PROBLEM: For almost a decade, practitioners have been reporting concerns with illegible labeling of unit-dose respiratory therapy medications packaged in low-density polyethylene (LDPE) plastic containers. The poor legibility of these product labels has repeatedly been brought to the attention of the USP–ISMP Medication Errors Reporting Program (MERP). In fact, the Food and Drug Administration (FDA) has received more than 100 error reports through the MERP and the FDA MedWatch programs combined.

The often indecipherable labeling is evident to practitioners such as nurses and respiratory therapists, as well as to patients and caregivers, who administer these medications. Unfortunately, pharmacists might not be aware of the extent of the problem because they do not usually see the individual unit-dose containers.

Many inhalation products intended for use by nebulization are packaged in LDPE plastic containers. Examples include albuterol (Proventil®, Schering), ipratropium bromide (Atrovent®, Boehringer Ingelheim), an albuterol–ipratropium combination (Duoneb®, Dey), levalbuterol (Xopenex®, Sepracor), cromolyn sodium (Intal®, Aventis), and budesonide (Pulmicort® Respules). These medications are usually dispensed in boxes that contain foil pouches, with each pouch holding multiple unit-dose containers. Transparent, raised letters, which include the drug name, concentration, lot number, and expiration date, are embossed into the plastic container, making the labeling virtually impossible to read (Figure 1).

The risk of a mix-up is heightened if staff members keep various respiratory medications in their laboratory coat pockets or if the medications are stored together in a “respiratory bin” in a refrigerator. To make matters worse, some manufacturers (e.g., AstraZeneca, Avitro, and Vital Signs) have introduced injectable products, such as heparin, used as an intravenous flush, and ropivacaine (Naropin®, AstraZeneca), a local anesthetic, packaged in LDPE ampules. These products carry the same risk of error because of their similarly sized and shaped containers as well as their nearly invisible labels.

The embossing method of labeling is used because the FDA no longer permits paper labels or printed ink on these containers. LDPE plastic is permeable to the volatile chemicals used in label adhesives, paper, and ink, and the inhalation solutions can become contaminated, resulting in potential harm to patients. In fact, FDA studies have shown that 29 of 37 samples tested positive for volatile chemicals. The presumed source of these chemicals was the packaging and labeling materials used, such as adhesives, varnishes, inks, and solvents.

Figure 1 Embossed labeling on plastic containers. The raised letters include the drug name, concentration, lot number, and expiration date, but they are very difficult to read.

Figure 2 Traditional printed paper-and-ink labels.
For these reasons, in 2002, the FDA published a notice in the Federal Register of a draft guidance for industry entitled, “Inhalation Drug Products Packaged in Semipermeable Container Closure Systems.” Measures to limit chemical contamination of the containers were recommended in the guidance, including alternative approaches to paper labels and inks, such as embossed labels. Since then, manufacturers and the FDA have essentially been following that recommendation. However, compared with the prior paper labels used on some products, embossed labels are almost impossible to read (Figure 2), often leading to medication errors.

**SAFE PRACTICE RECOMMENDATIONS:**
In 2004, the FDA’s Drug Safety and Risk Management Advisory Committee met to discuss how to prevent errors with drug products marketed in unit-dose plastic containers composed of LDPE. Although the committee did not determine a solution to the labeling problem, a number of alternative measures were considered. Until the FDA clears up this labeling problem, the following steps can be taken to prevent errors with these products:

- Some practitioners and patients have considered using marking pens on individual containers to color-code or mark a letter indicating the drug name or to affix labels to the containers as a means of easily identifying these medications. However, because other substances can permeate the plastic containers, it seems reasonable that the ink from a marker and volatile ingredients from the label adhesives would do the same. Therefore, these practices are not recommended.

  • In physicians’ offices, pharmacies, and patients’ homes, the plastic containers should be stored in their original boxes whenever possible.
  • Individual plastic ampules should not be kept with others in a single location because many products look alike and might be inadvertently mixed together.
  • Manufacturers of many products that are packaged in protective foil pouches because of their sensitivity to light recommend storing unopened containers in the pouch until they are ready to use.
  • In most cases, containers that are removed from the foil pouch should be used within one week.
  • In an effort to keep medications in their original packaging, pharmacists should avoid dispensing partial boxes. If boxes must be “broken up,” the plastic containers should be dispensed in a clearly labeled package and medications should be dispensed in their original, intact foil pouches.
  • Patients should be counseled about the proper use and storage of medications, and they should be alerted to the ease with which these products can be misidentified.
  • Pharmacists should advise patients about the need to store the medications in their original, clearly labeled packaging.
  • Patients may want to know how to identify the plastic containers or what to do if the wrong medication or too much of one medication is taken. Elderly patients and those with visual difficulty should be taught how to properly identify their respiratory medications, especially if they are using more than one product.

The reports described in this column were received through the USP–ISMP Medication Errors Reporting Program (MERP). Errors, close calls, or hazardous conditions may be reported on the ISMP (www.ismp.org) or the USP (www.usp.org) Web site or communicated directly to ISMP by calling 1-800-FAIL SAFE or via e-mail at ismpinfo@ismp.org.