

Asthma Sprays to Be Modified

THE inhalers that are an essential part of daily life for many of the 24 million Americans with asthma and other respiratory diseases are due for a major overhaul, raising concerns among some patients and doctors about whether the medications they depend on will continue to be available.

The proposed changes were announced last month by the Food and Drug Administration. The plan, which has been in the works for years, is to phase out current inhalers, which use chlorofluorocarbon, or CFC, gases as a propellant to spray out a fine mist of medication that is inhaled through a mouthpiece. To comply with environmental regulations, the current devices, about 70 different products called metered-dose inhalers, are to be replaced over a period of years by inhalers that do not contain CFC's, which deplete the stratospheric ozone layer. That layer shields Earth from ultraviolet radiation, a cause of skin cancer and cataracts. Reformulating the inhalers is expected to cost billions of dollars. The change is required by law, even though the devices are responsible for only a small fraction of the CFC pollution worldwide. The new inhalers will use different propellants or mechanical methods to generate a mist of liquid or powdered medication. F.D.A. officials declined to speculate about how long it would take to switch to the new devices.

"People shouldn't panic," said Dr. John Jenkins, director of the division of pulmonary drug products at the agency. "No one will be taken by surprise. This will take some years." But Dr. Jenkins acknowledged that news of the proposed plan, published in The Federal Register on March 6, might have alarmed some people. "Asthma, emphysema and chronic bronchitis are serious conditions," he said. "It's frightening for patients when they can't breathe, and they come to rely on medications. And when they hear the Government is going to take away their medication, people get scared. But there will be time. We're not proposing to eliminate CFC's until new products adequately serve patients' needs." Dr. Jenkins emphasized that the rules were not yet final; the F.D.A. is seeking public comment on its proposal before May 5. The agency's plan has support from medical groups, including the American Lung Association and the American Academy of Allergy, Asthma and Immunology, which say the proposed change can be made safely. "But I'm skeptical that the small amount of ozone damage produced by inhalers makes a lot of difference in the long run," said Dr. Betty Wray, president of the American College of Allergy, Asthma and Immunology and chief of the section of allergy and immunology at the Medical College of Georgia, in Augusta. Nonetheless, she thinks the transition can be made without harming patients.

Despite reassurances from professional groups, some patients remain uneasy. Nancy Sander, president of the Allergy and Asthma Network-Mothers of Asthmatics, a patient advocacy group with 5,000 members based in Fairfax, Va., said that the current F.D.A. proposal reflected more concern for the environment than for people with asthma. Surveys indicate that patients favor the development of new inhalers and the elimination of CFC's, she said, but they fear that the process the F.D.A. has suggested may phase out the old ones without first letting patients make sure that the new ones work as well. Ms. Sander also said patients were worried that some old medications would not be reformulated into new inhalers because of the expense of the change and would be lost from the market. "The F.D.A. needs to continue to understand the needs of patients and to monitor them the same way the Environmental Protection Agency monitors ozone," she said. The proposed changes are intended to bring the United States into compliance with the Montreal Protocol, a 1987 treaty signed by more than 150 countries to reduce CFC pollution. In keeping with the treaty, the production of the gases was banned for most nonmedical uses in the United States in 1996. Inhaled medications received an "essential use" exemption from the treaty because they form the cornerstone of treatment for most of the 12 million to 15 million people with asthma in the nation and a similar number with disorders like emphysema and chronic bronchitis. But the exemption was never meant to last forever, even though inhalers cause little pollution. Before CFC production for other purposes was banned, inhalers were estimated to account for a very small share, less than half of 1 percent to a few percent, of all the nation's CFC's. "But if we argued that our remaining uses are so tiny that they should be allowed, other countries could make arguments for their pet uses," said Drusilla Hufford, acting director of the stratospheric protection division of the Environmental Protection Agency. "That could delay recovery of the ozone layer, potentially quite substantially." Creating new inhalers is time-consuming and expensive because the devices are far more complicated than they appear. Each drug requires its own system to insure that the device delivers the correct dose, in particles of the correct size, to the correct part of the lung, every time. New propellants have to be proved safe for inhalation. Every new product must pass the F.D.A.'s new-drug approval process, even if the active medication has been used before. Drug companies have already spent \$1 billion to develop new inhalers and are expected to spend several billion more in coming years, according to figures presented to the F.D.A. by Dr. Janet Remetta, chairwoman of the International Pharmaceutical Aerosol Consortium, a trade group in Washington. She estimated that at least 11, and perhaps as many as 30, new products would be approved by 2000. Dr. Wray said: "The expense concerns me. I would expect that it eventually it will have to be passed along to patients." So far, only one new product with a non-CFC propellant has become available. That product, Proventil HFA, contains albuterol, the drug most widely used to treat asthma attacks. It was introduced in January by Schering-Plough, of Kenilworth, N.J., which beat its competitors to market. HFA refers to its new propellant, a hydrofluoroalkane gas, which is used in a new inhaler patented by the Minnesota Mining and Manufacturing Company of St. Paul. It took seven years and \$100 million to develop the new device, said Maria Westfall, the company's global program manager for CFC-free products. The new inhaler costs patients about \$25, the same as regular Proventil, but about \$7 more than generic albuterol. A spokesman for Schering-Plough declined to say how well it was selling; the company has been promoting the new inhaler in full-page ads in The New York Times and other major newspapers. With the first drug on the market and others not far behind, Schering-Plough and the 3M Company support the phase-out of the older inhalers. But rival companies, like Glaxo Wellcome, which is still working on its first new inhaler, have questioned the F.D.A.'s plan, citing concerns for the safety of patients. The marketing of the first new product helped convince F.D.A. officials that it was time to publish a proposal for implementing further changes, Dr. Jenkins said. "One is approved, and we know a lot of others are coming," he said.

"Now it makes sense to develop a policy on how to phase out chlorofluorocarbon products." The proposal divides most major asthma medications two groups; there are seven short-acting bronchodilators, including albuterol, that are used to treat asthma attacks, and five inhaled steroids that are used as preventives. The F.D.A. is suggesting that the drugs within each group are interchangeable and that once two of them became available in three new forms, including two inhalers, the others in the group might be phased out if they had not been converted to non-CFC forms. But the phase-out would not occur until the replacements had been on the market for at least a year and had proved acceptable to patients. In addition, supplies would have to be judged adequate, and a drug would not be eliminated if it was the only thing that worked for a group of patients. Five other asthma drugs fall into a third group, consisting of one-of-a-kind medications. Those drugs would not be phased out until CFC-free inhalers containing those drugs became available.