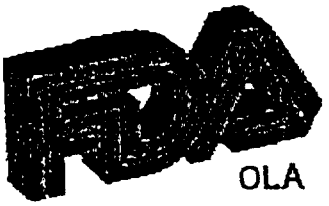
TELEFAX TRANSMITTAL SHEET



FOOD AND DRUG ADMINISTRATION
Office of Legislative Affairs
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Rockville, MD 20850
TEL: (301) 443-3793
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(301) 594-6778

PLEASE DELIVER THE FOLLOWING PAGES

TO: CDER ExSec DATE: August 13, 2002

TELEPHONE #: 46740 FAX#: 45493

FROM: Joy Stevens

COMMENTS: Please review the enclosed material and assist us with a draft reply. It is not clear to me just what FDA's role is in deciding how these products should be labeled. I spoke with Judy Schultz and she is very adamant that it is extremely difficult for elderly people to accurately read the raised lettering on these ampules. The family found the solution suggested in Alpharma's letter to be totally inadequate. Is FDA perhaps working on a solution?

NUMBER OF PAGES, INCLUDING COVER: 8

IF YOU DO NOT RECEIVE THE NUMBER OF PAGES INDICATED ABOVE, PLEASE CALL IMMEDIATELY

TOM HARKIN
IOWA

(202) 224-3254
TTY (202) 224-4633
Tom_Harkin@Harkin.Senate.Gov

COMMITTEES:
AGRICULTURE
APPROPRIATIONS
SMALL BUSINESS
LABOR AND HUMAN RESOURCES

United States Senate

WASHINGTON, DC 20510-1502

May 22, 2002

Lester Crawford
Deputy Commissioner, Food and Drug Administration
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

Dear Dr. Crawford:

Enclosed is a letter from one of my constituents who has a concern over the administration's policy on medication labeling. I respectfully ask you to review the administration's policy on this issue and send me a clarification so that I might be able to respond to my constituent's questions. It would be helpful if you could mark your correspondence with my office to the attention of Kristy Anderson.

Thank you in advance for your assistance on this matter.

Sincerely,

Tom

Tom Harkin
United States Senator

TH/kka

160 FIRST AVENUE, NE
SUITE 370
CEDAR RAPIDS, IA 52407-4884
(319) 365-4504

210 WALNUT ST.
733 FEDERAL BLDG.
DES MOINES, IA 50309
(515) 284-4574

131 E. 4TH ST.
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(319) 322-1338

350 WEST 6TH ST.
315 FEDERAL BLDG.
DUBUQUE, IA 52001
(319) 582-2130

320 6TH ST.
110 FEDERAL BLDG.
SIOUX CITY, IA 51101
(712) 252-1550

Senator Tom Harkin
350 West 6th Street, Rm 315
Dubuque, IA 52001

Subject: Easily Readable Labels of Medicines to Insure Correct Usage

Dear Senator Harkin:

Enclosed are samples of empty liquid packages from medicines which my Mom uses. (The one with the colored label is the only one we have left, please don't lose it.)

Previously the little plastic viles could be identified as different one from the other by the 'differently colored' labels which used to be stuck to each. (example enclosed.)

Now those different colored labels are not used in production. And, as you can see by the raised letters, it is hard to read the contents of the medicine being taken.

I'm very surprised the manufacturers changed this packaging and have questions:

1. Was there a simple mistake in production so labels were not applied?
2. Did common sense get dropped in lieu of a cost cutting measure? (At what cost to the customer?)
3. Was a market study performed to see how this affected customers?
   a. If a study was performed, I wonder if it was flawed as apparently not 'all' users of these medicines were considered and it seems that when working with medicines, 'all' users must be considered.
4. Describe the physical characteristics of most of the customers who use this product.
   a. Is there a particular age segment?
   b. Presuming this is an older age segment, could we generally project any difficulty for these people in reading the new packaging without labels? (I have difficulties as it is...!)
5. If the medicines are not taken appropriately because they cannot be adequately identified one from the other, will the medicines be ineffective? (Sometimes these particular medicines are combined, and other times, one or the other is taken individually.)
4. Not knowing any side affects, or other medicines which have had this labelling change, could there be lawsuits because of this inadequate labelling?

There seemed to be total disgregard to the customers affected by this change. Couldn't a notification have been sent along with prescriptions stating the reason for the change but then asking customers sincerely that if they had difficulties reading the labels, to call an 800 number at the manufacturer's office, or, have a readable post card by which they could forward their approval or dissapproval?

I am asking someone, somewhere please reconsider putting 'easily readable labels on these liquid packaging medicines' again.

Senator Harkin, I'm asking your office to help with communication to the FDA office.

3-4-2002...Inadequate Liquid Medicine Labelling, continued

Thank you for your consideration. Please let us know of any questions.

Sincerely,

Judy A. Schultz (daughter)

Violet and Charles Schultz (parents)

Products needing to be addressed:

1.) IPRATROPIUM BROMIDE, inhalant, 0.02%, manufactured by Automatic Liquid Packaging for Alpharma USPD, Inc.
2.) ALBUTEROL SULFATE, inhalation solution, 0.083%, manufacturered by Automatic Liquid Packaging for Apharma USPD, Inc.

Copies of this correspondence are going to:

Dr. Matthew Kirkendall
Dubuque Internal Medicine Clinic

John Mulert, Pharmacy Manager
Mercy Family Pharmacy

John Brda, Regulatory Director
Automatic Liquid Packaging
2200 Lakeshore Drive
Woodstock, IL 60098
815-338-9500

Donna Williams
Alpharma
10065 Red Run Blvds
Owings Mills, MD 21117
410-298-1000 x 1299

ALPHARMA
U.S. Pharmaceuticals Division

May 31, 2002

Judy Schultz

RE: Albuterol Sulfate Inhalation Solution, 0.83%
Ipratropium Bromide Inhalation Solution 0.02%

Dear Ms. Schultz:

This is in response to your call of February 25, 2002. We are sorry that you may have had a negative experience with our products and have reviewed your comments regarding the difficulty you experience with these product's packaging. We would like to take this opportunity to address your concerns. Your comments about the confusion that you experience in differentiating between these products have been passed on to both our Labeling Department and Marketing Departments.

These respiratory care products are designed in this manner to permit the packaging of a sterile product. The product cartons and foil packages are clearly marked with the product name and dosage. As the unit-dose vial has been designed to provide a sterile product, the product name, lot number and expiration date are embossed in the plastic. The raised letters that are part of the vial can never become smeared or defaced through normal handling or wetting and are always present and legible. These raised letters also provide a textured surface to assist in gripping the vial when opening by twisting off the top.

In addition, these products are packaged in easy tear foil wrappers. The foil serves to protect these products from light. It is important to always keep the unused vials in the foil envelope to prevent any possibility of product degradation from exposure to light and to help prevent errors in dispensing medications in vials.

The FDA has approved the packaging components and labeling for both products. Our packaging for each product meets or exceeds all current regulatory requirements. The exterior packaging is clearly marked with the product name, contents, and dosage. The individual vials are packaged in a foil pouch that protects the product from light. Color coding of the outer boxes and foil wrapper (blue for Albuterol and green for Ipratropium) should alleviate any confusion between the products. Additionally, the top of each vial is stamped with a large "A" for Albuterol and an "I" for Ipratropium and the full product name is stamped into the body of each vial. Keeping the vials in their packaging until you take the medicine is recommended and should help you better identify the products.

Thank you for having contacted us with your concerns. If you have any further questions or concerns please do not hesitate to contact us at 800-638-9096 Ext. 1299 and refer to PSF20360.

Sincerely
ALPHARMA USHP

Donna Williams, R.Ph.
Professional Services

2 of 3

Alpharma USPD Inc. 10065 Red Run Boulevard Owings Mills, Maryland 21117 Tel (410) 298-1000 Fax (800) 772-2773 C-5698, PSF20360

ISMP **MEDICATION SAFETY** ALERT!

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(ISMP®), a nonprofit organization
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E-mail: ismpinfo@ismp.org
Volume 7, Issue 10
May 15, 2002
Educating the healthcare community about safe medication practices

Atrocious labeling of plastic ampuls needs action now by FDA and manufacturers

Problem: For nearly a decade, practitioners have been reporting concerns with the labels on respiratory therapy medications packaged in plastic (low density polyethylene - LDPE) ampuls, making this one of the more frequent product problems reported to the USP-ISMP Medication Errors Reporting Program. These concerns are well founded. Many products from various manufacturers (Alpharma, AstraZeneca, Dey Labs, Genentech, Nephron, Roxane, Sepracor, Zenith-Goldline, and others) are packaged in look-alike plastic ampuls with little differences in shape or color. Even worse, the ampuls have the drug name(s), strength, lot number and expiration date embossed into the plastic in transparent, raised letters, making it virtually impossible to read.

Practitioners have reported confusion between plastic ampuls of ipratropium (ATROVENT), albuterol (PROVENTIL), levalbuterol (XOPENEX), budesonide (PULMICORT RESPULES), dornase alfa (PULMOZYME), and cromolyn (INTAL). See our web site for pictures. Staff may not notice that a newer product, DUONEB, contains both ipratropium and albuterol because the label is so hard to read. Some products in plastic ampuls, like Pulmicort, Xopenex, and ACCUNEB (albuterol), also are available in multiple dosage strengths, but poorly visible labels make it hard to tell the difference. The risk of a mix-up is heightened if staff keep various respiratory medications in their lab coat pockets or mixed together in a "respiratory bin" in a refrigerator. To make matters worse, some manufacturers (AstraZeneca, Avitro, Vital Signs) have introduced *injectable* products, such as heparin for IV flush use and NAROPIN (ropivacaine), a local anesthetic, packaged in LDPE ampuls that carry the same risk of error due to the poorly visible labels.

Safe Practice Recommendation: There's no doubt that better labeling of plastic ampuls is long overdue. So why has FDA allowed manufacturers to produce these products with unreadable, embossed labels? If a paper label is affixed to the ampul, or if the label information is embossed into the ampul using colored inks, there's concern that certain volatiles in the inks, adhesive and/or paper may ingress into the LDPE ampuls and potentially harm patients. While this concern is certainly valid, an unreadable embossed label is an unacceptable solution, even temporarily. If colored ink or paper labels *on the body* of a LDPE ampul is not safe at this time, then FDA should require such labeling *on the flashing portion* of the ampul that does not come into contact with drug solution. While this may require manufacturers to redesign the ampul's shape and retool the equipment used to produce it, the only safe alternative would be to disallow the use of LDPE ampuls.

Meanwhile, when other packaging alternatives exist (especially for injectables), practitioners and group purchasing organizations should avoid using products packaged in LDPE ampuls with embossed labels. For now, Dey Labs offers generic respiratory products (ipratropium, albuterol, cromolyn, and metaproterenol) in LDPE ampuls with readable, paper labels affixed. FDA is allowing Dey Labs to continue to produce these products in plastic ampuls with paper labels until more information is available (FDA will not allow Dey Labs to affix paper labels on newer products such as DuoNeb). Ensure that pharmacy staff order all respiratory medications and alert the manufacturers to ship the products separately (including different strengths) in well-marked boxes to promote accurate placement into storage. Keep the plastic ampuls in an outer package, which may be labeled more clearly, and avoid storing respiratory medications together in a single bin or lab coat pockets. If feasible, affix auxiliary labels to the products before dispensing.

Safety Briefs

•"AD" is used sometimes as an abbreviation for right ear (aura dexter). One problem with this abbreviation is that a handwritten lower case "a" can easily look like an "o." Thus, a patient might risk getting an otic medication into the right eye (OD-oculus dexter) instead of the right ear, as occurred in a recently reported error. The physician had ordered AURALGAN (antipyrine, benzocaine, glycerin) two drops AD for an emergency room patient, but the nurse administered the drops into the patient's right eye. When the error was discovered, the eye was flushed and the patient suffered no permanent harm. Using AS for left ear or AU for each ear might cause similar problems. In addition, AD has been misread as QD (if the tail of a handwritten lower case "a" looks like a "q") and PO (when poorly handwritten). In fact, in 1975, in one of the earliest errors we ever published (Cohen MR. Medication error reports. *Hosp Pharm* 1975;10:167), a patient nearly received ear drops by mouth! Recently, yet another type of error has surfaced with the abbreviation AD. Tired of writing out "as directed" when transcribing prescriptions received by telephone, a pharmacist began to abbreviate that term as AD. Later, a pharmacy technician misinterpreted the directions for an oral liquid prescription transcribed as "5 mL TID AD" and typed the directions as "one teaspoonful three times a day in right ear." It seems like AD would be a good abbreviation for all of us to avoid!

•At a mail order pharmacy, prescription directions for FOSAMAX (alendronate) 70 mg tablets (indicated for once a week dosing only) were erroneously typed with directions to take the medication daily. A pharmacist recognized the error before the drug was dispensed because the 70 mg package was available in the pharmacy only in a unit-of-use blister package containing four doses. Hypocalcemia, hypophosphatemia, upset stomach, heartburn, esophagitis, gastritis, or ulcer may have resulted from the overdose. In our April 3, 2002 issue, we wrote about erroneous daily dosing of methotrexate when weekly dosing is indicated. As mentioned, errors are possible because relatively few medications are dosed on a once weekly basis. This latest incident should support the recommendation to prescribe and dispense unit-of-use dose packs

Institute for Safe Medication Practices

ISMP MEDICATION SAFETY ALERT!

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E-Mail:
ismpinfo@ismp.org

Atrocious labeling of plastic ampuls needs action now by FDA and manufacturers

Printer Friendly Version

From the May 15, 2002 issue

PROBLEM: For nearly a decade, practitioners have been reporting concerns with the labels on respiratory therapy medications packaged in plastic (low density polyethylene - LDPE) ampuls, making this one of the more frequent product problems reported to the USP-ISMP Medication Errors Reporting Program. These concerns are well founded. Many products from various manufacturers (Alpharma, AstraZeneca, Dey Labs, Genentech, Nephron, Roxane, Sepracor, Zenith-Goldline, and others) are packaged in look-alike plastic ampuls with little difference in shape or color. Even worse, the ampuls have the drug name(s), strength, lot number and expiration date embossed into the plastic in transparent, raised letters, making it virtually impossible to read.

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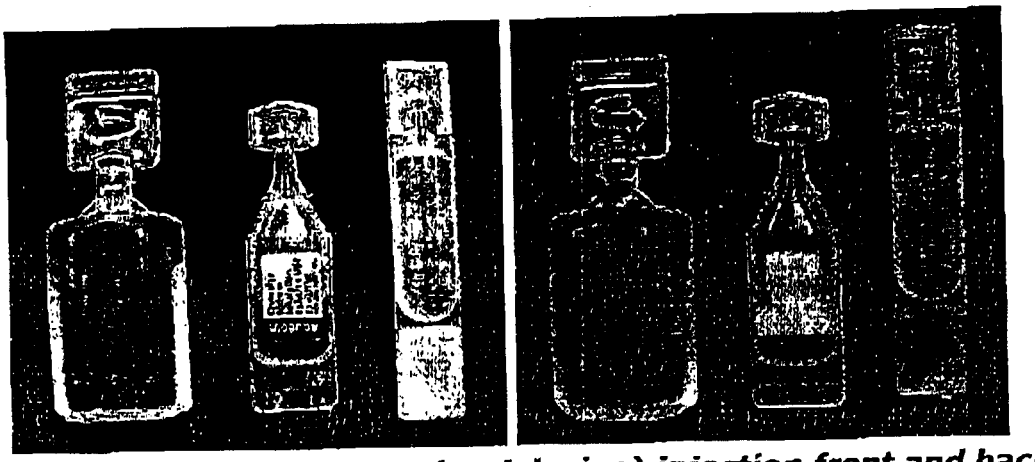

Figures one and two: Naropin (ropivicaine) injection front and back ampuls.

SAFE PRACTICE RECOMMENDATION: There's no doubt that better labelin of plastic ampuls is long overdue. So why has FDA allowed manufacturers to produce these products with unreadable, embossed labels? If a paper label is affixed to the ampul, or if the label information is embossed into the ampul using colored inks, there's concern that certain volatiles in the inks, adhesive and/or paper may ingress into the LDPE ampuls and potentially harm patient While this concern is certainly valid, an unreadable embossed label is an unacceptable solution, even temporarily. If colored ink or paper labels *on the body* of a LDPE ampul is not safe at this time, then FDA should require such labeling *on the flashing portion* of the ampul that does not come into contact with drug solution. While this may require manufacturers to redesign the ampul's shape and retool the equipment used to produce it, the only safe alternative would be to disallow the use of LDPE ampuls.

For some reason page 3 of this item did not print out. Please see website for last paragraph and picture showing further comparisons of ampuls.

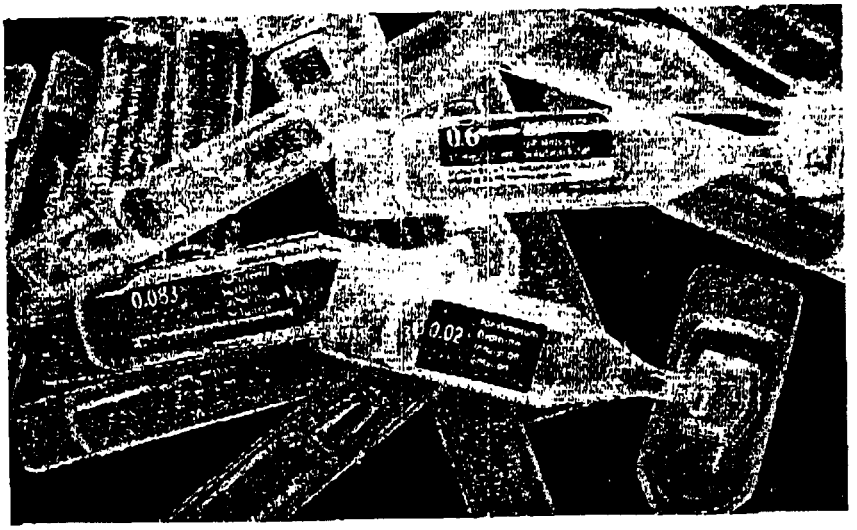

Figure three: paper labels currently on products from Dey Labs are
Contrasted against newer style of labeling which is unreadable.