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MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: October 17, 2000

SUBJECT: Summary report of FDA analytical survey of approved NDA/ANDA inhalation solutions marketed in Low Density Polyethylene (LDPE) containers without a protective overwrap.

To: The Record

From: Michael Smela, Jr.
Team Leader, ANDA Review Team 2
Division of Chemistry 1
Office of Generic Drugs

Background: Dey Laboratories, Inc. initiated a large scale recall of inhalation solutions in the summer of 1999 due to contamination of the products with 1-phenoxy-2-propanol. The recall was conducted with the knowledge of the FDA and followed a Health Hazard Evaluation of the situation in FDA/CDER. The Office of Generic Drugs (OGD) was concerned that other inhalation solution products that have been approved over the years may be similarly situated as the Dey products. It was decided to conduct a survey of marketed products.

Sampling: The OGD and the Division of Pulmonary and Allergy Drug Products (DPADP) identified all approved applications for LDPE packaged inhalation solutions that do not have protective overwraps. A total of 23 ANDAs and 1 NDA were identified covering 5 different drug substances (Attachment 1). It was learned that all Isoetharine products as well as Metaproterenol Sulfate of ——— were currently not in distribution. The CDER Office of Compliance issued an assignment to the appropriate ORA field offices for sampling of representative lots of the remaining products which were covered by 7 ANDAs and 1 NDA. A total of 37 samples representing 38 lots of the various drug products were collected and forwarded to ORA's Pacific Regional Laboratory Northwest for analysis.

020-0254

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Analysis: Samples were screened for potential volatile and semi-volatile contaminants using Gas Chromatography/Mass Spectrophotometry with a sensitivity of approximately 0.5 ppm (part per million). A similarly sensitive screening for potential contaminants was conducted using High Performance Liquid Chromatography (HPLC) with special emphasis for vanillin, 2-phenoxyethanol and 1-phenoxy-2-propanol as these compounds have previously been detected as contaminants in these types of products. Analytical responses were further characterized for chemical identification to the extent possible.

Results: Of the 37 samples tested, 29 tested positive for potential packaging chemical contamination (Attachment 2). The remaining 8 samples were free of impurities under the test conditions. One sample (Metaproterenol Sulfate ——, tested positive for 2-phenoxyethanol at 1.7 ppm. This finding is considered insignificant as this issue had been previously addressed in a CDER recommendation for a Class 3 recall which —— did not implement. The lot expired 6/00. The remaining samples were found to contain varying levels of 5 different chemical contaminants which are presumed to be packaging ingressers. Several samples are listed as —— Metaproterenol Sulfate and it is assumed that these lots are being distributed under the —— with generic labeling as —— and does not hold its own approved ANDA for this drug.

EVALUATION: The findings relative to the 5 chemical contaminants which are presumed to be packaging chemicals were submitted for Health Hazard Evaluation to DPADP (Attachment 3). Completed Health Hazard Evaluations as amended have been returned (Attachment 4).

Future Plans: It has yet to be decided what effect, if any, the Health Hazard Evaluation should have on the indicated drug products, and by what means such decisions, if any, should be communicated to the application holders. ——

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Attachment 1 Listing of Approved Applications

Application #	Drug Substance	Holder	Strength
89817	Isoetharine HCL	Dey	0.08%
89818	Isoetharine HCL	Dey	0.1%
89819	Isoetharine HCL	Dey	0.17%
89820	Isoetharine HCL	Dey	0.25%
89614	Isoetharine HCL	Astra	0.062%
89615	Isoetharine HCL	Astra	0.125%
89616	Isoetharine HCL	Astra	0.167%
89617	Isoetharine HCL	Astra	0.2%
89618	Isoetharine HCL	Astra	0.25%
87396	Isoetharine HCL	Roxane	0.1%
87025	Isoetharine HCL	Roxane	0.125%
88226	Isoetharine HCL	Roxane	0.167%
87324	Isoetharine HCL	Roxane	0.2%
88275	Isoetharine HCL	Roxane	0.25%
74209	Cromolyn Sodium	Dey	1%
74755	Ipratropium Bromide	Dey	0.02%
72652	Albuterol Sulfate	Dey	0.083%
71855	Metaproterenol Sulfate	ALPharma	0.4%
71726	Metaproterenol Sulfate	ALPharma	0.6%
18761	Metaproterenol Sulfate	Boehringer Ingelheim	0.4%, 0.6%
71275	Metaproterenol Sulfate	Astra	0.4%
71018	Metaproterenol Sulfate	Astra	0.6%
71786	Metaproterenol Sulfate	Dey	0.4%
70804	Metaproterenol Sulfate	Dey	0.6%

Attachment 2 Test Results

Sample #	Manufac.	drug	lot / exp	HPLC Results	GC/MSD Results
60605		metaproterenol		Clean* (0.5ppm LOQ)	~0.6ppm DEGBE
60606		metaproterenol		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
60607		metaproterenol		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
60608		metaproterenol		Clean (0.5ppm LOQ)	1.2ppm DEGBE ~0.6ppm Benzophenone
60609		metaproterenol		Clean (0.5ppm LOQ)	~0.5ppm DEGBE
60610		metaproterenol		Clean (0.5ppm LOQ)	~0.5ppm DEGBE
60611		metaproterenol		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
67155		metaproterenol		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
67156		metaproterenol		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
67157		metaproterenol		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
67158		metaproterenol		Clean (0.5ppm LOQ)	1.2ppm DEGBE ~0.5ppm Benzophenone
67159		metaproterenol		Clean (0.5ppm LOQ)	1.2ppm DEGBE
18524		metaproterenol		2.0ppm 2-HMPP**	~5ppm total PEG's ~2.2ppm 3-HMPP
67899		metaproterenol		1.0ppm 2-HMPP	~4ppm total PEG's ~1.0ppm 2-HMPP
67900		metaproterenol		0.33ppm 2-HMPP	~5ppm total PEG's
67902-1		metaproterenol		8.44ppm 2-HMPP	~2ppm total PEG's
67902-2		metaproterenol		0.52ppm 2-HMPP	~4ppm total PEG's
44103		metaproterenol		Clean (0.5ppm LOQ)	~0.6ppm DEGBE
44104		metaproterenol		Clean (0.5ppm LOQ)	2.1ppm DEGBE
47726		metaproterenol		Clean (0.5ppm LOQ)	~0.7ppm DEGBE
47727		metaproterenol		Clean (0.5ppm LOQ)	~0.5ppm DEGBE
47728		albuterol sulfate		Clean (0.5ppm LOQ)	0.89ppm DEGBE 1.6ppm DEGEEA
47729		albuterol sulfate		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
47730		ipratropium bromide		Clean (0.5ppm LOQ)	1.2ppm DEGBE
47731		ipratropium bromide		Clean (0.5ppm LOQ)	Nothing above ~0.5ppm
47732		cromolyn sodium		Clean (0.5ppm LOQ)	1.5ppm DEGBE
47733		cromolyn sodium		Clean (0.5ppm LOQ)	~0.6ppm DEGBE
67901		metaproterenol		Clean (0.5ppm LOQ)	1.3ppm DEGBE
69771		metaproterenol		Clean (0.5ppm LOQ)	1.2ppm DEGBE
69772		metaproterenol		Clean (0.5ppm LOQ)	2.9ppm DEGBE
69773		metaproterenol		Clean (0.5ppm LOQ)	1.6 ppm 2-PE
69774		metaproterenol		1.7 ppm 2-PE	1.5ppm DEGBE
69775		albuterol sulfate		Clean (0.5ppm LOQ)	1.3ppm DEGBE
69776		albuterol sulfate		Clean (0.5ppm LOQ)	1.1ppm DEGBE
69777		ipratropium bromide		Clean (0.5ppm LOQ)	1.5ppm DEGBE 0.86ppm DEGEEA
69778		ipratropium bromide		Clean (0.5ppm LOQ)	~0.5ppm DEGBE and DEGEEA
69779		cromolyn sodium		Clean (0.5ppm LOQ)	3.8ppm DEGBE
69780		cromolyn sodium		Clean (0.5ppm LOQ)	2.6ppm DEGBE

*Clean = No 2-phenoxyethanol, 1-phenoxyisopropanol or vanillin above the 0.5ppm limit of quant
**2-HMPP = 2-Hydroxy-2-methylpropiophenone - id'd by GC/MS and quantified by HPLC
PEG's = Polyethylene glycols HO-(CH2-CH2-O)n-H where n is ~4-8 (no standards available)
DEGBE = Di(ethylene glycol) butyl ether = 2-(2-butoxyethoxy) ethanol
DEGEEA = Di(ethylene glycol) ethyl ether acetate = 2-(2-ethoxyethoxy) ethanol acetate

Attachment 3 Request for Health Hazard Evaluation

1. **Benzophenone**...Found in 2 lots of ——— at 0.5-0.6ppm.

2. **Low Molecular Weight Polyethylene Glycols (n=4-8)**

Found in 3 lots of ——— 0.4% Metaproterenol at 4-5ppm and 2 lots of ——— 0.6% Metaproterenol at 2-4ppm.

3. **DEGBE (Di(ethylene glycol) butyl ether, or 2-(2-butoxyethoxy)ethanol):**

Found in 1 lot of 0.6% ——— Metaproterenol at 0.6ppm
Found in 3 lots of 0.6% ——Metaproterenol at 1.2 ppm.
Found in 2 lots of 0.4% —— Metaproterenol at 0.5ppm
Found in 4 lots of 0.4% ——Metaproterenol at 0.5-1.5ppm
Found in 4 lots of 0.6% —— Metaproterenol at 1.5-2.9ppm
Found in 3 lots of 0.083% —— Albuterol at 0.9-1.3ppm
Found in 3 lots of 0.02% —— Ipratropium at 0.5-1.5ppm
Found in 4 lots of 1% ——Cromolyn at 0.6-3.8ppm

4. **DEGEEA (Di(ethylene glycol) ethyl ether acetate, or 2-(2-ethoxyethoxy). ethanol acetate):**

Found in 1 lot of ——Albuterol at 1.6ppm
Found in 2 lots of —— Ipratropium at 0.5-0.9ppm

5. **2-HMPP (2-Hydroxy-2-methylpropiophenone):**

Found in 3 lots of 0.4% ——— Metaproterenol at 0.3-2ppm
Found in 2 lots of 0.6% ——— Metaproterenol at 0.4-0.5ppm

Note: 2-HMPP is not specifically listed as a process impurity for the synthesis of the drug substance. However, it is an old file and the reviewer believes that is is possible that this impurity may be formed as a by-product of the synthesis.

Attachment 4 Health Hazard Evaluations

MEDICAL OFFICER CONSULTATION

Date: August 4, 2000

To: OGD/Regulatory Support Branch HFD-615

From: Eugene J. Sullivan, MD, FCCP
Medical Officer, Division of Pulmonary and Allergy Drug Products

Luqi Pei, PhD, DVM
Pharmacologist/Toxicologist, DPADP

Through: Robin Huff, PhD
Supervisory Pharmacologist, DPADP

Through: Badrul Chowdhury, MD, PhD
Acting Medical Team Leader, DPADP

Through: Robert Meyer, MD
Director, DPADP

Subject: Health Hazard Evaluation for non-overwrapped, LDPE-packaged inhalation solutions

General Information

NDA/IND#: Multiple.
Sponsor: Multiple.
Protocol: N/A.
Drug Product: Albuterol sulfate, Cromolyn sodium, Ipratropium bromide, Metaproterenol sulfate.
Request From: Office of Generic Drugs.
Materials: Cover letter and 2-page summary of the analytical survey.

Background

At the request of OGD, an analytical survey of non-overwrapped, LDPE-packaged inhalation solutions was performed by ORA's Pacific Regional Laboratory. The purpose of the survey was to detect potential chemical contamination of these products. Samples of various drug products (see consult request) were obtained and assayed using Gas Chromatography/Mass Spectrometry and High Performance Liquid Chromatography with special emphasis on three chemicals which have been previously detected in these types of products: vanillin, 2-phenoxyethanol, and 1-phenoxy-2-propanol.

Of the 37 samples, 29 tested positive for chemical contamination. One sample tested positive for 2-phenoxyethanol at 1.7ppm. This finding has already been addressed by CDER in its recommendation

for a Class 3 recall of a [redacted] product. The remaining samples were found to contain varying levels of 5 different chemical contaminants: benzophenone, low molecular weight polyethylene glycols, DEGBE [Di(ethylene glycol) butyl ether or 2-(2-butoxyethoxy)ethanol)], DEGEEA [(Di(ethylene glycol) ethyl ether acetate or 2-(2-ethoxyethoxy) ethanol acetate], and 2-HMPP [2-hydroxy-2-methylpropiophenone]. These five contaminants were different than the three chemicals that the analytic method was specifically designed to detect. OGD has requested that DPADP perform a Health Hazard Evaluation.

In order to address this evaluation, DPADP convened a multidisciplinary group including representatives from the CMC, pharm/tox and medical disciplines.

Specific Comments

Four of the five chemicals identified are assumed to represent contaminants that have leached into the drug product from outside the LDPE vial. Labeling and packaging materials may be the source of some or all of these four contaminants. The fifth, 2-HMPP is presumed to be a synthetic impurity. The amount of information available regarding the toxicologic profiles of these five compounds is variable. Although the toxicologic evaluations of these chemicals are incomplete, there is no specific evidence to suggest that they pose a significant toxicologic risk at the concentrations detected. There is no information available regarding the potential for these chemicals to act as spasmogens in the airways of normal subjects or patients with asthma or chronic obstructive pulmonary disease. However, the concentrations of the contaminants detected were low (≤ 5ppm).

A completed Health Hazard Evaluation form is attached to this memorandum. The presence of these contaminants is concerning.

[redacted] The available toxicology data for each contaminant is summarized below, along with our opinion regarding the potential for human toxicity for each contaminant.

1. Benzophenone

Benzophenone is a respiratory irritant, and this irritancy is a dose-dependent phenomenon. The expected low level of exposure for benzophenone (0.12 µg/kg/day) is far below its permissible workplace level of 710 µg/kg/day recommended by the American Industrial Hygiene Association. This suggests that benzophenone at the observed levels would be unlikely to irritate the respiratory tract and trigger bronchospasms in COPD and asthmatic patients.

2. Polyethylene glycols

The safety of polyethylene glycols (PEGs), including PEG 200 and PEG 400, as inactive ingredients in drug products, has been established. Formulations of the approved and marketed products using PEGs include parental, oral, topical, dental, nasal and other preparations. PEGs are not components of any approved inhalation drug products, but reasonably sufficient data show that the low levels of PEGs (≤ 5 ppm) does not cause significant safety concern. Laboratory studies have shown that small molecular PEGs such as PEG 600 have no effect on the respiratory tract at an inhalation dose of 1.4 mg/kg/day in dogs. (This level is 1,400 times greater than the expected dose of 1 µg/kg/day in humans.) Clinical trials with formulations containing PEG 600 did not show any evidence of bronchospasm associated with the treatment. Because PEGs of small molecular weights are expected to possess similar toxicity profiles, available information suggests that the observed levels of PEGs are unlikely to be irritating to the respiratory system and thus, unlikely to cause bronchospasm in the intended populations.

3. DEGBE [Di(ethylene glycol)butyl ether]

DEGBE is the most prevalent leachable found in the survey. A total of 24 lots of drug products were found to contain the compound. DEGBE is apparently a respiratory irritant at high concentrations, but laboratory studies show that DEGBE has no effect on the respiratory tract at an air concentration of 18 ppm (26 mg/kg/day) for 5 weeks in rats. These inhalation toxicity studies show that the liver is the target organ of DEGBE toxicity. The inhalation NOAEL value is 3 mg/kg/day. This value is 5,000 times the expected exposure levels in humans (0.6 µg/kg/day). [Note: this NOAEL is based upon a 5-week study. It is possible that the NOAEL could decrease with chronic exposure.] These data show that DEGBE is not likely to irritate the respiratory tract and trigger bronchospasm in the intended population.

4. DEGEEA [Di(ethylene glycol)ethyl Ether Acetate

DEGEEA was found in a total of three lots of the inhalation solutions. Available information for DEGEEA is too limited to conduct a sound safety evaluation of the compound. The following information was found in databases:

DEGEEA is a solvent and a plasticizer. It irritates the eyes, mucous membranes and upper respiratory tract at high concentrations. Rats and guinea pigs exposed to an essentially saturated atmosphere at room temperature for 8 hours (approximately 207 mg/kg) revealed injury to the lung and kidneys at gross autopsy, but detailed information about the injuries is not available. No occupational exposure standards or permissible

levels for DEGEEA are available. The Hazardous Substance Data Bank (HSDB) states that "no hygienic standard of permissible exposure... has been suggested, nor would one seem necessary in view of the low volatility and the nature of the material".

The above information is insufficient to establish the safety of DEGEEA in asthmatic and COPD patients. The HSDB statement is inapplicable to the drug products of interest because DEGEEA will be delivered to the lung through the administration of these drug products. Although the expected exposure in the patient is relatively low (0.32 µg/kg/day), the possibility of DEGEEA triggering bronchospasm in asthmatic and COPD patients cannot be excluded due to the irritability of the compound. Because of the lack of data on the dose-response relationship for the irritability of DEGEEA, caution should be applied to the safety assessment of the compound.

5. 2-HMPP (2-hydroxy-2-methylpropiophenone)

Five lots of inhalation solutions were found to contain 0.3 - 2.0 ppm of 2-HMPP, a synthesis impurity. The safety evaluation of 2-HMPP should follow the ICH guidelines on the qualification of impurities. The 2-HMPP levels (0.05%) in the products of interest is below the identification and qualification threshold of 0.1%. This renders the 2-HMPP levels acceptable and no further discussion is necessary.

Conclusion:

A preclinical health hazard evaluation indicates that the levels of benzophenone, PEGs, DEGBE, and 2-HMPP do not raise sufficient safety concerns in the intended population to warrant a recall of the products involving these contaminants.

The absence of any known occurrence of harm to a patient and the absence of specific data to demonstrate toxic potential of these chemicals at the concentrations detected preclude a more aggressive recall action. However, several issues raise particular concern. First, the potential for these chemicals to cause bronchospasm, particularly in the patient populations using these drug products, is unknown. Second, it is not clear whether the products were tested at the end of their shelf-life. It is possible that the concentration of contaminants might be greater at the end of the expiry. Third, this analysis has demonstrated that chemical contaminants can and do leach into these drug products. It is possible that additional chemicals were also present, but were not detected by the assays used. Further,

- future changes in the materials used in labeling and packaging may result in contamination with different chemicals.

We believe that these issues are concerning enough to merit aggressive measures to ensure that future LDPE-packaged inhalation solutions remain free of leachable chemicals. It is quite possible that chemical contamination of inhalation solutions may have clinical consequences. The current absence of data to establish such clinical consequences is not completely reassuring. Because the potential adverse effect of these chemicals (bronchospasm) is also the indication for which the drug products are used, it would be very difficult to establish any link between the chemicals and bronchospasm. In light of the concerns regarding these and other chemical contaminants as well as the data that suggests that asthma mortality rates are increasing, it is advisable to make all efforts to assure the purity of these drug products. We recommend that you initiate efforts, separate and in addition to the proposed development of a guidance document on this permeability issue, to ensure that all single dose inhalation drug products in LDPE vials have a secondary full overwrap and not have paper labeling directly applied to them.

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EPAG

European Pharmaceutical Aerosol Group

Inhalation Drug Products Packaged in Semipermeable Container Closure Systems

The European Pharmaceutical Aerosol Group (EPAG) is pleased to have the opportunity to comment on this guidance for industry. EPAG is a voluntary non-profit making consortium of member companies open to "European Pharmaceutical Companies that develop new products for human use utilising the Pulmonary or Nasal route of delivery"

We submit the following specific comments:

- **Section I. Introduction.** We ask that clarification be added that the guidance does not apply to dry powder inhalers or pressurised metered dose inhalers.

- **Section I. Introduction.** We ask that definition of "semipermeable" be added to the document in order to clarify applicability of the guidance to new packaging materials.

- **Section I. Introduction (lines 30-31).** We ask that time frame and details on information required to adopt the guidance be added for products already approved and marketed in the United States.

- **Section III. Chemistry, Manufacturing and Controls Considerations (lines 125-128).** We ask that additional information be added to clarify the type and extent of study that should be performed to demonstrate that the secondary packaging can provide adequate protection from reactive gases, volatile compounds and foreign chemicals from the local environment.

- **Section III. Chemistry, Manufacturing and Controls Considerations (lines 129-132).** We ask that guidance be added for concentrations at which chemical contaminants from the secondary packaging components should be identified, quantified and qualified.

02D-0254 C1

Yours sincerely.
On behalf of EPAG

N. Bowles

Nola Bowles
3M Health Care Ltd, Morley Street, Loughborough, Leicestershire, England. LE11 1EP

11 October 2002

3M, AstraZeneca, Aventis, Bespak, Boehringer Ingelheim, Chiesi, Clinical Designs, GlaxoSmithKline, Hovione, Innovata Biomed, Ivax Pharmaceuticals, Novartis, Orion, Pharmachemie, Pfizer, SkyePharma, Sofotec, Trudell Medical International, Vectura.

EPAG

European Pharmaceutical Aerosol Group

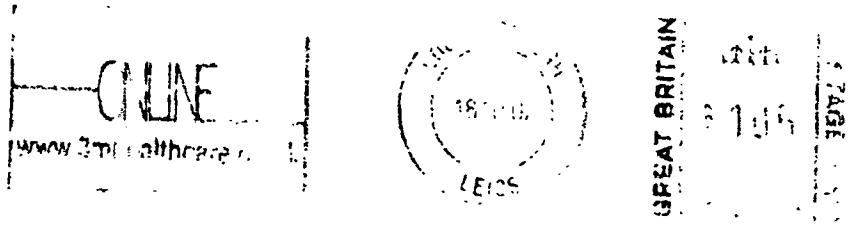
Comments on

Draft Guidance for Industry Inhalation Drug Products Packaged in Semipermeable Container Closure Systems

Docket Number 02D-0254

11 October 2002

3M, AstraZeneca, Aventis, Bespak, Boehringer Ingelheim, Chiesi, Clinical Designs, GlaxoSmithKline, Hovione, Innovata Biomed, Ivax Pharmaceuticals, Novartis, Orion, Pharmachemie, Pfizer, SkyePharma, Sofotec, Trudell Medical International, Vectura.



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October 23, 2002

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GlaxoSmithKline

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Re: Docket Number 02D-0254, Comments on Draft Guidance for Industry on Inhalation Products Packaged in Semipermeable Container Closure Systems

Dear Sir or Madam:

Enclosed please find comments from GlaxoSmithKline on the Draft Guidance for Industry on Inhalation Products Packaged in Semipermeable Container Closure Systems. The comments are provided for consideration by the FDA. The comments are listed in order by the line number in the attachment.

GlaxoSmithKline appreciates the opportunity to provide feedback and suggestions for this guidance. I am submitting this document both electronically and by hardcopy. Therefore, you will receive a copy of this letter and two copies of the comments through the USPS. If you have any questions about these submitted comments, please feel free to contact me at (919) 483-5857. Thank you for your consideration.

Sincerely,

Mary Faye S. Whisler

Mary Faye S. Whisler, Ph.D.
Assistant Director
New Submissions, North America

02D-0254

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Specific comments from GSK relating to the Draft Guidance for Industry on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems include the following.

I. Introduction:
Line 25 should be changed to "It is intended to provide guidance on (1) the considerations for selecting appropriate protective..."

II. Background
Lines 39- 53 should be changed to clarify and eliminate redundancy. The first paragraph in this section should end with the statement that ends on line 39 (statement ending in "...chemical impurities."). The next paragraph (lines 46 to 53) should changed to the following.

"Drug substances used in the treatment of patients with asthma or chronic obstructive pulmonary disease (COPD) are often formulated as inhalation solutions or suspensions. These drug products can be packaged in either unit-dose vials or multi-dose vials. In an inhalation drug product packaged in a semipermeable container, in addition to chemical impurities that can accumulate over time as a result of the degradation of formulation components or leaching from the container closure system, chemical impurities can enter from the local environment. For example, LDPE vials are permeable to some volatile chemicals (i.e., chemicals with moderate to high vapor pressure under typical climatic storage conditions). As a result of this permeability, chemicals originating from packaging materials, such as adhesives, varnishes, and solvents, have been found in inhalation drug products packaged in LDPE. These findings have resulted in drug recalls."

Lines 77 – 93 should be deleted. The information in these two paragraphs are speculative (as to the link of chemical contaminants, asthma, and asthma mortality) and should not be included in a CMC guidance document.

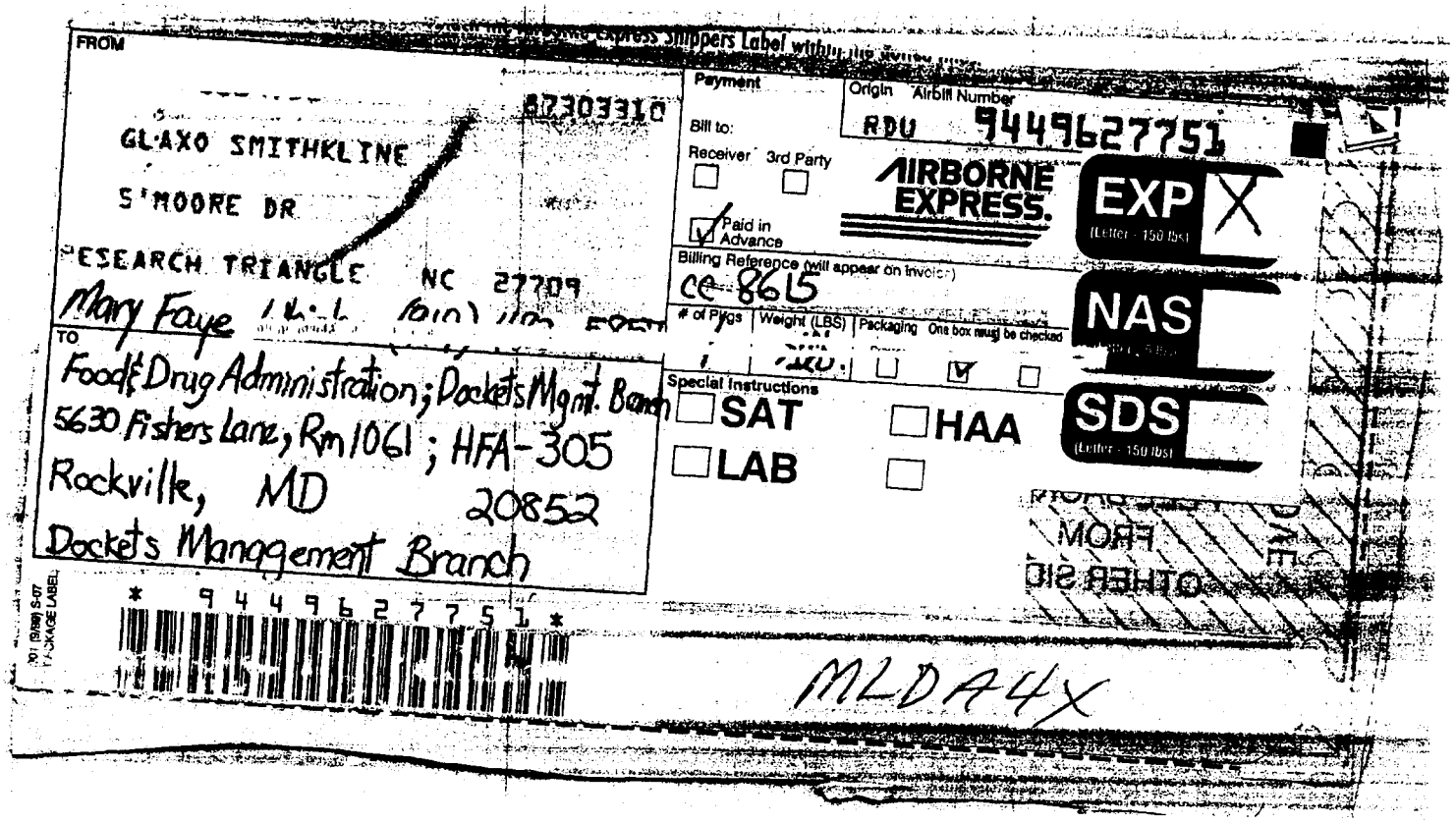
III. Chemistry, Manufacturing and Controls Considerations

Lines 96 to 110 should be rewritten because it is hard to assess the risk of the different types of contamination. Specific information follows. Lines 96 to 107 are confusing. We would agree that the extent of leaching should be limited, but limits do not keep the levels down. The issues with secondary packaging are confusing because we would increase the risk of one form of contamination (from the secondary packaging) to minimize the risk of other contamination (from the environment). The opening phrase in line 107 indicates that secondary packaging is optional, whereas lines 96 and 97 mandate

the use of secondary packaging. Additionally, lines 104-105 ("Controls are also important to prevent loss of water from the formulation.") is not really a part of the problem and is not mentioned again.

Lines 122-129 seem to require a lot of information for secondary packaging, that are not necessary for performance purposes. This information should be deleted. If these lines are not deleted, the guidance suggests a significant permeation study should be performed with multiple analysts. If this is required, the agency should give guidance on the type of analyst studies required.

Lines146 to 153 should also be deleted because the information is not necessary for performance purposes.


FROM
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Mary Faye
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Origin Airbill Number
RDU 9449627751
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EXP
NAS
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Billing Reference (will appear on invoice)
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# of Pkgs
Weight (LBS)
Packaging
Special Instructions
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HAA
LAB
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Docket Management

Docket: 02D-0254 - Draft Guidance on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems

Comment Number: EC -2

Accepted - Volume 1

Comment Record			
Commentor	Dr. Mary Faye Whisler	Date/Time	2002-10-23 13:02:36
Organization	GlaxoSmith Kline		
Category	Company		

Comments for FDA General	
Questions	
1. General Comments	October 23. 2002 Dockets Management Branch Food and Drug Administration HFA-305 5630 Fishers Lane, Rm 1061 Rockville, MD 20852 Re: Docket Number 02D-0254, Comments on Draft Guidance for Industry on Inhalation Products Packaged in Semipermeable Container Closure Systems Dear Sir or Madam; Enclosed please find comments from GlaxoSmithKline on the Draft Guidance for Industry on Inhalation Products Packaged in Semipermeable Container Closure Systems. The comments are provided for consideration by the FDA. The comments are listed in order by the line number in the attachment. GlaxoSmithKline appreciates the opportunity to provide feedback and suggestions for this guidance. I am submitting this document both electronically and by hardcopy. Therefore, you will receive a copy of this letter and two copies of the comments through the USPS. If you have any questions about these submitted comments, please feel free to contact me at (919) 483-5857. Thank you for your consideration. Sincerely, Mary Faye S. Whisler, Ph.D. Assistant Director New Submissions, North America Specific comments from GSK relating to the Draft Guidance for Industry on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems include the following. I. Introduction: Line 25 should be changed to "It is intended to provide guidance on (1) the considerations for selecting appropriate protective..." II. Background Lines 39- 53 should be changed to clarify and eliminate redundancy. The first paragraph in this section should end with the statement that ends on line 39 (statement ending in "...chemical

impurities."). The next paragraph (lines 46 to 53) should changed to the following. Drug substances used in the treatment of patients with asthma or chronic obstructive pulmonary disease (COPD) are often formulated as inhalation solutions or suspensions. These drug products can be packaged in either unit-dose vials or multi-

product packaged in a semipermeable container, in addition to chemical impurities that can accumulate over time as a result of the degradation of formulation components or leaching from the container closure system, chemical impurities can enter from the local environment. For example, LDPE vials are permeable to some volatile chemicals (i.e., chemicals with moderate to high vapor pressure under typical climatic storage). As a result of this permeability, chemicals originating from packaging materials, such as adhesives, varnishes, and solvents, have been found in inhalation drug products packaged in LDPE. These findings have resulted in drug recalls. Lines 77 – 93 should be deleted. The information in these two paragraphs are speculative (as to the link of chemical contaminants, asthma, and asthma mortality) and should not be included in a CMC guidance document. III. Chemistry, Manufacturing and Controls Considerations Lines 96 to 110 should be rewritten because it is hard to assess the risk of the different types of contamination. Specific information follows. Lines 96 to 107 are confusing. We would agree that the extent of leaching should be limited, but limits do not keep the levels down. The issues with secondary packaging are confusing because we would increase the risk of one form of contamination (from the secondary packaging) to minimize the risk of other contamination (from the environment). The opening phrase in line 107 indicates that secondary packaging is optional, whereas lines 96 and 97 mandate the use of secondary packaging. Additionally, lines 104-105 ("Controls are also important to prevent loss of water from the formulation.) is not really a part of the problem and is not mentioned again. Lines 122-129 seem to require a lot of information for secondary packaging, that are not necessary for performance purposes. This information should be deleted. If these lines are not deleted, the guidance suggests a significant permeation study should be performed with multiple analysts. If this is required, the agency should give guidance on the type of analyst studies required.

	Lines146 to 153 should also be deleted because the information is not necessary for performance purposes.

EC -2

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Novartis Pharmaceuticals Corporation
Global Regulatory CMC
One Health Plaza
East Hanover, NJ 07936-1080

Tel 973 781 7500
Fax 973 781 6325

NOVARTIS

[illegible], 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Subject: Response to Draft Guidance for Industry: "Inhalation Drug Products Packaged in Semipermeable Container Closure Systems, Federal Register, Friday, July 26, 2002, Docket No. 02D-0254

To whom it may concern:

Novartis is a world leader in the research and development of products to protect and improve health and well-being. As a global pharmaceutical corporation, Novartis is supportive of efforts to improve and to harmonize the technical requirements for registration of pharmaceutical products. After review of the above-cited guidance, we have the following comments:

General comment
Explanations of the scientific thought behind certain recommendations in the draft Guidance are valuable in promoting understanding of the FDA reasoning within the draft Guidance. However, some of these thoughts are open-ended. Focusing these ideas into more specific and measurable recommendations will improve the effectiveness of the Guidance, once finalized. As the document is made more specific, implementation of its recommendations by industry can be more uniform and regulatory review by FDA can be more consistent. Novartis' comments are made to draw clarity to these open points in the draft document.

Line-specific comments
Line specific comments are provided in tabular form below.

02D-0254

C 3

Line number	Comment
24	The term 'semipermeable' needs to be defined against a uniform standard. This information may be added in a Glossary at the end of the Guidance. Recommendations may include both materials of construction and test methodology (such as reference to standard USP tests) to assess permeability and loss of formulation components.
30, 38	As this draft Guidance addresses the sub-set of medications intended for pulmonary-compromised patients (asthma, COPD—reference line 46), systemic drugs intended for delivery by the pulmonary/nasal route should be specifically excluded from the scope of this Guidance, in the Introduction. Additionally, non-aqueous liquid inhalation products such as MDDPIs and DPIs should be excluded.
31	A regulatory mechanism needs to be proposed to qualify those products already approved and marketed in semi-permeable containers. Commercial materials may also be used in the development of new standards as noted earlier. The Agency should also consider alternative proposals to demonstrate that package concerns are not relevant to the clinical aspects of a particular marketed product (lines 77-87), should a sponsor wish to discuss them.
44, 57, 93, 127-132	Agency comments on volatile organic chemicals, potential contaminants in the local environment, identified and unidentified contaminants from secondary packaging and labeling adhesives, and the potential of formulation components to interact with these to form new impurities describe potential scenarios to introduce trace quantities of impurities into product formulations. To direct efforts in identification and quantification of impurities and reduce speculative studies, it would be useful to relate impurity quantification to known standards such as the ICH Guideline on Residual Solvents, a to-be-developed FDA list of suspect chemicals, or other scientific baseline.
141-144	Complete avoidance of paper labels on unit containers may prove impractical as multiple products become approved, and product identifiers become necessary to avoid misuse or errors in administration. Debossed or embossed molding on translucent or opaque white semipermeable containers may provide too little product differentiation. The Agency should consider establishment of standards or testing for direct-printing inks or label adhesives to qualify their use on liquid inhalation product container labels.

These comments are being provided in duplicate in written form and electronically as directed in the Federal Register Notice.

Thank you for the opportunity to comment. If you have any questions, please contact me at (973) 781-3379 or at e-mail: joan.materna@pharma.novartis.com

Sincerely,

(original signed)

Joan A. Materna
Senior Associate Director
Global Regulatory CMC

NOVARTIS

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Tel 973 781 7500
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October 24, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Subject: Response to Draft Guidance for Industry: "Inhalation Drug Products Packaged in Semipermeable Container Closure Systems, Federal Register, Friday, July 26, 2002, Docket No. 02D-0254

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Line-specific comments

Line specific comments are provided in tabular form below.

02D-0254

C 3

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141-144	Complete avoidance of paper labels on unit containers may prove impractical as multiple products become approved, and product identifiers become necessary to avoid misuse or errors in administration. Debossed or embossed molding on translucent or opaque white semipermeable containers may provide too little product differentiation. The Agency should consider establishment of standards or testing for direct-printing inks or label adhesives to qualify their use on liquid inhalation product container labels.

These comments are being provided in duplicate in written form and electronically as directed in the Federal Register Notice.

Thank you for the opportunity to comment. If you have any questions, please contact me at (973) 781-3379 or at e-mail: joan.materna@pharma.novartis.com

Sincerely,

(original signed)

Joan A. Materna
Senior Associate Director
Global Regulatory CMC

NOVARTIS PHARMACEUTICALS CORP

1 HEALTH PLZ
EAST HANOVER NJ 07936
973-781-5743

SHIP DATE 24OCT2002
ACCOUNT # 116213141
ACTUAL WGT 0 15 LBS

Part # 156148 RJT 02/01

TO:

DOCKETS MANAGEMENT BRANCH
FOOD AND DRUG ADMINISTRATION
5630 FISHERS LANE
ROOM 1061
ROCKVILLE MD 20857

973-781-8251

FedEx

PRIORITY OVERNIGHT

FRI

REF 6940148540
System # 617627 24OCT2002
TRK# 6215 9630 7810 Form 201

DELIVER BY:
IAD 25OCT2002
A2

20857-MD-US ZM GAIA

0 15 LBS
1 OF 1
PO # 8540
J MATERNA

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm 1061
Rockville, Maryland 20855

Docket # 02D-0254

NOVARTIS PHARMACEUTICALS CORP

1 HEALTH PLZ
EAST HANOVER NJ 07936
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SHIP DATE 240CT2002
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20857-MD-US ZM GAIA

0 15 LBS
1 OF 1
PO # 8540
J MATERNA

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm 1061
Rockville, Maryland 20855

Docket # 02D-0254

From: joan.materna@pharma.novartis.com
Sent: Thursday, October 24, 2002 4:48 PM
To: fdadockets@oc.fda.gov
Subject: Novartis Pharmaceuticals Corp. comments on Docket 02D-0254 (Inhalation Products/Semipermeable Containers)

To Whom It May Concern,

Novartis Pharmaceuticals Corporation is submitting comments on the subject Guidance in the attached PDF file.

(See attached file: Novartis comments inhalation Docket 02D-0254.pdf)

Hard copy comments are also being provided to the Dockets Management Branch.

Should you have any questions, I may be reached at 973-781-3379.

Kind regards,
Joan A. Materna

From: joan.materna@pharma.novartis.com
Sent: Thursday, October 24, 2002 4:45 PM
To: fdadockets@oc.fda.gov
Subject: Novartis comments on FDA Docket 02D-0254 (Inhalation Drug Products/Semipermeable Containers)

To Whom It May Concern,

Novartis Pharmaceutical Corporation submits the attached electronic file containing comments on the subject guidance.

Hard copies are being submitted to the Dockets Management Branch.

(See attached file: Novartis comments inhalation Docket 02D-0254.pdf)

Should you have any questions, I may be reached at 862-778-3379.

Regards,
Joan A. Materna

9

IPAC-RS
International Pharmaceutical Aerosol Consortium on Regulation & Science

Comments on Draft Guidance for Industry

Inhalation Drug Products Packaged in Semipermeable Container Closure Systems

(FDA Docket No. 02D-0254)

Submitted by the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS)

24 October 2002

I. INTRODUCTION

The International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS) is an association of companies that research, develop and manufacture aerosol drug products for oral inhalation or intranasal delivery. The importance of these drug products is growing with the expanding range of conditions they are used to treat, including asthma, chronic obstructive pulmonary disease (COPD), rhinitis, migraine, diabetes and others.

Current members of IPAC-RS are: Aradigm, AstraZeneca, Aventis, Boehringer Ingelheim, Eli Lilly, GlaxoSmithKline, Inhale Therapeutic Systems, Inc., Kos Pharmaceuticals, Norton Healthcare, Pfizer, and Schering-Plough Corporation. IPAC-RS companies and the Food and Drug Administration (FDA) share a common goal: to meet the medical needs of patients in a timely manner by facilitating the arrival of new drug products to the market while maintaining scientifically justified standards of safety, efficacy and quality.

II. GENERAL COMMENTS

IPAC-RS welcomes the opportunity to offer comments on the Draft Guidance for Industry entitled *Inhalation Drug Products Packaged in Semipermeable Container Closure Systems.*[1]

IPAC-RS commends the Agency for developing guidance documents focused on a specific regulatory issue, which should facilitate timely discussion and efficient finalization of Draft Guidances. We hope that the Agency will continue this approach in the future by issuing topic-specific Guidances with a well-defined scope.

We are concerned, however, that this particular Draft Guidance is redundant to several other FDA Guidances, which address the issue of leachables testing as well as requirements for primary and secondary packaging, such as the following Guidances:

- Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products Chemistry, Manufacturing, and Controls Documentation;[2]
- Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products Chemistry, Manufacturing, and Controls Documentation;[3] and
- Container Closure Systems for Packaging Human Drugs and Biologics Chemistry, Manufacturing, and Controls Documentation.[4]

The value of an additional Guidance that mostly repeats general statements made elsewhere, is questionable. Moreover, as elaborated in our specific comments below, the new language included in this Draft Guidance confuses rather than clarifies the matter (*e.g.*, do LDPE containers need secondary packaging or not?) or introduces vague but potentially

1 See http://www.fda.gov/cder/guidance/4168dft.pdf.
2 See http://www.fda.gov/cder/guidance/2180dft.pdf.
3 See http://www.fda.gov/cder/guidance/4234fnl.pdf.
4 See http://www.fda.gov/cber/gdlns/cntanr.pdf.

burdensome requirements without substantive justification (*e.g.*, what analytes and methods should be used to assess the effectiveness of a secondary overwrap system to prevent environmental contamination?)

We also feel it is not appropriate for this Guidance to speculate on the medical implications of leachables, as there are no established facts on linkage between incidence and mortality of asthma and leachables.

III. SPECIFIC COMMENTS

In an effort to point out areas for improvement in the present Draft Guidance, we offer the following specific comments.

Clarify Applicability

Lines 23-31

> *This document provides recommendations for industry on inhalation drug products that are packaged in semipermeable primary container closure systems, such as low-density polyethylene (LDPE) containers. ...These recommendations apply to inhalation drug products (e.g., solutions, suspensions, sprays), both those in development and those already approved and marketed in the United States.*

The Guidance should set a clear definition of when a container is considered semipermeable. It should also elaborate as to whether any material besides LDPE is considered "semipermeable" for the purposes of this Guidance.

Further, we request that the Guidance include an explicit statement that it applies only to liquid, aqueous based inhalation drug products and does not apply to metered dose inhalers (MDIs) and dry powder inhalers (DPIs). In addition, newer products for systemic delivery, which treat patients who do not necessarily have hypersensitive airways or have chronic disease, should be explicitly excluded from the applicability of this Guidance.

Furthermore, while the Agency specifically mentions that the Guidance applies to the products already approved and marketed in the U.S., it does not specify a process by which these products can comply with the Guidance. For example, it would be helpful if the Agency described in detail the information that should be submitted, as well as the timeframe and procedure (*e.g.*, first submitting a proposed study protocol to the Agency for comment, and then submitting the data in the Annual Report).

Explain referenced FDA study

Lines 55-58

> *In an FDA study involving random sampling of a number of different inhalation products in non- overwrapped LDPE vials, the majority of these products were found to contain chemical contaminants of various types. The sources of these contaminants were the primary and secondary packaging and labeling components.*

In light of the importance the Agency attributes to this study, the Guidance should describe in more detail what type of secondary packaging was involved if it was not overwrap. (The memorandum referenced in the Draft Guidance in footnote 2 does not provide such information). Clarifying this point is especially important because the Draft Guidance specifically recommends (in line 150) that each individual semipermeable container be overwrapped.

Better define and justify requirements

The Draft Guidance contains a number of open-ended recommendations, which should be clarified in order to provide better guidance for the industry as well as consistency in the regulatory review. Specific examples follow.

Lines 125-129

> *Additionally, if secondary packaging is added, appropriate data must be provided in NDAs, ANDAs, or their supplements to demonstrate that the specified foil-laminate can provide adequate protection from reactive gases, volatile compounds, and foreign chemicals that can enter into the drug products from the packaging materials and/or from the local environment (see 21 CFR 314.420).*

The Guidance should include a specific list of "reactive gases, volatile compounds and foreign chemicals" against which the packaging should be tested. Otherwise, the number of chemicals to test is limitless. The Guidance should identify gases, chemicals and compounds the Agency views as most relevant for these drug products (21 CFR 314.420 does not provide such guidance). Moreover, the Agency should clarify what types of tests are required and what constitutes "appropriate data."

The Guidance would be improved if such specific recommendations were linked to available scientific data and documented studies of potential safety concerns. For example, a method of toxicity classes similar to that adopted by the International Conference on Harmonization for organic solvents,[5] could be used to provide substantive guidance and inform decisions about details of recommended packaging testing.

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[5] International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, *Q3C: Impurities: Guidelines for Residual Solvents.* Internet: http://www.ich.org/pdfICH/Q3C.pdf (1997).

Without further specificity, there is a real potential for the scope of the required testing to grow out of proportion and impose unjustifiable regulatory burden on the developers and manufacturers of these types of drug products.

Lines 129-132

> *...any leaching of contaminants into the formulation...be adequately documented, quantified, and qualified.*

The Guidance should include the threshold levels at which the leachables are to be identified, quantified, and qualified. Otherwise, the amount, scope, intensity and associated costs of the required testing will be driven by the ever-increasing detection capabilities of analytical technology and not by any clinical or quality concern.

The industry has repeatedly requested that the threshold approach to leachables in orally inhaled and nasal drug products be adopted by the Agency.[6, 7, 8] This approach received positive comments during a 2000 meeting of the FDA Advisory Committee for Pharmaceutical Science.[9] Most recently, FDA, industry, USP and academic representatives have undertaken an evaluation of the details of this approach and associated methods through the Product Quality Research Institute.[10] We also note that use of thresholds has a well established precedent in general guidelines developed by the International Conference on Harmonization for impurities in new drug products.[11]

To consolidate best scientific regulatory approaches to leachables testing, we strongly urge the Agency to acknowledge and use the concept of identification, quantification and qualification thresholds in this and future Guidances. Moreover, based on its extensive data base, the Agency could propose a practicable set of

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6 CMC Leachables and Extractables Technical Team of the ITFG/IPAC-RS Collaboration, *Leachables and Extractables Testing: Points to Consider*. Internet: http://ipacrs.com/PDFs/Points_to_Consider_FINAL.PDF (2001).

7 IPAC, *Comments on a draft Guidance for Industry Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products Chemistry, Manufacturing, and Controls Documentation (Docket No. 98D-0997)*. Internet: http://ipacrs.com/PDFs/IPAC_Final_Comments_on_CMC.PDF (1999).

8 IPAC, *Comments on a draft Guidance for Industry Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products Chemistry, Manufacturing, and Controls Documentation (Docket No. 99D-1454)*. Internet: http://ipacrs.com/PDFs/IPAC_Final_Comments_on_CMC.PDF (1999).

9 Advisory Committee for Pharmaceutical Science. *Transcripts of the Meeting on November 15, 2000*. Internet: http://www.fda.gov/ohrms/dockets/ac/00/transcripts/3657t1.pdf (2000).

10 PQRI Leachables and Extractables Working Group, *Development of Scientifically Justifiable Thresholds for Leachables and Extractables*. Internet: http://www.pqri.org/minutes/pdfs/dptc/lewg/workplan02.pdf (2002).

11 International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, *Q3B(R): Impurities in New Drug Products*. Internet: http://www.ich.org/word/Q3Brstep2.doc (1999).

identification, quantification and qualification thresholds for leachables in orally inhaled and nasal drug products.

Lines 140-155

> *FDA also recommends that the number of semipermeable containers packaged within a single protective secondary package (e.g., a foil-laminate overwrap pouch) be limited to restrict the exposure of unused containers to environmental contaminants if the protective secondary packaging should be compromised. To prevent such environmental contamination of the drug product, the ideal approach would be to overwrap each semipermeable container individually within the protective secondary packaging. However, if more than one unit is packaged per pouch, the number of units per pouch should be limited so that the amount of time the vials are exposed to the unprotected environment before use is kept to a minimum.*

We request that the Agency provide further guidance on what would be considered an acceptable "limited" number of units per pouch.

Furthermore, in view of the study referenced by the Guidance in lines 55-61, it would be interesting to know if an evaluation of chemical contamination was performed on inhalation products using both secondary packaging and overwrap, to justify the recommendation of individually wrapping containers within secondary packaging. Since no material is entirely free of compounds that can potentially migrate, it should be evaluated whether use of overwrap significantly diminishes contamination from the environment, has little effect, or adds new contaminants to the immediate environment of the primary semipermeable container.

IV. CONCLUSIONS

We sincerely hope that our comments will be helpful to the Agency. We believe our suggestions will help clarify and further strengthen the Draft Guidance and increase its usefulness and scientific relevance.

We look forward to the publication of a final Guidance that will effectively serve the current and future needs of the inhalation drug product industry and ultimately the consumers of these important drug products.

From: Lyapustina, Svetlana [SLyapustina@dc.gcd.com]
Sent: Thursday, October 24, 2002 8:24 PM
To: 'fdadockets@oc.fda.gov'
Subject: FDA Docket No. 02D-0254: IPAC-RS Comments on Draft Guidance "Inha lation Drug Products Packaged in Semipermeable Container Closure Systems"

Dear Madam/Sir:

Attached please find a set of comments from the International Pharmaceutical Aerosol Consortium on Regulation and Science (IPAC-RS) on the FDA Draft Guidance for Industry entitled "Inhalation Drug Products Packaged in Semipermeable Container Closure Systems" (FDA Docket No. 02D-0254). The comments are being attached in two formats - PDF and MS Word.

Please let me know if you have any questions or have trouble opening the attachments.

Kind regards,

Svetlana Lyapustina, Ph.D.
IPAC-RS Science Advisor
.....
1301 K Street, NW
Suite 900, East Tower
Washington DC, 20005
.....
Phone: 202-408-7179
Fax: 202-289-1504
Email: SLyapustina@gcd.com
.....

MEDERR DDP REPORT

Access Number: 040892
28-Oct-02 02:51:59 PM **erf**

Date Received at USP: 16-May-9 **Date of Report**

Product Name: VENTOLIN NEBULES	**Container Type:** UNIT-DOSE
Generic Name(s): ALBUTEROL SULFATE	**Container Size:** 3 ML
Manufacturer: ALLEN & HANBURYS	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength:	**Sample Available:** Yes
Product Name: ATROVENT	**Container Type:** UNIT-DOSE
Generic Name(s): IPRATROPIUM BROMIDE	**Container Size:** 2.5 ML
Manufacturer: BOEHRINGER ING	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength:	**Sample Available:** Yes

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error?

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error?

When and how was the error discovered?

Where did the error occur?

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 040892

28-Oct-02 02:52:00 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

POTENTIAL ERROR: ALTHOUGH THE BOXES THAT THE UNIT-DOSE VIALS ARE PACKAGED IN ARE VERY DIFFERENT, THE UNIT-DOSE VIALS THEMSELVES LOOK IDENTICAL EXCEPT FOR THE SHAPE OF THE SNAP OFF TOP. IT IS FEARED THAT PRACTITIONERS, ESPECIALLY RESPIRATORY THERAPISTS WILL CONFUSE THE TWO WHEN THEY ARE TAKEN OUT OF THE BOX TO BE USED FOR PATIENTS. THE REPORTER RECOMMENDS THAT THE CLEAR PLASTIC UNIT-DOSE VIALS SHOULD HAVE PAPER LABELS ON THEM, SO THAT ONE CAN READ THE NAME OF THE DRUG.

MEDERR DDP REPORT

Access Number: 040914
28-Oct-02 02:52:00 PM **erf**

Date Received at USP: 09-Jun-94 **Date of Report**

Product Name: ATROVENT	**Container Type:** UNIT-DOSE
Generic Name(s): IPRATROPIUM BROMIDE	**Container Size:**
Manufacturer: BOEHRINGER ING	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength: 0.5 MG/2.5 ML	**Sample Available:** No
Product Name: VENTOLIN	**Container Type:** UNIT-DOSE
Generic Name(s): ALBUTEROL SULFATE	**Container Size:**
Manufacturer: ALLEN & HANBURYS	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength: 2.5 MG/3 ML	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error?

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error?

When and how was the error discovered?

Where did the error occur?

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 040914

28-Oct-02 02:52:00 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

POTENTIAL ERROR: THE PACKAGING OF ATROVENT INHALATION SOLUTION AND VENTOLIN NEBULES IS VERY SIMILAR. THE POTENTIAL PROBLEM IS THAT SINCE BOTH AGENTS ARE USED IN JUST NEBULIZER TREATMENTS, THEY COULD EASILY BE CONFUSED. THE WRITING ON THE PLASTIC CONTAINER IS IN CLEAR WRITING AND DIFFICULT TO READ; THEREFORE IF THE PACKAGING IS SIMILAR AND THE WRITING DIFFICULT TO READ, THE TWO CAN BE EASILY CONFUSED. THE REPORTER RECOMMENDS EITHER ADD A DIFFERENT COLOR TO THE WRITING ON THE PLASTIC CONTAINER OR ADD COLOR TO THE TAB ON THE END OF EACH CONTAINER.

MEDERR DDP REPORT

Access Number: 041020
28-Oct-02 02:52:00 PM **erf**

Date Received at USP: 19-Aug-9 **Date of Report**

Product Name: ATROVENT	**Container Type:** AMPUL
Generic Name(s): IPRATROPIUM BROMIDE	**Container Size:**
Manufacturer: BOEHRINGER ING	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength:	**Sample Available:** No
Product Name: ALBUTEROL SULFATE	**Container Type:** AMPUL
Generic Name(s): ALBUTEROL SULFATE	**Container Size:**
Manufacturer: VARIOUS	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength:	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error?

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error?

When and how was the error discovered?

Where did the error occur?

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 041020

28-Oct-02 02:52:00 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

BOTH AMPULS LOOK VERY SIMILAR. THIS COULD CAUSE AN ERROR. THE PERSONNEL IN THE RESPIRATORY THERAPY DEPARTMENT ASKED THE PHARMACY TO PACKAGE THEM DIFFERENTLY TO AVOID CONFUSION. THIS INCIDENT HAS BEEN REPORTED TO THE INSTITUTION. THE REPORTER RECOMMENDS BOTH MANUFACTURERS SHOULD BE NOTIFIED THAT THE LABELING, SIZING OR COLORING OF BOTH DRUGS NEED TO BE CHANGED TO DIFFERENTIATE BETWEEN THE TWO.

MEDERR DDP REPORT

Access Number: 041119
28-Oct-02 02:52:00 PM **erf**

Date Received at USP: 02-Nov-9 **Date of Report**

Product Name: ATROVENT	**Container Type:**
Generic Name(s): IPRATROPIUM BROMIDE	**Container Size:**
Manufacturer: BOEHRINGER ING	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength: 0.5 MG/2.5 ML	**Sample Available:** No
Product Name: VENTOLIN	**Container Type:**
Generic Name(s): ALBUTEROL SULFATE	**Container Size:**
Manufacturer: ALLEN & HANBURYS	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength: 2.5 MG/3 ML	**Sample Available:** No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome: N/A

If the medication did not reach the patient, describe the intervention.

Who discovered the error? Pharmacist

When and how was the error discovered? N/A

Where did the error occur? Hospital pharmacy

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:
N/A

MEDERR DDP REPORT

Access Number: 041119

28-Oct-02 02:52:00 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

POTENTIAL ERROR ONLY. IPRATROPIUM BROMIDE AND ALBUTEROL SULFATE LOOK IDENTICAL AND CAN BE EASILY INTERCHANGED.

MEDERR DDP REPORT

Access Number: 041258
28-Oct-02 02:52:00 PM **erf**

Date Received at USP: 02-Feb-95 **Date of Report**

Product Name:	VENTOLIN NEBULES	**Container Type:**	
Generic Name(s):	ALBUTEROL SULFATE	**Container Size:**	
Manufacturer:	ALLEN & HANBURYS	**NDC Number:**	
Labeler:		**Adm. Route:**	INHALATION
Dosage Form:	SOLUTION	**Lot Number(s):**	
Strength:		**Sample Available:**	No
Product Name:	ATROVENT	**Container Type:**	
Generic Name(s):	IPRATROPIUM BROMIDE	**Container Size:**	
Manufacturer:	BOEHRINGER ING	**NDC Number:**	
Labeler:		**Adm. Route:**	INHALATION
Dosage Form:	SOLUTION	**Lot Number(s):**	
Strength:	0.5 MG/2.5 ML	**Sample Available:**	No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome: NA

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered? NA

Where did the error occur? HOSPITAL PHARMACY

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:
NA

MEDERR DDP REPORT

Access Number: 041258

28-Oct-02 02:52:00 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

THE REPORTER IS WRITING IN ORDER TO EXPRESS HIS CONCERNS OVER POSSIBLE MEDICATION ERRORS OCCURRING FROM THE UNINTENDED DISPENSING OF VENTOLIN NEBULE (3 ML FOR INHALATION) FOR ATROVENT (0.5 MG/2.5 ML FOR INHALATION). THE REPORTER IS AWARE THAT THE PRODUCT HAS A V FOR VENTOLIN AT THE TOP FOR EASE OF OPENING, HOWEVER, BECAUSE OF THE SIMILARITY (ALMOST IDENTICAL) COLOR, SIZE, SHAPE AND RAISED LETTERING, THE REPORTER IS SURE THAT IT IS JUST A MATTER OF TIME BEFORE SERIOUS MEDICATION ERRORS OCCUR WITH THE PRODUCT. THEREFORE, THE REPORTER IS REQUESTING THE FIRMS TAKE A SERIOUS LOOK AT THE PACKAGING FOR THIS PRODUCT WITH THE INTENTION OF CHANGING SOMETHING SO AS TO ALLOW EASIER IDENTIFICATION.

MEDERR DDP REPORT

Access Number: 041294
28-Oct-02 02:52:01 PM **erf**

Date Received at USP: 17-Feb-95 **Date of Report**

Product Name:	ATROVENT	**Container Type:**	UNIT-DOSE
Generic Name(s):	IPRATROPIUM BROMIDE	**Container Size:**	
Manufacturer:	BOEHRINGER ING	**NDC Number:**	
Labeler:		**Adm. Route:**	INHALATION
Dosage Form:	SOLUTION	**Lot Number(s):**	
Strength:	0.5 MG/2.5 ML	**Sample Available:**	No
Product Name:	SODIUM CHLORIDE	**Container Type:**	UNIT-DOSE
Generic Name(s):	SODIUM CHLORIDE	**Container Size:**	
Manufacturer:	VARIOUS	**NDC Number:**	
Labeler:		**Adm. Route:**	INHALATION
Dosage Form:	SOLUTION	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome: NA

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered? NA

Where did the error occur? HOSPITAL PHARMACY

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:
NA

MEDERR DDP REPORT

Access Number: 041294

28-Oct-02 02:52:01 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

A POTENTIAL EXISTS THAT ATROVENT, WHICH IS IN A CLEAR CONTAINER SIMILAR TO THE CONTAINERS OF MANY BRANDS OF SODIUM CHLORIDE, COULD BE MISTAKEN FOR SODIUM CHLORIDE. NO ERROR OCCURRED. THE REPORTER RECOMMENDS THAT THE ATROVENT LABELING SHOULD HAVE SOME COLOR ADDED.

MEDERR DDP REPORT

Access Number: 041578
28-Oct-02 02:52:01 PM **erf**

Date Received at USP: 24-Aug-9 **Date of Report**

Product Name: ATROVENT	**Container Type:**
Generic Name(s): IPRATROPIUM BROMIDE	**Container Size:**
Manufacturer: BOEHRINGER ING	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength: 0.5 MG/ML	**Sample Available:** No
Product Name: SODIUM CHLORIDE	**Container Type:**
Generic Name(s): SODIUM CHLORIDE	**Container Size:**
Manufacturer: WYETH AYERST	**NDC Number:**
Labeler:	**Adm. Route:** INHALATION
Dosage Form: SOLUTION	**Lot Number(s):**
Strength: 0.9%	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 041578

28-Oct-02 02:52:01 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

THE UNIT-DOSE CONTAINERS OF ATROVENT AND SODIUM CHLORIDE LOOK VERY SIMILAR CREATING A POTENTIAL FOR ERROR. [redacted] THIS CAN BE A DANGEROUS MIX-UP IF A PATIENT WITH SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE MISSES DOSES OF HIS OR HER ORDERED ATROVENT BECAUSE A NURSE HURRIEDLY GRABS SODIUM CHLORIDE. OR, IF A PATIENT REQUIRING ONLY A SALINE NEBULIZER TREATMENT IN ORDER TO HELP HIM OR HER EXPECTORATE A SPUTUM SAMPLE IS GIVEN ATROVENT BY MISTAKE, THAT PATIENT MAY SUFFER SIDE EFFECTS SUCH AS NERVOUSNESS, DIZZINESS, HEADACHE, NAUSEA, OR HEART PALPITATIONS. IF FACILITIES STOCK SIMILAR LOOKING UNIT-DOSE SOLUTIONS OF NEBULIZER MEDICATIONS, CONSIDER CONTAINERS IN DIFFERENT COLORS. THE MEDICATION WAS NOT ADMINISTERED TO OR USED BY THE PATIENT. THE REPORTER RECOMMENDS TO CHANGE THE PACKAGING, ORDER DIFFERENT BRANDS, STORE THE TWO MEDICATIONS IN DIFFERENT AREAS, AND READ THE LABEL CAREFULLY BEFORE ADMINISTRATION.

MEDERR DDP REPORT

Access Number: 042242
28-Oct-02 02:52:01 PM **erf**

Date Received at USP: 06-Jan-97 **Date of Report** 02-Jan-97

Product Name: Gastrocrom	**Container Type:** Plastic ampul
Generic Name(s): Cromolyn Sodium	**Container Size:**
Manufacturer: Medeva Pharmaceuticals	**NDC Number:** 53014-0678-70
Labeler:	**Adm. Route:** Oral
Dosage Form: Concentrate	**Lot Number(s):**
Strength: 100 mg/5 mL	**Sample Available:** No
Product Name: Cromolyn Sodium	**Container Type:** Plastic ampul
Generic Name(s): Cromolyn Sodium	**Container Size:**
Manufacturer: Dey	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 10 mg/mL	**Sample Available:** No
Product Name: Intal	**Container Type:** Plastic ampul
Generic Name(s): Cromolyn Sodium	**Container Size:**
Manufacturer: Fisons	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 10 mg/mL	**Sample Available:** No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

MEDERR DDP REPORT

Access Number: 042242

28-Oct-02 02:52:01 PM **erf**

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

Change the packaging of Gastrocrom, perhaps by utilizing a screw-on top, so that it looks more like oral packaging.

REMARKS

Problem:

A reporter received information on a new product named Gastrocrom 100 mg/5 mL, an oral concentrate, packaged in a plastic ampul. He noticed that the ampul is exactly the same size and shape as the plastic ampuls of Intal and Cromolyn Sodium for inhalation. The reporter feels that someone using the oral concentrate and also frequently using the inhalation solution, could accidentally or deliberately use the oral concentrate in an inhalation machine and receive a five-fold overdose.

Dey Laboratories letter to USP dated 2/28/97: The Dey Laboratories vial is a completely different shape and size from the other two product vials. Dey Laboratories' Cromolyn Sodium Inhalation Solution USP is labeled with a yellow and blue paper label on each vial. This vial contains the product name and strength information.
Medeva Pharmaceuticals letter to USP dated 4/15/97: Gastrocrom Oral Concentrate ampuls are significantly larger than the other ampuls in question. Gastrocrom ampuls measure approximately 4" x 1/2" and contain five (5) mLs of product while the other ampuls are approximately 2 1/4" x 1/2" and contain only two (2) mLs of product. Additionally, the Gastrocrom ampuls are clearly labeled as being an oral concentrate and for oral use only.

MEDERR DDP REPORT

Access Number: 050615
28-Oct-02 02:52:01 PM **erf**

Date Received at USP: 17-Nov-9 **Date of Report** 13-Nov-9

Product Name:	Pulmozyme	**Container Type:**	Ampul
Generic Name(s):	Dornase Alfa	**Container Size:**	2.5 mL
Manufacturer:	Genentech	**NDC Number:**	50242-100-37
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	1 mg/mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant.

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

The labeling on Pulmozyme is confusing and dangerous.

MEDERR DDP REPORT

Access Number: 051073
28-Oct-02 02:52:01 PM **erf**

Date Received at USP: 01-Apr-98 **Date of Report** 31-Mar-9

Product Name:	Ipratropium Bromide	**Container Type:**	2.5 mL
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Roxane	**NDC Number:**	0054-8402-11
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.02%	**Sample Available:**	No

Product Name:	Sodium Chloride Inhalation Solution	**Container Type:**	
Generic Name(s):	Sodium Chloride Inhalation Solution	**Container Size:**	
Manufacturer:	Unknown	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 051073

28-Oct-02 02:52:01 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

Labeling of the Ipratropium Bromide vials could lead to medication errors. The clear plastic vials are labeled with raised lettering; no paper label is attached. This makes reading the contents extremely difficult. The vials also resemble several brands of Saline inhalation vials, which could lead to potential errors.

Roxane Laboratories, Inc. letter sent to reporter dated March 27, 1998: Suggestion that we replace the embossing with a printed label will be forwarded to our Product Management Committee for review.

MEDERR DDP REPORT

Access Number: 052296
28-Oct-02 02:52:01 PM **erf**

Date Received at USP: 27-Apr-99 **Date of Report** 27-Apr-99

Product Name:	Naropin	**Container Type:**	Polyamp Duofit
Generic Name(s):	Ropivacaine Hydrochloride	**Container Size:**	Various
Manufacturer:	Astra	**NDC Number:**	
Labeler:		**Adm. Route:**	Injection
Dosage Form:	Injectable	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Product Name:	Xylocaine-MPF	**Container Type:**	Polyamp Duofit
Generic Name(s):	Lidocaine Hydrochloride	**Container Size:**	Various
Manufacturer:	Astra	**NDC Number:**	
Labeler:		**Adm. Route:**	Injection
Dosage Form:	Injectable	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Product Name:	Ipratropium Bromide	**Container Type:**	
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Dey	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.5 mg/2.5 mL	**Sample Available:**	No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

MEDERR DDP REPORT

Access Number: 052296

28-Oct-02 02:52:01 PM **erf**

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

Change the packaging, label well, and distribute notices of the potential for error.

REMARKS

Problem:

The Polyamp Duofit packaging of Naropin (Ropivacaine Hydrochloride) and Xylocaine MPF (Lidocaine Hydrochloride) is very similar to that of Ipratropium Bromide inhalation solution and could potentially be confused.

Dey letter sent to USP dated May 25, 1999. Although there are other distinct differences between Dey's packaging of the injectable products, the vial size is the most obvious and evident difference which would prevent Dey's Ispratropium Bromide from being mistaken for one of the injectable products mentioned. Of course, it is always vitally important for the health care provider and pharmacist to carefully inspect the labeling of a medication before administration in order to prevent errors; however, given the great size difference, Dey does not believe there is any potential for confusion or error involving Dey's Ipratropium Bromide and Naropin and Xylocaine MPF.

MEDERR DDP REPORT

Access Number: 052830
28-Oct-02 02:52:01 PM **erf**

Date Received at USP: 27-Jan-00 **Date of Report** 27-Jan-00

Product Name:	Ipratropium Bromide	**Container Type:**	
Generic Name(s):	Ipratropium Bromide	**Container Size:**	2.5 mL
Manufacturer:	Roxane	**NDC Number:**	00054-8402-11
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.02%	**Sample Available:**	No

Product Name:	Cromolyn Sodium	**Container Type:**	
Generic Name(s):	Cromolyn Sodium	**Container Size:**	2 mL
Manufacturer:	Arcola Labs	**NDC Number:**	00070-9996-06
Labeler:	Automatic Liquid Packaging	**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	20 mg/2 mL	**Sample Available:**	No

Product Name:	Xopenex	**Container Type:**	
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0512-24
Labeler:	Automatic Liquid Packaging	**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.63 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

MEDERR DDP REPORT

Access Number: 052830

28-Oct-02 02:52:02 PM **erf**

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

A respiratory therapist brought this concern to the attention of the pharmacy. The inhalation solutions, Ipratropium Bromide, Cromolyn Sodium, and Xopenex unit-dose vials look almost identical to each other and the labels on the vials are difficult to read.

Roxane Laboratories letter to the reporter dated 2/25/00: Comments about the embossing on the vial will be forwarded to the Product Management Committee for review.
Sepracor letter to the reporter dated 4/24/00: In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible. Please be aware that many product changes, including labeling changes such as this, require FDA approval before marketed to consumers and therefore require additional time to implement.
Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible.

MEDERR DDP REPORT

Access Number: 052894
28-Oct-02 02:52:02 PM **erf**

Date Received at USP: 22-Feb-00 **Date of Report** 22-Feb-00

Product Name:	Atrovent	**Container Type:**	Unit-dose ampuls
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Boehringer Ingelheim	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Product Name:	Xopenex	**Container Type:**	Unit-dose ampuls
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	
Manufacturer:	Sepracor Inc.	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 052946
28-Oct-02 02:52:02 PM **erf**

Date Received at USP: 20-Mar-0 **Date of Report** 20-Mar-0

Product Name:	Gastrocrom	**Container Type:**	
Generic Name(s):	Cromolyn Sodium	**Container Size:**	5 mL
Manufacturer:	Medeva Pharmaceuticals	**NDC Number:**	
Labeler:		**Adm. Route:**	Oral
Dosage Form:	Solution	**Lot Number(s):**	
Strength:		**Sample Available:**	No
Product Name:	Xopenex	**Container Type:**	
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? Pharmacist

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/I

When and how was the error discovered?

Where did the error occur? N/I

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 052946

28-Oct-02 02:52:02 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

Gastrocrom and Xopenex have similar packaging and can be easily mixed up. The error was noted when someone was putting away returned medications. The patient did not receive the incorrect drug.

Medeva Pharmaceuticals, Inc. letter to USP dated 5/10/00: A review of complaint files did not reveal any other complaints of this type for Gastrocrom Oral Concentrate. As such, this is considered to be an isolated incident.

MEDERR DDP REPORT

Access Number: 053003
28-Oct-02 02:52:02 PM **erf**

Date Received at USP: 06-Apr-00 **Date of Report** 06-Apr-00

Product Name: Ipratropium Bromide	**Container Type:**
Generic Name(s): Ipratropium Bromide	**Container Size:** 2.5 mL
Manufacturer: Roxane	**NDC Number:** 00054-8402-11
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.02%	**Sample Available:** No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:
Need an actual label instead of an imprint.

REMARKS

Problem:
The labeling on Ipratropium Bromide is an imprint, which is difficult to read. This could lead to an error.

Roxane Laboratories letter to the reporter dated 5/5/00: The suggestion that the company enhance the embossing or replace the product with a printed label will be forwarded to the Product Management Committee for review.

MEDERR DDP REPORT

Access Number: 053280
28-Oct-02 02:52:02 PM **erf**

Date Received at USP: 28-Aug-0 **Date of Report** 28-Aug-0

Product Name: Cromolyn Sodium	**Container Type:** unit-dose vial
Generic Name(s): Cromolyn Sodium	**Container Size:** 2 mL
Manufacturer: Dey	**NDC Number:** 49502-0689-02
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 20 mg/2 mL	**Sample Available:** No

Product Name: Ipratropium Bromide	**Container Type:** unit-dose vial
Generic Name(s): Ipratropium Bromide	**Container Size:** 2.5 mL
Manufacturer: Roxane	**NDC Number:** 00054-8402-11
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.02%	**Sample Available:** No

Was the medication administered to or used by patient? No

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? Pharmacist

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? Pharmacist

When and how was the error discovered? The pharmacist realized the error later on in the day.

Where did the error occur? Outpatient pharmacy

Was another practitioner involved in the error? No

If yes, what type of practitioner?

Was patient counseling provided? Yes

If yes, before or after error was discovered? Both

Number of occurrences:

Patient information that might be relevant:
The patient is a 5-year-old male.

MEDERR DDP REPORT

Access Number: 053436
28-Oct-02 02:52:02 PM **erf**

Date Received at USP: 24-Oct-00 **Date of Report** 24-Oct-00

Product Name: Albuterol Sulfate	**Container Type:** unit-dose
Generic Name(s): Albuterol Sulfate	**Container Size:** 3 mL
Manufacturer: Steripak Limited	**NDC Number:** 00172-6405-44
Labeler: Zenith Goldline	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.083%	**Sample Available:** No

Product Name: HypoTears PF	**Container Type:** unit-dose
Generic Name(s): Polyvinyl Alcohol PEG 400 Dextrose	**Container Size:** 0.45 mL
Manufacturer: Ciba	**NDC Number:** 58768-0132-30
Labeler:	**Adm. Route:** Ophthalmic
Dosage Form: Drops	**Lot Number(s):**
Strength: 1%	**Sample Available:** No

Was the medication administered to or used by patient? No

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? Nurse, registered

Describe Outcome: The medication was not administered.

If the medication did not reach the patient, describe the intervention. The floor registered nurse brought the appearance of the two unit-dose drugs to the attention of the superiors. Nursing then brought this to the reporter's attention.

Who discovered the error? Nurse, registered

When and how was the error discovered? The registered nurse recognized the Albuterol and questioned why it should be in the medication drawer since that would be in violation of the policy. The nurse also observed that this patient was using Hypo Tears PF.

Where did the error occur? Nursing home

Was another practitioner involved in the error? Yes

If yes, what type of practitioner? Respiratory therapist or LPN

Was patient counseling provided? No

MEDERR DDP REPORT

Access Number: 053436

28-Oct-02 02:52:02 PM **erf**

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

The patient is a female in her 70's with dry eyes.

Reporter's recommendations or policies to prevent future similar errors:

Have the manufacturer improve the labeling of both products so that the label can be clearly read and the containers distinguished. The Albuterol for inhalation now being used is manufactured by Dey and contains a nice blue adhesive label that is easy to read.

REMARKS

Problem:

A registered nurse was passing medications on the general floor of a nursing home. The nurse opened the medication drawer and found a plastic unit-dose vial of Albuterol for inhalation. The patient is not on Albuterol for Inhalation, but is using Hypo Tears PF. The registered nurse noticed that the containers of both products are very difficult to read and similar in appearance (size, shape, color, imprinting style). Both products have clear plastic with identifying information molded into the container itself. The products could be easily misidentified by a busy nurse on a short-staffed unit and the inhalation product instilled into the eye. The registered nurse caught the error by recognizing the Albuterol container and realizing that this product should not be in the patient's medication drawer by the policy.

Zenith Goldline Pharmaceuticals letter to USP dated 11/16/00: This will acknowledge receipt of the correspondence, the file number 053436.

MEDERR DDP REPORT

Access Number: 053529
28-Oct-02 02:52:02 PM **erf**

Date Received at USP: 05-Dec-00 **Date of Report** 05-Dec-00

Product Name:	Pulmicort	**Container Type:**	Plastic respules
Generic Name(s):	Budesonide	**Container Size:**	
Manufacturer:	Astra	**NDC Number:**	00186-1988-04
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Suspension	**Lot Number(s):**	
Strength:	0.25 mg/2 mL	**Sample Available:**	No
Product Name:	Pulmicort	**Container Type:**	Plastic respule
Generic Name(s):	Budesonide	**Container Size:**	
Manufacturer:	Astra	**NDC Number:**	00186-1989-04
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Suspension	**Lot Number(s):**	
Strength:	0.5 mg/2 mL	**Sample Available:**	No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? Technician, pharmacy

Describe Outcome:

If the medication did not reach the patient, describe the intervention. Respiratory therapist caught the mistake and the error was avoided.

Who discovered the error? Respiratory therapist

When and how was the error discovered? The error was discovered when the respiratory therapist went to the drawer to administer respiratory treatment requiring budesonide respules.

Where did the error occur? Hospital

Was another practitioner involved in the error? No

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053529

28-Oct-02 02:52:02 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

If the company can't mark the plastic respule with a color or identifying mark, then the different strengths should be separated when shipped, placed in well-marked bins, and have some sort of identifying sticker placed on them when dispensed. Care should be taken when crediting and returning the respule to the storage bin. The storage bins are now marked more clearly and e-mail has been sent out warning pharmacy technicians and pharmacists about the potential for error.

REMARKS

Problem:

Pulmicort respules 0.25 mg/2 mL and 0.5 mg/2 mL are very similar in packaging size and were mixed up in the pharmacy storage bins. The incorrect strength was placed in the patient's medication drawers. The respiratory therapist caught the mistake and the error was avoided.

MEDERR DDP REPORT

Access Number: 053698

28-Oct-02 02:52:02 PM **erf**

Date Received at USP: 06-Feb-01 **Date of Report** 06-Feb-01

Product Name: Albuterol Sulfate	**Container Type:** Plastic ampul
Generic Name(s): Albuterol Sulfate	**Container Size:**
Manufacturer: Zenith	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength:	**Sample Available:** No

Product Name: Ipratropium Bromide	**Container Type:** Plastic ampul
Generic Name(s): Ipratropium Bromide	**Container Size:**
Manufacturer: Roxane	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength:	**Sample Available:** No

Was the medication administered to or used by patient? No

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error? No

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053698

28-Oct-02 02:52:03 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

Modify packaging; give each distinguishing characteristics.

REMARKS

Problem:

This problem was brought to the attention of the reporter by the Respiratory Department. The following inhalation products are packaged similarly and could contribute to a medication error: Albuterol Sulfate inhalation solution by Zenith and Ipratropium Bromide inhalation solution by Roxane. The two products are in ready to use vials and the boxes are different, but since most respiratory technicians break open the foil packs and carry the vials, there needs to be some distinguishing features to the individual packaging (colored plastic in the vial or a label on the outside of the vial similar to Dey's Albuterol inhalation soultion).

MEDERR DDP REPORT

Access Number: 053735
28-Oct-02 02:52:03 PM **erf**

Date Received at USP: 14-Feb-01 **Date of Report** 14-Feb-01

Product Name:	Ipratropium Bromide	**Container Type:**	Ampul
Generic Name(s):	Ipratropium Bromide	**Container Size:**	2.5 mL
Manufacturer:	Roxane	**NDC Number:**	00054-8402-11
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.02%	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

Roxane's Ipratropium Bromide Inhalation solution 0.02% unit-dose vials 2.5 mL has poor labeling. This medication almost caused a medication error in the emergency room. Once the outer foil packaging is removed it is very difficult to read the clear, raised letters on each unit. The hospital will try to order another brand that has each unit more clearly marked.

MEDERR DDP REPORT

Access Number: 053736

28-Oct-02 02:52:03 PM **erf**

Date Received at USP: 14-Feb-01 **Date of Report** 14-Feb-01

Product Name:	Ipratropium Bromide	**Container Type:**	Vial
Generic Name(s):	Ipratropium Bromide	**Container Size:**	2.5 mL
Manufacturer:	Roxane	**NDC Number:**	00054-8402-11
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.02%	**Sample Available:**	No

Product Name:	Xopenex	**Container Type:**	Vial
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0512-24
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.63 mg/mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053736

28-Oct-02 02:52:03 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

The reporter wrote to suggest the labeling of respiratory inhalation treatment vials be considered as an issue by ISMP (Institute of Safe Medication Practices). Specifically, labeling of respiratory medication pre-mix vials by imprinting the labeling information during the molding process for the vial. Many people find this very difficult to read. Many inhalation solutions come in pre-mixed vials, which are labeled only by the imprinting of product information on the exterior of the vial. [redacted] The addition of a paper label or a color identifier would greatly aid in the discrimination of one vial from another.

MEDERR DDP REPORT

Access Number: 053793

28-Oct-02 02:52:03 PM **erf**

Date Received at USP: 05-Mar-0 **Date of Report** 05-Mar-0

Product Name:	Xopenex	**Container Type:**	vial
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0512-24
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.63 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:
Encourage manufacturers to change its labeling habits.

REMARKS

Problem:

Fortunately, this has not been either a potential or actual occurrence. However, the reporter has received a number of phone messages from respiratory therapists and pulmonologists on staff regarding the labeling of the Xopenex (Levalbuterol) jets. Any efforts to encourage the manufacturer to change its labeling habits would be most appreciated.

Information per call to reporter: The product is packaged in a clear plastic container. There is no label on the container; the product information is imprinted on the plastic, which is difficult to read.

Sepracor letter to the reporter dated 7/12/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible and would further differentiate the Xopenex Inhalation Solution products.

MEDERR DDP REPORT

Access Number: 053811

28-Oct-02 02:52:03 PM **erf**

Date Received at USP: 13-Mar-0 **Date of Report** 13-Mar-0

Product Name: Xopenex	**Container Type:** Unit-dose vial
Generic Name(s): Levalbuterol Hydrochloride	**Container Size:** 3 mL
Manufacturer: Sepracor Inc.	**NDC Number:** 63402-0512-24
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.63 mg	**Sample Available:** No

Product Name: Xopenex	**Container Type:** Unit-dose vial
Generic Name(s): Levalbuterol Hydrochloride	**Container Size:** 3 mL
Manufacturer: Sepracor Inc.	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 1.25 mg	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053811

28-Oct-02 02:52:03 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

The reporter feels that the manufacturer should create vials of different strengths that are more readily seen as different.

REMARKS

Problem:

A potential error caused by the packaging of the drug Xopenex (Levalbuterol manufactured by Sepracor) in the 1.25 mg and 0.63 mg unit-dose vials. While the outer wrappers (box and inner foil wrapper) of the two strengths differ in appearance, the vials themselves are distinguishable only upon very careful examination of the labels. The reporter feels that the manufacturer should create vials of different strengths that are more readily seen as different. Any help that would end this confusion would be appreciated.

Sepracor letter to the reporter dated 7/12/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible and would further differentiate the Xopenex Inhalation Solution products.

MEDERR DDP REPORT

Access Number: 053887
28-Oct-02 02:52:03 PM **erf**

Date Received at USP: 29-Mar-0 **Date of Report** 29-Mar-0

Product Name:	Xopenex	**Container Type:**	unit-dose vial
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0512-24
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.63 mg/3 mL	**Sample Available:**	No
Product Name:	Xopenex	**Container Type:**	unit-dose vial
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0513-24
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	1.25 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? Respiratory therapist

Describe Outcome:

If the medication did not reach the patient, describe the intervention. The physician inspected the unit-dose package, determined that it was not the right dose and prevented the error.

Who discovered the error? Physician

When and how was the error discovered?

Where did the error occur? Hospital

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053887

28-Oct-02 02:52:03 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

The medications require different packaging or labeling. Printing the name and strength of the medication in color would be most useful. A consideration to prevent potential errors in the future is to remove the medication from the hospital formulary because safe and effective alternatives exist.

REMARKS

Problem:

Prior to administration of a dose of Xopenex, a physician noticed that the respiratory therapist had mistakenly opened the wrong strength of medication. By inspecting the unit-dose package, the physician prevented the error. The error almost occurred because the two product strengths are virtually identical in appearance, the only significant difference being "0.63" embossed on one vial and "1.25" embossed on the other. Both packages are already difficult to read, being clear plastic with raised lettering. The potential exists to give 50% or 200% of the prescribed dose.

Sepracor letter to the reporter dated 7/18/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible and would further differentiate the Xopenex Inhalation Solution.

MEDERR DDP REPORT

Access Number: 053888
28-Oct-02 02:52:03 PM **erf**

Date Received at USP: 29-Mar-0 **Date of Report** 29-Mar-0

Product Name: Xopenex	**Container Type:** Vial
Generic Name(s): Levalbuterol Hydrochloride	**Container Size:** 3 mL
Manufacturer: Sepracor Inc.	**NDC Number:** 63402-0512-24
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.63 mg/3 mL	**Sample Available:** No

Product Name: Ipratropium Bromide	**Container Type:**
Generic Name(s): Ipratropium Bromide	**Container Size:**
Manufacturer: Roxane	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.02%	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053888

28-Oct-02 02:52:03 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

Xopenex (Levalbuterol) SVN (small volume nebulizer) package is very hard to read. The label is on clear plastic with raised lettering for drug name and strength. This product comes in two strengths. The packaging is identical to Roxane's product Ipratropium SVN (clear plastic with raised lettering). This is a set up for a medication error.

Sepracor letter to the reporter dated 7/18/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible.

MEDERR DDP REPORT

Access Number: 053893

28-Oct-02 02:52:03 PM **erf**

Date Received at USP: 30-Mar-0 **Date of Report** 30-Mar-0

Product Name: Pulmicort Respules	**Container Type:**
Generic Name(s): Budesonide	**Container Size:** 2 mL
Manufacturer: Astra	**NDC Number:** 00186-1988-04
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Suspension	**Lot Number(s):**
Strength: 0.25 mg/2 mL	**Sample Available:** No

Product Name: Pulmicort Respules	**Container Type:**
Generic Name(s): Budesonide	**Container Size:** 2 mL
Manufacturer: Astra	**NDC Number:** 00186-1989-04
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Suspension	**Lot Number(s):**
Strength: 0.5 mg/2 mL	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053893

28-Oct-02 02:52:04 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

The medications require different packaging and/or labeling. Printing the name and strength of the medication in color would be most useful. A consideration to prevent potential errors in the future is to remove the medication from the hospital formulary.

REMARKS

Problem:

Pulmicort Respules are manufactured in two strengths. The two product strengths are virtually identical in appearance, the only significant difference being "0.25" embossed on one vial and "0.5" embossed on the other. Both packages are already difficult to read, being clear plastic with small raised lettering. The potential exists to give 50% or 200% of the prescribed dose.

MEDERR DDP REPORT

Access Number: 053970

28-Oct-02 02:52:04 PM **erf**

Date Received at USP: 17-Apr-01 **Date of Report** 17-Apr-01

Product Name: Xopenex	**Container Type:** Ampul
Generic Name(s): Levalbuterol Hydrochloride	**Container Size:**
Manufacturer: Sepracor Inc.	**NDC Number:** 63402-0513-96
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 1.25 mg/3 mL	**Sample Available:** No

Product Name: Ipratropium Bromide	**Container Type:** Ampul
Generic Name(s): Ipratropium Bromide	**Container Size:**
Manufacturer: Roxane	**NDC Number:** 00054-8404-11
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.5 mg/2.5 mL	**Sample Available:** No

Was the medication administered to or used by patient? Yes

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? Respiratory therapist

Describe Outcome: No adverse outcome reported.

If the medication did not reach the patient, describe the intervention.

Who discovered the error? Respiratory therapist?

When and how was the error discovered? Unknown

Where did the error occur? Hospital

Was another practitioner involved in the error? No

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053970

28-Oct-02 02:52:04 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

The packaging of Xopenex and Ipratropium Bromide are very similar. The manufacturer should add color ink or a label to one or both of these products. The facility has made the following changes in order to prevent this error from occurring in the future: 1) Two "info-grams" sent to all pharmacy locations via the order entry computer system to notify the pharmacy staff of the similar appearance of these products (Xopenex and Ipratropium). 2) The hospital has ordered a new brand of Ipratropium (Dey). 3) Central pharmacy will dispense all Xopenex in a zip lock bag with a label indicating that it contains Albuterol.

REMARKS

Problem:

Xopenex was administered to the patient by the respiratory therapist instead of Ipratropium. No harm reported. The containers are very similar. Both are in clear plastic ampuls for nebulization. It is difficult to read the writing on the ampuls because it is the same color as the plastic ampul.

Sepracor letter to the reporter dated 7/19/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible.

MEDERR DDP REPORT

Access Number: 053971

28-Oct-02 02:52:04 PM **erf**

Date Received at USP: 17-Apr-01 **Date of Report** 17-Apr-01

Product Name:	Xopenex	**Container Type:**	Ampul
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0513-96
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	1.25 mg/3 mL	**Sample Available:**	No

Product Name:	Ipratropium Bromide	**Container Type:**	Ampul
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Roxane	**NDC Number:**	00054-8404-11
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.5 mg/2.5 mL	**Sample Available:**	No

Was the medication administered to or used by patient? No

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? Technician, pharmacy

Describe Outcome:

If the medication did not reach the patient, describe the intervention. The error was discovered by the pharmacist during check of medication carts.

Who discovered the error? Pharmacist

When and how was the error discovered?

Where did the error occur? Hospital pharmacy

Was another practitioner involved in the error? No

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 053971

28-Oct-02 02:52:04 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

Xopenex and Ipratropium Bromide both have similar packaging. The manufacturer should add colored ink or a label to one or both of these products. The facility has made the following changes in order prevent this error from occurring in the future: 1) Two "info-grams" sent to all pharmacy locations via the order entry computer system to notify the pharmacy staff of the similar appearance of these products (Xopenex and Ipratropium). 2) The hospital has ordered a new brand of Ipratropium (Dey). 3) Central pharmacy will dispense all Xopenex in a zip lock bag with a label indicating that it contains Albuterol.

REMARKS

Problem:

Xopenex was dispensed in the medication cart instead of Ipratropium. The medications were initially placed into the cart by the pharmacy technician. The pharmacist checking the carts noted that there were two ampuls of each medication in the cart. The containers are extremely similar. Both are clear plastic ampuls for nebulization. It is difficult to read the writing on the ampuls because it is the same color as the plastic ampul

Sepracor letter to the reporter dated 7/19/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible.

MEDERR DDP REPORT

Access Number: 053972

28-Oct-02 02:52:04 PM **erf**

Date Received at USP: 17-Apr-01 **Date of Report** 17-Apr-01

Product Name:	Xopenex	**Container Type:**	Ampul
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0513-96
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	1.25 mg/3 mL	**Sample Available:**	No

Product Name:	Ipratropium Bromide	**Container Type:**	Ampul
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Roxane	**NDC Number:**	00054-8404-11
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.5 mg/2.5 mL	**Sample Available:**	No

Product Name:	Pulmozyme	**Container Type:**	Ampul
Generic Name(s):	Dornase Alfa	**Container Size:**	
Manufacturer:	Genentech	**NDC Number:**	50242-0100-39
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	2.5 mg/2.5 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

MEDERR DDP REPORT

Access Number: 053972

28-Oct-02 02:52:04 PM **erf**

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

The manufacturer should add colored ink or a label to the products. The facility has made the following changes in order to prevent an error from occurring: 1) Two "info-grams" sent to all pharmacy locations via the order entry computer pharmacy staff of the similar appearance of these products (Xopenex, Ipratropium, and Pulmozyme). 2) The hospital has ordered a new brand of Ipratropium (Dey). 3) Central pharmacy will dispense all Xopenex in a zip lock bag with a label indicating that it contains Albuterol.

REMARKS

Problem:

The packaging for Dornase Alfa (Pulmozyme) 2.5 mg/2.5 mL container by Genetech (NDC (National Drug Code) 50242-0100-39) is very similar to Xopenex and Ipratropium. All are in clear plastic ampuls for nebulization. It is difficult to read the writing on the ampuls because it is the same color as the plastic ampul.

Genentech, Inc. letter to USP dated 5/29/01: The company has completed the investigation of the report. Pulmozyme is an enzyme indicated for the treatment of patients with cystic fibrosis which was approved by the FDA in December 1993. During the approval process, the FDA reviewed the packaging and ampule configuration for Pulmozyme and found it to be acceptable. The ampules are labeled with the product name, lot number, expiration date, and strength. In addition, the secondary packaging for Pulmozyme is clearly labeled with the appropriate information for proper identification. The report was conveyed to the Regulatory Affairs department, and it was concluded that no action is necessary. Both the packaging and the ampules for Pulmozyme are well labeled with the name and strength which should be verified before administration.

Sepracor letter to the reporter dated 7/19/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible.

MEDERR DDP REPORT

Access Number: 054161
28-Oct-02 02:52:04 PM **erf**

Date Received at USP: 13-Jun-01 **Date of Report** 13-Jun-01

Product Name:	Xopenex	**Container Type:**	
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.63 mg/3 mL	**Sample Available:**	No

Product Name:	Atrovent	**Container Type:**	
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Roxane	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.02%	**Sample Available:**	No

Product Name:	Xopenex	**Container Type:**	
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	1.25 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

MEDERR DDP REPORT

Access Number: 054161

28-Oct-02 02:52:04 PM **erf**

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

Levalbuterol (Xopenex) medication nebulizers look almost exactly like the Ipratropium medication nebulizers from Roxane. There is a serious potential for error.

Sepracor letter to the reporter dated 7/18/01. The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and the red for the 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible.

MEDERR DDP REPORT

Access Number: 054263
28-Oct-02 02:52:04 PM **erf**

Date Received at USP: 06-Aug-0 **Date of Report** 03-Aug-0

Product Name:	Albuterol Sulfate	**Container Type:**	
Generic Name(s):	Albuterol Sulfate	**Container Size:**	
Manufacturer:	Alpharma USPD, Inc.	**NDC Number:**	00472-0831-60
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	2.5 mg/3 mL	**Sample Available:**	No
Product Name:	Ipratropium Bromide	**Container Type:**	Vial
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Alpharma USPD, Inc.	**NDC Number:**	00472-0751-23
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.5 mg/2.5 mL	**Sample Available:**	No
Product Name:	Xopenex	**Container Type:**	
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-2513-24
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	1.25 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

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Access Number: 054263

28-Oct-02 02:52:04 PM **erf**

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

Add some sort of coloring to the vials or use an actual label on the vials instead of the raised lettering.

REMARKS

Problem:

Alpharma's Albuterol Sulfate and Ipratropium, and Sepracor's Xopenex are packaged in identical plastic vials with raised letters. Only the product name is different. The Alpharma products have an "A" or an "I" on the appropriate tab on the vials, but it is only on one side of the tab.

Sepracor letter to the reporter dated 9/20/01: The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil puch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and red for the 1.25 mg/3 mL). The LPDE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluationg the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible. Please be aware that many product changes, including labeling changes such as this, require FDA (Food and Drug Administration) approval before being marketed to consumers and therefore require additional time to implement.

MEDERR DDP REPORT

Access Number: 054293
28-Oct-02 02:52:04 PM **erf**

Date Received at USP: 13-Aug-0 **Date of Report** 13-Aug-0

Product Name:	Albuterol Sulfate	**Container Type:**	Plastic ampul
Generic Name(s):	Albuterol Sulfate	**Container Size:**	3 mL
Manufacturer:	Zenith Goldline	**NDC Number:**	00172-6405-44
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.083%	**Sample Available:**	No
Product Name:	Ipratropium Bromide	**Container Type:**	Plastic ampul
Generic Name(s):	Ipratropium Bromide	**Container Size:**	2.5 mL
Manufacturer:	Alpharma USPD, Inc.	**NDC Number:**	00472-0751-23
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.02%	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

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Access Number: 054293

28-Oct-02 02:52:05 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

The packaging and labeling for Ipratropium Bromide and Albuterol Sulfate inhalation solutions are practically identical and hard to read. The drug names and dosing information are extremely hard to read due to the almost transparent font. There is a high potential of confusion among these two products.

MEDERR DDP REPORT

Access Number: 054341

28-Oct-02 02:52:05 PM **erf**

Date Received at USP: 29-Aug-0 **Date of Report** 23-Aug-0

Product Name:	Ipratropium Bromide	**Container Type:**	Plastic ampul
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Alpharma USPD, Inc.	**NDC Number:**	00472-0751-60
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.5 mg/2.5 mL	**Sample Available:**	No

Product Name:	Albuterol Sulfate	**Container Type:**	Plastic ampul
Generic Name(s):	Albuterol Sulfate	**Container Size:**	
Manufacturer:	Alpharma USPD, Inc.	**NDC Number:**	00472-0831-30
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	2.5 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 054341

28-Oct-02 02:52:05 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

Attach a label to the container or add some color. The pharmacy is considering purchasing a different product at an additional cost because of the packaging concern.

REMARKS

Problem:

The packaging of Ipratropium Bromide 0.02% and Albuterol 0.083% is similar. Also, both are in clear containers with raised lettering making it difficult to read the name of the drug.

MEDERR DDP REPORT

Access Number: 054342

28-Oct-02 02:52:05 PM **erf**

Date Received at USP: 29-Aug-0 **Date of Report** 23-Aug-0

Product Name:	DuoNeb	**Container Type:**	Plastic ampul
Generic Name(s):	Ipratropium Bromide Albuterol Sulfate	**Container Size:**	
Manufacturer:	Dey	**NDC Number:**	49502-0672-60
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.5 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:
Attach a label to the container and add some color.

REMARKS

Problem:

The raised lettering on the clear plastic container of DuoNeb makes it difficult to read the name of the product and the ingredients. If you do not look closely, you might not notice that DuoNeb contains Ipratropium Bromide and Albuterol Sulfate.

MEDERR DDP REPORT

Access Number: 054336
28-Oct-02 02:52:05 PM **erf**

Date Received at USP: 24-Aug-0 **Date of Report** 24-Aug-0

Product Name: Ipratropium Bromide	**Container Type:** Plastic ampul
Generic Name(s): Ipratropium Bromide	**Container Size:** 2.5 mL
Manufacturer: Alpharma USPD, Inc.	**NDC Number:** 00472-0751-23
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.02%	**Sample Available:** No

Product Name: Xopenex	**Container Type:** Plastic ampul
Generic Name(s): Levalbuterol Hydrochloride	**Container Size:** 3 mL
Manufacturer: Sepracor Inc.	**NDC Number:** 63402-0513-24
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 1.25 mg	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

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Access Number: 054336

28-Oct-02 02:52:05 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

Not allowing clear vials with clear writing.

REMARKS

Problem:

This potential error was reported by the respiratory staff. The hospital recently switched companies that supply respiratory products due to a contract change. The Ipratropium Bromide inhalation solution 0.02% 2.5 mL unit-dose vials distributed by Alpharma (00472-0751-23) look identical to Xopenex inhalation solution unit-dose vials (63402-0513-34). Both vials are opaque with non-colored, raised lettering. They are very hard to read even when there was not a similar product. The respiratory staff is afraid that one will be accidentally substituted for the other one.

Sepracor letter to the reporter dated 9/20/01: The current packaging for Xopenex (Levalbuterol HCL) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for the 0.63 mg/3 mL and red for the 1.25 mg/3 mL). The LPDE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the product, Sepracor is currently evaluationg the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible. Please be aware that many product changes, including labeling changes such as this, require FDA (Food and Drug Administration) approval before being marketed to consumers and therefore require additional time to implement.

MEDERR DDP REPORT

Access Number: 054380

28-Oct-02 02:52:05 PM **erf**

Date Received at USP: 07-Sep-01 **Date of Report** 07-Sep-01

Product Name: Albuterol Sulfate	**Container Type:** Plastic ampul
Generic Name(s): Albuterol Sulfate	**Container Size:** 3 mL
Manufacturer: Alpharma USPD, Inc.	**NDC Number:** 00472-0831-23
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.083%	**Sample Available:** No
Product Name: Cromolyn Sodium	**Container Type:** Plastic ampul
Generic Name(s): Cromolyn Sodium	**Container Size:** 2 mL
Manufacturer: Alpharma USPD, Inc.	**NDC Number:** 00472-0750-60
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 10 mg/mL	**Sample Available:** No
Product Name: Pulmozyme	**Container Type:** Plastic ampul
Generic Name(s): Dornase Alfa	**Container Size:** N/I
Manufacturer: Genentech	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: N/I	**Sample Available:** No
Product Name: Pulmicort Respules	**Container Type:** Plastic ampul
Generic Name(s): Budesonide	**Container Size:** N/I
Manufacturer: Astra Zeneca	**NDC Number:**
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Suspension	**Lot Number(s):**
Strength: N/I	**Sample Available:** No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

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Access Number: 054380

28-Oct-02 02:52:05 PM **erf**

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided?

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

There is a potential for errors regarding the respiratory care unit-dose medications Albuterol and Cromolyn (manufactured by Alpharma), Pulmicort respules (manufactured by Astra), and Pulmozyme (manufactured by Genentech). These products are packaged in clear plastic single-use ampuls whose labeling on each ampul is terrible. The letters are raised on the plastic container, but not a different color. The letters are the same material as the plastic container. The reporter has had many respiratory care therapists complain of this; they are concerned that a wrong dose or wrong medication will be administered to the patient.

MEDERR DDP REPORT

Access Number: 054425

28-Oct-02 02:52:05 PM **erf**

Date Received at USP: 28-Sep-01 **Date of Report** 28-Sep-01

Product Name:	DuoNeb	**Container Type:**	Plastic ampul
Generic Name(s):	Albuterol Sulfate Ipratropium Bromide	**Container Size:**	3 mL
Manufacturer:	Novartis	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	3 mg/0.5 mg	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

The pharmacies at the facility have reported that the pack size for the inhalation product DuoNeb is difficult to read and there exists the risk of error in using this drug. DuoNeb consists of a 3 mL inhalant solution (Ipratropium and Albuterol) packaged in a clear plastic vial, with several vials in a foil pouch. The pouch is clearly labeled DuoNeb with the ingredients, lot number, expiration date, and other information. The problem is when the clear vials are removed from the packaging. The vials are clear plastic containing a clear solution. The lettering on the vials is not printed, but

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Access Number: 054425

28-Oct-02 02:52:05 PM **erf**

raised in clear plastic. This makes it difficult to clearly see the name of the drug, ingredients, lot number, and expiration date. While the foil pouch is clearly marked, the facility has noted the practice of opening the pouch, taking the vials out and then discarding the pouch. The result is loose vials that are not clearly marked. In addition, the labeling on the foil package shows the Albuterol Sulfate content to be 3.0 mg. The small print makes the strength appear to be 30 mg. The practice of adding trailing zeros to the strength of drugs is commonly implicated in medication errors. The facility feels that this type of packaging and labeling may lead to medication errors if the wrong vial is picked up.

MEDERR DDP REPORT

Access Number: 054577

28-Oct-02 02:52:05 PM **erf**

Date Received at USP: 26-Oct-01 **Date of Report** 26-Oct-01

Product Name: Pulmicort Respules	**Container Type:** Plastic ampul
Generic Name(s): Budesonide	**Container Size:** 2 mL
Manufacturer: Astra Zeneca	**NDC Number:** 00186-1988-04
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Suspension	**Lot Number(s):**
Strength: 0.25 mg/2 mL	**Sample Available:** No

Product Name: Pulmicort Respules	**Container Type:** Plastic ampul
Generic Name(s): Budesonide	**Container Size:** 2 mL
Manufacturer: Astra Zeneca	**NDC Number:** 00186-1989-04
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Suspension	**Lot Number(s):**
Strength: 0.5 mg/2 mL	**Sample Available:** No

Was the medication administered to or used by patient? No

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? Pharmacist

Describe Outcome:

If the medication did not reach the patient, describe the intervention. The error was caught at patient counseling.

Who discovered the error? Pharmacist

When and how was the error discovered? The error was discovered while discussing the medication strength with the patient.

Where did the error occur? Pharmacy, community

Was another practitioner involved in the error? No

If yes, what type of practitioner?

Was patient counseling provided? Yes

If yes, before or after error was discovered? Both

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 054577

28-Oct-02 02:52:05 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

Take time to check prescriptions and institute the use of a bar scanner.

REMARKS

Problem:

The pharmacy had regular staffing and the pharmacist chose the wrong strength and quantity needed to fill the prescription. The prescription called for Pulmicort Respules 0.5 mg/2 mL with a quantity of 120 mL. The prescription was filled instead as Pulmicort 0.25 mg/2 mL with a quantity of 60 mL.

MEDERR DDP REPORT

Access Number: 054588
28-Oct-02 02:52:05 PM **erf**

Date Received at USP: 31-Oct-01 **Date of Report** 31-Oct-01

Product Name:	Xopenex	**Container Type:**	Plastic ampul
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0512-24
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.63 mg/3 mL	**Sample Available:**	No

Product Name:	Xopenex	**Container Type:**	Plastic ampul
Generic Name(s):	Levalbuterol Hydrochloride	**Container Size:**	3 mL
Manufacturer:	Sepracor Inc.	**NDC Number:**	63402-0513-24
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	1.25 mg/3 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 054588

28-Oct-02 02:52:06 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

The reporter may have not had an incident, but they see a potential for errors with the product Xopenex (Levalbuterol HCL (Hydrochloride)) by Sepracor. Sepracor produces two strengths of the medication, 0.63 mg/3 mL and 1.25 mg/3 mL, in unit-dose packages. The unit-dose packages look the same. The difference in dose is stamped on the vial, but it is the same color as the rest of the package. You have to look very hard in good light to note the difference.

Sepracor letter to the reporter dated 06-Dec-01: The current packaging for Xopenex (Levalbuterol Hydrochloride) Inhalation Solution consists of the low-density polyethylene (LDPE) unit-dose vial, an outer foil pouch, and a packaging carton. The cartons and foil pouches both differentiate the strengths using label text and colored markings (yellow for 0.63 mg/3 mL and red for 1.25 mg/3 mL). The LDPE unit-dose vials list the product strength in three separate locations on each unit-dose vial and again on the bottom flashing used to connect the 12 unit-dose vials. In order to increase the visible differentiation of the two strengths, Sepracor is currently evaluating the feasibility of ink printing the dose strength onto the top flashing portion of each vial. This could make the information more readily visible. Please be aware that many product changes, including labeling changes such as this, require FDA (Food and Drug Administration) approval before being marketed to consumers and therefore require additional time to implement.

MEDERR DDP REPORT

Access Number: 054601
28-Oct-02 02:52:06 PM **erf**

Date Received at USP: 06-Nov-0 **Date of Report** 06-Nov-0

Product Name: Cromolyn Sodium	**Container Type:** Plastic ampul
Generic Name(s): Cromolyn Sodium	**Container Size:** 2 mL
Manufacturer: Alpharma USPD, Inc.	**NDC Number:** 00472-0752-60
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 20 mg/2 mL	**Sample Available:** No

Product Name: Ipratropium Bromide	**Container Type:** Plastic ampul
Generic Name(s): Ipratropium Bromide	**Container Size:** 2.5 mL
Manufacturer: Alpharma USPD, Inc.	**NDC Number:** 00472-0751-60
Labeler:	**Adm. Route:** Inhalation
Dosage Form: Solution	**Lot Number(s):**
Strength: 0.02%	**Sample Available:** No

Was the medication administered to or used by patient? Yes

Date of Event: [redacted]

What type of staff or health care practitioner made the initial error? Intern, pharmacy

Describe Outcome: The patient benefited and became better with the medication.

If the medication did not reach the patient, describe the intervention.

Who discovered the error? Physician

When and how was the error discovered? The error was discovered when the physician called the patient's parents the day after the office visit for a follow-up.

Where did the error occur? Pharmacy, community

Was another practitioner involved in the error? Yes

If yes, what type of practitioner? Pharmacist

Was patient counseling provided? Yes

If yes, before or after error was discovered? After

Number of occurrences:

Patient information that might be relevant:
The patient is a 2-year-old Caucasian female.

MEDERR DDP REPORT

Access Number: 054601

28-Oct-02 02:52:06 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

Decrease distractions to allow the verifying pharmacist to check the medication being dispensed more carefully.

REMARKS

Problem:

A physician called in a prescription to the pharmacy and the intern tried to take it over the phone, but did not understand the physician. The pharmacist took over and received the prescription. The intern was confused. The prescription was typed into the computer as Ipratropium (Atrovent) instead of Cromolyn (Intal). The prescription was filled, but not properly checked before dispensing it to the patient's parent. Both Ipratropium Bromide and Cromolyn Sodium solution boxes look similar. Thus, it is hypothesized that the medication was picked before the prescription was typed in and then typed in based on the wrong medication selected.

MEDERR DDP REPORT

Access Number: 054698

28-Oct-02 02:52:06 PM **erf**

Date Received at USP: 26-Dec-01 **Date of Report** 26-Dec-01

Product Name:	DuoNeb	**Container Type:**	Plastic ampul
Generic Name(s):	Albuterol Sulfate Ipratropium Bromide	**Container Size:**	3 mL
Manufacturer:	Dey	**NDC Number:**	49502-0672-30
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

Several of the respiratory medications available have similar, if not d[illegible] packaging. With the addition of DuoNeb to this group, the facility has yet another item to add into the category. The reporter understands that the FDA (Food and Drug Administration) has a lot to do with this by disallowing inks directly on the packaging and other stability requirements. The facility currently does not add any ancillary labeling to this product because more steps in the process add more opportunities for error. Fortunately for the facility, the therapists, who can be alerted with relative

ease, give most of these respiratory products that are dispensed from pharmacy.

Dey letter to USP dated 21-Jan-02: It is very important that health care professionals carefully read the labeling of the drug product prior to dispensing to a customer. The labeling for DuoNeb was developed in consultation with the Food and Drug Administration (FDA). The labeling was approved by the FDA and may not be altered without prior approval from the FDA. The company does not anticipate a change in the labeling for DuoNeb in the foreseeable future.

MEDERR DDP REPORT

Access Number: 054744
28-Oct-02 02:52:06 PM **erf**

Date Received at USP: 28-Jan-02 **Date of Report** 28-Jan-02

Product Name:	Albuterol Sulfate	**Container Type:**	Plastic ampul
Generic Name(s):	Albuterol Sulfate	**Container Size:**	
Manufacturer:	Nephron Pharmaceutical Corporation	**NDC Number:**	00487-9501-25
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.083%	**Sample Available:**	No

Product Name:	Ipratropium Bromide	**Container Type:**	
Generic Name(s):	Ipratropium Bromide	**Container Size:**	
Manufacturer:	Nephron Pharmaceutical Corporation	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:	0.02%	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 054744

28-Oct-02 02:52:06 PM **erf**

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

The facility is concerned about the new packaging for the unit-dose inhalation solutions. The specific brand the facility is now stocking is Nephron Pharmaceuticals Corporation. The Albuterol Sulfate 0.083% solution and the Ipratropium Bromide 0.02% solution both come in clear, unit-dose vials. The vials are the same shape, with the Ipratropium Bromide a little taller. The Ipratropium Bromide has an embossed "I" on the top, and the Albuterol Sulfate an embossed "A." This was discovered by respiratory therapists looking at the vials.

MEDERR DDP REPORT

Access Number: 054754

28-Oct-02 02:52:06 PM **erf**

Date Received at USP: 13-Feb-02 **Date of Report** 13-Feb-02

Product Name:	Heparin Sodium	**Container Type:**	Plastic ampul
Generic Name(s):	Heparin Sodium	**Container Size:**	
Manufacturer:	Automatic Liquid Packaging	**NDC Number:**	
Labeler:	American Pharmaceutical Partners	**Adm. Route:**	Injection
Dosage Form:	Injectable	**Lot Number(s):**	
Strength:	10 units/mL	**Sample Available:**	No

Product Name:	Plastic Ampul for Respiratory Medications	**Container Type:**	Plastic ampul
Generic Name(s):	Plastic Ampul for Respiratory Medications	**Container Size:**	
Manufacturer:	Various	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Solution	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Product Name:	SmartAmp	**Container Type:**	Plastic ampul
Generic Name(s):	SmartAmp	**Container Size:**	
Manufacturer:	Avitro	**NDC Number:**	
Labeler:		**Adm. Route:**	Injection
Dosage Form:	Injectable	**Lot Number(s):**	
Strength:		**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

MEDERR DDP REPORT

Access Number: 054754

28-Oct-02 02:52:06 PM **erf**

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

Reporter's recommendations or policies to prevent future similar errors:

REMARKS

Problem:

The SmartAmp looks exactly like a respiratory therapy "pillow," however is being used as an injectable. There are three areas that the reporter has concerns: (1) look-alike of injectable to respiratory medication, (2) labeling insufficiencies, and (3) injectable not having a rubber stopper (open to air container used for direct IV (intravenous) injection).

Information per call to reporter on 06-Feb-02: The product involved is Heparin Sodium preservative free 10 units/mL. Although Heparin Sodium is a drug shortage product, a drug representative from Avitro informed the reporter that Heparin Sodium is available in the SmartAmp. The reporter is not identifying any specific respiratory product, but notes that the SmartAmp resembles the respiratory unit-dose packaging.

MEDERR DDP REPORT

Access Number: 054911

28-Oct-02 02:52:06 PM **erf**

Date Received at USP: 19-Apr-02 **Date of Report** 19-Apr-02

Product Name:	Pulmicort Respules	**Container Type:**	Plastic ampul
Generic Name(s):	Budesonide	**Container Size:**	
Manufacturer:	Astra Zeneca	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Suspension	**Lot Number(s):**	
Strength:	0.25 mg/2 mL	**Sample Available:**	No

Product Name:	Pulmicort Respules	**Container Type:**	Plastic ampul
Generic Name(s):	Budesonide	**Container Size:**	
Manufacturer:	Astra Zeneca	**NDC Number:**	
Labeler:		**Adm. Route:**	Inhalation
Dosage Form:	Suspension	**Lot Number(s):**	
Strength:	0.5 mg/2 mL	**Sample Available:**	No

Was the medication administered to or used by patient?

Date of Event:

What type of staff or health care practitioner made the initial error? N/A

Describe Outcome:

If the medication did not reach the patient, describe the intervention.

Who discovered the error? N/A

When and how was the error discovered?

Where did the error occur? N/A

Was another practitioner involved in the error?

If yes, what type of practitioner?

Was patient counseling provided? No

If yes, before or after error was discovered?

Number of occurrences:

Patient information that might be relevant:

MEDERR DDP REPORT

Access Number: 054911

28-Oct-02 02:52:06 PM **erf**

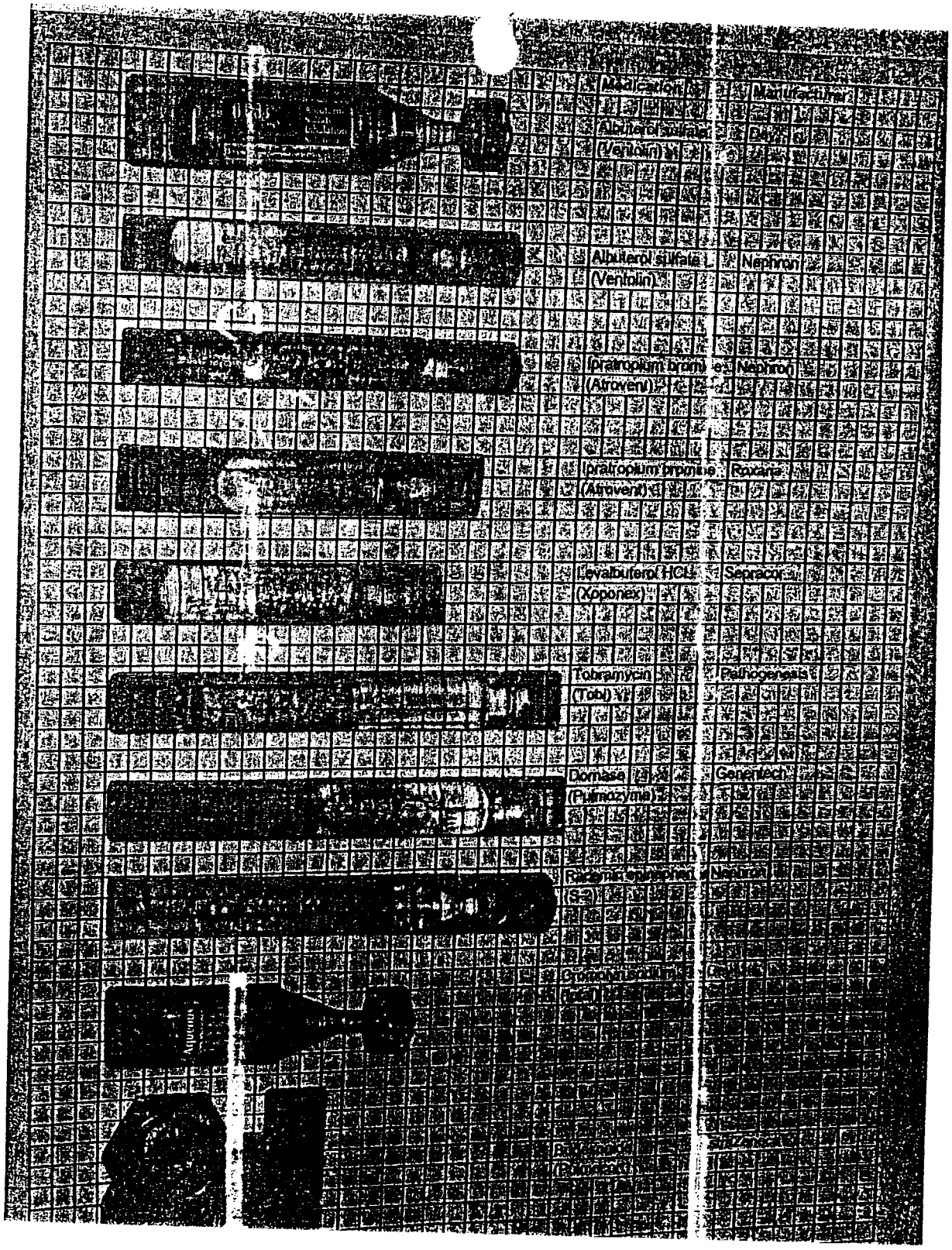
Reporter's recommendations or policies to prevent future similar errors:

REMARKS

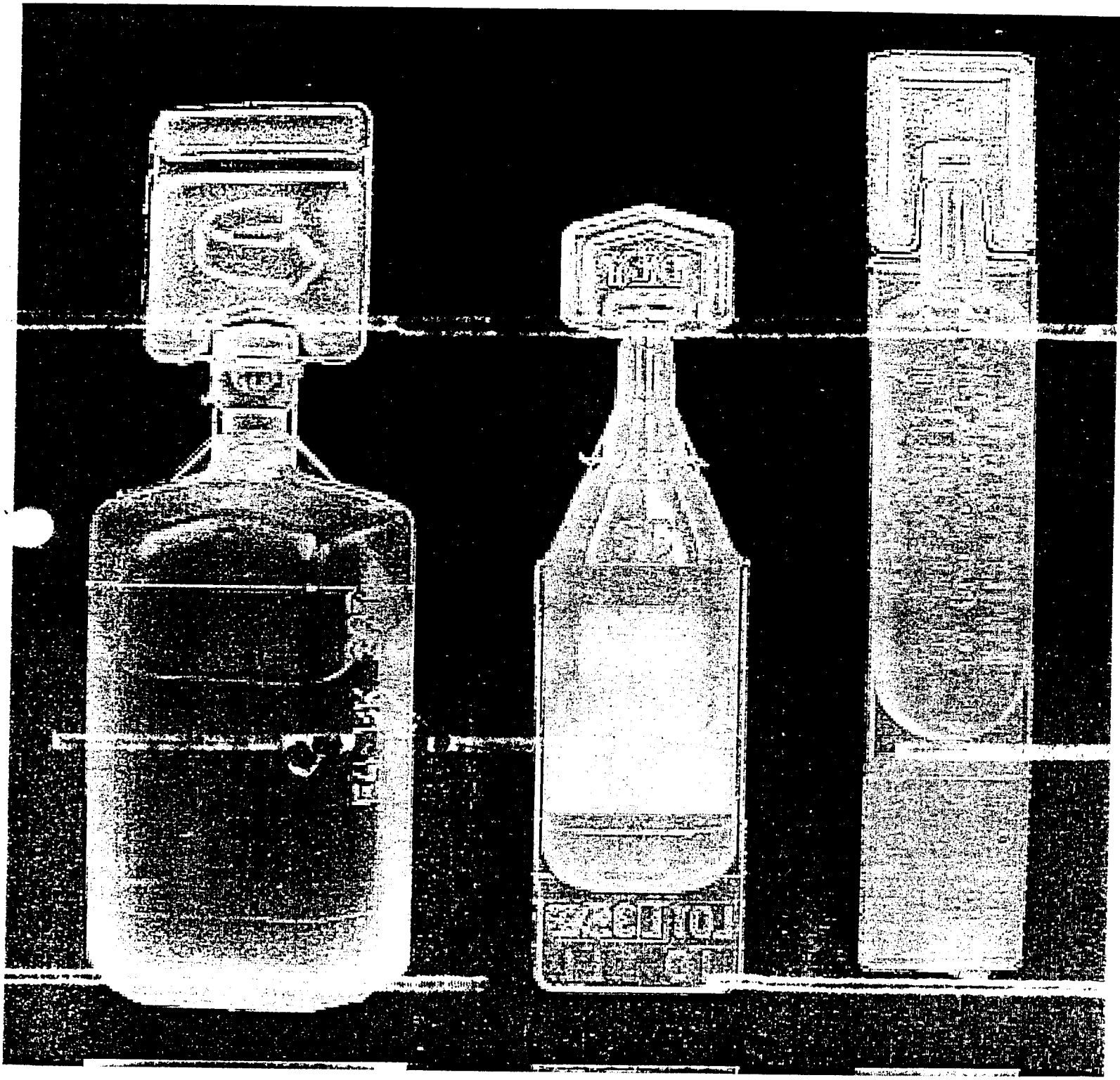
Problem:

The respiratory staff asked the facility to initiate a medication alert for some inhalation products. The unit-dose packaging for the two strengths of Pulmicort Respules (0.25 mg/2 mL and 0.5 mg/2 mL) is very similar. Both are made of clear plastic and have raised lettering. Neither have any coloration for easy identification. The facility's respiratory therapists often carry individual unit-dose containers in their pockets without the outside packaging

Information per email from reporter: Albuterol unit-dose, manufactured by Dey, has colored packaging that makes it easy to identify.


Medication
Manufacturer
Albuterol sulfate
(Ventolin)
Albuterol sulfate L
(Ventolin)
Nephron
Ipratropium bromi
(Atrovent)
Nephron
Ipratropium bromide
(Atrovent) c
Roxane
Levalbuterol HCL
(Xoponex)
Sepracor
Tobramycin
(Tobi)
Pathogenesis
Dornase
(Pulmozyme)
Genentech
Racemic epinephrine
(S-E)
Nephron

Cromolyn
Sodium
Inhalation
Solution USP
Aqueous



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1125 07 001 28 25 63 200 Crossing Boulevard Bridgewater, NJ 08807

FAX

Date: October 28, 2002

Number of pages including cover sheet: 6

To: Dockets Management Branch, FDA

Phone: (301) 827-6860

Fax phone: (301) 827-6870

CC:

From: Jackie Knoble Mail Stop BX4-306A

Phone: (908) 231-2228

Fax phone: (908) 231-4040

REMARKS: ☐ Urgent ☐ For your review ☐ Reply ASAP ☐ Please comment

Dear Sir/Madam:

Attached please find comments regarding "*Draft Guidance for Industry on Inhalation Drug Products packaged in Semipermeable Container Closure Systems [67FR 48920, July 26, 2002]*".

Should you have any questions, please call me at your convenience.

Regards,

Jackie Knoble

Aventis Pharmaceuticals

Aventis

October 24, 2002

Via fax and UPS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 02D-0254
Draft Guidance for Industry on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems [67FR 48920, July 26, 2002]

Dear Sir/Madam:

Aventis Pharmaceuticals Inc. appreciates the opportunity to comment on the above-referenced draft guidance entitled "Inhalation Drug Products Packaged in Semipermeable Container Closure Systems".

This draft guidance provides recommendations on the appropriate protective secondary packaging, the embossing and/or debossing of the primary container in lieu of paper labels, and the number of unit-dose containers within each protective secondary package. The development of the draft guidance on inhalation drug products packaged in semipermeable container closure systems is welcomed. The underlying principles are generally sound and acceptable. We offer the following comments/clarification for your consideration.

02D-0254 C4

I. Introduction

Page 1, lines 23 to31

This document provides recommendations for industry on inhalation drug products that are packaged in semipermeable permeable primary container closure systems, such as low-density polyethylene (LDPE) containers. It is intended to provide guidance on (1) the appropriate protective secondary packaging, (2) the embossing and/or debossing of the primary container in lieu of paper labels, and (3) the number of unit-dose containers within each protective secondary package.

These recommendations apply to inhalation drug products (e.g., solutions, suspensions, sprays), both those in development and those already approved and marketed in the United States.

We would like to have further clarification of the scope of this guidance and definition of semipermeable.

The guidance refers to semipermeable container closure systems such as LDPE containers. We feel that this is an inadequate definition of the material covered by this guidance as many other polymers, such as medium density polymers are also semipermeable. It would be also helpful if semipermeable is further defined.

Further, reference is made that the guidance applies to inhalation drug products e.g. solutions, suspensions, sprays. We understand that this does not refer to products given nasally as these are dealt with in other guidance (July 2002 Guidance for Industry on Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products – Chemistry, Manufacturing, and Controls Documentation). Similarly, lines 46 and 47 refer to asthma and chronic obstructive pulmonary disease (COPD), which is the current practice, but newer inhaled therapies, especially for systemic diseases, would also be covered by this guidance.

We propose rewording this paragraph as follows:

"*This document provides recommendations for industry on ~~inhalation~~ **orally inhaled unit and multi-dose drug products that are packaged in semipermeable polymer** primary container closure systems. ~~such as low density polyethylene (LDPE) containers.~~ **Semipermeable refers to those polymers through which chemical contaminants either from the container closure system or the environment can permeate.** It is intended to provide guidance on (1) the appropriate protective secondary packaging, (2) the embossing and/or debossing of the primary container in lieu of paper labels, and (3) the number of unit dose containers within each protective secondary package.*

*These recommendations apply to ~~inhalation drug~~ **orally inhaled** drug products (e.g., solutions, suspensions, ~~sprays~~), both those in development and those already approved and marketed in the United States.*"

Page 1, paragraph 2, lines 30 to 31
These recommendations apply to inhalation drug products (e.g., solutions, suspensions, sprays), both those in development and those already approved and marketed in the United States.

This guidance refers to those drug products already approved and marketed in the United States without reference to the process, including timeframe, by which manufactures should ensure and demonstrate those drug products currently marketed and not complying with the guidance become compliant.
We believe that guidance is required to inform manufacturers of currently marketed drug products on the process that they should follow to ensure that the marketed drug products become compliant with the requirements of this guidance.

II. Background

Pages 2-3, paragraph 5, lines 77 to 87
The clinical consequences of chemical contamination of inhalation drug products are uncertain. Although there are no data on the potential for the identified chemical contaminants to act as spasmogens in the airways of patients with the target diseases for these medications (i.e., asthma and/or COPD), many of these chemical contaminants are potential respiratory irritants. No previously reported adverse reactions can be conclusively attributed to chemical contaminants. However, given the known sensitivity of these patients to respiratory irritants and sensitizers, it is possible that these chemical contaminants may induce bronchospasm. The potential adverse effect of these chemical contaminants (i.e., bronchospasm) is also the indication for which the drug product is used. Therefore, in the clinical setting it is very difficult to establish whether bronchospasm after the use of a drug product is due to chemical contaminants or to the disease itself.

We agree with the purpose of the guidance but feel that arguments supporting the clinical consequences for chemical contamination controls are overstated. The draft guidance recognizes that there is no previously reported adverse reactions conclusively attributed to chemical contaminants, nor that it would be "very difficult" to establish whether bronchospasm after the use of a drug product was due to chemical contaminants. A more **rationale basis should be made on the potential of chemical contaminants to cause adverse events, and that these proposals would remove or even further reduce the risk.**

III. Chemistry, Manufacturing, and Controls Considerations

Page 3, paragraph 1, lines 99 to 105

Special consideration should be given to the components and composition of the materials used in the protective secondary packaging and the manufacturing processes involved (e.g., adhesive lamination, heat-seal lamination, various temperature conditions). Adequate control of each of these components and manufacturing processes is critical to prevent the entry of volatile environmental contaminants and volatile chemical constituents from packaging components into the drug product. Controls are also important to prevent loss of water from the formulation.

We believe that this refers to the selection process of the components and materials. We propose rewording this paragraph as follows:

*"Special consideration should be given to the **selection of** components and composition of the materials used in the protective secondary packaging and the manufacturing processes involved (e.g., adhesive lamination, heat-seal lamination, various temperature conditions). Adequate control of each of these components and manufacturing processes is critical to prevent the entry of volatile environmental contaminants and volatile chemical constituents from packaging components into the drug product. **Additionally, formation of volatile substances during the heat sealing process should be investigated and controlled.** Controls are also important to prevent loss of water from the formulation."*

Page 4, paragraph 1, lines 129 to 132

FDA recommends that any leaching of contaminants into the formulation from the primary container, any entry of chemical contaminants from protective secondary packaging components or other packaging components (e.g., the carton) be adequately documented, quantified, and qualified.

It would be helpful here to refer to any other guidance or procedures that provide information on qualification and quantification of the contaminants, and what likely action levels should be in place for various contaminants classes.
The activity should be linked with the Product Quality Research Institute (PQRI) Working Group that is considering leachables and extractables from orally inhaled and nasal drug products.. We strong suggest that the PQRI activity includes inhalation drug products packaged in semipermeable container closure systems, and that more specific recommendations on qualification and quantification with action limits are provided in this guidance.

On behalf of Aventis Pharmaceuticals Inc. we appreciate the opportunity to comment on the draft Guidance for Industry on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems and are much obliged for your consideration.

Sincerely,

Steve Caffé, M.D.
Vice President, Head US Regulatory Affairs

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Schering-Plough

Integrated Therapeutics Group, Inc

October 24, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 02D-0254; Draft Guidance for Industry on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems

Dear Sir/Madam:

Schering-Plough has reviewed the Draft Guidance for Industry on Inhalation Drug Products Packaged in Semipermeable Container Closure Systems, and we are providing the following comments for your consideration.

1. In the Introduction (lines 30-31) it is stated that the recommendations in the draft guidance apply to inhalation drug products both in development, and those that are already approved and marketed in the United States. The guidance is not clear, however, on what should be done for products that are already approved. Will companies be required to add secondary packaging, change from paper labels to embossing, or implement new controls?

2. In the Chemistry, Manufacturing, and Controls Considerations section (lines 142-144) the Agency recommends alternative approaches to paper labels, such as embossing or debossing or "other means to display the requisite labeling information." It would be helpful if the Agency provided examples of "other means."

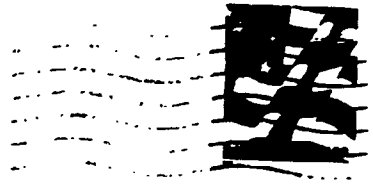
Schering Plough appreciates the opportunity to comment on this draft guidance and hopes you will consider our comments when finalizing the guidance document.

Sincerely,

Gretchen Trout

Gretchen Trout
Director, Regulatory Relations and Policy
Worldwide Regulatory Affairs

02D-0254 C5



Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

20857X0001

12

ARADIGM

December 3, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Ref: Docket No. 02D-0254

Comments on Draft Guidance for Industry on:
Inhalation Drug Products Packaged in Semipermeable Container Closure Systems

Dear Sir or Madam:

Aradigm Corporation (Aradigm) appreciates the opportunity to provide the following comments on the **Draft Guidance for Industry, Inhalation Drug Products Packaged in Semipermeable Container Closure Systems.**

Aradigm recognizes that this guidance highlights a clinical concern primarily with inhalation product for the treatment of asthma and COPD. However, the CMC considerations in the draft guidance related to the specific issue of packaging in semipermeable container/closure system do not provide additional clarity to the information in the current guidances referenced in Section IV and are therefore redundant. Aradigm recommends that requirements specific to inhalation drug products packaged in semi-permeable material be clearly defined and that a clear distinction be made between chemical contaminants from packaging versus contaminants from the local environment. We also recommend that for completeness, the available guidances be modified rather than the issuance of an additional guidance.

Background

Lines 47-48 and 79-80: This guidance appears to be specific to patients with pulmonary disease (i.e., asthma and/or COPD) and to unit-dose vials. Clarity is requested on the applicability of this guidance to products not developed to treat pulmonary disease packaged in semi-permeable containers other than vials.

02D-0254

C 6

3929 POINT EDEN WAY | HAYWARD, CA 94545
510-265-9000 TEL | FAX 510-265-0277

Lines 55-60: We agree that careful choice of primary packaging can and should address the risk of contaminants from the primary packaging. The purpose of extractable and leachable testing is to address this specific issue. Clarity is requested to the reference to [illegible] contaminants. Which specific chemical [illegible] environmental contaminants are of concern or have been identified?

Section III CMC Considerations

Line 77-93: This paragraph implies that the products developed to treat pulmonary disease, which may be contaminated by chemicals from the environment, may be a reason for the increase in the asthma mortality rate. However, patients are continually exposed to these same contaminants in the environment and most likely at increased levels. In addition, no data exist that attribute adverse reactions to chemical contaminants from the product type identified in this guidance, yet the Agency is imposing this [illegible] requirement on the manufacturers of these types of products which will increase the cost of drug development and therefore impact cost to the patient.

Line 96-99: Clarity is requested on the applicability of this guidance specifically to unit-dose vials where shelf-life storage is in LDPE primary packaging and secondary carton.

This guidance needs to evaluate other considerations such as shelf-life storage conditions and in-use periods, which minimize the exposure of product to the local environment. The requirement for secondary packaging should be product specific and take into consideration therapeutic indication.

Aradigm appreciates the opportunity to provide comments to this guidance. Please feel free to contact me to discuss or seek clarification to our comments.

Sincerely,

Darlene Rosario
Director, Regulatory Affairs

ARADIGM
3929 POINT EDEN WAY
HAYWARD, CA 94545

Food and Drug Administration
Dockets Management Branch (HFA-305)
6530 Fishers Lane, Room 1061
Rockville, MD 20852

Docket No. 02D-0254

13

U.S Pharmacopeia
The Standard of Quality℠

January 2, 2003

1142

Dockets Management Branch
HFA-305
Food and Drug Administration
5600 Fishers Lane, Room 1061
Rockville, Maryland 20857

Re: Docket # 02D-0254

Dear Sir/Madam:

We are sending this letter to document the continuing concerns of the USP Safe Medication Use Expert Committee (SMU EC) and healthcare practitioners regarding the inability to identify products in plastic ampuls that is secondary to inadequate labeling.

Plastic ampul packaging has been frequently used for respiratory therapy drugs. The ampuls often do not bear labels but are labeled by debossing/embossing the actual plastic container. This imprinting is perceived by healthcare practitioners reporting to the USP Medication Errors Reporting Program as being difficult to read and sometimes illegible. In response to these perceptions, the FDA reported that the glue used to attach labels on plastic ampuls was leaching into the drug. Additionally, inks used to print directly on the plastic were also found to leach. To solve the leaching problem, manufacturers typically emboss imprinting into the plastic ampuls and/or flange. Because these are now being used not only for respiratory therapy drugs, but also for injectable and oral solutions, it is imperative that labels be readily readable. The enclosed case studies and pictures are taken from the USP Medication Errors Reporting Program and will attest to the nature of the problem.

The Safe Medication Use Expert Committee unanimously voted to encourage the FDA to establish an alternate method of labeling these plastic ampuls, so that these products are clearly identifiable. The SMU EC also suggests that the FDA cease approving products in these containers because their use continues to be the subject of numerous medication errors.

Thank you for your attention in this matter. If you have questions please call Shawn C. Becker, B.S.N., R.N., USP Liaison to the USP SMU EC at 301-816-8216 or e-mail to scb@usp.org.

Sincerely,

Eric Sheinin

Eric Sheinin, Vice President
USP Information and Standards Development

cc: Yana Mille

12601 Twinbrook Parkway
Rockville, MD 20852

301-881-0666
www.usp.org

02D-0254

C7

Dockets Management Branch
HFA-305
Food and Drug Administration
5600 Fishers Lane, Room 1061
Rockville, Maryland 20857

Pharmacopeia
...e Standard of Quality℠

October 28, 2002

Yana Ruth Mille, Chief
FDA Compendial Operations Staff, HFD-354
Office of Pharmaceutical Science
Center for Drug Evaluation & Research
Parklawn Bldg. (WOC II, Room 3070)
5600 Fishers Lane
Rockville, Maryland 20857

Re: Plastic Ampul Labeling

Dear Ms. Mille:

On behalf of the USP Safe Medication Use Expert Committee (SMU EC), I am sending this letter to inform you of the continuing concerns of the Committee and also healthcare practitioners regarding the inability to identify drug products in plastic ampuls that is secondary to inadequate labeling.

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Sincerely,

Eric B Sheinin

Eric Sheinin, Vice President
USP Information and Standards
Development

F

Pharmacopeia
The Standard of Quality℠

January 2, 2003

Dockets Management Branch
HFA-305
Food and Drug Administration
5600 Fishers Lane, Room 1061
Rockville, Maryland 20857

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Sincerely,

Eric B Sheinin

Eric Sheinin, Vice President
USP Information and Standards Development

cc: Yana Mille

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