

STATE OF OREGON  
Marion County Circuit Courts  
DEC 11 2007  
**FILED**

IN THE CIRCUIT COURT OF THE STATE OF OREGON  
FOR THE COUNTY OF MARION

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STATE OF OREGON ex rel HARDY  
MYERS, Attorney General for the State of  
Oregon,

Plaintiff,

v.

APOTHECURE, INC. and GARY OSBORN,  
individually,

Defendants.

Case No. 07C23297

COMPLAINT ALLEGING VIOLATIONS OF  
THE UNLAWFUL TRADE PRACTICES ACT  
(ORS 646.605 TO 646.656)

CLAIM NOT SUBJECT TO MANDATORY  
ARBITRATION

13 Plaintiff, State of Oregon, for its Complaint alleges claims for relief based upon violation  
14 of Oregon's Unlawful Trade Practices Act (UTPA), ORS 646.605 to 646.656. Plaintiff alleges  
15 that at all times material herein:

ALLEGATIONS COMMON TO ALL CLAIMS

17 1.

18 HARDY MYERS is the Attorney General for the State of Oregon and sues in his official  
19 capacity pursuant to ORS 646.632.

20 2.

21 DEFENDANT ApotheCure, Inc. is a Texas corporation with its principle place of  
22 business in Dallas, Texas. ApotheCure has operated as a compounding pharmacy for 16 years.  
23 The firm has 35 employees including 5 pharmacists and 11 pharmacy technicians. ApotheCure's  
24 annual sales total approximately \$6 million; 60 to 70% of sales are generated from products that  
25 the firm produces. At all relevant times, DEFENDANT ApotheCure did business in Oregon  
26 selling and promoting prescription drugs, over-the-counter drugs, and nutritional supplements.

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3.

DEFENDANT Osborn manages, controls, and directs all business activities and operations of ApotheCure, Inc, including business operations in Oregon. Hereinafter, defendants ApotheCure, Inc. and Gary Osborn shall be referred to collectively as DEFENDANTS.

4.

The Circuit Court for the State of Oregon has personal jurisdiction over DEFENDANTS pursuant to ORCP 4A. DEFENDANTS engaged in substantial activities within the State by operating a business that provides services that are primarily for personal, family, and household use. All transactions took place in the course of DEFENDANTS' business.

5.

DEFENDANTS were given the Notice required by ORS 646.632(2) and failed to submit to the Attorney General an acceptable Assurance of Voluntary Compliance.

6.

The conduct of DEFENDANTS described in this Complaint was willful within the meaning of ORS 646.605(10).

**SUMMARY OF THE ACTION**

7.

DEFENDANTS sold dangerous prescription drugs in Oregon without possessing the license from the Oregon Board of Pharmacy necessary to operate in Oregon as a pharmacy or a drug manufacturer. While operating as an unlawful pharmacy and/or drug manufacturer, DEFENDANTS promoted and sold powerful drugs for indications (uses) not approved by the Food and Drug Administration ("FDA") and for which DEFENDANTS lacked competent and reliable evidence of safety and efficacy. Among the dangerous prescriptions drugs DEFENDANTS unlawfully sold in Oregon was colchicine. Even for uses and dosages approved by FDA, colchicine is a highly toxic drug that must be used with great care to avoid injury and death. DEFENDANTS sold colchicine to treat back pain, an off-label indication for which

1 colchicine is largely ineffective. Worse yet, in February of 2007, DEFENDANTS shipped into  
2 Oregon 31 vials of mislabeled colchicine that was eight times more concentrated than indicated  
3 on each vial's label. At least three patients died as a result of poisoning by this mislabeled super-  
4 potent colchicine. Besides selling mislabeled super-potent colchicine, DEFENDANTS also sold  
5 colchicine that was less potent than indicated on the label. The sale of mislabeled colchicine was  
6 not an isolated incident but reflected a pattern and practice of substandard care. DEFENDANTS  
7 operating procedures fail to comply with basic good pharmacy standards and practices.  
8 Moreover, DEFENDANTS use their status as a pharmacy to operate as an unlicensed drug  
9 manufacturer to formulate, fabricate, and promote new drugs without performing the clinical  
10 trials necessary to establish that these new drugs are safe and effective for the uses for which  
11 they are promoted. Among the unapproved drugs that DEFENDANTS unlawfully manufacture  
12 and promote is adrenal cortex, a drug that was removed from the market place for safety reasons.

### 13 BACKGROUND

14 8.

15 Compounding pharmacies operate in a grey area between the practice of pharmacy and  
16 business of drug manufacturing. Manufacturers of drugs are regulated by FDA while pharmacies  
17 are regulated by state Boards of Pharmacy.

18 9.

19 To ensure the safety, sterility, and purity of drugs, manufacturers are subject to regular  
20 inspection by the FDA. Compounding pharmacies, however, operate with considerably less  
21 regulatory oversight. State Boards of Pharmacy generally do not subject pharmacies to the same  
22 level of inspection as manufacturers are subject to by the FDA.

23 10.

24 Drug manufacturers may not market new drugs unless they submit a New Drug  
25 Application ("NDA") to the FDA supported by clinical trials that demonstrate to FDA's  
26 satisfaction that the new drug is safe and effective. Drug manufacturers are only permitted to

1 market drugs for the specific indications approved by FDA and may not promote drugs "off-  
2 label" for unapproved uses.

3 11.

4 Pharmacy compounding is the process of combining, mixing, or altering ingredients in a  
5 drug to create a new compound for an individual patient to address the patient's unique needs.  
6 For example, a patient with difficulty swallowing might require a drug that was approved in the  
7 form of a pill to be compounded into a liquid suspension. Another example would be to  
8 reformulate a drug so that it does not contain an ingredient for which the individual patient is  
9 allergic. The traditional practice of compounding involves the receipt of a prescription for a  
10 specific patient, compounding the drug, and labeling the prescription with the patient's name and  
11 directions for use. Under the Food Drug and Cosmetic Act ("FDCA"), such modifications  
12 require submission of an NDA; however, because FDA recognizes the importance of traditional  
13 compounding for patients with unique needs, FDA exercises its administrative discretion and  
14 allows pharmacies to compound "new drugs" in small batches for individual patients without  
15 submission of an NDA. To ensure this exception does not allow manufacturers to circumvent  
16 regulation of new drugs by masquerading as a pharmacy engaged in the practice of  
17 compounding, FDA publishes a Compliance Policy Guide for FDA Staff and Industry that lists  
18 various factors that distinguish a pharmacy engaged in the traditional practice of compounding  
19 from a manufacturer. Among these factors are: (1) whether the pharmacy engages in  
20 "[c]ompounding of drugs in anticipation of receiving prescriptions, except in very limited  
21 quantities in relation to the amounts of drugs compounded after receiving valid prescriptions;"  
22 (2) whether the pharmacy compounds "drugs that were withdrawn or removed from the market  
23 for safety reasons"; and (3) whether the pharmacy engages in "[c]ompounding drug products that  
24 are commercially available in the marketplace or that are essentially copies of commercially  
25 available FDA-approved drug products." (The Guide is attached as Exhibit 1).

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Page 4  
COMPLAINT

1 12.

2 DEFENDANTS' compound, promote, and sell prescription drugs, over-the-counter drugs  
3 and nutritional supplements internationally and throughout the United States, including Oregon.  
4 DEFENDANTS are not a small local pharmacy compounding individual prescriptions for  
5 patients with unique needs. Rather, DEFENDANTS' drug business is primarily volume sale of  
6 drugs they manufacture in batches and sell to "alternative" health care providers for uses  
7 unapproved by FDA. DEFENDANTS' operations are more consistent with those of a  
8 manufacturer than a pharmacy since most of their operations relate to formulating, fabricating,  
9 and promoting new drugs in bulk. Unlike licensed pharmaceutical companies that comply with  
10 FDA regulations, DEFENDANTS do not conduct clinical trials, let alone well designed clinical  
11 trials, to establish the safety and efficacy of their products. Rather, DEFENDANTS rely upon  
12 DEFENDANT Osborn's experience as CEO of an alternative medical practice, anecdotal  
13 reports, and attendance at trade shows, to substantiate the safety and efficacy of their new drugs.  
14 Traditional pharmacy compounding (meaning the pharmacy receives a prescription for a specific  
15 patient, and then compounds the drug that is labeled with the patient's name and directions for  
16 use) is a small fraction of DEFENDANTS' business.

17 **UNLICENSED PRACTICE OF PHARMACY**

18 13.

19 Although DEFENDANTS do business as a pharmacy internationally and throughout the  
20 United States, they are only licensed to do business as a pharmacy in the states of Texas,  
21 California, Hawaii, and Florida. DEFENDANTS applied for but were denied a license by the  
22 state of Indiana.

23 14.

24 All pharmacies, manufacturers and other "drug outlets" that do business in Oregon must  
25 be licensed by the Oregon Board of Pharmacy.

26 ///

1 15.

2 DEFENDANTS never obtained the license from the Oregon Board of Pharmacy  
3 necessary to lawfully operate as a pharmacy or drug manufacturer in Oregon.

4 16.

5 Despite the fact that they lacked the necessary license, DEFENDANTS sold hundreds of  
6 thousands of dollars worth of prescription and over-the-counter drugs in Oregon. From  
7 November 25, 2004 through May 17, 2007, DEFENDANTS sold \$368,854.88 worth of  
8 prescription and over-the-counter drugs in Oregon; engaged in 222 sales transactions with  
9 Oregon patients; and engaged in 1,526 sales transactions with Oregon naturopathic physicians  
10 and medical doctors. Before November 25, 2004, DEFENDANTS engaged in an as of yet  
11 unknown number of unlicensed drug sales in Oregon.

12 17.

13 By engaging in the practice of pharmacy in Oregon, DEFENDANTS misrepresented by  
14 implication that they had the status of a pharmacy licensed to do business in Oregon. When  
15 selling prescription and over-the-counter drugs in Oregon, DEFENDANTS did not disclose that  
16 they lacked the license necessary to lawfully sell these products.

17 **UNLAWFUL DRUG MANUFACTURING**

18 18.

19 Despite the fact that adrenal cortex drugs had been removed from the market place for  
20 safety reasons and federal law expressly prohibits pharmacies from compounding such drugs,  
21 DEFENDANTS manufactured, promoted and sold in Oregon adrenal cortex drugs.

22 19.

23 DEFENDANTS manufacture, promote and sell prescription and over-the-counter drugs  
24 that have not been approved by FDA as safe and effective and promote drugs unlawfully for  
25 "off-label" indications that lack competent and reliable scientific evidence of safety and efficacy.

26 ///

1 COLCHICINE

2 20.

3 A recent report issued by the Center for Disease Control and Prevention (CDC) of the  
4 U.S. Department of Health and Human Services indicates that, “[c]olchicine for injection has  
5 been available in the United States since the 1950s. Although not approved by FDA, intravenous  
6 (IV) colchicine is an accepted treatment for acute gout symptoms. . . . more recently, outpatient  
7 use of IV administration [of colchicine] has been advocated by alternative medicine providers  
8 but is not an accepted practice. Colchicine has well-known toxicities that limit its safe  
9 therapeutic use. IV doses that exceed the standard single-use therapeutic dose of 2 to 4 mg per  
10 episode of gout have resulted in life-threatening toxicity.” (Citations removed). The CDC paper  
11 goes on to report that [u]se of colchicine for treatment of low back pain and intervertebral disc  
12 herniation was described initially in the 1970s. A single case series in 1979 suggested some  
13 effectiveness with low doses of oral and IV colchicine in reducing pain; subsequent prospective  
14 double-blind studies showed no improvement over placebo with oral use and only short-lived  
15 improvement with IV therapy. Nevertheless, numerous Internet sources continue to recommend  
16 use of IV colchicine for back pain, referencing these early studies as evidence of the drug’s  
17 effectiveness. (Citations removed). The complete report is attached as Exhibit 2.

18 21.

19 DEFENDANTS targeted “alternative” health care providers in Oregon and around the  
20 country with sales brochures promoting their products, including colchicine.

21 22.

22 Between November 25, 2005 and May 17, 2007, DEFENDANTS made 44 sales of IV  
23 colchicine in Oregon. During these transactions, DEFENDANTS failed to disclose that  
24 colchicine is dangerous and largely ineffective for treatment of backpain.

25 ///

26 ///

1 23.

2 At the time DEFENDANTS sold IV colchicine in Oregon, the same formulation sold by  
3 DEFENDANTS was commercially available from a licensed manufacturer.

4 24.

5 By offering compounded IV colchicine for sale in Oregon, DEFENDANTS implicitly  
6 represented it was not commercially available from a licensed manufacturer.

7 25.

8 When promoting and selling compounded IV colchicine in Oregon, DEFENDANTS did  
9 not disclose that the same product was available from a licensed manufacturer or that  
10 DEFENDANTS' IV colchicine was subject to a lower level of regulatory oversight and  
11 inspection than IV colchicine sold by a licensed manufacturer.

12 26.

13 On or about February 8, 2007, DEFENDANTS shipped 31 vials of IV colchicine to the  
14 Center for Integrative Medicine in Portland, Oregon. Each of these 31 vials was mislabeled  
15 "1mg/2ml," that is 0.5mg/ml, when in fact, the dosage was 4mg/ml, a concentration eight times  
16 greater than the labeled dose. Colchicine at such a high dose is highly toxic. At least three  
17 patients died from colchicine poisoning after they were infused with mislabeled colchicine sold  
18 by DEFENDANTS to the Center for Integrative Medicine.

19 27.

20 In addition to mislabeled super- potent colchicine, DEFENDANTS sold colchicine in  
21 Oregon that was significantly less potent than labeled. In January 2007, DEFENDANTS sold  
22 the Center for Integrative Medicine 35 vials of IV colchicine labeled 1mg/ ml that was in fact .38  
23 mg/ ml. In February 2007, DEFENDANTS, sold the Center of Integrative Medicine another 39  
24 vials of similarly mislabeled IV colchicine.

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**BAD PRACTICES**

28.

When doing business in Oregon, DEFENDANTS implicitly represent that their operating procedures are adequate to ensure the safety of their products and meet professional standards of care. In fact, DEFENDANTS operating procedures are inadequate and fail to meet accepted standards for both compounding pharmacies and drug manufacturers.

29.

The Oregon colchicine poisonings were not the first time a patient died after “alternative treatment” with one of DEFENDANTS’ IV drugs. In August, 2005, a five year old Pennsylvania boy died while being infused with EDTA compounded by DEFENDANTS. The boy was given EDTA as part of an unapproved treatment for autism. In 2004, the National Institute of Medicine had already determined that this type of treatment for autism was scientifically without merit. Had DEFENDANTS followed good pharmacy practice, this five year old boy would not have died.

30.

The Oregon colchicine poisonings were also not the first time multiple patients suffered serious adverse events from a batch of IV drug compounded by DEFENDANTS. In August 2004, nine adverse events and three hospitalizations were reported in patients infused with IV phosphatidylcholine compounded by DEFENDANTS. After this incident, FDA tried to inspect DEFENDANTS’ operations but DEFENDANTS refused to permit the inspection and FDA took no further action.

31.

After the Oregon colchicine poisonings, FDA attempted to conduct a systemic inspection of DEFENDANTS’ operations, including operations not directly related to colchicine. Again DEFENDANTS resisted the inspection. This time, however, FDA obtained a search warrant, conducted the inspection, and identified the following deficiencies:



1 33.

2 After patients suffer adverse events from their drugs, DEFENDANTS fail to take  
3 necessary remedial actions and report the adverse event to regulatory authorities. On or about  
4 November 2006, an Oregonian was sickened by IV CaEDTA compounded by DEFENDANTS;  
5 however, DEFENDANTS only corrective action was to refund the price of the product and  
6 DEFENDANTS never reported the incident to regulatory authorities.

7 **CAUSE OF ACTION**

8 **UNLAWFUL TRADE PRACTICES**

9 **FIRST CLAIM FOR RELIEF**

10 **ORS 646.608(1)(b)**

11 **COUNT I**

12 34.

13 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
14 preceding paragraphs 1 through 33 as if fully alleged herein.

15 35.

16 DEFENDANTS violated ORS 646.608(1)(b) by causing likelihood of confusion  
17 regarding the source, sponsorship, approval or certification of prescription and over-the-counter  
18 drugs that they promoted or sold Oregon. Each time DEFENDANTS promoted or sold  
19 prescription or over-the-counter drugs in Oregon without clearly and conspicuously disclosing  
20 that these drugs were produced by a pharmacy or manufacturer unlicensed to do business in  
21 Oregon is a separate and distinct violation of ORS 646.608(1)(b).

22 **COUNT II**

23 36.

24 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
25 preceding paragraphs 1 through 33 as if fully alleged herein.

26 ///

1 37.

2 DEFENDANTS violated ORS 646.608 (1) (b) by causing likelihood of confusion  
3 regarding whether their prescription and over-the-counter drugs had undergone regulatory  
4 approval by FDA. Each time DEFENDANTS promoted or sold a prescription or over-the-  
5 counter drug in Oregon that had not been approved by FDA and did not fall within a recognized  
6 exception for approval, without disclosing that the drug was not approved by FDA and did not  
7 fall within a recognized exception for approval, was separate and distinct violation of ORS  
8 646.608(1)(b).

9 **COUNT III**

10 38.

11 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
12 preceding paragraphs 1 through 33 as if fully alleged herein.

13 39.

14 DEFENDANTS violated ORS 646.608 (1) (b) by causing likelihood of confusion  
15 regarding approval of adrenal cortex drugs for lawful sale in the United States. Each time  
16 DEFENDANTS promoted or sold in Oregon adrenal cortex drugs without disclosing that the  
17 drug was on a list of drugs withdrawn from the marketplace for safety reasons was a separate and  
18 distinct violation of ORS 646.608(1)(b).

19 **COUNT IV**

20 40.

21 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
22 preceding paragraphs 1 through 33 as if fully alleged herein.

23 41.

24 DEFENDANTS violated ORS 646.608 (1) (b) by causing likelihood of confusion  
25 regarding their certification to compound prescription drugs that were copies of drugs  
26 commercially available from licensed manufacturers. Every time DEFENDANTS sold or

1 promoted a prescription drug in Oregon that was a copy of a drug commercially available from a  
2 licensed manufacturer, and did not disclose that as a pharmacy, DEFENDANTS were not  
3 certified or licensed to compound drugs that were commercially available from manufacturers,  
4 was a separate and distinct violation of ORS 646.608(1)(b).

5 **SECOND CLAIM FOR RELIEF**

6 **ORS 646.608(1)(e)**

7 **COUNT V**

8 42.

9 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
10 preceding paragraphs 1 through 33 as if fully alleged herein.

11 43.

12 DEFENDANTS violated ORS 646.608(1)(e) by representing that goods and services had  
13 characteristics, ingredients, uses, benefits, quantities or qualities that they did not have when they  
14 sold mislabeled vials of colchicine with concentrations that differed from their labels. Each vial  
15 of mislabeled colchicine that DEFENDANTS sold in Oregon was a separate and distinct  
16 violation of ORS 646.608(1)(e).

17 **COUNT VI**

18 44.

19 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
20 preceding paragraphs 1 through 33 as if fully alleged herein.

21 45.

22 DEFENDANTS violated ORS 646.608(1)(e) by representing that goods and services had  
23 characteristics, benefits, and qualities that they did not have when they sold and promoted in  
24 Oregon compound drugs in formulations commercially available from licensed drug  
25 manufacturers without disclosing that the drug was also available from a commercial  
26 manufacturer. Each time DEFENDANTS sold or promoted a compounded drug in Oregon that

1 was also commercially available from a licensed manufacturer, without disclosing that the drug  
2 was also available from a licensed commercial manufacturer and thus should not be compounded  
3 by a pharmacy, is a separate and distinct violation of ORS 646.608(1)(e).

4 **COUNT VII**

5 46.

6 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
7 preceding paragraphs 1 through 33 as if fully alleged herein.

8 47.

9 DEFENDANTS violated ORS 646.608(1)(e) by representing that their goods and  
10 services had characteristics, benefits, and qualities that they did not have by misrepresenting that  
11 DEFENDANTS' operations complied with good pharmacy and manufacturing practice and that  
12 DEFENDANTS' drugs were of the quality of a pharmacy or manufacturer that follows good  
13 practices. Each time DEFENDANTS dispensed or sold a prescription drug or over-the-counter  
14 drug in Oregon without disclosing that their practices failed to comply with good pharmacy and  
15 manufacturing practices was a separate and distinct violation of ORS 646.608(1)(e).

16 **COUNT VIII**

17 48.

18 Plaintiff, STATE, realleges and incorporates each and every allegation contained in the  
19 preceding paragraphs 1 through 33 as if fully alleged herein.

20 49.

21 DEFENDANTS violated ORS 646.608(1)(e) by representing that their goods and  
22 services had characteristics, benefits, and qualities that they did not have by promoting and  
23 selling colchicine and other prescription drugs to treat indications that were not approved by  
24 FDA and for which the drugs were not safe<sup>l</sup> or effective.

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**COUNT IX**

50.

Plaintiff, STATE, realleges and incorporates each and every allegation contained in the preceding paragraphs 1 through 33 as if fully alleged herein.

51.

DEFENDANTS violated ORS 646.608(1)(e) by representing that a person has an approval, status, and qualification that the person does not have by misrepresenting that ApotheCure, Inc. had the approval, status, and qualifications of a pharmacy or manufacturer licensed to practice in the state of Oregon. Each time DEFENDANTS did business in Oregon as a pharmacy or manufacturer without disclosing that ApotheCure Inc. was not an Oregon licensed pharmacy or manufacturer was a separate and distinct violation of ORS 646.608(1)(e).

**THIRD CLAIM FOR RELIEF**

**ORS 646.608(1)(g)**

**COUNT X**

52.

Plaintiff, STATE, realleges and incorporates each and every allegation contained in the preceding paragraphs 1 through 33 as if fully alleged herein.

53.

DEFENDANTS violated ORS 646.608(1)(g) by representing that goods are of a particular standard, quality or grade if they are of another by misrepresenting the standard, quality, or grade of IV and injection drugs compounded or manufactured with sterile water that was only fit for irrigation. Each sale of a drug compounded or manufactured with saline solution that was only fit for irrigation was a separate and distinct violation of ORS 646.608(1)(g).

**COUNT XI**

54.

Plaintiff, STATE, realleges and incorporates each and every allegation contained in the

1 preceding paragraphs 1 through 33 as if fully alleged herein.

2 55.

3 DEFENDANTS violated ORS 646.608(1)(g) by representing that goods are of a  
4 particular standard, quality or grade if they are of another by misrepresenting the standard,  
5 quality, or grade of drugs compounded or manufactured in multiple doses from sterile water  
6 marked as a single dose container. Each sale of a drug compounded or manufactured in multiple  
7 doses from sterile water from a single dose container was a separate and distinct violation of  
8 ORS 646.608(1)(g).

9 **PRAYER FOR RELIEF**

10 56.

11 **WHEREFORE**, plaintiff prays for relief as follows:

- 12 (a) For a judgment against DEFENDANTS for civil penalties of up to \$25,000 for each  
13 willful violation of the Unlawful Trade Practices Act ORS 646.605 et seq;
- 14 (b) For a judgment against DEFENDANTS for disgorgement of the value of all unlawful  
15 Oregon sales of prescription and over-the-counter drugs;
- 16 (c) For a judgment against DEFENDANTS for reasonable attorney fees pursuant to ORS  
17 646.632(8);
- 18 (d) For a judgment requiring DEFENDANTS to refund all direct or indirect consumer  
19 purchases of drugs unlawfully sold by DEFENDANTS in Oregon;
- 20 (e) For a judgment requiring DEFENDANTS to comply with all applicable Oregon law  
21 regulating the practice of pharmacy;
- 22 (f) For a judgment prohibiting DEFENDANTS from compounding drugs for sale in  
23 Oregon prior to receipt of a valid prescription for the compound drug;
- 24 (g) For a judgment prohibiting DEFENDANTS from promoting or compounded drugs  
25 for sale in Oregon that are commercially available in the marketplace or that are  
26 essentially copies of commercially available FDA-approved drug products;

- 1 (h) For a judgment requiring DEFENDANTS to comply with U.S. Pharmacopoeia  
2 regulation 797;
- 3 (i) For a judgment prohibiting DEFENDANTS, in connection with the manufacturing,  
4 labeling, advertising, promotion, offering for sale, sale, or distribution of their  
5 products, from making any representation, expressly or by implication, concerning  
6 their products' efficacy, performance, safety or benefits, unless, at the time the  
7 representation is made, DEFENDANTS possess and rely upon competent and reliable  
8 scientific evidence that substantiates the representation. For purposes of this  
9 judgment, "*competent and reliable scientific evidence*" shall mean tests, analysis,  
10 research, studies, or other evidence based on the expertise of professionals in the  
11 relevant area, that have been conducted and evaluated in an objective manner by  
12 persons qualified to do so, using procedures generally accepted in the profession to  
13 yield accurate and reliable results and shall include at least two adequate, and well-  
14 controlled, double-blind clinical studies;
- 15 (j) For a judgment permanently restraining and enjoining DEFENDANTS, individually  
16 or in any business or corporate capacity, from making any express or implied  
17 statements in the offer or sale of their products that have the capacity, tendency or  
18 effect of deceiving or misleading consumers or that fail to state any material fact, the  
19 omission of which deceives or tends to deceive;
- 20 (k) For a judgment that all injunctions herein shall apply to DEFENDANTS individually  
21 and through any present or future corporation or other organization or entity whose  
22 acts, practices or policies are directed, formulated or controlled by either defendant or  
23 in which DEFENDANTS are a principal or own any interest; to DEFENDANTS'  
24 successors and assigns, agents, representatives and employees, directly or through  
25 any affiliate, corporation, subsidiary, division or other related entity consumer; and,

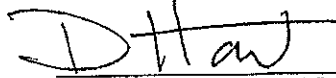
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1 (l) For a judgment granting any other and further relief, as the court may deem  
2 appropriate.

3 Dated December 11, 2007.

4 Respectfully submitted,

5 HARDY MYERS  
6 Attorney General

7 

8 David A. Hart, OSB No. 00275  
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**Compliance Policy Guide**  
**Compliance Policy Guidance for FDA Staff and Industry<sup>1</sup>**

**CHAPTER - 4**  
**SUB CHAPTER - 460**

**Sec. 460.200 Pharmacy Compounding**

**Guidance for FDA Staff and Industry**  
**Compliance Policy Guides Manual**

**Sec. 460.200**  
**Pharmacy Compounding**

Submit written comments regarding this guidance document to the Dockets Management Branch (HFA-305), 5630 Fishers Lane, rm.1061, Rockville, MD 20852.

Additional copies of this document may be obtained by sending a request to the Division of Compliance Policy (HFC-230), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or from the Internet at: [http://www.fda.gov/ora/compliance\\_ref/cpg/default.htm](http://www.fda.gov/ora/compliance_ref/cpg/default.htm)

U.S. Department of Health and Human Services  
Food and Drug Administration  
Office of Regulatory Affairs  
Center for Drug Evaluation and Research  
May 2002

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**CHAPTER - 4**  
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## Sec. 460.200 Pharmacy Compounding

***This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.***

## INTRODUCTION

This document provides guidance to drug compounders and the staff of the Food and Drug Administration (FDA) on how the Agency intends to address pharmacy compounding of human drugs in the immediate future as a result of the decision of the Supreme Court in *Thompson v. Western States Medical Center*, No. 01-344, April 29, 2002. FDA is considering the implications of that decision and determining how it intends to regulate pharmacy compounding in the long term. However, FDA recognizes the need for immediate guidance on what types of compounding might be subject to enforcement action under current law. This guidance describes FDA's current thinking on this issue.

## BACKGROUND

On March 16, 1992, FDA issued a compliance policy guide (CPG), section 7132.16 (later renumbered as 460.200) to delineate FDA's enforcement policy on pharmacy compounding. That CPG remained in effect until 1997 when Congress enacted the Food and Drug Administration Modernization Act of 1997.

On November 21, 1997, the President signed the Food and Drug Administration Modernization Act of 1997 (Pub. L. 105-115) (the Modernization Act). Section 127 of the Modernization Act added section 503A to the Federal Food, Drug, and Cosmetic Act (the Act), to clarify the status of pharmacy compounding under Federal law. Under section 503A, drug products that were compounded by a pharmacist or physician on a customized basis for an individual patient were entitled to exemptions from three key provisions of the Act: (1) the adulteration provision of section 501(a)(2)(B) (concerning the good manufacturing practice requirements); (2) the misbranding provision of section 502(f)(1) (concerning the labeling of drugs with adequate directions for use); and (3) the new drug provision of section 505 (concerning the approval of drugs under new drug or abbreviated new drug applications). To qualify for these statutory exemptions, a compounded drug product was required to satisfy several requirements, some of which were to be the subject of FDA rulemaking or other actions.

Section 503A of the Act took effect on November 21, 1998, one year after the date of the enactment of the Modernization Act. In November

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1998, the solicitation and advertising provisions of section 503A were challenged by seven compounding pharmacies as an impermissible regulation of commercial speech. The U.S. District Court for the District of Nevada ruled in the plaintiffs' favor. FDA appealed to the U.S. Court of Appeals for the Ninth Circuit. On February 6, 2001, the Court of Appeals declared section 503A invalid in its entirety (*Western States Medical Center v. Shalala*, 238 F.3rd 1090 (9th Cir. 2001)). The government petitioned for a writ of certiorari to the U.S. Supreme Court for review of the circuit court opinion. The Supreme Court granted the writ and issued its decision in the case on April 29, 2002.

The Supreme Court affirmed the 9th Circuit Court of Appeals decision that found section 503A of the Act invalid in its entirety because it contained unconstitutional restrictions on commercial speech (i.e., prohibitions on soliciting prescriptions for and advertising specific compounded drugs). The Court did not rule on, and therefore left in place, the 9th Circuit's holding that the unconstitutional restrictions on commercial speech could not be severed from the rest of section 503A. Accordingly, all of section 503A is now invalid.

FDA has therefore determined that it needs to issue guidance to the compounding industry on what factors the Agency will consider in exercising its enforcement discretion regarding pharmacy compounding.

#### DISCUSSION

FDA recognizes that pharmacists traditionally have extemporaneously compounded and manipulated reasonable quantities of human drugs upon receipt of a valid prescription for an individually identified patient from a licensed practitioner. This traditional activity is not the subject of this guidance.

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FDA believes that an increasing number of establishments with retail pharmacy licenses are engaged in manufacturing and distributing unapproved new drugs for human use in a manner that is clearly outside the bounds of traditional pharmacy practice and that violates the Act. Such establishments and their activities are the focus of this guidance. Some "pharmacies" that have sought to find shelter under and expand the scope of the exemptions applicable to traditional retail pharmacies have claimed that their manufacturing and distribution practices are only the regular course of the practice of pharmacy. Yet, the practices of many of these entities seem far more consistent with those of drug manufacturers and wholesalers than with those of retail pharmacies. For example, some firms receive and use large quantities of bulk drug substances to manufacture large quantities of unapproved drug products in advance of receiving a valid prescription for them.

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Moreover, some firms sell to physicians and patients with whom they have only a remote professional relationship. Pharmacies engaged in activities analogous to manufacturing and distributing drugs for human use may be held to the same provisions of the Act as manufacturers.

**POLICY:**

Generally, FDA will continue to defer to state authorities regarding less significant violations of the Act related to pharmacy compounding of human drugs. FDA anticipates that, in such cases, cooperative efforts between the states and the Agency will result in coordinated investigations, referrals, and follow-up actions by the states.

However, when the scope and nature of a pharmacy's activities raise the kinds of concerns normally associated with a drug manufacturer and result in significant violations of the new drug, adulteration, or misbranding provisions of the Act, FDA has determined that it should seriously consider enforcement action. In determining whether to initiate such an action, the Agency will consider whether the pharmacy engages in any of the following acts:

1. Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving valid prescriptions.
2. Compounding drugs that were withdrawn or removed from the market for safety reasons. Appendix A provides a list of such drugs that will be updated in the future, as appropriate.
3. Compounding finished drugs from bulk active ingredients that are not components of FDA approved drugs without an FDA sanctioned investigational new drug application (IND) in accordance with 21 U.S.C. § 355(i) and 21 CFR 312.
4. Receiving, storing, or using drug substances without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA-registered facility.
5. Receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements.
6. Using commercial scale manufacturing or testing equipment for compounding drug products.
7. Compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.
8. Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products. In certain circumstances, it may be

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appropriate for a pharmacist to compound a small quantity of a drug that is only slightly different than an FDA-approved drug that is commercially available. In these circumstances, FDA will consider whether there is documentation of the medical need for the particular variation of the compound for the particular patient.

9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.

The foregoing list of factors is not intended to be exhaustive. Other factors may be appropriate for consideration in a particular case.

Other FDA guidance interprets or clarifies Agency positions concerning nuclear pharmacy, hospital pharmacy, shared service operations, mail order pharmacy, and the manipulation of approved drug products.

#### REGULATORY ACTION GUIDANCE:

District offices are encouraged to consult with state regulatory authorities to assure coherent application of this guidance to establishments that are operating outside of the traditional practice of pharmacy.

FDA-initiated regulatory action may include issuing a warning letter, seizure, injunction, and/or prosecution. Charges may include, but need not be limited to, violations of 21 U.S.C. §§ 351(a)(2)(B), 352(a), 352(f)(1), 352(o), and 355(a) of the Act.

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Reissued: 5/29/2002

#### APPENDIX A

##### LIST OF COMPOUNDING DRUGS THAT WERE WITHDRAWN OR REMOVED FROM THE MARKET FOR SAFETY REASONS

- Adenosine phosphate: All drug products containing adenosine phosphate.
- Adrenal cortex: All drug products containing adrenal cortex.
- Aminopyrine: All drug products containing aminopyrine.
- Astemizole: All drug products containing astemizole.
- Azaribine: All drug products containing azaribine.
- Benoxaprofen: All drug products containing benoxaprofen.
- Bithionol: All drug products containing bithionol.
- Bromfenac sodium: All drug products containing bromfenac sodium.
- Butamben: All parenteral drug products containing butamben.
- Camphorated oil: All drug products containing camphorated oil.
- Carbetapentane citrate: All oral gel drug products containing carbetapentane citrate.
- Casein, iodinated: All drug products containing iodinated casein.

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Chlorhexidine gluconate: All tinctures of chlorhexidine gluconate formulated for use as a patient preoperative skin preparation.

Chlormadinone acetate: All drug products containing chlormadinone acetate.

Chloroform: All drug products containing chloroform.

Cisapride: All drug products containing cisapride.

Cobalt: All drug products containing cobalt salts (except radioactive forms cobalt and its salts and cobalamin and its derivatives).

Dexfenfluramine hydrochloride: All drug products containing dexfenfluramine hydrochloride.

Diamthazole dihydrochloride: All drug products containing diamthazole dihydrochloride.

Dibromsalan: All drug products containing dibromsalan.

Diethylstilbestrol: All oral and parenteral drug products containing 25 milligrams or more of diethylstilbestrol per unit dose.

Dihydrostreptomycin sulfate: All drug products containing dihydrostreptomycin sulfate.

Dipyron: All drug products containing dipyron.

Encainide hydrochloride: All drug products containing encainide hydrochloride.

Fenfluramine hydrochloride: All drug products containing fenfluramine hydrochloride.

Flosequinan: All drug products containing flosequinan.

Gelatin: All intravenous drug products containing gelatin.

Glycerol, iodinated: All drug products containing iodinated glycerol.

Gonadotropin, chorionic: All drug products containing chorionic gonadotropins of animal origin.

Grepafloxacin: All drug products containing grepafloxacin.

Mepazine: All drug products containing mepazine hydrochloride or mepazine acetate.

Metabromsalan: All drug products containing metabromsalan.

Methamphetamine hydrochloride: All parenteral drug products containing methamphetamine hydrochloride.

Methapyrilene: All drug products containing methapyrilene.

Methopholine: All drug products containing methopholine.

Mibefradil dihydrochloride: All drug products containing mibefradil dihydrochloride.

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Nitrofurazone: All drug products containing nitrofurazone (except topical drug products formulated for dermatologic application).

Nomifensine maleate: All drug products containing nomifensine maleate.

Oxyphenisatin: All drug products containing oxyphenisatin.

Oxyphenisatin acetate: All drug products containing oxyphenisatin acetate.

Phenacetin: All drug products containing phenacetin.

Phenformin hydrochloride: All drug products containing phenformin hydrochloride.

Pipamazine: All drug products containing pipamazine.

Potassium arsenite: All drug products containing potassium arsenite.

Potassium chloride: All solid oral dosage form drug products containing potassium chloride that supply 100 milligrams or more of potassium per dosage unit (except for controlled-release dosage forms and those products formulated for preparation of solution prior to ingestion).

Povidone: All intravenous drug products containing povidone.

Reserpine: All oral dosage form drug products containing more than 1 milligram of reserpine.

Sparteine sulfate: All drug products containing sparteine sulfate.

Sulfadimethoxine: All drug products containing sulfadimethoxine.

Sulfathiazole: All drug products containing sulfathiazole (except those formulated for vaginal use).

Suprofen: All drug products containing suprofen (except ophthalmic solutions).

Sweet spirits of nitre: All drug products containing sweet spirits of nitre.

Temafloxacin hydrochloride: All drug products containing temafloxacin.

Terfenadine: All drug products containing terfenadine.

3,3',4',5-tetrachlorosalicylanilide: All drug products containing 3,3',4',5-tetrachlorosalicylanilide.

Tetracycline: All liquid oral drug products formulated for pediatric use containing tetracycline in a concentration greater than 25 milligrams/milliliter.

Ticrynafen: All drug products containing ticrynafen.

Tribromsalan: All drug products containing tribromsalan.

Trichloroethane: All aerosol drug products intended for inhalation containing trichloroethane.

Troglitazone: All drug products containing troglitazone.

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Urethane: All drug products containing urethane.

Vinyl chloride: All aerosol drug products containing vinyl chloride.

Zirconium: All aerosol drug products containing zirconium.

Zomepirac sodium: All drug products containing zomepirac sodium.

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<sup>1</sup> This guidance has been prepared by the Office of Regulatory Policy and the Office of Compliance in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

<sup>2</sup> With respect to such activities, 21 U.S.C. 360(g)(1) exempts retail pharmacies from the registration requirements of the Act. The exemption applies to "Pharmacies" that operate in accordance with state law and dispense drugs "upon prescriptions of practitioners licensed to administer such drugs to patients under the care of such practitioners in the course of their professional practice, and which do not manufacture, prepare, propagate, compound, or process drugs or devices for sale other than in the regular course of their business of dispensing or selling drugs or devices at retail" (emphasis added). See also 21 U.S.C. §§ 374(a)(2) (exempting pharmacies that meet the foregoing criteria from certain inspection provisions) and 353(b)(2) (exempting drugs dispensed by filling a valid prescription from certain misbranding provisions).

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# MMWR

Weekly

October 12, 2007 / 56(40);1050-1052

## Deaths from Intravenous Colchicine Resulting from a Compounding Pharmacy Error --- Oregon and Washington, 2007

Colchicine for injection has been available in the United States since the 1950s. Although not approved by the Food and Drug Administration (FDA), intravenous (IV) colchicine has been an accepted treatment for acute gout symptoms. Several additional IV uses have been studied, including treatment of familial Mediterranean fever, pericarditis, primary biliary cirrhosis, amyloidosis, and Behçet's syndrome (1--3). More recently, outpatient use of IV administration for chronic back pain has been advocated by alternative medicine providers but is not an accepted practice. Colchicine has well-known toxicities that limit its safe therapeutic use. IV doses that exceed the standard single-use therapeutic dose of 2--4 mg per episode of gout have resulted in life-threatening toxicity (2). In March 2007, two persons from Washington and Oregon died after receiving IV colchicine for back pain from an alternative medicine clinic in Oregon. This report describes the investigation, which determined that a measuring error by a Texas compounding pharmacy resulted in a fatal colchicine concentration that was eight times greater than the recognized standard level. A subsequent review of medical records revealed that a third death from colchicine toxicity in a patient treated at the Oregon clinic also occurred in March and likely was associated with the same compounding error. These deaths highlight the potential risk from use of IV colchicine for back pain and the possibly fatal consequences of measuring errors in compounding pharmacy products.

### Patient A, Washington

On March 19, 2007, a woman aged 77 years arrived at an emergency department (ED) with sudden onset of nausea, vomiting, numbness, and mild hypotension. She had been receiving treatment for back pain with what was intended to be 2-mg IV doses (4 mL of 0.5 mg/mL labeled concentration) of colchicine administered every other day in a 6-day period (i.e., 3 total doses). She had received part of her treatment at an alternative medicine clinic in Portland, Oregon, and then took IV colchicine to her home in Washington, where she received the third dose shortly before she became ill and sought treatment at the ED. She had obtained the colchicine from a relative who was an employee in the clinic where she received her initial treatment.

Initial laboratory test results revealed only slightly increased hepatic enzyme levels. The woman was admitted to the intensive care unit (ICU) for observation. The next day, her condition deteriorated, with onset of acute renal insufficiency, an elevated creatinine level (2.6 mg/dL), acidosis (pH = 7.07), leukocytosis (25,100/ $\mu$ L), abnormal liver function (aspartate aminotransferase [AST] = 1,933 units/L, alanine transaminase [ALT] = 2,295 units/L), rhabdomyolysis (creatinine kinase = 740 units/L), and myocardial toxicity (peak troponin I = 53.6 ng/mL).

The woman experienced severe abdominal pain and refractory hypotension; she died from cardiac arrest later the same day. Postmortem colchicine plasma level was 44 ng/mL; the therapeutic colchicine plasma level is <5 ng/mL (4).

### Patient B, Oregon

On March 30, 2006, a woman aged 56 years with a history of fibromyalgia and neck pain arrived at an ED with nausea, vomiting, profuse diarrhea, and chest pain. She had been receiving weekly IV colchicine for back pain from naturopathic and allopathic physicians at the same Oregon clinic as patient A. During the 2 preceding months, she had received a series of six weekly colchicine infusions, in doses intended to be 2 mg each, for an intended cumulative dose of 12 mg. Before arrival at the ED, she had just received the last dose at the clinic and had begun experiencing symptoms within an hour of infusion; a clinic staff member instructed her to go to the ED. Initial laboratory test results for blood urea nitrogen (BUN), creatinine, electrolytes, complete blood count, and troponin were within normal ranges, although her white blood cell (WBC) count was elevated (14,100/ $\mu$ L). The woman was admitted to the hospital for rehydration and continued observation. The leukocytosis increased to a peak count of 18,400/ $\mu$ L, with 40% band forms and evidence of myelocytes, metamyelocytes, and echinocytes on a peripheral smear. During the next 72 hours, she experienced leukopenia and thrombocytopenia (nadir WBC count = 1,400/ $\mu$ L, platelet count = 74,000/ $\mu$ L), renal insufficiency (BUN = 38 mg/dL, creatinine = 2.4 mg/dL), rhabdomyolysis (creatinine kinase = 1,485 units/L), lactic acidosis (venous lactate = 6.9 mmol/L), abnormal liver function (AST = 626 units/L, ALT = 290 units/L), and myocardial toxicity (peak troponin I of >50 ng/mL). A cardiac echocardiogram performed on the second hospital day indicated mild wall motion abnormalities with a normal ejection fraction. Her serum colchicine level 3 days after the last infusion was 11 ng/mL.

On the third hospital day, the woman was intubated because of worsening hypoxia and evidence of developing acute respiratory distress syndrome (ARDS) on chest radiograph. Her hemodynamic status deteriorated, and she became hypotensive, requiring dopamine and norepinephrine infusions to maintain a systolic blood pressure of 100 mmHg. During the day, she became increasingly anuric and hypoxic with worsening ARDS and was unable to maintain normal oxygen saturation levels, with a fraction of inspired oxygen (FiO<sub>2</sub>) of 100%. On the evening of the third hospital day, her oxygen saturation levels continued to decrease; she experienced bradycardia and cardiac arrest and died. Her postmortem colchicine blood level was 32 ng/mL.

### Investigation and Control Measures

Investigation into the causes of death of the two patients and a suspected third patient indicated that they each received IV colchicine infusions obtained from the same alternative medicine clinic in Oregon. The clinic had purchased the drug from a Texas compounding pharmacy.

The Washington case occurred when an employee in the clinic gave colchicine from the implicated lot to her relative (patient A) to take home. The patient had received previous infusions from different lots and had not become ill, but the infusion from the new lot resulted in sudden onset of symptoms on March 19. The unusual circumstances of the woman's death were discussed on March 26 at a weekly Oregon-Washington poison center teleconference, alerting toxicologists and poison centers in three states.

On March 30, the Oregon patient (patient B) was treated at the same alternative medicine clinic as patient A. On April 2, when staff members at the Oregon Poison Center were consulted about patient

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B, they notified the county public health department of the two cases. The Oregon Board of Naturopathic Examiners was notified and voluntarily posted a warning on its website the same day.

Investigators from the Oregon office of the state medical examiner learned that the deaths both occurred after the patients had received colchicine supplied by the Oregon clinic. The medical examiner's office confiscated from the clinic approximately 70 remaining vials of the colchicine, which were from several lots. Toxicology tests of colchicine vials from the same lot used to treat the patients indicated a concentration of 4 mg/mL. However, the vial labels indicated a concentration of 0.5 mg/mL; therefore, each intended infusion of a 2-mg dose of colchicine was actually 16 mg. The clinic supplied its medical records, including records of a third patient who was treated the same day as patient B and who also died. The clinic closed voluntarily in April 2007 and subsequently ceased operations.

The third suspected case occurred in a man aged 55 years who received a colchicine infusion on March 30 (the same day as patient B). He experienced severe vomiting, diarrhea, and chest pain within 1 hour of infusion and sought treatment at an ED. Because he had a history of coronary heart disease and recently had received a cardiac stent, his initial evaluation included a coronary catheterization, which was normal. He died within 24 hours of receipt of his last colchicine infusion; his death was attributed initially to cardiac causes. Media coverage of the deaths associated with the Oregon clinic prompted a nurse who had treated this man to call the poison center and report possible colchicine toxicity. After the investigation, the medical examiner reissued the man's death certificate, listing colchicine toxicity as cause of death. Although an autopsy was performed, no body fluids were available to confirm colchicine toxicity.

After the drug concentration in the colchicine vials used was determined to be eight times the labeled concentration, investigators attributed the deaths to an error at the Texas compounding pharmacy. On April 30, in coordination with FDA, the Texas State Board of Pharmacy issued a recall of all colchicine that had been sold or produced by the compounding pharmacy within the last year and shipped throughout the United States. No other cases have since been linked to this product.

**Reported by:** NJ McKeown, DO, BZ Horowitz, MD, F Garlich, MD, Oregon Poison Center; CR Young, MD, Oregon Medical Examiner. WO Robertson, MD, Washington Poison Center.

### Editorial Note:

FDA policy allows an ingredient from an FDA-approved drug to be compounded to fill a prescription from a licensed practitioner for use by a specifically named patient. Compounding pharmacies are either registered or licensed by state pharmacy boards. Compounded drugs are not evaluated for safety and efficacy and, unlike pharmaceutical manufacturers, traditional compounding pharmacies are not inspected by FDA to ensure that they have the capacity to consistently produce high-quality drugs. However, certain compounding pharmacies that engage in large-scale manufacturing are subject to regulations that FDA imposes on pharmaceutical manufacturers.

Although FDA has approved drugs that contain a combination of colchicine and probenecid for oral use, no FDA-approved colchicine products for IV use exist. The Texas State Board of Pharmacy and the Texas attorney general are investigating the deaths described in this report; the Oregon attorney general has issued an injunction against the Texas pharmacy from doing business in Oregon.

Colchicine, a naturally occurring alkaloid derivative of the autumn crocus *Colchicum autumnale* and the glory lily *Gloriosa superba*, has been used to treat gout for centuries. The drug has a narrow

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therapeutic range; in toxic levels, colchicine can disproportionately affect rapidly dividing cells and have substantial effects on multiple organ systems. In 2005, the American Association of Poison Control Centers Toxic Exposure Surveillance System reported 312 exposures and four deaths related to colchicine (5), annual totals that had remained stable during the preceding 15 years (6). A review of FDA Adverse Event Reporting System data from 1983 to 2000 indicated that IV administration of colchicine in amounts that exceeded the maximum recognized dose resulted in 20 deaths from colchicine toxicity, 17 of these during treatment for gout (2). In 2001, an incident involving an error of 10 times the standard therapeutic dose occurred in Pennsylvania and resulted in an FDA recall from an Arizona compounding pharmacy (7).

The recognized maximum cumulative IV dose is 4 mg for a single course of therapy, with a 7-day colchicine-free interval after each full IV course (8). However, deaths have been reported with cumulative doses as low as 5.5 mg (2). Older adults, patients with preexisting renal and hepatic failure, and patients with concomitant use of nonsteroidal antiinflammatory drugs or oral colchicine might have a higher risk for toxicity and death (2).

Use of colchicine for treatment of low back pain and intervertebral disc herniation was described initially in the 1970s. A single case series in 1979 suggested some effectiveness with low doses of oral and IV colchicine in reducing pain (9); subsequent prospective double-blind studies showed no improvement over placebo with oral use (10) and only short-lived improvement with IV therapy (3). Nevertheless, numerous Internet sources continue to recommend use of IV colchicine for back pain, referencing these early studies as evidence of the drug's effectiveness.

The cases described in this report highlight the risk for serious health consequences from use of IV colchicine for back pain. Although no FDA-approved indication for use of IV colchicine exists, multiple clinics continue to offer such therapy for various musculoskeletal disorders. These deaths underscore the potentially fatal ramifications of errors by compounding pharmacies, which generally are not subject to the same oversight and manufacturing practices as pharmaceutical manufacturers. The public health response to these drug-related deaths and the sharing of public health information among several states, which included poison control centers, medical examiners' offices, and county health departments, likely prevented additional deaths.

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