

Dissenting Views on H.R. 6190

The Montreal Protocol, signed in 1987, is widely recognized as a tremendously successful international environmental agreement that has dramatically reduced the production and use of substances that deplete the stratospheric ozone layer, such as chlorofluorocarbons (CFCs). The Environmental Protection Agency (EPA) regulations implementing the Montreal Protocol prohibit the production and import of CFCs with an exception for essential metered dose inhalers (MDIs). Under the Clean Air Act and its implementing regulations, the Food and Drug Administration (FDA) determines whether a MDI is essential.

On November 19, 2008, FDA issued a final rule removing the essential use designation for epinephrine MDIs containing CFCs. FDA concluded that there are no substantial technical barriers to formulating epinephrine as a product that does not release ozone-depleting substances. At that time, the only remaining CFC-containing epinephrine MDI on the market was Primatene Mist. As requested by Armstrong, the manufacturer of Primatene Mist, FDA set a phase-out date of December 31, 2011, one year longer than was originally proposed in 2007. Primatene Mist was phased-out on December 31, 2011, and it has not been on the market for the past eight months.

Prior to its phase-out, Primatene Mist was the only epinephrine metered dose inhaler available over-the-counter without a prescription. According to Armstrong, the company has between 1.2 million and 1.5 million units of Primatene Mist left in its inventory with a potential market value of between \$15 million and \$18 million.¹

The bill directs the Administrator of the EPA to allow for the distribution, sale, and consumption in the United States of remaining inventories of over-the-counter epinephrine inhalers containing CFCs manufactured pursuant to essential use exemptions. The term “remaining inventories” is not defined. The bill also prohibits EPA from taking any enforcement action or otherwise seeking to restrict the distribution, sale, or consumption of such inhalers pursuant to the Clean Air Act or any other federal law implementing the Montreal Protocol. In response to any request by a distributor or seller of Primatene Mist, the bill would require EPA to issue a letter to the requesting party stating that EPA will not initiate an enforcement action relating to the distribution or sale of any such inhaler prior to August 1, 2013. Under the bill, these provisions would cease to be effective on August 1, 2013.

The bill’s approach raises a number of significant concerns.

First, the bill would overturn an established regulatory framework in order to allow a single manufacturer to sell off its remaining inventory of the CFC-containing inhaler Primatene Mist. FDA has established a clear and open process for determining whether inhalers containing CFCs are essential. Over the years, more than a dozen types of inhalers containing CFCs have been phased-out under this process. The schedules were never changed for these thirteen inhalers, and none of these other manufacturers were allowed to sell off their inventories after the

¹ Letter from Jason Shandell, Vice President and General Counsel, Amphastar Pharmaceuticals, Inc., to Rep. Henry A. Waxman (Jul. 16, 2012).

phase-out date. All of these CFC inhalers were phased-out prior to the phase-out of Primatene Mist. The remaining two CFC-propelled inhalers are scheduled for phase-out at the end of 2013.

Even though Armstrong was not singled out by the FDA process or required to do anything that other companies were not required to do, the bill would change the rules so that Armstrong could sell off its inventory of Primatene Mist. The bill would directly benefit just one company – Armstrong, the maker of Primatene Mist. For example, the bill could benefit Armstrong by allowing the company to maintain its market share until it can obtain FDA approval for a CFC-free epinephrine inhaler.

Companies that made the necessary investments to develop CFC-free inhalers contend that the bill would unfairly provide special treatment to a single company. The International Pharmaceutical Aerosol Consortium (IPAC), a group of MDI manufacturers, argues: “Granting extraordinary, unwarranted and special treatment to a single company would send an extremely negative signal to the manufacturers that responded to the US Government’s call many years ago to be a partner in meeting the Montreal Protocol commitments.”²

On July 26, 2012, FDA officials briefed Committee members and staff about the phase-out of Primatene Mist. They also raised concerns about overturning FDA’s established regulatory process for setting deadlines for the phase-out of inhalers containing CFCs.

Second, the Committee heard testimony and received additional information from a host of medical organizations that putting Primatene Mist back on the market would not be in the interests of patients. At a July 18, 2012, legislative hearing, Dr. Monica Kraft, a professor of medicine at Duke University and President of the American Thoracic Society, testified that “[i]nhaled epinephrine is not a safe drug for the treatment of asthma.”³ She explained that Primatene Mist can “cause a significantly increased heart rate,” which “can lead to cardiac stress and heart attacks in older patients or patients with heart disease.” According to Dr. Kraft, the American Medical Association twice “encouraged FDA to consider removing inhaled epinephrine from the market.” She also testified that “[n]o current clinical practice guideline for the diagnosis and treatment of asthma recommends the use of epinephrine.” Dr. Kraft expressed concern that “[p]utting Primatene Mist back on the market – for an indefinite period of time – will send a very confusing message to patients.” She explained that many people who suffer from asthma have already transitioned to other, more effective treatments. Chris Ward, who testified on behalf of the Asthma and Allergy Foundation of America, echoed this concern, stating: “Lifting the ban now will lead to confusion.”⁴

² International Pharmaceutical Aerosol Consortium, *Re-introducing CFC-Based Epinephrine (Primatene Mist) in the United States Is Counterproductive to Patient Health and US Policy* (July 2012) (fact sheet).

³ Dr. Monica Kraft, President of the American Thoracic Society, Committee on Energy and Commerce Subcommittee on Energy and Power, *Legislative Hearing on H.R. __, the U.S. Agricultural Sector Relief Act of 2012, and H.R. __, the Asthma Inhalers Relief Act of 2012*, 112th Cong. (Jul. 18, 2012).

⁴ Chris Ward, Asthma and Allergy Foundation of America, Committee on Energy and Commerce Subcommittee on Energy and Power, *Legislative Hearing on H.R. __, the U.S.*

On July 30, 2012, the American Lung Association, the American Thoracic Society, the American Academy of Pediatrics, the Asthma and Allergy Foundation of America, and other public health groups wrote to Committee members to oppose the legislation, stating: “Our organizations strongly believe that allowing this product to return to the marketplace is not in the best interests of patients with asthma or public health.”⁵ These organizations agreed with Dr. Kraft that Primatene Mist is not recommended or considered safe for the treatment of asthma because of the potential of epinephrine to cause excessive heart stimulation.

At the July 26, 2012, briefing for members and staff, FDA officials explained that Primatene Mist was determined to meet the regulatory definition of “safe and effective” in 1967, but the standard of care for asthma has changed considerably over the past 50 years. As a result, physicians and expert guidelines do not recommend Primatene Mist for the treatment of asthma. The FDA officials also raised concerns about patients being confused by the temporary re-introduction of a product that has been off the shelves for eight months.

In anticipation of the December 31, 2011, phase-out of Primatene Mist, EPA and FDA took a number of actions to inform consumers of the approaching transition. In addition to public and stakeholder meetings convened by the agencies, FDA approved a message for Primatene Mist cartons and containers indicating to consumers that Primatene Mist would not be available after December 31, 2011. Under the bill, after being off the market for over eight months, Primatene Mist would go back on the market, but only for as long as the inventory lasted. Then it would once again disappear from the shelves.

To address concerns about patient confusion and safety, Rep. Pallone offered an amendment at the full Committee markup of the bill. The amendment would have prevented the provisions of the bill from taking effect unless FDA finds that the temporary reintroduction of Primatene Mist is unlikely to cause significant patient confusion and will provide an overall public health benefit. The amendment required FDA to make a determination within 30 days. The amendment was defeated by voice vote.

Third, despite concerns from the proponents of the bill that no over-the-counter asthma inhalation treatment has been available since the phase-out of Primatene Mist, an alternative is now entering the market. On July 19, 2012, at the Subcommittee markup of this legislation, it was revealed that Nephron, a company in Florida, has developed a hand-held, battery-operated

Agricultural Sector Relief Act of 2012, and H.R. ___, the Asthma Inhalers Relief Act of 2012, 112th Cong. (Jul. 18, 2012).

⁵ Letter from Alpha-1 Association, Alpha -1 Foundation, American Academy of Allergy Asthma and Immunology, American Academy of Pediatrics, American Association for Respiratory Care, American College of Allergy Asthma and Immunology, American Lung Association, American Thoracic Society, Asthma and Allergy Network/Mothers of Asthmatics, Asthma and Allergy Foundation of America, COPD Foundation, National Association for the Medical Direction of Respiratory Care, and National Home Oxygen Patients Association to Rep. Ed Whitfield and Rep. Bobby Rush (July 30, 2012).

atomizer that uses vials of a variant of epinephrine (racepinephrine hydrochloride).⁶ The product is a portable, over-the-counter device and is explicitly being marketed as an affordable alternative to Primatene Mist. According to Nephron, the product, called Asthmanefrin, will soon be available nation-wide at Walmart, CVS, and other retail outlets.⁷ Under a 1986 FDA rulemaking, simple epinephrine delivery mechanisms like nebulizers or atomizers can be placed on the market without pre-approval by FDA.

Nephron made a significant investment to bring this product to market, relying on the established regulatory regime. The bill's intervention in the market would affect companies that have followed the rules and made investments based on those rules.

To avoid picking winners and losers, Rep. Castor offered an amendment at the full Committee markup of the bill. The amendment would have prevented the provisions of the bill from taking effect if an alternative over-the-counter inhalation asthma treatment is available on the date of enactment. The amendment was defeated by voice vote.

Finally, it is unlikely that the bill would result in the widespread availability of Primatene Mist sought by proponents of the legislation. According to Armstrong, 2-3 million people used Primatene Mist, but fewer than 1.5 million Primatene Mist inhalers remain in Armstrong's inventory. As a result, as many as half of all previous users of Primatene Mist would not be able to obtain even one inhaler if Armstrong was allowed to sell off its remaining inventory. It is unclear whether Primatene Mist would be available nationwide and which pharmacies or drug stores would carry it. Some retailers may opt not to sell inventoried units of Primatene Mist because "Armstrong's inventory of Primatene Mist will expire at varying times between January and August of 2013."⁸ Additionally, the inventory would not immediately be available. According to Armstrong, the company would need to move the inventoried units to a subsidiary in order to re-label the units to eliminate the labeling statement that Primatene Mist would not be available after December 31, 2011.⁹ Thus, the real effect of this bill would be to provide a regulatory earmark to Armstrong rather than a "rescue inhaler" that would be available in the middle of the night to someone suffering from an asthma attack, as the bill's proponents contend..

⁶ Letter from Lou Kennedy, Chief Executive Officer of Nephron Pharmaceuticals Corporation, to Rep. Kathy Castor (Jul. 17, 2012).

⁷ Nephron Pharmaceuticals Corporation, *Nephron Announces Asthmanefrin, an Alternatives to Primatene Mist* (Aug. 20, 2012).

⁸ Letter from Jason Shandell, Vice President and General Counsel, Amphastar Pharmaceuticals, Inc., to Rep. Henry A. Waxman (Jul. 16, 2012).

⁹ *Id.*

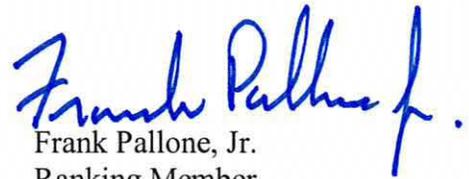
For the reasons stated above, we dissent from the views contained in the Committee's report.



Henry A. Waxman
Ranking Member



Bobby L. Rush
Ranking Member
Subcommittee on Energy
and Power



Frank Pallone, Jr.
Ranking Member
Subcommittee on Health