

# Unlawful Pharmacy Manufactured Nebulizer Medications: Physician Liability and Patient Safety Issues

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**Physicians practicing medicine today are exposed to many legal risks. Medical malpractice cases have been predicated in part on claims of failure to warn patients of risks associated with a procedure or course of treatment, failure to obtain informed consent and failure to exercise reasonable care. Related to these bases for liability is a new area of concern involving nebulizer medications. The purpose of this paper is to help physicians understand this new concern and protect themselves and their patients from the risks it poses.**

## Introduction

*In recent years, a clandestine pharmacy manufacturing industry has emerged, one that replaces a patient's prescription(s) for FDA-approved nebulizer medications with unlawful pharmacy-manufactured substitutes. Operating under the guise of pharmacy compounding, these businesses manufacture, distribute and dispense millions of doses of non-FDA-approved nebulizer medications through local and national mail-order home healthcare companies and pharmacies. Illegal pharmacy manufacturing of nebulizer medications has resulted in serious consequences for both patients and physicians.*

*Whether or not a physician knows about the substitution, the physician is liable if the substituted drug causes harm to the patient. Healthcare providers have been exposed to increased liability predicated on their duty to know the characteristics of a prescribed therapy, their failure to inform patients of the special risks posed by a pharmacy-manufactured drug and the lack of a medical rationale for substituting an unlawful pharmacy-manufactured drug for a readily available FDA-approved commercial drug.*

*Health risks to patients are real. Unlawful pharmacy-manufactured nebulizer medications are not proven safe and effective. Outcomes data from using these medications are unknown.<sup>1</sup> Combinations of nebulizer products never tested for safety and efficacy can result in accelerated degradation and/or inactivation of the potential to reduce therapeutic efficacy.<sup>2</sup>*

*Unlawful pharmacy-manufactured nebulizer medications do not meet the sterility requirements determined by FDA for all*

*aqueous-based drugs for inhalation, thereby exposing already compromised patients to the risks of a potentially contaminated drug.<sup>3</sup>*

*The medications may contain known airway irritants such as ethanol (most commonly used to dilute budesonide) and other preservatives.<sup>4</sup> The resulting symptoms of coughing, wheezing and shortness of breath cannot be differentiated from those of the diseases these medications are intended to treat.*

*The purpose of this paper is to describe specific areas of physician liability related to unlawful pharmacy-manufactured medications created and sold under the guise of legitimate pharmacy compounding.*

## Mass Manufacturing of Unlawful Unit-Dose Nebulizer Medications

Over the last decade, an increasing number of pharmacy operations have begun manufacturing millions of doses of illegal unit-dose nebulizer medications outside the requirements of the Federal Food, Drug, and Cosmetic Act.

These businesses employ various tactics to obtain physician and patient authorization to replace FDA-approved commercial products with illegal products.

One point of entry begins with some durable medical equipment (DME) companies that deliver oxygen or nebulizer equipment to patients' homes. Elderly and disabled patients, their family caregivers and parents of young children with asthma are particularly drawn to DME offers of lower prices, free home delivery of

1 See e.g., FDA, Center for Drug Evaluation and Research, Guidance For Industry: Nasal Spray And Inhalation Solution, Suspension, and Spray Drug Products - Chemistry, Manufacturing, and Controls Documentation (July 2002).  
2 John H. Perrin, *Comments on drugs difficult to compound and the quality of chemicals used in compounding*, 25 DRUG DEV. AND INDUS. PHARM. 553, (1999); Myrna A. Dolovich, P. Eng, et al., *Consensus Statement: Aerosols and Delivery Devices*, 45 RESPIR. CARE 589, 589-90 (2000).  
3 Sterility requirements are set forth in 21 C.F.R. § 200.51.  
4 See Eugene Sullivan, PhD, FDA, Testimony before FDA Drug Safety and Risk Management Advisory Committee 20-21 (May 5, 2004) ("Chemical components in inhalation drug products may be associated with a variety of adverse effects, including irritant and immunologic effects, leading to acute bronchospasm and airway inflammation and hyper-responsiveness, other toxicologic injury, or even potentially carcinogenicity"). See also the following abstracts: T. Kawajiri et al., *Pathology and mechanism of lung toxicity following inhalation of hair spray in rats*, 16 INHAL. TOXICOL. 147 (2004); Ronald D. Reynolds, MD, and Richard M. Smith, MD, *Nebulized bacteriostatic saline as a cause of bronchitis*, 40 J. FAM. PRACT. 35 (1995); J. Pauluhn, *Comparative analysis of pulmonary irritation by measurements of Pehh and protein in bronchoalveolar lavage fluid in brown Norway rats and Wistar rats exposed to irritant aerosols*, 16 INHAL. TOXICOL. 159 (2004); Neil E. Alexis, PhD, et al., *Effect of inhaled endotoxin on airway and circulating inflammatory cell phagocytosis and CD11b expression in atopic asthma subjects*, 112 J. ALLERGY AND CLIN. IMMUNOL. 353 (2003).

nebulizer medications and automatic filing of reimbursement forms with the patient's insurance company. The patient signs several forms authorizing the DME's pharmacy or affiliate to fill and deliver the prescription. Another form is faxed to the physician's office acknowledging the patient's need for the DME/Pharmacy service. The physician signs the form, unaware that the patient will receive an unlawful pharmacy-manufactured medication that is not FDA-approved and has not been shown to be safe and effective. There is no disclosure of potential patient health risks or physician liability risks.

Another strategy employed by some DME and pharmacy businesses is to employ sales staff to call on physician offices to promote respiratory services such as overnight pulse oximetry testing to determine a patient's eligibility for home oxygen services. Sales representatives may leave nebulizer medication vial samples, sales literature and preprinted and preselected prescription tablets for unlawful pharmacy-manufactured nebulizer medications. At no time is the physician or patient informed of potential health risks or medical liability associated with unlawful pharmacy-manufactured nebulizer medications.

Television, radio, print and Internet advertising are other methods whereby these DME/pharmacy businesses acquire names of patients who use nebulizer medications.

Busy family and primary care physician practices with geriatric patients are favored targets of these schemes. However, allergists and pulmonologists report that their patients or referred patients are often victims of these schemes as well. Many physicians were not aware any of their patients were using unlawful pharmacy-manufactured nebulizer medications until they began checking patient records and asking patients to bring samples of their nebulizer medications to appointments.

## FDA Concerns

The Food and Drug Administration has stated, "We are aware of the problems associated with the compounding of inhalation products and are concerned about firms that, under the guise of compounding, are involved in the large-scale production of these drugs, often when an FDA-approved commercially manufactured product is already available to meet the patient's medical needs. Our specific concerns include questions about the sterility and potency of compounded inhalation products."<sup>5</sup>

FDA has taken enforcement action with numerous pharmacy businesses whose activities expanded beyond those associated with retail or compounding pharmacies. In fact, FDA recently issued warning letters to firms to stop manufacturing and distributing thousands of doses of compounded, unapproved inhalation drugs nationwide. FDA determined that the firms were producing mass amounts of inhalation drugs and that their actions went beyond traditional compounding.<sup>6</sup> In a press release regarding the warning letters, FDA noted that it is aware of certain pharmacies compounding *millions* of doses of inhalation drugs per

year, prompting Dr. Steven Galson, Director of FDA's Center for Drug Evaluation and Research, to assert, "Compounded inhalation drugs are not reviewed by the FDA for safety and effectiveness, often are not produced according to good drug manufacturing practice and typically are not sterile. This may expose patients to unnecessary risk. To avoid these risks, we encourage patients to use FDA-approved drugs whenever possible."<sup>7</sup>

Although some pharmacy manufacturers have claimed that FDA has no authority to regulate them because they are compounding, that is to say they are mixing the medication for the patient according to a valid prescription, recent court decisions have upheld FDA's position that these operations are illegal drug manufacturers and are fully subject to the agency's requirements when they manufacture large quantities or do not use an FDA-approved bulk drug.<sup>8</sup>

FDA permits legitimate pharmacy compounding only where (1) it is done on the specific order of a physician for an individual patient, (2) the active ingredient comes from an FDA-approved source and (3) the finished drug product is not a copy of a commercially available FDA-approved drug.<sup>9</sup>

Accordingly, pharmacies engaged in manufacturing and distributing drugs for human use are held to the same FDA requirements as qualified manufacturers.<sup>10</sup> In particular, a recent court decision held that a pharmacy suspected by FDA to be engaged in the manufacture of drugs under the guise of compounding is not exempt from FDA inspection authority under the Federal Food, Drug, and Cosmetic Act.<sup>11</sup>

In short, a drug may legally be compounded only if the commercially available FDA-approved version is not adequate to meet the specific medical needs of an individual patient. This rarely occurs, particularly with nebulizer medications. The illegal pharmacy-manufactured nebulizer medications available in the marketplace today are not proven to be therapeutic equivalents of FDA-approved commercially available medications. They are not manufactured in compliance with FDA standards for safety, effectiveness and sterility. Thus, the safety, efficacy and sterility of these vials cannot be assured. Testing has shown they often contain bacteria and airway irritants.

Physicians and their patients are frequently unaware that their trusted pharmacy would substitute a prescription for an FDA-approved commercially available nebulizer medication with an illegal pharmacy-manufactured alternative for which the safety, effectiveness and sterility are unknown. When a pharmacy substitutes an unlawfully manufactured drug for an FDA-approved commercially available nebulizer medication and fails to disclose possible health risks, they deny patients and healthcare providers the opportunity to make informed medical decisions, undermine the physician/patient relationship and erode patient trust in pharmacists.

No one knows the scale and scope of the illegal pharmacy manufacturing industry or how often adverse events take place. Not only is the source of bulk chemicals used in these pharmacies to

5 Statement from FDA e-mailed to Nancy Sander, President, Allergy & Asthma Network Mothers of Asthmatics, on February 7, 2005.

6 See Letter from Carol A. Heppe, Cincinnati District Office, FDA, to Philip L. Carter, President and CEO, Rotech Healthcare, Inc. (August 9, 2006); Letter from Emma R. Singleton, Director, Florida District, FDA, to Joseph Capper, CEO, CCS Medical (August 9, 2006).

7 "FDA Warns Three Pharmacies to Stop Mass-Producing Unapproved Inhalation Drugs," *FDA News* (August 10, 2006), available at [www.fda.gov/bbs/topics/NEWS/2006/NEW01428.html](http://www.fda.gov/bbs/topics/NEWS/2006/NEW01428.html).

8 See e.g., *Wedgewood Village Pharmacy, Inc. v. United States*, 421 F.3d 263 (3d Cir. 2005).

9 FDA, Center for Drug Evaluation and Research, *Guidance for FDA Staff and Industry, Compliance Policy Guides Manual*, § 460.200: Pharmacy Compounding (May 2002).

10 FDA, Center for Drug Evaluation and Research, *Guidance for FDA Staff and Industry, Compliance Policy Guides Manual*, § 460.200: Pharmacy Compounding (May 2002).

11 *Wedgewood Village Pharmacy*, 421 F.3d 263.

manufacture their products not disclosed, products most often do not comply with basic safety measures such as use of lot numbers, proper dosing instructions or the name of the manufacturer or packager. These pharmacies do not comply with FDA regulations governing drug manufacturers and thus believe they are not required to report adverse reactions or other problems with their drugs.<sup>12</sup>

Pharmacy manufacturing or compounding that does not conform to FDA requirements results in illegally manufactured products, i.e., unlawful drugs. Physician authorization does not legitimize otherwise illegal compounding practices. FDA will consider enforcement action whenever the scope and nature of a pharmacy's activities raise concerns normally associated with a drug manufacturer and will result in significant violations of the new drug, adulteration or misbranding provisions of the Federal Food, Drug, and Cosmetic Act.

Allergy & Asthma Network Mothers of Asthmatics, a 501(c)(3) nonprofit patient education and advocacy organization founded in 1985, convened a national group of medical professional and patient organizations concerned about these issues. The working group is known as the Consumer Health Alliance for Safe Medication (CHASM)<sup>13</sup>. CHASM member organizations are engaged in a national grassroots campaign to raise awareness of this important issue. In addition, CHASM submitted a Citizen Petition to FDA<sup>14</sup> asking them to inform prescribers and patients about this issue and to require businesses that legally compound nebulizer medications to clearly label products so that both patients and prescribers are aware of critical material facts (i.e., no claims are made as to the uses, safety, efficacy or bioavailability of this product; this is not an FDA-approved nebulizer medication; this product has not been proven to be sterile or a therapeutic equivalent of FDA-approved nebulizer medications).

### Take Action Now: Protect Patient Safety and Reduce Physician Liability

An informed physician is the greatest defense to threats posed by illegal pharmacy-manufactured nebulizer medications.

1. Establish practice policies regarding patient referrals to DME agencies, authorizing faxed prescription forms, access of DME or pharmacy sales representatives to the medication sample closet, or use of preprinted and preselected nebulizer prescription tablets. Inform medical and office staff about policies intended to protect patient safety and reduce physician liability.
2. Inform patients about health risks associated with use of unlawful nebulizer medications. Post patient education materials in waiting areas and exam rooms.
3. Stamp or clearly write "Do Not Compound This Nebulizer Medication" on all prescriptions for nebulizer medications.
4. Ensure that your patients are using the nebulizer medications you prescribed. Ask patients or family caregivers to bring samples of all nebulizer medications they are currently using to each appointment.

5. Do not accept preprinted and preselected prescription pads or tablets or fax forms from DMEs or pharmacies. The patient's prescription is the only authorization a legitimate pharmacy needs to provide a commercially available FDA-approved nebulizer medication.
6. Physicians and medical staff should read and understand all forms, including the fine print, before signing. The physician's signature may unintentionally be authorizing substitution of an illegal and clinically inappropriate drug.
7. Be suspect of DMEs and/or pharmacy businesses promoting unsubstantiated medical claims or outcomes for nebulizer medications such as reduced nebulization time, lower cost, improved patient quality of life, improved patient compliance or convenience. Ask for the evidence.
8. Be aware that product labeling such as, "This medication was made specifically for you at your physician's request" or similar wording indicates that the product is not FDA-approved.
9. When prescribing nebulizer medications, show patients and caregivers what the prescribed medication vial and packaging should look like.
10. Advise patients to confirm their FDA-approved medication is in stock before releasing their prescription to any pharmacy or home healthcare representative and to reject any offers to substitute their physician-prescribed nebulizer medication.
11. Advise staff to carefully scrutinize DME requests to make late entries to patient records because insurance reimbursement has been denied. This may happen when a patient's record does not reflect a medical need for a compounded nebulizer medication or when the prescription log does not indicate the medication submitted for reimbursement was ever prescribed. Often, the DME will provide the exact wording for office staff to use.
12. Be aware that Medicare, Medicaid or third party reimbursement for a product does not imply that the nebulizer medication is FDA-approved. It is up to the physician to make certain that the prescription is written in a manner that ensures the patient receives the medication the physician intends for the patient to use.
13. Report DME and pharmacy businesses engaged in illegal substitution of nebulizer medications. Contact AANMA to initiate the process.

### Conclusions

Pharmacy businesses engaged in mass manufacturing under the guise of extemporaneous compounding target busy medical practices likely to include patients with asthma, COPD, emphysema, cystic fibrosis and other conditions for which a nebulizer medication may be prescribed. They employ a variety of schemes to dupe physicians into prescribing and patients into using unlawful pharmacy-manufactured nebulizer products in place of commercially available FDA-approved medications.

12 As authorized under section 505(k) of the FDCA, FDA has adopted detailed regulations requiring applicants to maintain records and report "adverse drug experiences" to the agency. See 21 C.F.R. § 314.80.

13 CHASM Members: Allergy & Asthma Network Mothers of Asthmatics (AANMA); American Academy of Allergy, Asthma and Immunology (AAAAI); American College of Allergy, Asthma and Immunology (ACAAI); American Latex Allergy Association (A.L.E.R.T., Inc.); American Partnership for Eosinophilic Disorders (APFED); American Association for Respiratory Care (AARC); Association of Asthma Educators (AAE); American Academy of Nurse Practitioners (AANP); Asthma and Allergy Foundation of America (AAFA); COPD-ALERT; National Association for Medical Direction of Respiratory Care (NAMDRRC); and National Emphysema/COPD Association (NECA).

14 See CHASM Citizen Petition re Labeling and Advertisements for Compounded, Aqueous-Based Drugs for Inhalation, FDA Docket #2005p-0116 (March 24, 2005).

The financial rewards for these pharmacy manufacturing operations are greater than their fear of state and federal enforcement. As they proliferate, so do rates of patient exposure to health risks and physician exposure to liability risks.

Physicians, medical staff and patients can protect against health and liability risks by insisting on commercially available FDA-approved brand and generic nebulizer medications, no substitutes. Reporting pharmacy businesses to Allergy & Asthma Network Mothers of Asthmatics is easy and effective.

**To learn more about how to file a report, contact Sandra Fusco-Walker at Allergy & Asthma Network Mothers of Asthmatics, 800.878.4403 x105 or [sfwalker@aanma.org](mailto:sfwalker@aanma.org).**

### About CHASM

Allergy & Asthma Network Mothers of Asthmatics, a leading nonprofit patient education, advocacy and outreach organization, formed the Consumer Health Alliance for Safe Medication (CHASM), a working group comprising:

- Allergy & Asthma Network Mothers of Asthmatics ([www.breatherville.org](http://www.breatherville.org))
- American Academy of Allergy, Asthma and Immunology ([www.aaaai.org](http://www.aaaai.org))

- American Association for Respiratory Care ([www.aarc.org](http://www.aarc.org))
- American College of Allergy, Asthma and Immunology ([www.acaai.org](http://www.acaai.org))
- American Latex Allergy Association ([www.latexallergyresources.org](http://www.latexallergyresources.org))
- American Partnership for Eosinophilic Disorders ([www.apfed.org](http://www.apfed.org))
- American Academy of Nurse Practitioners ([www.aanp.org](http://www.aanp.org))
- Association of Asthma Educators ([www.asthmaeducators.org](http://www.asthmaeducators.org))
- Asthma and Allergy Foundation of America ([www.aafa.org](http://www.aafa.org))
- COPD-ALERT ([www.copd-alert.com](http://www.copd-alert.com))
- National Association for Medical Direction of Respiratory Care ([www.namdr.org](http://www.namdr.org))
- National Emphysema/COPD Association ([www.necacommunity.org](http://www.necacommunity.org))

You can find more information about CHASM at [www.breatherville.org/CHASM](http://www.breatherville.org/CHASM). For more information about the Food and Drug Administration (FDA) and the Federal Food, Drug, and Cosmetic Act, visit [www.fda.gov](http://www.fda.gov).

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## Examples of FDA-Approved Brand-Name and Generic Unit-Dose Medications



**The Real Thing...**

|  |                                    |  |  |  |   |  |   |
|--|------------------------------------|--|--|--|---|--|---|
|  | Expiration date embossed onto vial |  | Medication lot number embossed onto vial |  | Medication name and dosage embossed onto vial |  | Pharmaceutical manufacturer name embossed onto vial |
|--|------------------------------------|--|--|--|---|--|---|

Refer to PDR for other examples

## Examples of Unapproved Nebulizer Medications



**More Clues**



Paper labels leach glue and ink toxins into nebulizer solutions; FDA-approved nebulizer medications do not have paper labels.