

WORKING P A P E R

Use of Compound Drugs, Medical Foods, and Co- Packs in California's Workers' Compensation Program

An Overview of the Issues

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PREFACE

The purpose of this paper is to explore the issues surrounding the use of compound drugs, co-packs and medical foods under the California workers' compensation (WC) program and to assess whether policy changes are needed to promote medically appropriate and efficient use of these products.

There is considerable controversy over the growing use of compound drugs by WC patients. The Chairs of the Committees with jurisdiction over WC asked the Commission on Health and Safety and Workers' Compensation (CHSWC) to prepare a background paper on the use of compound drugs, co-packs and medical foods. CHSWC asked RAND for assistance in preparing the paper. RAND is engaged in on-going evaluation of the impact of recent changes affecting medical care provided California's injured workers. Some of the preliminary findings from that study informed the preparation of this paper and conversely, some of the findings in this paper will be included in the final report for the other study. This paper should be of interest to policymakers and others interested in medical care provided under California's workers' compensation program.

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SUMMARY

There is considerable controversy over the growing use of compound drugs, medical foods, and co-packs for workers' compensation (WC) patients. Pharmacy compounding has traditionally involved combining drug ingredients to meet the needs of specific patients for medications that are not otherwise commercially available. Unlike commercially available drugs, these products are not approved by the Food and Drug Administration (FDA) but rather are regulated by the state pharmacy board. Recently, some pharmacies have been making and marketing stock compound drugs for the WC patient population. Similarly, the use of medical foods (a food that is specially formulated and processed for seriously ill patients with a specific medical condition with distinctive nutritional requirements) and co-packages (co-packs) of a medical food and a generic drug is rapidly increasing among WC patients. A recent report issued by the California Workers' Compensation Institute (CWCI) found that payments for compound drugs, convenience packaging of drugs and medical foods (co-packs), and medical foods grew from 2.3 percent to 12.0 percent of medication expenses between the first quarter of January 2006 and the first quarter of 2009 (Ireland & Swedlow, August 2010).

Multiple parties are involved in delivering and paying for these products, each with financial interests at stake in how the products are used in California's WC program. Other health programs have adopted policies that provide more assurance that drugs are medically appropriate and payments are reasonable. As a result, they are not experiencing comparable issues related to use of these products.

The issues surrounding compound drugs, medical foods, and co-packs rest on uncertainties regarding whether the products are medically appropriate and whether payments are reasonable. Clarifying the rules and removing inappropriate financial incentives should help assure that workers receive the drugs and other pharmaceuticals that are needed to "cure or relieve" their illness or injury.

Medical Necessity. With respect to the medical necessity issues, the WC program needs general coverage requirements for compound drugs and medical foods and other nutritional products. The criteria could draw from FDA policy guidance on compounding drugs and the National Association of Boards of Pharmacy's Model Act. For example, the provision might require that the finished drug product:

- Include a least one drug substance (or active ingredient) that is the sole active ingredient in an FDA-approved drug. This would eliminate OTC compound drugs.
- Include only active ingredients that are components of FDA-approved drugs that have been made in an FDA-registered facility. This would allow compounding only of bulk ingredients that are used in FDA-approved finished products and are manufactured in FDA-registered facilities.
- Is not a drug that was withdrawn or removed from the market for safety reasons.
- Is not a copy of a commercially available FDA-approved drug product.
- Include only active ingredients that have been supported as safe and effective for the prescribed indication by the FDA-approval process or by adequate medical and scientific evidence in the medical literature. This would allow off-label usage when supported by medical evidence but also clarify that a product is not covered unless there is evidence to support that it is medically appropriate.
- Prior authorization could be required when the active ingredient is not addressed in the Medical Treatment Utilization Schedule (MTUS) guidelines adopted by the Administrative Director.

The MTUS should be updated and expanded to address compound drugs as a product class. In addition to addressing the evidence-base

supporting the efficacy of ingredients frequently used in compounding, the guidelines should consider whether FDA-approved drugs should be tried prior to prescribing the compound drug and whether restrictions are appropriate on consecutive dispensing of 72-hour supplies of compound drugs (assuming the practice continues to be allowed). Similarly, the MTUS should address the medical appropriateness of medical foods. MTUS guidelines should not be necessary for co-packs as long as medical foods are addressed; instead, as discussed below, the Official Medical Fee Schedule (OMFS) allowances for these products should be clarified.

OMFS allowances. Review of sample bills and OMFS pricing policies indicates there is problem with how bulk ingredients are priced. The allowances in the MediCal database are based on average wholesale prices (AWP or self-reported "sticker" prices) for a single manufacturer. The OMFS is vulnerable to establishing excessive allowances as long as pricing relies on these AWP's and does not take advantage of multi-source pricing. Excessive allowances create incentives to market compound drugs to the WC population. This issue could be addressed by using an approach that is similar to the pricing formula used to establish the federal upper limit on multi-source drugs provided under Medicaid. Clarification is also needed to address ingredients that are not included in the MediCal database. For co-packs, consideration should be given to adopting the principle underlying the repackaged drug policy: base the allowance for the co-pack on the individual pricing for the medical food and the generic drug.

Physician incentives. Physician-dispensing creates financial incentives that affect the use of compound drugs and the other products results. California's pharmacy code (beginning at Business & Professions Code section 4000) includes within the definition of pharmacy compounding the preparation of drugs "for distribution of not more than a 72-hour supply to the prescriber's patients, as estimated

by the prescriber.” Review of sample bills indicates there may be issues with both the quantity and the frequency of the drugs that are dispensed by some physicians. Recognizing patient convenience is a reason for dispensing the initial supply, a reasonable approach would be to cover an initial physician-dispensed supply but not refills.

The financial incentives for physician-dispensing of compounded drugs could also be reduced significantly by limiting the amount payable under the OMFS to the amount that the provider paid for the products plus a reasonable mark-up. Even if the policy were not applied to compound drugs, it should be considered for medical foods for which there are no quantity limitations on physician-dispensing and determining an appropriate price is problematic.

Financial incentives may also be involved in physician prescribing of pharmacy-dispensed compound drug products and medical foods. California Labor Code section 139.3 precludes a physician from referring patients for certain designated services (e.g. clinical laboratory and diagnostic imaging) if the physician or his immediate family has a financial interest with the entity that receives the referral. Adding pharmacy goods and services (including OTC drugs and nutritional products) to the list of designated services would provide more assurance that prescribed products are medically appropriate.

California’s WC experience with repackaged drugs suggests that “quick fixes” may address issues in the short-term but that the issues are likely to re-emerge in another fashion unless the underlying incentives are addressed. The use of repackaged drugs declined significantly when it was no longer profitable for physicians to prescribe them. However, fixing the payment policy on physician-dispensing of repackaged drugs fueled the increased use of compound drugs, medical foods, and co-packs. The benefits gained from making policy changes to ensure these products are medically appropriate and payments are reasonable are also likely to be temporary unless greater attention is given to improving the overall incentives through selective contracting with high-quality efficient providers and appropriately rewarding their performance.

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I am grateful to the individuals who shared their perspectives on the use of compound drugs, medical foods and co-packs in the workers' compensation program and provided relevant documents that facilitated an understanding of current policies and issues. This paper could not have been prepared without their contributions. Christine Baker, Executive Director of the Commission on Health, Safety, and Workers' Compensation and Judge Lachlan Taylor on the Commission staff provided needed assistance in scheduling interviews and obtaining sample bills for review. I appreciate the insightful comments provided by RAND colleagues Susan Gates and Paul Heaton on an earlier draft of this working paper and the assistance provided by Christina Walker in conducting internet searches and preparing the paper for publication.

LIST OF ACRONYMS

Acronym	Definition
AWP	Average wholesale price
CHSWC	Commission on Health and Safety and Workers' Compensation
CMS	Centers for Medicare and Medicaid Services
CWCI	California Workers' Compensation Institute
DWC	Division of Workers' Compensation
FDA	Federal Drug Administration
MTUS	Medical Treatment Utilization Schedule
"N"	Not recommended
NDC	National Drug Code
NSAID	Non-steroidal anti-inflammatory drugs
ODG	Official Disability Guidelines
OMFS	Official Medical Fee Schedule
OTC	Over-the-counter
PBM	Pharmacy benefits manager
WC	Workers' compensation

1. INTRODUCTION

A recent report issued by the California Workers' Compensation Institute (CWCI) found that payments for compound drugs, convenience packaging of drugs and medical foods (co-packs), and medical foods grew from 2.3 percent to 12.0 percent of medication expenses between the first quarter of January 2006 and the first quarter of 2009 (Ireland & Swedlow, August 2010). According to the CWCI report, the average amount paid during the first quarter of 2009 was \$551 for a compound drug, \$420 for a co-pack, and \$322 for a medical food.

There is considerable controversy over the growing use of compound drugs for WC patients. During the 2010 legislative session, AB 2779 (Solario) was introduced (but did not come to a general vote after committee review) that would have tightened the coverage requirements and fee schedule allowances for compound drugs (California State Assembly, 2009-2010). Subsequently, the Chairs of the Committees with jurisdiction over WC asked the Commission on Health and Safety and Workers' Compensation (CHSWC) to prepare a background paper on the use of compound drugs, co-packs and medical foods (DeSaulnier & Solorio, September 17, 2010). CHSWC was asked to address the differences in utilization of these products in WC compared to other healthcare systems and to include if possible policy recommendations. CHSWC asked RAND for assistance in preparing the paper.

In this working paper, we consider the following questions:

- What are compound drugs, co-packs and medical foods? How are they regulated?
- What products are commonly furnished to WC patients? Are they safe and effective? When are they medically necessary and appropriate?
- How is payment determined under the Official Medical Fee Schedule (OMFS)?
- What tools do payers and employers have to ensure the products are medically appropriate and payments are reasonable?

- Are other health programs experiencing comparable increases in the use of compound drugs? How do the tools and policies that they use compare to those used under WC?
- Are there policy shortcomings in the WC program that should be addressed and if so, how?

Information for this working paper was gathered through an environmental scan of articles in the medical literature and trade press and information obtained from relevant websites such as those of compounding pharmacies, the Division of Workers' Compensation (DWC), and other health programs. Examining these issues is challenging because multiple parties are involved in delivering and paying for these products, each with financial interests at stake in how the products are used in California's WC program (see Figure 1). To obtain the insights from individuals with different perspectives on the use of compound drugs, medical foods, and co-packs for the WC population, a limited number of interviews was conducted with one or more individuals from most of the groups listed in Figure 1: providers, payers, third-party billers, and pharmacy benefits managers (PBM) as well as other experts on the use of these products. Injured workers and compounding pharmacies were not interviewed but a pharmacist was consulted in reviewing sample bills. Resource constraints precluded an independent systematic review of the medical literature regarding the safety and efficacy of specific compound drug products and analyses of WC administrative data.

Figure 1. Key Participants in Dispensing and Paying for Compound Drugs Under the Workers' Compensation Program

Patients: An injured worker is entitled to receive all medical care reasonably required to cure or relieve the effects of his or her injury free of charge. The patient is focused on receiving effective care and does not have a direct financial interest in assuring that it is furnished in the least costly manner. Because of convenience, the patient may prefer prescription and physician-dispensed drugs that are billed directly to the payer and want to avoid out-of-pocket expenses for OTC drugs that must be submitted to the payer for reimbursement. In the long term, workers have an indirect interest in controlling WC costs because these costs ultimately affect wage and benefit levels.

Pharmacies: Any pharmacy that meets state law requirements can compound drugs; a pharmacy that specializes in the practice is known as "compounding pharmacy." Some pharmacies produce and stock standard compound drug products that are marketed to physicians instead of products that are customized based on each patient's individual needs.

Physicians: Under California law, physicians are authorized to dispense up to a 3-day supply of compound medications. In-office dispensing offers an additional revenue stream for physicians to supplement their revenues from providing patient care services.

Pharmacy benefit managers (PBMs): PBMs manage most WC drug benefits in California. They operate under contract with payers to manage pharmacy claims by establishing formularies, authorizing benefits, and negotiating prices with network pharmacies. The PBM retains the difference between what it pays for drugs and the contracted amount (typically a discount off the OMFS allowance). The PBM has a financial interest in keeping administrative costs down and OMFS allowances above market prices for drug products. The difference between the market price and OMFS allowance provides a margin for financing operations and receiving a return on investment. As a result, PBMs also have an interest in keeping claims in-network so that they can take advantage of negotiated prices.

Payers (insurers and self-insured employers): Employers or their insurers are responsible for providing all medical care reasonably required to cure or relieve the effects of a workplace injury. Payers have a financial interest in controlling drug costs by denying medically unnecessary or unreasonably priced drug products in the least administratively burdensome manner.

Pharmacy management companies: These organizations purchase outstanding bills at a discount (e.g., bills for compound drugs dispensed by physicians or pharmacies). They may submit bills (and pursue settlements through the lien process when necessary) directly or use a third party biller. They benefit from continuing uncertainty in coverage and payment determinations for compound drugs and substantial differences between the cost to the provider (pharmacy or physician) for dispensing compound drugs and amounts payable by the WC program.

Brokers: These organizations act as a broker between the physician and the pharmacy. They typically arrange for the pharmacy to provide stock compound drugs to a physician and purchase the accounts receivable from the dispensing physician. They may bill directly but often use a third-party biller to collect from the WC payer.

2. COMPOUND DRUGS, MEDICAL FOODS AND CO-PACKS

COMPOUND DRUGS

What are compound drugs? How are they regulated?

Pharmacy compounding has traditionally involved combining drug ingredients to meet the needs of specific patients for medications that are not otherwise commercially available. It has been undertaken on a patient-by-patient basis for patients who, for example, might be allergic to inactive ingredients in FDA-approved drugs or may need a different dosage strength or route of administration.

The Federal Drug Administration (FDA) has the responsibility for assuring that prescribed and over-the counter (OTC) commercially sold drugs in the United States are "safe and effective." Prescription drugs must go through a pre-marketing new drug approval process. FDA-approval is for specific indications. For example, the FDA has approved a topical 1.5% diclofenac solution for the treatment of osteoarthritis of the knee and a topical diclofenac sodium gel for osteoarthritis pain amenable to topical treatment, such as pain of the hands or knees. Physicians often prescribe *off-label* usage of the drugs for other indications.

FDA-approved commercially available drug products may include a combination of ingredients. An example of a high-volume WC drug with more than one ingredient is hydrocodone/acetaminophen. These FDA-approved products should be distinguished from products created by compounding of two or more ingredients by a pharmacy.

The FDA does not regulate pharmacy-compounded products in recognition of the important public health function performed by traditional compounding (United States Food and Drug Administration, May 31, 2007). Rather, compounding pharmacies are subject to state laws governing the practice of pharmacy. However, some specialized pharmacies have been making and distributing compound drugs for a broader patient population that the FDA argues should be subject to its

approval process for new drugs. See Figure 2 for the "red flags" that the FDA considers in deciding whether to take an enforcement action, We have included only those that are potentially relevant to WC policies. (United States Food and Drug Administration, 2010)

Figure 2. Selected FDA "Red Flags" for Enforcement Action on Compounded Drugs

1. Compounding drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to amounts compounded after receiving valid prescriptions.
2. Compounding drugs that were withdrawn or removed from the market for safety reasons.
3. Compounding finished drugs from bulk active ingredients that are not components of an FDA-approved drug.
4. Using drug substances without assuring they were manufactured in FDA-approved facilities.
5. 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.
6. Compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products.

CPG 460.200 Pharmacy Compounding Compliance Policy Guides Manual

Most OTC drugs marketed in compliance with FDA regulatory standards for labeling and ingredients within a specific category or "therapeutic class" are deemed to be "safe and effective" and do not need separate approval. The FDA standards include guidance for when OTC drugs may be combined by manufacturers. Generally, active ingredients in the same therapeutic class should not be combined unless the combination offers some advantage over the active ingredients used alone at its therapeutic dose (United States Federal Drug Administration, 1978).

An establishment that manufactures, prepares, compounds, processes or repackages drugs is required to register annually with the FDA and provide a current list of all drugs it produces for commercial

distribution (United States Food and Drug Administration, February 2008, May 2007; United States Food and Drug Administration, Office of the Commissioner, May 2009). A registered establishment is subject to inspection at least every two years. Each product is identified through a unique, three-segment number, called the National Drug Code (NDC), which is a universal product identifier for human drugs. The NDC code contains information on the drug labeler (manufacturer, relabeler, or repackager), product (specific strength, dosage form, and formulation for a particular labeler) and package size. Every FDA-approved drug must have a NDC code, but having a code does not mean that the product is FDA-approved. Compound drug formulations commonly use bulk drug substances (comparable to active ingredients in FDA-approved drugs), each of which should have a unique NDC (if it has been properly listed with the FDA). However, bulk ingredients are not FDA-approved because they are not commercially available finished drug products. Also, pharmacies that operate under applicable local law and only manufacture, prepare, propagate, compound, or process drugs for sale in the regular course of pharmacy are exempt from registering and listing the drugs with the FDA.

The relevant provisions of the California regulations pertaining to pharmacy compounding largely mirror the FDA distinctions between compounding drugs (subject to state law) and manufacturing drugs (subject to FDA approval as "safe and effective"). The Code specifies that no drug will be compounded prior to receipt by the pharmacy of a valid prescription for an individual patient; however, it also allows a pharmacy to prepare and store a limited quantity of a compounded drug product in advance of receipt of a patient-specific prescription if it is necessary to ensure continuity of care for an identified population of patients of the pharmacy based on a documented history of prescriptions for that patient population. Further, the Code allows the pharmacy to furnish a "reasonable quantity" of compounded drug product to a prescriber for in-office use or dispensing (not more than a 72-

hour supply).¹ Thus, a physician preference for a particular formulation, rather than the specific needs of an individual patient, can lead to a pharmacy producing a large quantity of compound drugs for either direct or in-office dispensing.

What products are commonly furnished to WC patients?

The most commonly prescribed compound drugs used by WC patients are topical analgesic creams and lotions. The products are challenging to identify in administrative databases because the compound product does not have a single NDC identifier; rather, each ingredient is listed separately by its NDC code. The CWCI analysis relied on the NDC listing maintained by the Centers for Medicare and Medicaid Services (CMS) for bulk drug ingredients to identify potential compound drugs. The most common bulk ingredients identified in the CWCI analysis are listed in Table 1 below. These may be combined with other substances, including menthol (which creates a cooling sensation), methyl salicylate (an anti-inflammatory that creates a warming sensation), and camphor (an anti-itch agent). Figure 3 shows information from a compound pharmacy website suggesting how topical gels might be combined. Not all compound products involve a prescription drug. For example, Physician's Science and Nature produces an OTC topical pain relief lotion Dendracin Neurodendraxcin®, which combines three drug substances, none of which individually require a prescription: methyl salicylate, menthol, and capsaicin lotion. Under California's pharmacy rules, however, only prescription drugs can be compounded so that this product is not available over-the-counter and can only be dispensed by prescription.

¹ The 72-hour limit conforms to a provision in the Business and Professions Code section 4052(a) (1) limiting physician dispensing of compound drugs to no more than a 72-hour supply.

Figure 3. Topical Compound Products Listed At www.theapothecaryshop.com/pain-topical-gels.html 		
TYPICAL COMBINATIONS	DRUG	STRENGTH
K.I.C.K. Gel	Ketoprofen	10%
	Ibuprofen	10%
	Cyclobenzaprine	2%
	Piroxicam	2%
K.I.C.K.-II Gel (Alternate)	Ketoprofen	10%
	Ibuprofen	10%
	Cyclobenzaprine	2%
	Piroxicam	2%
	Lidocaine	5%
Keto/Lido	Ketoprofen	20%
	Lidocaine	10%
Ketamine/Lido	Ketamine	10%
	Lidocaine	10%
Keto/Gaba/Clon	Ketoprofen	20%
	Gabapentin	6%
	Clonidine	0.2%
Keto/Gaba/Clon	Ketoprofen	10%
	Ketamine	10%
	Amitriptyline	2%
	Baclofen	2%
	Clonidine	0.2%
	Gabapentin	6%
Benzo/Lido/Tetra	Benzocaine	20%
	Lidocaine	10%
	Tetracaine	6%

While traditional compound drugs are customized for individuals, the environmental scan conducted for this paper found indications that products are pre-compounded and mass-marketed in California. Figure 4

shows an order form for physician-dispensed compound topical ointment. What constitutes a 3-day supply is left to physician judgment, in this case, 30 grams (~ 2.4 oz) or 60 grams (~ 4.8 oz). The amount that constitutes a three-day supply depends on the labeling regarding dosage amount and frequency and the affected area. As a "customized" drug, the information is not readily available to make this assessment. It is assumed that the physician will discuss the dosing requirements when dispensing the product; there are no detailed labeling requirements for the compound. For an FDA-approved drug, however, this information would be easily obtainable in not only the packaging information provided with the drug but also on the FDA and other medical websites.

Figure 4. Sample Order Form for Compound Drug Products

RX COMPOUND 72-HOUR SUPPLY ONLY				
COMPOUND	DESCRIPTION	GRAM SIZE		QTY
AMITRIPTYLINE - DT	Amitriptyline - Dextromethorphan - Tramadol 4/20/5 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
AMITRIPTYLINE - TL	Amitriptyline - Tramadol - Lidocaine 5/15/2 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
CAPSAICIN - D3	Capsaicin - Diclofenac Sodium - Camphor - Menthol 0.0375/30 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
CAPSAICIN - T3	Capsaicin - Tramadol - Camphor - Menthol 0.0375 /15 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
CAPSAICIN - DT3	Capsaicin - Diclofenac Sodium - Tramadol - Camphor - Menthol 0.0375 /30/4 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
DICLOFENAC 30 %	Diclofenac Sodium 30 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
FLURBIPROFEN - D	Flurbiprofen - Diclofenac 20/10 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
FLURBIPROFEN - D ²	Flurbiprofen - Diclofenac - Dexamethasone 20/10/0.4 %	<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	
OTHER (LIST INGREDIENTS, STRENGTH, & DIRECTION)		<input type="checkbox"/> 30 gm	<input type="checkbox"/> 60 gm	

Are compound drugs safe and effective? When are they medically appropriate?

As noted earlier, traditional compounding is regulated by state law governing the practice of pharmacy. Unlike other drug products, compound drugs do not require a FDA determination that the product is

"safe and effective." Instead, California's regulations hold the pharmacy accountable for monitoring and ensuring the integrity, potency, quality, and labeled strength of compounded drug products. Nevertheless, the FDA has expressed concern that poor pharmacy practices might result in contamination or products that lack the required strength, quality, and purity. Because pharmacies are not required to report adverse events associated with the compound drugs to either the FDA or the state, there is no systematic collection of information on potential safety issues with compound drugs (United States Food and Drug Administration, 2006; May 31, 2007).

Topical analgesics provide relief by acting locally over the painful site with lower risk of systemic adverse effects on the gastrointestinal system and drug interactions than oral non-steroidal anti-inflammatory drugs (NSAIDs). Table 1 summarizes the policies related to the use of topical analgesics under the Medical Treatment Utilization Schedule (MTUS) guidelines for chronic pain adopted by the Division of Workers' Compensation (DWC) (California Division of Workers' Compensation, July 18, 2009). The MTUS guidelines set presumptive standards for the duration and scope of medically appropriate care but are potentially refutable if it can be shown that the preponderance of the scientific evidence establishes that a variance from the guidelines is reasonably required to cure or relieve the injured worker's condition. The guidelines are an adaptation of evidence-based treatment guidelines from the Work Loss Data Institute's Official Disability Guidelines (ODG) Treatment in Workers' Comp - Chapter on Pain (Chronic) and were adopted effective July 18, 2009 (California Division of Workers' Compensation, July 18, 2009). The guidelines indicate that topical analgesics as a class are largely experimental in use with few randomized controlled trials to determine efficacy or safety. The guidelines specify that a compounded product is not recommended if it contains a drug (or drug class) that is not recommended. Most high volume compound drug ingredients identified in the CWCI analysis are not recommended because there is no evidence base to support their use (e.g., gabapentin, baclofen) or are recommended

only after other treatments have been tried unsuccessfully (capsaicin, lidocaine, ketamine HCL).

Table 1. Summary of MTUS Chronic Pain Guidelines Related to Topical Analgesics

Gabapentin	Not recommended. There is no peer-reviewed literature to support use.
Ketoprofen	Not recommended. It has a high incidence of photocontact dermatitis. Topical treatment can result in systemic effects comparable to the oral forms.
Capsaicin	[OTC] Recommended only as an option in patients who have not responded or are intolerant to other treatments. No current indication that the 0.0375% formulation provides any further efficacy than a 0.025% formulation.
Cyclobenzaprine HCL	[Not addressed in topical application] Cyclobenzaprine as an oral form is recommended as an option, using a short course of therapy. The addition of cyclobenzaprine to other agents is not recommended.
Lidocaine	Recommended for localized peripheral pain after there has been evidence of a trial of first-line therapy (using anti-depressants or anti-convulsants).
Ketamine HCL	Only recommended for treatment of neuropathic pain in refractory cases in which all primary and secondary treatment have been exhausted.
Flurbiprofen	[NSAID not expressly addressed in guidelines]
Baclofen	Not recommended. There is no peer-reviewed literature to support use.

MEDICAL FOODS AND CO-PACKS

A medical food product is specially formulated and processed for the patient who is seriously ill or who requires the food as a major treatment modality and is:

- A food for oral or tube feeding.
- Labeled for the dietary management of a specific medical condition "for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation."
- Intended for use under a physician's supervision. (United States Food and Drug Administration, May 2007)."

Medical foods must:

- Be labeled with a statement of identity and content but are exempt from the labeling requirements for health claims and nutrient content claims.
- Comply with all applicable requirements for the manufacture of foods. Ingredients must be approved food additives or a food additive exempt for investigational use.

The FDA has a specific compliance program for medical foods but individual products are not approved or registered with the FDA. ²

Co-packs are convenience packaging of a medical food product and a generic drug into a single package that requires a prescription. The labeler then creates a new NDC for the co-pack. While the generic drug is FDA-approved, the co-pack of a medical food and FDA-approved drug is not unless the manufacturer obtains FDA approval for the product as a new drug. The FDA has issued warning letters to Physician Therapeutics LLC, a Los Angeles-based packager of co-packs to seek approval for its co-packs or cease marketing them (see Appendix D) (Cruse, April 8, 2010). Physician Therapeutics LLC was identified in the CWCI analysis as the main producer of medical foods and co-packs for California's WC program (Ireland & Swedlow, August 2010).

² Facilities that manufacture/process or pack foods are also required to register with the FDA.

What products are commonly furnished to WC patients?

Table 2. Description of Common Medical Foods and Co-Packs Provided to WC Patients

Medical Food	Ingredients	Marketing Summary
Theramine®	GABA, arginine, choline, glutamine, grape seed extract, cocoa, cinnamon, histidine, serine, 5-HTP, and hydrolyzed whey protein	Designed to aid in nutritional management of chronic pain syndromes including fibromyalgia.
GABAdone®	Choline Bitartrate, Glutamic Acid, 5-Hydroxytryptophan, GABA, Grape Seed Extract, Griffonia Extract, Whey Protein, Valerian Extract, Ginkgo Biloba and Cocoa	Designed to provide dietary management of sleep disorders.
Sentra PM®	Choline, acetylcholine, 5-HTP, ginkgo biloba, glutamic acid, cocoa, and dextrose	Designed to provide dietary management of sleep disorders.
Sentra AM®	Choline, acetylcarnitine, ginkgo biloba, glutamic acid, cocoa, and dextrose	Designed to provide dietary management of sleep fatigue.
Co-Packs	Ingredients	Marketing Summary
Theratramadol™	Theramine® & Tramadol	Designed for the management of moderate to moderately severe pain in adults
Theraproxen™	Theramine® & Naproxen	Used for pain management and relief of pain caused by arthritis, tendonitis, and other similar diseases
Theracodophen™	Theramine®, Hydrocodone & Acetaminophen	Used to relieve moderate to severe pain
Therabenzaprime™	Theramine® & Cyclobenzaprine	Designed for relief of muscle spasms
Gabitidine	Gabadone® & Fluoxetine	Used for the treatment of ulcers, esophogitis, and heartburn.

(Physician Therapeutics, 2010)

The top medical foods/co-packs distributed by Physician Therapeutics LLC to WC patients according to the CWCI analysis are shown in Table 2 together with summary of the marketing explanation of

the product from material submitted by the labeler or information on its website.

Are they safe and effective? When are they medically appropriate?

Medical foods are required to use only approved food additives and ingredients that are generally recognized as safe. Because the products do not require FDA-approval, there is a paucity of medical evidence to support whether they are effective. In this regard, Targeted Medical Pharma Inc, the parent company for Physician Therapeutics LLC has been awarded grants under the Affordable Care Act's Qualifying Therapeutic Discovery Projects program to examine the reduction of gastrointestinal bleeding with Theramine® and effectiveness of the Gabadone® and Sentra® products in addressing sleep-related issues.

The MTUS for chronic pain does not specifically address medical foods or co-packs. The ODG guidelines contain some recommendations on specific medical foods, but DWC did not incorporate them into the MTUS because the ODG guidelines did not provide information on how the medical food should be used for chronic pain (as opposed to co-morbid conditions such as sleep disorders) or evidence regarding treatment intensity.

3. DETERMINING PAYMENT UNDER THE OFFICIAL MEDICAL FEE SCHEDULE (OMFS)

California's OMFS for outpatient drugs is tied to the MediCal fee schedule for pharmaceuticals. The allowance is determined using a unit price (per metric decimal) based on the lowest cost for the ingredient or, if "no substitutions" is indicated on the prescription, a "no substitution" cost for the brand name.

- For simple prescriptions, the MediCal price is the applicable unit price times the number of metric decimal units plus a dispensing fee of \$7.25 for patients who are not in a nursing home. Most unit prices are based on 83% of the average wholesale price (AWP) for a drug. The AWP is the manufacturer's suggested "sticker price" for wholesalers to charge pharmacies. The AWP is self-reported data compiled by commercial publishers of drug pricing data, such as First DataBank's *Blue Book* and Thomson Medical Economics' *Red Book* and does not reflect actual pharmacy acquisition costs for drugs. Lower unit prices apply to certain multi-source (generic) drugs.
- For prescription compound drugs, MediCal determines the price for each ingredient separately (based on the applicable unit price and quantity) and adds a compounding fee based on the dosage form and route of administration and, if applicable, a sterility fee to the professional services fee.

The amount paid is the lesser of the computed price or the pharmacy's usual and customary charge to the general public for such prescriptions.

The MediCal billing form for compound drugs requires that an appropriate code be used for each ingredient listing on the billing form. If no NDC number exists for the ingredient, the pharmacy is instructed to enter a Universal Product Code or Universal Product number or, in the absence of any code, a brief description of the ingredient. When billing for a non-NDC ingredient, the pharmacy must attach a catalog page, invoice or other supporting document showing the

price and related quantity of the ingredient. Ingredients that are not on MediCal's List of Contract Drugs are paid at \$0 unless there has been prior authorization.

MediCal's general policy is that the payment rate for OTC drugs, which require a prescription before they are reimbursable, is determined using the same formula as for prescription drugs but without a dispensing fee. Compounded OTC products are not specifically addressed but OTC topical analgesics are not covered unless expressly listed in the List of Contract Drugs.

While the OMFS generally follows the MediCal fee schedule, WC-specific provisions are also relevant to determining policies for compound drugs. The MediCal formulary is limited to drug manufacturers who participate in its Medicaid drug rebate program and, as a result, not all drugs provided to WC patients appear in the MediCal database. The OMFS § 9789.40(b) provisions pertaining to drugs that do not appear in the MediCal database are found in Appendix B. Another difference is that the AD has decided not to require pharmacies to submit their usual and customary charge as defined by MediCal when billing for prescribed drugs.³ With regard to billing for compound drugs, DWC has issued instructions that have not been codified in regulations that specify:

- Each ingredient needs an NDC number.
- Ingredients for which there is no NDC number at all are not separately reimbursable. The assumption is that these are inactive ingredients such as distilled water.
- Ingredients whose NDC number doesn't appear in the Medi-Cal database should be priced per the methodology spelled out in section 9789.40.

³ California Welfare And Institutions Code Section 14105.455 defines usual and customary as the lower of a) the lowest price reimbursed to the pharmacy by other third-party payers in California, excluding Medi-Cal managed care plans and Medicare Part D prescription drug plans and b) the lowest price routinely offered to any segment of the general public.

The OMFS section 9789.40(b) provisions were added to address a loophole in the fee schedule for repackaged drugs that were procured from an original labeler and repackaged for in-office dispensing. However, there are several problems in applying these provisions to compound drugs, medical foods, and co-packs.

- *Compound Drugs.* For compound drug ingredients that have been assigned an NDC that is not in the MediCal database:
 - o The first pricing default is to use the NDC unit cost in the MediCal database for the underlying drug. This logic works for repackaged drugs where there is an underlying ingredient by definition, but it is not germane for most ingredients used in compounded drugs.
 - o The second pricing default is based the ingredient cost on 83 percent of the lowest priced therapeutically equivalent drug as determined in the FDA's *Orange Book*. Again, this logic works for repackaged commercially available prescription drugs but does not work well for compound drug ingredients. The *Orange Book* is limited to examining the therapeutic equivalence of FDA-approved prescription drug products. Bulk ingredients are not FDA-approved prescription drugs and are not ranked for therapeutic equivalence.
- *Medical Foods.* Neither of the default pricing schemes applies to medical foods because they are not FDA-approved drugs.
- *Co-packs.* The regulations and instructions do not explicitly address co-packs. However, the co-pack is essentially repackaging of two products and it could be argued that the two components of the co-pack should be priced separately based on the pricing defaults in § 9789.40(b). This would provide an allowance for the generic drug but not the medical food component of the product.

Figure 5. OMFS Pricing for Amitriptyline-DT Cream (30 grams)

NDC No	Label name	Price date (start)	Number of units	Unit price	Product
49452046001	AMITRIPTYLINE HCL POWDER	2/26/2009	1.2	12.6077	15.12924
49452249501	DEXTROMETHORPHAN POWDER	2/26/2009	6	12.3902	74.3412
51927340400	TRAMADOL HCL POWDER	1/3/2007	1.5	24.236	36.354
51927333800	PCCA LIPODERM BASE	6/1/2006	21.3	0.3735	7.95555

Total of ingredients: **\$133.78**

The compounding fee for route of administration form **Topical** with a dose MDU of **30** is \$0.00

The allowed sterility fee (lesser of the usual and customary sterility fee and the maximum sterility fee) for route of administration form **Topical** with a dose MDU of **30** is \$0.00

The dispensing fee for a patient **Not in** a nursing home on and after 9/1/2004 is \$7.25

The dosage compounding fee for dosage form **Cream** with a dose MDU of **30** is \$1.64

Therefore the total allowed compound dispensing fee is: **8.89**

Equals subtotal: **\$142.67**

Source: <http://www.dir.ca.gov/dwc/pharmfeesched/PFScompound.ASP>
Information is supplied on 1/18/2011 for a date of service of 5/21/2010.

To illustrate how the OMFS fee schedule policies work, we priced a bill for the first product listed in Figure 4. The information needed to price the product is taken from a script for 30 grams of Amitriptyline-DT cream that was included in a bill dated 5/21/2010 along with charges for Capsaicin-T3 (30 grams) and Flurbiprofen-D (30 grams). A copy of the bill is in Appendix C.1. DWC pricing from the MediCal fee schedule for this product indicates an OMFS allowance of \$142.67 for what should be no more than a 72-hour supply (Figure 5).

Table 3. MediCal Prices per Gram for Amitriptyline HCL Powder (as of 10/27/2010)

NDC	Labeler	Unit Price (\$)	Effective date
	Spectrum Chemical and Laboratory Products		
49452046001		12.6077	2/25/2009
51927160300	PCCA	10.458	9/1/2010
63275993602	B&B Pharmaceuticals, Inc.	7.968	9/1/2010
51552046402	Gallipot	2.0916	3/12/2008
62991200401	Letco Medical	1.494	9/26/2009

In this example, each ingredient in the cream had an NDC in the MediCal database. A short-coming of the pricing policy, however, is that the unit prices for the bulk ingredients are generally based on a single manufacturer's reported price, even when multiple sources are available. This leaves the door open for manufacturers to report excessively high AWP amounts. The AWP is a self-reported sticker price that is not verified by the commercial databases that are used for pricing pharmacy bills. Table 3 summarizes the unit prices in the MediCal database for one of the ingredients in the compound priced in Figure 4. The labeler (Spectrum Pharmacy) whose product was used in the compound has the highest unit price of the labelers in the MediCal database and also had the highest volume of compound drug bulk ingredients in the CWCI analysis. Moreover, using the price reported by a single manufacturer does not take advantage of the pricing rules that apply to multi-source generic drugs.⁴ The unit price for a 100 mg tablet of Amitriptyline HCL is .1568 in the MediCal database effective 1/12/09, i.e., the cost of 1.2 grams in an FDA-approved form is \$1.88 compared to \$15.13 for the same quantity as a bulk ingredient.

⁴ Under Medicaid rules, certain multi-source drugs are subject in the aggregate to an upper limit on the payment that will qualify for full federal participation in matching grants and others are subject to a state-imposed maximum allowable ingredient cost (MAIC) limit.

As noted earlier, not all active drug ingredients have been assigned an NDC. Nevertheless, OMFS regulations and instructions assume that all ingredients will have an NDC identifier. If non-NDC products are determined to be covered as safe and medically appropriate under the WC program, the prices could be determined consistent with MediCal pricing rules. However, some payers, including the Texas WC program, limit coverage to ingredients that have been assigned an NDC.

To better understand the billing and pricing issues raised by compound drugs, medical food and co-packs, we obtained a convenience sample of bills that had been submitted for both pharmacy-dispensed and physician-dispensed products. Portions of selected bills are found in Appendix C and are representative of other bills that we examined. The types of billing issues that they raise include:

- NDCs are not reported for all ingredients (Appendix C.2). This means the payer does not have the information required to process the bill and must return it for further development. It was not uncommon for the electronic bills that we reviewed to include only a single NDC with the breakdown of the total units by ingredient included in supporting documentation. This billing practice increases the likelihood that the bill will be improperly processed and overpaid paid using the price for the single NDC code (typically, a high cost ingredient) for the total number of units rather than the actual number of units for each ingredient.⁵
- Physician-dispensing of the same product multiple times (Appendix C.2). The underlying rationale for the California's Code provision that permits a physician to dispense up to 72-hour supplies of compound drugs is that it allows the patient

⁵ This may be occurring most often when billers and payers are not using the National Council for Prescription Drug Programs (NCPDP) version 5.1 standard for electronic billing of compound drugs. This standard allows for multiple ingredients to be listed by NDC while earlier versions did not.

to begin a course of treatment immediately before obtaining a larger supply from a pharmacy. The spirit of the law is violated when a physician dispenses the same product multiple times. We do not know whether the patient in the example also filled prescriptions at a pharmacy in between obtaining the compounds from the physician or made the "72-hour supply" last until obtaining a refill from the physician.

- The total number of units billed for the individual ingredients are inconsistent with the total number of reported units for the compound (Appendix C.4). This typically occurs when the bill reports the total number of units accurately but reports for individual ingredients the number of units reflected in the NDC rather than the actual number of units that were used. In the Appendix C.4 example, the bill reports 710 grams of various powders and granules being added to a 96 ml gel. While this is improbable (the product would be a heavy paste with unsafe amounts of drugs), the billing practice increases the probability that the bill will be overpaid. This is because the pricing algorithm multiplies the metric units for each ingredient by its unit price.

4. TOOLS TO ENSURE DRUGS ARE MEDICALLY APPROPRIATE AND PAYMENTS ARE REASONABLE

WHAT TOOLS ARE AVAILABLE TO WC PAYERS?

When payers are confronted with payment requests for compound drugs that fall outside of established medical and payment protocols, they have several tools for ensuring that payments are appropriate and reasonable. With regard to medical necessity determinations, Labor Code section 4600 stipulates that worker is entitled to "all medical care reasonably required to cure or relieve" the effects of the injury or illness. Labor Code section 4600b further stipulates that the MTUS adopted by the Administrative Director define the therapies that are reasonably required to cure or relieve work-related injuries. The guidelines are presumptively correct in medical necessity disputes but are rebuttable by "a preponderance of evidence establishing that a variance from the guidelines is reasonably required." For injuries not covered by the MTUS, Labor Code section 4604.5(e) requires that care be in accordance with "other evidence-based medical treatment guidelines recognized by the national medical community and that are scientifically based." As noted in Chapter 2, the MTUS chronic care guidelines contain recommendations on the medical appropriateness of some but not all ingredients used in common compound drugs. There are no explicit guidelines for when compound drugs, medical foods and co-packs are appropriate, in large part because there is a limited evidence base on which to establish treatment guidelines. Medical necessity disputes over these products revolve around whether the products should be covered only if there is evidence supporting that they are medically appropriate or whether they should be covered unless there is evidence that they are not safe and effective. If a payer wishes to contest the medical necessity of any product prescribed by a physician, it may do so only if it bears the cost of a formal utilization review process.

Most payers contract with pharmacy benefit management companies (PBMs) to manage their pharmaceutical claims and perform functions such as medical review, negotiating prices, providing a pharmacy network, and establishing a formulary. The range of functions performed by the PBM depends on the contractual arrangement between the PBM and payer. Compound drugs raise special challenges in managing the benefit. By definition, because they traditionally have been a customized product based on individual patient needs, compound drugs are generally not part of the PBM's formulary. As a result, when a pharmacy script is submitted electronically at point of sale by a network pharmacy, it triggers an approval process that delays processing. Some PBMs have processes to handle the script quickly while others transmit the script for review through the payer's normal prior authorization process. To avoid undue delay in providing the compound, some pharmacies go "out-of-network", dispense the compound drug, and submit a paper claim to the payer instead of using point-of-sale electronic processing through the PBM. Paper scripts are much more costly to process, more prone to result in duplicate payments, and when submitted out-of-network, bypass the PBM-negotiated prices. Moreover, physician-dispensed drugs do not go through the PBM but are submitted directly to the payer. Typically, the payer does not have the capacity to process these bills electronically and has to process them as paper claims. Delays in the bill processing system and the complexities of billing and paying for compound drugs has contributed to the growth of pharmacy management companies specializing in WC compound drugs, medical foods, and co-packs. These entities have arrangements with both pharmacies and physician offices to purchase outstanding receivables and pursue collection on disputed bills through the lien process. According to CHSWC analyses, nearly 25 percent of the medical treatment liens involve pharmacies or physician-dispensed drugs. The volume for compound drugs, co-packs and medical foods is sufficiently high for the Presiding Judge in the Los Angeles office of the Workers' Compensation Appeals Board to hold conferences on whether it is feasible to consolidate liens involving these products. (CHSWC, 2011).

Labor Code Section 4600.2 specifies that when a payer has contracted with pharmacies or a pharmacy benefit network in compliance with standards issued by the Administrative Director, affected injured employees "shall be provided medicines and medical supplies in the manner prescribed in the contract for as long as medicines or medical supplies are reasonably required to cure or relieve the injured employee from the effects of the injury." The *Jose Brambila v. Vons, Inc., PSI* decision affirmed the right of Safeway to establish and enforce the rules of the pharmacy benefit network. However, other payers appear reluctant to follow the Safeway approach in the absence of rules implementing the pharmacy benefit network provisions. This helps explain why a participating pharmacy is able to go "out-of-network" in dispensing and billing for compound drugs.

Arguably, medical provider networks are the most important tool currently available to address compound products. An employer has the right to establish medical provider networks and control care provided to injured workers throughout the course of the claim. Preliminary qualitative findings from on-going RAND research evaluating the impact of the recent statutory changes on medical care provided injured workers found that most payers have not used this tool effectively to assure that appropriate care is furnished in a cost effective manner. They have focused more on broad networks with fee discounting than on selective contracting with efficient providers. We identified in our interviews for this paper several self-insured employers with more selective contracting with physicians who agree to use the PBM-designated pharmacies and to not dispense drugs to patients directly. These self-insured employers are not seeing any widespread use of compound drugs in their WC patient population.

WHAT TOOLS DO OTHER HEALTH PROGRAMS USE?

Other payers use a variety of tools to address the use of compound drugs. Some rely on tiered pricing, which assigns the patient more financial liability for compound drugs than for other drugs. While this

strategy is not appropriate for WC patients, other medical review strategies that they are employing include prior approval, step therapy (where a compound drug is covered only after FDA-approved products have been tried unsuccessfully), post-payment audits, and limitations on physician-dispensing. The policies of selected health programs that provide coverage in California regarding compound drugs that RAND researchers identified in their environmental scan are summarized in Table 4.

Table 4. Summary of Other Health Program Policies for Compound Drugs

Health Program	Coverage
Medicare	Only FDA-approved ingredients are covered under Part D.
MediCal	Prior authorization required for drugs that are not in the MediCal formulary. Only specified OTC drugs are covered.
Aetna	<p>Generally, compounded drug products are considered medically necessary if all of the following criteria are met:</p> <ol style="list-style-type: none"> 1. The product contains at least one prescription ingredient. 2. The prescription ingredient is FDA-approved for medical use in the United States. 3. The compounded product is not a copy of commercially available FDA-approved drug product. 4. The safety and effectiveness of use for the prescribed indication is supported by FDA-approval or adequate medical and scientific evidence in the medical literature. <p>Ketamine topical gel is not covered because Aetna has concluded that there is inadequate evidence of its effectiveness.</p>
Anthem Blue Cross	Co-pay for compound drugs at participating retail pharmacies is \$25. Compound drugs are not covered when provided by non-participating pharmacies.
CIGNA	Pre-certification required if submitted price is more than \$200.
Pacificare	Pre-authorization required. Non-formulary drug approved only if there is not a formulary alternative

A common theme in the interviews conducted for this study was that significant compound drugs, medical foods, and co-packs usage is generally found only in the workers' compensation programs, and that

the prevalence of these products is higher in California's WC program than in other states. Florida and Texas were commonly identified as other states with high usage rates but several interviewees noted that it is a growing but generally unrecognized problem elsewhere. To date, Florida has not made any policy changes to address either compound drugs or repackaged drugs. Effective January 1, 2011, Texas adopted a closed formulary that restricts the availability of drugs that are not in the formulary. With respect to compound drugs, the rules provide that the formulary excludes any compound that contains a drug identified with a status of "N" (not recommended) in the current edition of the ODG guidelines. Drugs that are excluded from the formulary require prior authorization in both the network and non-network settings. In contrast, formulary drugs (including compound drugs whose ingredients have no "N" status indicators) may be prescribed without prior authorization but are subject to medical necessity review. The Texas WC agency considered requiring prior authorization for all compound drugs but reconsidered after the public comment period.

5. DISCUSSION

In preparing this background paper on compound drugs, medical foods, and co-packs, we were struck that some parties face significant financial incentives to promote use of these products in questionable situations. As noted in Chapter 1, there are multiple parties are involved in delivering and paying for these products, each with financial interests at stake in how the products are used in California's WC program (see Figure 1). Other health programs have adopted policies that provide more assurance that drugs are medically appropriate and payments are reasonable. As a result, they are not experiencing comparable issues related to use of these products.

The issues surrounding compound drugs, medical foods, and co-packs rest on the incentives created by uncertainties regarding whether the products are medically appropriate and payments are reasonable. Clarifying both topics through statutory and administrative changes would reduce the incentives. Given the volume of liens being filed for these products and the frictional and transaction costs that are being added to the system, initial changes in the Labor Code followed by rulemaking may be warranted. There are precedents in both medical necessity and fee schedule provisions for an approach that establishes policies in the Labor Code that are effective until the Administrative Director adopts policies through the rulemaking process. This approach quickly addresses a growing problem while recognizing not all provisions are self-implementing and providing flexibility to address evolving situations.

Medical Necessity

With respect to medical necessity issues, a potential statutory change would be to specify general coverage requirements for compound drugs and medical foods and other nutritional products. The provision for compound drugs could draw from the FDA policy guidance and the National Association of Boards of Pharmacy (NABP)'s Model Act (including, if

determined appropriate, an exclusion for physician-dispensed compounds). For example, the provision might require that the finished drug product:

- Include a least one drug substance (or active ingredient) that is the sole active ingredient in an FDA-approved drug. This would eliminate OTC compound drugs.
- Include only bulk ingredients that are components of FDA-approved drugs that have been made in an FDA-registered facility. This would allow compounding of bulk ingredients only if they are used in FDA-approved finished products and are manufactured in FDA-registered facilities (i.e., have an NDC code).
- Is not a drug that was withdrawn or removed from the market for safety reasons.
- Is not a copy of a commercially available FDA-approved drug product.
- Include only drug substances that have been supported as safe and effective for the prescribed indication by the FDA-approval process or by adequate medical and scientific evidence in the medical literature. This would allow off-label usage when supported by medical evidence but also clarify that a product is not covered unless there is evidence to support it is medically appropriate. Prior authorization could be required when the active ingredient is not addressed in the MTUS.

The MTUS should be updated and expanded through the rulemaking process to address compound drugs as a product class. The MTUS guidelines for chronic conditions were a major step forward in providing guidance on when compounded drugs are medically appropriate. Because they were not effective until July 2009, after the CWCI analyses were conducted, it is too soon to know whether they have changed prescribing practices. However, these guidelines are applicable to chronic conditions and could be construed as not applying to patients who have not been determined to have chronic pain even if a

recommendation on a specific active ingredient is relevant. In addition to addressing the evidence-base supporting the efficacy of ingredients frequently used in compounding, the guidelines might consider whether FDA-approved drugs should be tried prior to prescribing the compound drug and whether restrictions are appropriate on consecutive dispensing of 72-hour supplies of compound drugs (assuming the practice continues to be allowed). Similarly, the MTUS should address the medical appropriateness of medical foods. MTUS guidelines should not be necessary for co-packs if medical foods are addressed; instead, as discussed below, OMFS allowances for these products should be clarified.

OMFS allowances

Review of sample bills and OMFS pricing policies indicates there is an underlying problem with how bulk ingredients are priced; namely, the allowances in the MediCal database are based on manufacturer-specific reported AWP even when there are multiple suppliers. This is not a particular concern for MediCal because of it has a relatively low volume of compound drugs but it has become an issue for the WC program. The OMFS is vulnerable to establishing excessive allowances as long as it relies on AWP prices reported by a single manufacturer and does not take advantage of multi-source pricing. Large differences between the "sticker" price and the actual cost to the pharmacy for the ingredient create incentives to market compound drugs to the WC population. Another problem that should be addressed quickly is the lack of clear guidance on how to price compound drug ingredients that are not in the MediCal database that is contributing to fee schedule disputes. Secondary issues relate to the administrative burden involved in processing incomplete bills and could be addressed either by statute or regulation.

Pricing for multi-source bulk ingredients could be modeled on the formula used to establish the Federal Upper Limit (FUL) on therapeutically equivalent multi-source drugs in the Medicaid program. The current formula establishes the FUL at 150% of the lowest priced alternative. For pricing of multi-source FDA-approved drugs, products

must have therapeutic equivalence; that is, the products contain the same active ingredients, are of the same dosage form, route of administration, are identical in strength or concentration and can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling. The definition of therapeutic equivalence does not apply to bulk ingredients that will be compounded into a finished drug product. For pricing these ingredients, the important considerations are whether the products contain the same drug substance (active ingredient) and dosage form and are manufactured by FDA-registered establishments. Using these criteria, the OMFS allowance could be determined separately for each medically appropriate active ingredient based on the number of metric units and the unit price for the ingredient determined as follows:

1. If a bulk ingredient is used and there are three or more suppliers listed in the current version of a national pricing compendium for the same active ingredient and dosage form, the unit price would be 150 percent of the unit price of the lowest cost alternative (assuming the greater of the largest packaging available from a supplier or 100 grams).
2. For other ingredients that are in MediCal database, the unit price in MediCal database would apply.
3. If an ingredient is not in the MediCal database and has fewer than three suppliers, the unit price would be 83 percent of the AWP for the manufacturer as published in the current version of a national compendium of drug pricing.

To reduce misunderstandings and frictional costs, consideration should also be given to requiring the payer to identify the information source and NDCs used for each unit price determination at the time of payment.

Because medical foods are not a drug, pricing these products is problematic. Some products have been assigned an NDC by manufacturers and are carried by national compendium. For example, Redbook's 2010 edition lists Theramine® as a prescription drug. A prescription may be

required because the product requires physician supervision, but it is not considered a drug. The issue is whether these products should be priced using the AWP approach or some other pricing method.

Clarification is also needed regarding how co-packs should be priced. Consideration should be given to adopting the principle underlying the repackaged drug policy: the allowance would be based on the allowances for the individual underlying products, i.e., the medical food and the generic drug.

In addition to the medical necessity issues and payment issues specific to drugs, the lack of rulemaking to establish contractual requirements for pharmacy benefit networks has made some payers reluctant to enforce their network policies. This could be addressed either by clarifying statutory intent in the absence of rulemaking or by DWC giving priority to developing the implementing regulations.

Physician Incentives

Physician-dispensing creates financial incentives that affect the use of compound drugs, medical foods, and co-packs. On this issue, compound drugs have a somewhat different status than FDA-approved drugs and medical foods. For example, the FDA's compliance guidance for pharmacy compounding lists compounding of drugs for resale as grounds for considering an enforcement action related to manufacturing drugs without FDA approval. Consistent with this policy, the NABP's Model Act provisions on *Good Compounding Practices Applicable to State-Licensed Pharmacies* specifies that "pharmacists shall not offer compounded drug products to other State-licensed persons or commercial entities for subsequent resale, except in the course of professional practice for a practitioner to *administer* to an individual patient, in limited quantities." The Model Act defines manufacturing (as opposed to compounding) to include producing a drug for resale by pharmacies, practitioners, or other persons. California has chosen not to follow these provisions of the Model Act in the pharmacy code. Instead, the definition of pharmacy compounding includes the preparation of drugs "for distribution of not more than a 72-hour supply to the prescriber's patients, as estimated by the prescriber." Consideration should be

given to conforming the pharmacy code to the Model Act provisions or conforming WC coverage to the Model Act provisions. Recognizing patient convenience is involved in the dispensing of the initial supply, a reasonable WC-specific approach would be to cover the initial physician-dispensed supply but not refills.

The financial incentives for physician-dispensing of compound drugs could also be reduced significantly by limiting the amount payable under the OMFS to the amount that the provider paid for the products plus a reasonable mark-up. This would continue patient convenience associated with physician-dispensing but also would add administrative burden for providers and payers alike in processing the bills. Even if the policy were not applied to compound drugs, it should be considered for medical foods.

Financial incentives may also be involved in physician prescribing of pharmacy-dispensed compounded drug products. Labor Code section 139.3 precludes a physician from referring patients for certain designated services (e.g. clinical laboratory and diagnostic imaging) if the physician or his immediate family has a financial interest with the entity that receives the referral. Consideration should be given to adding pharmacy goods and services (including OTC drugs and nutritional products) to the list of designated services.

California's WC experience with repackaged drugs suggests that "quick fixes" may address issues in the short-term but that the issues are likely to re-emerge in another fashion unless the underlying incentives are addressed. The use of repackaged drugs declined significantly when it was no longer profitable for physicians to prescribe them. However, fixing the payment policy on physician-dispensing of repackaged drugs as fueled the increased usage of compound drugs, medical foods, and co-packs. The benefits gained from making policy changes to ensure these products are medically appropriate and payments are reasonable are also likely to be temporary unless greater attention is given to improving the overall incentives through selective contracting with efficient providers and appropriately rewarding their performance.

Appendix

A. CALIFORNIA PHARMACY REGULATIONS

California Code of Regulations, Title 16, Division 17

Article 4.5 Compounding

1735. Compounding in Licensed Pharmacies (Effective 07/06/10)

(a) "Compounding" means any of the following activities occurring in a licensed pharmacy, by or under the supervision of a licensed pharmacist, pursuant to a prescription:

- (1) Altering the dosage form or delivery system of a drug
- (2) Altering the strength of a drug
- (3) Combining components or active ingredients
- (4) Preparing a drug product from chemicals or bulk drug substances

(b) "Compounding" does not include reconstitution of a drug pursuant to a manufacturer's direction(s) for oral, rectal topical, or injectable administration, nor does it include tablet splitting or the addition of flavoring agent(s) to enhance palatability.

(c) "Compounding" does not include, except in small quantities under limited circumstances as justified by a specific, documented, medical need, preparation of a compounded drug product that is commercially available in the marketplace or that is essentially a copy of a drug product that is commercially available in the marketplace.

(d) The parameters and requirements stated by this Article 4.5 (Section 1735 et seq.) apply to all compounding practices. Additional parameters and requirements applicable solely to sterile injectable compounding are stated by Article 7 (Section 1735 et seq.).

Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

1735.1. Compounding Definitions (Effective 07/06/10)

(a) "Integrity" means retention of potency until the expiration date noted on the label.

(b) "Potency" means active ingredient strength within +/- 10% of the labeled amount.

(c) "Quality" means the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, and absence of active ingredients other than those noted on the label.

(d) "Strength" means amount of active ingredient per unit of a compounded drug product.

Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4052, and 4127, Business and Professions Code.

1735.2. Compounding Limitations and Requirements (Effective 07/06/10)

(a) Except as specified in (b) and (c), no drug product shall be compounded prior to receipt by a pharmacy of a valid prescription for an individual patient where the prescriber has approved use of a compounded drug product either orally or in writing. Where approval is given orally, that approval shall be noted on the prescription prior to compounding.

(b) A pharmacy may prepare and store a limited quantity of a compounded drug product in advance of receipt of a patient-specific prescription where and solely in such quantity as is necessary to ensure continuity

of care for an identified population of patients of the pharmacy based on a documented history of prescriptions for that patient population.

(c) Pursuant to Business and Professions Code section 4052(a)(1), a "reasonable quantity" of compounded drug product may be furnished to a prescriber for office use upon prescriber order, where "reasonable quantity" is that amount of compounded drug product that:

(1) is sufficient for administration or application to patients in the prescriber's office, or for distribution of not more than a 72-hour supply to the prescriber's patients, as estimated by the prescriber; and

(2) is reasonable considering the intended use of the compounded medication and the nature of the prescriber's practice; and

(3) for any individual prescriber and for all prescribers taken as a whole, is an amount which the pharmacy is capable of compounding in compliance with pharmaceutical standards for integrity, potency, quality and strength of the compounded drug product.

(d) A drug product shall not be compounded until the pharmacy has first prepared a written master formula record that includes at least the following elements:

(1) Active ingredients to be used.

(2) Inactive ingredients to be used.

(3) Process and/or procedure used to prepare the drug.

(4) Quality reviews required at each step in preparation of the drug.

(5) Post-compounding process or procedures required, if any.

(6) Expiration dating requirements.

(e) Where a pharmacy does not routinely compound a particular drug product, the master formula record for that product may be recorded on the prescription document itself.

(f) The pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded drug product until it is dispensed.

(g) All chemicals, bulk drug substances, drug products, and other components used for drug compounding shall be stored and used according to compendial and other applicable requirements to maintain their integrity, potency, quality, and labeled strength.

(h) Every compounded drug product shall be given an expiration date representing the date beyond which, in the professional judgment of the pharmacist performing or supervising the compounding, it should not be used. This "beyond use date" of the compounded drug product shall not exceed 180 days from preparation or the shortest expiration date of any component in the compounded drug product, unless a longer date is supported by stability studies of finished drugs or compounded drug products using the same components and packaging. Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

(i) The pharmacist performing or supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug product.

(j) Prior to allowing any drug product to be compounded in a pharmacy, the pharmacist-in-charge shall complete a self-assessment form for compounding pharmacies developed by the board (form 17m-39 rev. 10/07). That form contains a first section applicable to all compounding, and a

second section applicable to sterile injectable compounding. The first section must be completed by the pharmacist-in-charge before any compounding is performed in the pharmacy. The second section must be completed by the pharmacist-in-charge before any sterile injectable compounding is performed in the pharmacy. The applicable sections of the self-assessment shall subsequently be completed before July 1 of odd-numbered each year, within 30 days of the start of a new pharmacist-in-charge, and within 30 days of the issuance of a new pharmacy license. The primary purpose of the self-assessment is to promote compliance through self-examination and education. Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

1735.3. Records of Compounded Drug Products (Effective 07/06/10)

(a) For each compounded drug product, the pharmacy records shall include:

- (1) The master formula record.
- (2) The date the drug product was compounded.
- (3) The identity of the pharmacy personnel who compounded the drug product.
- (4) The identity of the pharmacist reviewing the final drug product.
- (5) The quantity of each component used in compounding the drug product.
- (6) The manufacturer and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements in this paragraph are sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.
- (7) The equipment used in compounding the drug product.
- (8) A pharmacy assigned reference or lot number for the compounded drug product.
- (9) The expiration date of the final compounded drug product.
- (10) The quantity or amount of drug product compounded.

(b) Pharmacies shall maintain records of the proper acquisition, storage, and destruction of chemicals, bulk drug substances, drug products, and components used in compounding.

(c) Chemicals, bulk drug substances, drug products, and components used to compound drug products shall be obtained from reliable suppliers. The pharmacy shall acquire and retain any available certificates of purity or analysis for chemicals, bulk drug substances, drug products, and components used in compounding. Certificates of purity or analysis are not required for products that are approved by the Food and Drug Administration.

(d) Pharmacies shall maintain and retain all records required by this article in the pharmacy in a readily retrievable form for at least three years from the date the record was created.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

1735.4. Labeling of Compounded Drug Products (Effective 07/06/10)

(a) In addition to the labeling information required under Business and Professions Code section 4076, the label of a compounded drug product shall contain the generic name(s) of the principal active ingredient(s).

(b) A statement that the drug has been compounded by the pharmacy shall be included on the container or on the receipt provided to the patient.

(c) Drug products compounded into unit-dose containers that are too small or otherwise impractical for full compliance with subdivisions (a) and (b) shall be labeled with at least the name(s) of the active ingredient(s), concentration of strength, volume or weight, pharmacy reference or lot number, and expiration date.

Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052, 4076 and 4127, Business and Professions Code.

1735.5. Compounding Policies and Procedures (Effective 07/06/10)

(a) Any pharmacy engaged in compounding shall maintain a written policy and procedure manual for compounding that establishes procurement procedures, methodologies for the formulation and compounding of drugs, facilities and equipment cleaning, maintenance, operation, and other standard operating procedures related to compounding.

(b) The policy and procedure manual shall be reviewed on an annual basis by the pharmacist-in-charge and shall be updated whenever changes in processes are implemented.

(c) The policy and procedure manual shall include the following:

(1) Procedures for notifying staff assigned to compounding duties of any changes in processes or to the policy and procedure manual.

(2) Documentation of a plan for recall of a dispensed compounded drug product where subsequent verification demonstrates the potential for adverse effects with continued use of a compounded drug product.

(3) The procedures for maintaining, storing, calibrating, cleaning, and disinfecting equipment used in compounding, and for training on these procedures as part of the staff training and competency evaluation process.

(4) Documentation of the methodology used to test integrity, potency, quality, and labeled strength of compounded drug products.

(5) Documentation of the methodology used to determine appropriate expiration dates for compounded drug products.

Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

1735.6. Compounding Facilities and Equipment (Effective 07/06/10)

(a) Any pharmacy engaged in compounding shall maintain written documentation regarding the facilities and equipment necessary for safe and accurate compounded drug products. Where applicable, this shall include records of certification(s) of facilities or equipment.

(b) Any equipment used to compound drug products shall be stored, used, and maintained in accordance with manufacturers' specifications.

(c) Any equipment used to compound drug products for which calibration or adjustment is appropriate shall be calibrated prior to use to ensure accuracy. Documentation of each such calibration shall be recorded in

writing and these records of calibration shall be maintained and retained in the pharmacy.

Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

1735.7. Training of Compounding Staff (Effective 07/06/10)

(a) Any pharmacy engaged in compounding shall maintain written documentation sufficient to demonstrate that pharmacy personnel have the skills and training required to properly and accurately perform their assigned responsibilities relating to compounding.

(b) The pharmacy shall develop and maintain an on-going competency evaluation process for pharmacy personnel involved in compounding, and shall maintain documentation of any and all training related to compounding undertaken by pharmacy personnel.

(c) Pharmacy personnel assigned to compounding duties shall demonstrate knowledge about processes and procedures used in compounding any drug product.

Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

1735.8. Compounding Quality Assurance (Effective 07/06/10)

(a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug products.

(b) The quality assurance plan shall include written procedures for verification, monitoring, and review of the adequacy of the compounding processes and shall also include written documentation of review of those processes by qualified pharmacy personnel.

(c) The quality assurance plan shall include written standards for qualitative and quantitative integrity, potency, quality, and labeled strength analysis of compounded drug products. All qualitative and quantitative analysis reports for compounded drug products shall be retained by the pharmacy and collated with the compounding record and master formula.

(d) The quality assurance plan shall include a written procedure for scheduled action in the event any compounded drug product is ever discovered to be below minimum standards for integrity, potency, quality, or labeled strength.

Authority cited: Sections 4005 and 4127, Business and Professions Code.
Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

B. OMFS REGULATIONS

California code of regulations, Title 8, §9789.40 (excerpt)

(b) For a pharmacy service or drug that is not covered by a Medi-Cal payment system, the maximum reasonable fee paid shall not exceed the drug cost portion of the fee determined in accordance with this subdivision, plus \$7.25 professional fee for dispensing or \$8.00 if the patient is in a skilled nursing facility or in an intermediate care facility. The maximum fee shall include only a single professional dispensing fee for dispensing for each dispensing of a drug.

(1) If the National Drug Code for the drug product as dispensed is not in the Medi-Cal database, and the National Drug Code for the underlying drug product from the original labeler appears in the Medi-Cal database, then the maximum fee shall be the drug cost portion of the reimbursement allowed pursuant to section 14105.45 of the Welfare and Institutions Code using the National Drug Code for the underlying drug product from the original labeler as it appears in the Medi-Cal database, calculated on a per unit basis, plus the professional fee allowed by subdivision (b) of this section.

(2) If the National Drug Code for the drug product as dispensed is not in the Medi-Cal database and the National Drug Code for the underlying drug product from the original labeler is not in the Medi-Cal database, then the maximum fee shall be 83 percent of the average wholesale price of the lowest priced therapeutically equivalent drug, calculated on a per unit basis, plus the professional fee allowed by subdivision (b) of this section.

(c) For purposes of this section:

(1) "therapeutically equivalent drugs" means drugs that have been assigned the same Therapeutic Equivalent Code starting with the letter "A" in the Food and Drug Administration's publication "Approved Drug Products with Therapeutic Equivalence Evaluations" ("Orange Book".)

The Orange Book may be accessed through the Food and Drug Administration's website: <http://www.fda.gov/cder/orange/default.htm>;

(2) "National Drug Code for the underlying drug product from the original labeler" means the National Drug Code of the drug product actually utilized by the repackager in producing the repackaged product.

C. SAMPLE BILLS FOR COMPOUND DRUGS

C.1

A. Bill for three physician-dispensed drugs on the same day.

This bill is included because it illustrates that billing for compound drugs typically involves multiple products. It is also an example of a bill that includes all the information needed to price the OMFS allowance. The bill also raises an issue regarding what constitutes a 30-day supply (the maximum amount of any compound that can be physician-dispensed). The 30-gram size is the smaller of the stock compound creams distributed by the compounding pharmacy to physician offices (the other is a 60-day supply). However, as illustrated below in 1.B, other bills typically reported a 120 gram or 180 gram sizes as a 30-day supply.

DOS	CPT	Procedure/Description	GRAMS	NDC No:	UNITS	Price Breakdown	Amount
05 21 10	99070	AMITRIPTYLINE-DT 30GM			30		\$285.30
05 21 10		AMITRIPTYLINE 4%	1.2	49452046001		\$32.48	
05 21 10		DEXTROMETHORPHAN 20%	6	49452249501		\$150.90	
05 21 10		TRAMADOL 5%	1.5	51927340400		\$74.92	
05 21 10		PCCA LIPODERM BASE	21.30	51927333800		\$18.11	
05 21 10		COMPOUND DISPENSING FEE				\$ 8.89	
05 21 10	99070	CAPSAICIN-T3 30GM			30		\$262.20
05 21 10		CAPSAICIN POWDER 0.0375%	0.01125	51927180700		\$6.76	
05 21 10		MENTHOL 2.0%	0.6	49452444001		\$4.60	
05 21 10		CAMPHOR 2.0%	0.6	49452185001		\$2.24	
05 21 10		TRAMADOL 15%	4.5	51927340400		\$219.90	
05 21 10		PCCA LIPODERM BASE	24.28875	51927333800		\$19.81	
05 21 10		COMPOUND DISPENSING FEE				\$ 8.89	
05 21 10	99070	FLURBIPROFEN-D 20-10% 30GM			30		\$317.40
05 21 10		FLURBIPROFEN 20%	6	51927270100		\$212.12	
05 21 10		DICLOFENAC 10%	3	62991202403		\$77.66	
05 21 10		PCCA LIPODERM BASE	21	51927333800		\$18.73	
05 21 10		COMPOUND DISPENSING FEE				\$ 8.89	
Total Due Now:							\$864.90

B. Bill reporting 120 grams of Amitriptyline DT as a 30-day supply.

99070A	Amitriptyline DT LDS	EDS:		
		30 DAYS	120 gms	\$998.40
51552-0464-07	Amitriptyline HCL Powder 4%		2.5gms	
49452-2500-03	Dextrómethorphan HBR Powder 4%		.625gms	
49452-7861-02	Tramadol HCL Powder 5%		3.125gms	

C.2 Incomplete Bill for a Pharmacy-Dispensed Compound

This bill is included as an illustration of bills submitted with only the total number of units and the NDC for only one ingredient. For electronic billing, it was not uncommon for the first portion of the bill to contain only one NDC but for the supporting documentation to contain the remaining NDCs and other information needed to process the bill. This billing practice increases the likelihood that the bill will be improperly processed and overpaid paid using the price for the single NDC code (typically, a high cost ingredient) for the total number of units rather than the actual number of units for each ingredient.

Date	RX #:	Description/NDC#	Qty	Physician	Charge	Payment	Balance
6/2/2008	717152	DICLIGABAP/DEXAMTH 10/1.5/0.1% C NDC#:48452246501	120		312.00	0.00	312.00
6/2/2008	717153	CAPS/CAMP/MENT/LID 0.05%2%1%2 NDC#:51927180700	120		356.00	0.00	356.00
6/2/2008	717154	DELIVERY NDC#:00000000000	1		50.00	0.00	50.00
Remit Payment to:					Total Charges:		\$718.00
					Total Payments:		\$0.00
					Invoice Total:		\$718.00

C.3 Physician-dispensing of the same product multiple times

The underlying rationale for the California's Code provision that permits a physician to dispense up to 72-hour supplies of compound drugs is that it allows the patient to begin a course of treatment immediately before obtaining a larger supply from a pharmacy. The spirit of the law is violated when a physician dispenses the same product multiple times. We do not know whether the patient also filled prescriptions at a pharmacy in between obtaining the compounds from the physician or made the "72-hour supply" last until obtaining a refill from the physician.

DOS	CODE	Description	CHARGE	PAYMENT	ADJUST	BALANCE
05/30/07	99070	D-Ketorub 10 gm jar 00007	69.55	0.00	0.00	69.55
05/30/07	99070	D-Lidorub 10 gm jar 00009	69.55	0.00	0.00	69.55
05/30/07	99070	D-Wasabi Mild 10 gm jar 00003	69.55	0.00	0.00	69.55
07/18/07	99070	D-Ketorub 10 gm jar 00007	69.55	0.00	0.00	69.55
07/18/07	99070	D-Lidorub 10 gm jar 00009	69.55	0.00	0.00	69.55
02/27/08	99070	Capsaicin Compound 30g NDC:SEE ATTACH	120.00	0.00	0.00	120.00
02/27/08	99070	Cyclobenzaprine Compound 30g NDC:SEE ATTACH	120.00	0.00	0.00	120.00
02/27/08	99070	Gabapentin Compound 30g NDC:SEE ATTACH	120.00	0.00	0.00	120.00
04/09/08	99070	Capsaicin Compound 30g NDC:SEE ATTACH	120.00	0.00	0.00	120.00
04/09/08	99070	Cyclobenzaprine Compound 30g NDC:SEE ATTACH	120.00	0.00	0.00	120.00
04/09/08	99070	Gabapentin Compound 30g NDC:SEE ATTACH	120.00	0.00	0.00	120.00
Amount Due:						\$1,067.75

C4. Total Units Do Not Match the Sum of the Units for Individual Ingredients.

In this example, the first bill probably reports the total number of units accurately but reports for individual ingredients the number of units reflected in the NDC rather than the actual number of units that were used. It is highly improbable that 710 grams of various powders and granules would be added to a 96 ml gel (it would make it a heavy paste). The billing practice increases the probability that the bill will be overpaid. This is because the pricing algorithm multiplies the metric units for each ingredient by its unit price. When this particular bill was submitted upon appeal, the third-party biller had changed the total number of units for the product to 806 ML instead of supplying the actual number of units used for each ingredient (which presumably would total 120 ML).

Date of Service	RX #	Description	Quantity	Unit	Dr. Name	Amount Due
04/25/08	0020600	** COMPOUND **	120.000	ML		
		NDC# 49452391704	100.000	GM	KETOPROFEN POW	179.68
		NDC# 49452240703	10.000	GM	CYCLOBENZAPR POW HCL	238.21
		NDC# 49452404002	100.000	GM	LIDOCAINE POW	105.74
		NDC# 49452399901	500.000	GM	LECITHIN GRA	41.83
		NDC# 51552054905	96.000	ML	POLOX GEL 20% COMPOUND FEE	8.78 7.25
			<i>total = 806</i>			

Workers Compensation Claim

Date of Service	RX #	Description	Quantity	Unit	Dr. Name	Amount Due
04/25/08	0020600	** COMPOUND **	806	GM		
		NDC# 49452391704	100	GM	KETOPROFEN POW	179.68
		NDC# 49452240703	10	GM	CYCLOBENZAPR POW HCL	238.21
		NDC# 49452404002	100	GM	LIDOCAINE POW	105.74
		NDC# 49452399901	500	GM	LECITHIN GRA	41.83
		NDC# 51552054905	96	ML	POLOX GEL 20% COMPOUND FEE	8.76 7.25
			<i>*ingredients need to total 120ml.</i>			

D. WARNING LETTER TO PHYSICIAN THERAPEUTICS, LLC



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Inspections, Compliance, Enforcement, and Criminal Investigations

Physician Therapeutics, LLC 4/8/10



Department of Health and Human Services

Public Health Service
Food and Drug Administration
Los Angeles District
Pacific Region
19701 Fairchild
Irvine, CA 92612-2506
Telephone: 949-608-2900
FAX: 949-608-4415

WARNING LETTER

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

April 8, 2010

W/L 14-1

William Shell, M.D.
CEO
Physician Therapeutics, LLC
2980 N. Beverly Glen Circle, Suite 301
Los Angeles, California 90077-1735

Dear Dr. Shell:

On **(b)(4)**, FDA issued a warning letter to **(b)(4)**, (copy attached). As explained more fully in that warning letter, certain drug products that **(b)(4)** has manufactured are new drugs that lack approved applications as required under the Federal Food, Drug, and Cosmetic Act (the Act). Based on information obtained during FDA's inspection of from **(b)(4)**, your firm contracted or otherwise arranged with **(b)(4)** manufacture one or more drug products that your firm distributes. These drug products include, but are not necessarily limited to:

- Theracodophen-650 Convenience Pack (Hydrocodone 10 mg, Acetaminophen 650 mg, and Theramine);
- Strazepam Convenience Pack (Temazepam 15 mg and Sentra PM);
- Gabazolamine-0.5 Convenience Pack (Alprazolam 0.5 mg and GABAdone);
- Gaboxetine Convenience Pack (Fluoxetine 10 mg and GABAdone);
- Trazamine Convenience Pack (Tradazone 50 mg and Sentra PM);
- Senophylline Convenience Pack (Theophylline 100 mg and Sentra PM);

- Therapentin-60 (Gabapentin 200 mg and Theramine);
- Prazolamine (Carisoprodol 350 mg and Theramine);
- Sentradine (Ranitidine 150 mg and Sentra PM);
- Therafeldamine (Piroxicam 20 mg and Theramine)

The above products are drugs within the meaning of section 201(g) of the Act, [21 U.S.C. § 321(g)] because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases. Further, they are "new drugs" within the meaning of section 201(P) of the Act [21 U.S.C. § 321(P)] because they are not generally recognized as safe and effective for use under the conditions prescribed, recommended, or suggested in their labeling. Under sections 301 (a) and (d) and 505(a) of the Act [21 U.S.C. §§ 331(a), (d) and 355(a)], a new drug may not be introduced into or delivered for introduction into interstate commerce unless an FDA approved application is in effect for the drug. Based on our information, you do not have any FDA-approved applications on file for these drug products.

Additionally, because the above prescription drug products are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners, adequate directions cannot be written for them so that a layman can use these products safely for their intended uses, as described in 21 C.F.R. § 201.5. Consequently, their labeling fails to bear adequate directions for their intended uses, causing them to be misbranded under section 502(1)(1) of the Act [21 U.S.C. § 352(1)(1)]. Because the products lack required approved applications, they are not exempt under 21 C.F.R. § 201.115 from the requirements of section 502(1)(1) of the Act. The introduction or delivery for introduction into interstate commerce of these products without approved new drug applications violates sections 301(a) and (d) of the Act [21 U.S.C. §§ 331(a) and (d)].

Further, as explained in the warning letter dated **(b)(4)** to **(b)(4)** the above drug products are adulterated under 21 U.S.C. § 351(a)(2)(B), and thus your firm may not introduce or deliver them for introduction into interstate commerce, 21 U.S.C. § 331(a).

The violations cited in this letter are not intended to be an all-inclusive statement of violations that may exist in connection with your products. In particular, violations cited in this letter are not necessarily limited to drug products manufactured by **(b)(4)** and may apply to all drug products that you market and distribute without FDA-approved applications. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence or the occurrence of other violations. It is your responsibility to assure that your firm complies with all requirements of federal law and FDA regulations.

You should take prompt action to Correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice, including, without limitation, seizure, and, injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations, as well as copies of related documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the time within which you will complete the correction. If you no longer market the above products, your response should so indicate, including the reasons that, and the date on which, you ceased production.

Your reply should be sent to:

Daniel Cline, Acting Director
Los Angeles District Domestic Compliance Branch
U.S. Food & Drug Administration
19701 Fairchild
Irvine, CA 92612

If you have any questions regarding this letter, please contact John J. Stamp, Compliance Officer, at (949) 608-4464.

Sincerely,

/S/
Alonza E. Cruse
District Director

Enclosure

cc: Acting Branch Chief
Food and Drug Branch
California Department of Public Health
1500 Capitol Avenue-MS 7602
P.O. Box 997413
Sacramento, CA 95899-7413

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BIBLIOGRAPHY

- Aetna. (2010). Pharmacy Clinical Policy Bulletins: Aetna Non-Medicare Prescription Drug Plan. *Compounded Drug Products* Retrieved October 20, 2010, from www.aetna.com/products/rxnonmedicare/data/2010/MISC2010/compound2010.html
- Anthem Blue Cross. (July 2009). Modified Rx 14 for REMIF Prescription Drug Benefits Mandatory Generic Substitution. *Prescription Benefits* Retrieved January 2011, from http://ci.sebastopol.ca.us/sites/default/files/griffinj/2009-10_abc_prescription_summary_mod_rx-14_10-25_for_e8_7-1-09.pdf
- Blue Shield of California. (2010-2011). Blue Shield Drug Formulary Member Booklet Retrieved January 2011, from https://www.blueshieldca.com/bsc/pharmacy/download/Member_Formulary.pdf
- California Commission of Health and Safety and Workers' Compensation (2011). *Liens Report*. Retrieved January 2011 from <http://www.dir.ca.gov/chswc/allreports.html>.
- California Division of Workers' Compensation. (July 18, 2009). Medical treatment utilization schedule regulations, Title 8, California Code of Regulations Sections 9792.20-9792.26, from http://www.dir.ca.gov/dwc/DWCPropRegs/MTUS_Regulations/MTUS_Regulations.htm
- California Division of Workers' Compensation (2011). *Compound Pharmacy Lien Pleadings*. Retrieved January 2011 from <http://www.dir.ca.gov/dwc/Liens/Liens.html>
- California Medical Association. (2007). 2007 California Physician's Legal Handbook *Chapter 11: Drug Prescribing/Dispensing*. California.
- California Medical Association. (2008). 2008 California Physician's Legal Handbook *Chapter II: Drug Prescribing/Dispensing*. California.
- California State Assembly. (2009-2010). California Assembly Bill 2779 *Labor Code 5307.13*. California.
- Cruse, A. E. (April 8, 2010). Warning Letter to Physician Therapeutics, LLC Retrieved January 12, 2011, from <http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm208680.htm>
- DeSaulnier, M., & Solorio, A. (September 17, 2010, September 17, 2010). [Letter form the California Legislature].
- Ireland, J., & Swedlow, A. (August 2010). The Cost and Utilization of Compound Drugs, Convenience Packs, and Medical Foods in California Workers' Compensation *CWCI Research Notes: California Workers' Compensation Institute*.
- National Association of Boards of Pharmacy, *The Model State Pharmacy Act and Model Rules*. <http://www.nabp.net/publications/model-act/>
- PacificCare Health Systems. (2009). Selected Formulary and Non-Formulary Medications Requiring Preauthorization Retrieved January 2011, from

- http://www.pacificare.com/vgn/images/portal/cit_60701/600712493_S_elected_Meds_WA.pdf
- Physician Therapeutics. (2010). Medical Food and Generic Drug Convenience Packs for The Management of Nutritional Requirements in Disease States Retrieved January 14, 2011, from http://ptlcentral.com/index.php#Convenience_Packs
- United States Food and Drug Administration. (2000). Pharmacy and Physician Compounding of Drug Products from <http://www.reginfo.gov/public/do/eAgendaViewRule?pubId=200010&RIN=0910-AB58>
- United States Food and Drug Administration (1979). OTC Combination Drug Products. Federal Register vol 43, number 229.
- United States Food and Drug Administration. (2006). 2006 Limited FDA Survey of Compounded Drug Products Retrieved October 14, 2010, from <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm204237.htm>
- Federal Food, Drug, and Cosmetic Act (21 USC) § 360 Section 510. Registration of Producers of Drugs and Devices (February 2008).
- United States Food and Drug Administration. (May 31, 2007). The Special Risks of Pharmacy Compounding. *Consumer Health Information*, from www.fda.gov/consumer/updates/compounding053107.html
- United States Food and Drug Administration. (May 2007). Guidance for Industry: Frequently Asked Questions about Medical Foods Retrieved October 14, 2011, from <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/MedicalFoods/ucm054048.htm>
- United States Food and Drug Administration. (2010). Compliance Policy Guidance for FDA Staff and Industry: Sec. 460.200 Pharmacy Compounding Retrieved January 2011, from <http://www.fda.gov/ICECI/ComplianceManuals/CompliancePolicyGuidanceManual/ucm074398.htm>
- United States Food and Drug Administration, Office of the Commissioner. (May 2009). Guidance for Industry: Providing Regulatory Submissions in Electronic Format - Drug Establishment Registration and Drug Listing: United States Department of Health and Human Services.
- United States Food and Drug Administration, Center for Drug Evaluation and Research, Approved Drug Products with Therapeutic Equivalence Evaluations. Orange Book, 30th Edition. Retrieved January 2011 from <http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/UCM071436.pdf>.