



California State Board of Pharmacy

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BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY

DEPARTMENT OF CONSUMER AFFAIRS

GOVERNOR EDMUND G. BROWN JR.

Communication and Public Education Committee
Meeting Materials for the September 18, 2014 Meeting

Members

Rosalyn Hackworth, Public Member, Chair
Albert Wong, PharmD, Professional Member
Ramon Castellblanch, PhD, Public Member
Allen Schaad, RPh, Professional Member

1. FOR DISCUSSION: Review of the parameters for patient consultation as required by 16CCR Section 1707.2

The board adopted this regulation on patient consultation in the early 1990s and it has not been revised since then. President Stan Weisser has suggested the board initiate a review.

Attachment 1

Attachment 1 contains a copy of 16CCR Section 1707.2.

2. FOR DISCUSSION AND POSSIBLE ACTION: Resumption of the Committee's Assessment of California's Patient-Centered Labeling Requirements

Attachment 2

Background:

Title 16 California Code of Regulations section 1707.5 specifies requirements for patient-centered labels for prescription drug containers. When the board promulgated these requirements, there was much public comment from numerous stakeholders. As such, the board included in subdivision (e) a requirement that the board re-evaluate the requirements by December 2013 to ensure optimal conformance with Business and Professions Code Section 4076.5, which directed the board to promulgate regulations for improved prescription container label design that would be patient-centered.

Numerous presentations were made at the July 31, 2014, Patient-Centered Prescription Label Forum. Materials from those presentations are provided in **Attachment 2**. Materials from past meetings are available in the attachments from the July 31 Patient-Centered Label Forum.

At the October 2013 board meeting, the board voted to amend two items of 1707.5(a) – requiring 12-point font for all elements of the patient centered label and an express prohibition that nothing but the designated patient-centered elements appear in the 50% of the label space dedicated to the patient-centered labels. At the January 2014 board meeting, these two changes were moved to notice for public comment to initiate a rulemaking, and are not a part of the discussion scheduled for this committee meeting.

This proposed language is:

1707.5.(a)(1) Each of the following items, and only these four items, shall be clustered into one area of the label that comprises at least 50 percent of the label. Each item shall be printed in ~~at least a 10-point sans serif typeface or, if requested by the consumer,~~ at least a 12-point sans serif typeface, and listed in the following order:

- A. Name of the patient
- B. Name of the drug and strength of the drug. For the purposes of this section, name of the drug” means either the manufacturer’s trade name of the drug, or the generic name and the name of the manufacturer.
- C. The directions for use
- D. The condition or purpose, if it is indicated on the prescription.

This rulemaking is currently undergoing the required review by the state’s administrative agencies.

At this meeting:

At the conclusion of the Patient-Centered Label Forum, President Weisser asked that this committee provide further discussion and possible recommendations for the board.

a. Should Section 1707.5(a)(1)(B) Require Listing of the Manufacturer’s Name in the Patient-Centered Clustered Area of the Label When a Generic Drug Is Dispensed?

Current statutory law for prescription container labels requires that if a generic drug is dispensed, then the manufacturer’s name must also appear somewhere on the label. If a brand name is dispensed, then no manufacturer’s name is required on the label.

In a prior meeting, the committee had recommended to the board the removal from the patient-centered area of the label in 1707.5 (a)(1)(B) of “and the name of the manufacturer” when a generic is dispensed.

The manufacturer name is still required by Business and Professions Code section 4076 to appear elsewhere on the label every time a generic is dispensed. At past board meetings, there was disagreement as to whether the manufacturer name needed to be in the patient-centered section.

At this meeting:

Possible language to remove the manufacturer’s name from the patient-centered area (but it would still be required to appear elsewhere on the label) is provided below:

- (a) Labels on drug containers dispensed to patients in California shall conform to the following format:
 - (1) Each of the following items shall be clustered into one area of the label that comprises at least 50 percent of the label. Each item shall be printed in at least a 10-point sans serif typeface or, if requested by the consumer, at least a 12-point typeface, and listed in the following order:
 - (A) Name of the patient
 - (B) Name of the drug and strength of the drug. For the purposes of this section, “name of the drug” means either the manufacturer’s trade name of the drug, or the generic name ~~and the name of the manufacturer.~~

b. When a Generic Drug Is Dispensed, Should the Brand Name of the Generic Equivalent Be Included on the Label Phrased as “Generic for _____”?

The committee has discussed this issue, but has not taken action to require that when a generic drug is dispensed that “generic for [insert brand name]” is required on the label to ensure patients do not mistakenly take both forms of the medication. For example “Alendronate Tab 70 mg. generic for Fosamax.”

c. Should Purpose or Condition Be a General Requirement for Labels?

The addition of this component as a required element to the label has been discussed periodically for years.

d. Should the Existing Requirements for “Added Emphasis” in the Patient-Centered Area of the Prescription Label Be Modified?

At the January 2014 committee meeting, there was no committee or public discussion on this item. It is repeated here just to ensure the committee has no interest in modifications to this element.

e. Translations on Labels:

1. Translated Directions for Use Are Available on the Board’s Website. Should the Board Require Use of Them to Aid Patients with Limited English Proficiency?
2. Should There Be a Specific Requirement for Labels to Be Translated? If So, What Components Are Needed (e.g., Also printed in English, Only Directions, and Exemption from Liability for Translation Errors)?

f. Should the Board Adopt Liquid Measurement Standards as Recommended by NCPDP?

The National Council for Prescription Drug Programs in March 2014 released liquid dosing instructions to provide recommendations and guidance for standardizing the dosing designation (the amount and volumetric units) used on prescription container labels of oral liquid medications dispensed from community pharmacies. The goal is to improve patient safety and outcomes by decreasing the potential for error when patients and caregivers take and administer these medications.

The board’s existing regulation is silent on liquid dosing instructions.

g. Should the Board Consider Technology Standards to Enhance the Patient-Centered Requirements?

At past committee meetings, the committee has discussed that some pharmacies are able to provide pictures of the pill on the prescription label, instead of the verbal description of the medication -- which is a statutory requirement for all labels. The committee has not determined that requiring items like a picture of the pill on the label to replace the description is technologically feasible at many pharmacies.

3. FOR DISCUSSION AND POSSIBLE ACTION: Development of the Draft of a Board Policy Statement Recommending the Elimination of Tobacco and E-Cigarette Sales from California Pharmacies

At the July 2014 board meeting, board members voted to adopt a policy to recommend the elimination of tobacco and e-cigarette sales from California pharmacies and referred the item to this committee for follow-up.

A draft of a possible statement that the committee can use as a starting point for discussion will be available at the meeting.

4. FOR INFORMATION: Update on *The Script*

The next edition of *The Script* is expected to be completed this fall. It will highlight new California laws.

5. FOR INFORMATION: Update on the Board's Consumer Education Brochure on Counterfeit Drugs

Final edits are being made to a new brochure on counterfeit drugs and it will soon undergo legal review.

6. FOR INFORMATION: Public Continuing Education Training Session by the California State Board of Pharmacy and DEA Held September 2 and 3, 2014, in Santa Barbara

The Board of Pharmacy and the DEA held two continuing education training sessions on September 2 and 3 in Santa Barbara on diversion prevention. Titled "Pharmacy Diversion Awareness Conference" The event was attended by 142 people – 81 on the first day and 61 on the second day.

7. FOR INFORMATION: Update on Media Activity

A report on recent media contacts handled by the office will be presented at the meeting.

8. FOR INFORMATION: Public Outreach Activities Conducted by the Board

- July 10, August 29: Executive Officer Virginia Herold and Public Information Officer Joyia Emard attended the California Prescription Drug Abuse Work Group meetings
- July 15: Board Inspector Brandon Mutrux, PharmD, spoke on prescription drug abuse and other pharmacy issues at a Senior Scam Stopper program held in Southern California

- August 21: Executive Officer Virginia Herold provided a presentation at the California Conference of Local Health Officers monthly meeting regarding the board's implementation of SB 493 and the state's immunization registry
- August 25: Executive Officer Virginia Herold provided a presentation about the board's activities regarding prescription drug abuse to the first meeting of the Dental Board of California's prescription drug abuse committee
- August 28: Board Member Dr. Ramon Castellblanch presented at the Generation Rx educational event at Touro University, in Vallejo
- September 11: Public Information Officer Joyia Emard attended the Overdose Prevention Messaging Workshop

9. FOR REVIEW AND DISCUSSION: Articles on Issues of Interest

Attachment 3

Attachment 3 contains articles of interest for the Communication and Public Education Committee.

10. FOR REVIEW AND DISCUSSION: The 43rd Annual Report of the Research Advisory Panel of California

Attachment 4

California law, pursuant to Health & Safety Code Sections §11480 & §11481, requires proposed research projects using certain opioid, stimulant and hallucinogenic drugs classified as Schedule I and Schedule II Controlled Substances as their main study drug(s), to be reviewed and authorized by the Research Advisory Panel of California in the Attorney General's Office. The Board of Pharmacy has an appointee on the panel.

The Research Advisory Panel primarily seeks to ensure the safety and protection of participating human research subjects and adequate security of the controlled substances used in the study. The Panel members evaluate the scientific validity of each proposed project and may reject proposals where the research is poorly conceived, would produce conclusions of little scientific value or would not justify the exposure of California subjects to the risk of research.

During 2013, the panel reviewed 32 research study submissions. Twenty-eight were approved by the panel. Among the approved studies, 10 studies were academic research studies, nine studies were substance abuse treatment research protocols and nine studies were multi-clinical drug trial research studies.

At the end of 2013, the panel was monitoring 89 research projects

Attachment 4 contains the copy of the 2013 report.

11. Public Comment for Items Not on the Agenda, Matters for Future Meetings*

**(Note: the committee may not discuss or take action on any matter raised during the public comment section that is not included on this agenda, except to decide to place the matter on the agenda of a future meeting. Government Code Sections 11125 and 11125.7(a))*

Adjournment

3 p.m.

Attachment 1

1707.2 Duty to Consult.

(a) A pharmacist shall provide oral consultation to his or her patient or the patient's agent in all care settings:

(1) upon request; or

(2) whenever the pharmacist deems it warranted in the exercise of his or her professional judgment.

(b)(1) In addition to the obligation to consult set forth in subsection (a), a pharmacist shall provide oral consultation to his or her patient or the patient's agent in any care setting in which the patient or agent is present:

(A) whenever the prescription drug has not previously been dispensed to a patient; or

(B) whenever a prescription drug not previously dispensed to a patient in the same dosage form, strength or with the same written directions, is dispensed by the pharmacy.

(2) When the patient or agent is not present (including but not limited to a prescription drug that was shipped by mail) a pharmacy shall ensure that the patient receives written notice: of his or her right to request consultation; and a telephone number from which the patient may obtain oral consultation from a pharmacist who has ready access to the patient's record.

(3) A pharmacist is not required by this subsection to provide oral consultation to an inpatient of a health care facility licensed pursuant to section 1250 of the Health and Safety Code, or to an inmate of an adult correctional facility or a juvenile detention facility, except upon the patient's discharge. A pharmacist is not obligated to consult about discharge medications if a health facility licensed pursuant to subdivision (a) or (b) of Health and Safety Code Section 1250 has implemented a written policy about discharge medications which meets the requirements of Business and Professions Code Section 4074.

(c) When oral consultation is provided, it shall include at least the following:

(1) directions for use and storage and the importance of compliance with directions; and

(2) precautions and relevant warnings, including common severe side or adverse effects or interactions that may be encountered.

(d) Whenever a pharmacist deems it warranted in the exercise of his or her professional judgment, oral consultation shall also include:

(1) the name and description of the medication;

(2) the route of administration, dosage form, dosage, and duration of drug therapy

(3) any special directions for use and storage;

(4) precautions for preparation and administration by the patient, including techniques for self-monitoring drug therapy;

(5) prescription refill information;

(6) therapeutic contraindications, avoidance of common severe side or adverse effects or known interactions, including serious potential interactions with known nonprescription medications and therapeutic contraindications and the action required if such side or adverse effects or interactions or therapeutic contraindications are present or occur;

(7) action to be taken in the event of a missed dose.

(e) Notwithstanding the requirements set forth in subsection (a) and (b), a pharmacist is not required to provide oral consultation when a patient or the patient's agent refuses such consultation.

Attachment 2

Revisiting Patient-Centered Labeling Requirements in California



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Patient-Centered Label Forum

Maureen Schanck, PharmD
Professional Affairs Manager

NABP's Preamble

The National Association of Boards of Pharmacy (NABP) recognizes and supports pharmacists serving as the health care professionals responsible for providing patient care that ensures optimal medication therapy outcomes. NABP also recognizes the ongoing and critical need for patients' medications to be managed by a licensed pharmacist and state regulatory agencies to aggressively enforce standards of care.



NABP Mission Statement

NABP is the independent, international, and impartial association that assists its member boards and jurisdictions for the purpose of protecting the public health.



2008-2009 Task Force on Uniform Prescription Labeling Requirements

- Convened Following Resolution 104-3-08 from the 104th Annual Meeting in 2008
- The Task Force Recommended Amending NABP's Model Act.

Recommendation #1

A) Critical Information for Patients- Should be emphasized (highlighted or bold), in sans serif font (such as “arial”), minimum 12-point font and should never be truncated.

Example: ABCDE Vs ABCDE

Examples of Critical Information

1) Patient name

- (-a-) legal name of the patient; or
- (-b-) if patient is an animal, include the last name of the owner, name of the animal, and animal species.

Examples of Critical Information

2) Directions for use.

- (-a-) directions for use as indicated by the prescriber and medication purpose/indication if included on prescription drug order.

- (-b-) language should be simplified, avoiding unfamiliar words and medical jargon; when applicable, use numeric instead of alphabetic characters.

Examples of Critical Information

3) Drug Name

- (-a-) if written for a brand name and a generic drug is dispensed, include phrase “Generic for [brand name];”
- (-b-) include drug name suffixes, such as CD, SR, XL, XR, etc.

Examples of Critical Information

4) Drug Strength

5) “Use by” date

(-a-) Date by which medication should be used; not expiration date of medication or prescription.

(-b-) Format as “Use by: MM/DD/YY



Recommendation #2

B) Important information must appear on label but should not supersede Critical information.

Examples of Important Information

- 1) Pharmacy Name- or dispensing practitioner's entity name.
- 2) Pharmacy Telephone Number
- 3) Prescriber Name

Format -“Prescriber: [prescriber name]”

- 4) “Fill Date”-

Format- “Date filled: MM/DD/YY

Examples of Important Information

5) Prescription Number

6) Drug Quantity

Format- “Qty:[number]”

7) Number of Remaining Refills

a) use whole numbers only and managing partial fills through pharmacy record system.

“Refills:[number remaining]”



NABP®

Examples of Important Information

8) Written or graphic product description.

9) Auxiliary information.

10) Any cautions or provisions required by state or federal law.

Recommendation #3

The following information may also appear on the prescription label.

- A) Bar Codes
- B) Pharmacy Address
- C) Store Number

Pharmacy Name:

Date Filled: MM/DD/YY

Phone:

Rx No.:

Cautions:

Purpose:

Patient Q. Name

Prescriber:

**Take 1 tablet in the morning and
2 tablets at bedtime.**

Drug Name and Strength

Generic for:

Qty:

Discard after: MM/DD/YY

Refills:

Description:

Pharmacy Name:

Phone:

Patient Q. Name

Rx No.:

Date Filled: MM/DD/YY

Prescriber:

Drug Name and Strength

Generic for:

Qty:

Refills:

Discard after: MM/DD/YY

Purpose:

Take 1 tablet in the morning and 2 tablets at bedtime.

Cautions:

Description:

Comment #1

- Boards may want to consider supporting legislation which contains this type of language for incorporation into their State Food and Drug Act, so that it shall apply to all Persons who Dispense Drugs, including Practitioners who prescribe and Administer as well as Dispense Drugs.

Comment #2

- Boards of pharmacy and licensees should recognize that “take as directed” may not provide sufficient information for the appropriate use of the medication. “Take as directed” is appropriate when specific directions are included on a unit-of-use package or dispensed package or in situations when directions are not able to be included on the label and the pharmacist presents directions to the patient and documents that such directions were given. “Take as directed” should not be used in lieu of patient counseling.
- It is understood that prescription drug orders often do not include the indication for use.

Comment #3

- Information traditionally included on the patient label must continue to be maintained and safeguarded by the record keeping system. Boards of pharmacy should require that record keeping systems prohibit any alteration or modification of these data unless an appropriate audit trail and justification exists. Record keeping systems should also prohibit any deletion of information except in accordance with state and federal requirements for data management and retention.

Comment #4

Boards of pharmacy should recognize that some pharmacies “do business as” a name other than the corporate name.



Comment #5

Phone number of the dispensing pharmacy recognizing that a central fill pharmacy may be involved in the filling process; boards of pharmacy should not require more than one telephone number on the label.

Comment #6

“Fill date” and “use by” date should be the only dates appearing on the prescription label. Other dates often found on labels, such as the original and expiration dates of the prescription drug order can be misunderstood by patients and clutter the label with unnecessary information.

Comment #7

- Auxiliary information, including auxiliary labels, should be evidence based, standardized, and demonstrated to complement the prescription label.

States That Require Translation Services For Pharmacies

- 1) California– BReg 1707.5

- 2) New York–PracAct 6829
 - A) Applies to pharmacies that are part of a group of eight or more pharmacies.
 - B) Provide
 - C) and label translation services for languages spoken by at least 1% of the region's census data.
 - D) Can be provided by staff or third party.
 - E) Must display sign with notification of right to translation service.
 - E) Face-to-Face communication is not required.

- Questions?
- Thank you!



Redesigned Prescription Label: Evidence for patient preference and improved comprehension

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Dr. Amir Zargarzadeh,
Dr. Prashant Sakharkar
Dr. Bik–Wai Tai
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- ❖ Senior center staff

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Prescription Label

- ▶ Rx labels serve as an immediate and important source of medication information for patients
 - ▶ Prescription (Rx) labels are used to communicate key information
 - Medication name
 - Dosage
 - Directions
 - Precautions
- 

What is a GOOD Prescription Label?

- ▶ Easy to use
 - Simple
 - Convenient
- ▶ Without need for assistance
- ▶ Intended to supplement provider counseling
- ▶ Communicates to patient:
 - What is the med
 - When to take the med
 - How to take the med
 - How much to take
 - WHY to take the med

Some facts about Rx Labels

- ▶ **Differences in Rx label formats and instructions among pharmacies**
- ▶ **Patients often do not receive adequate medication counseling from healthcare providers (e.g. physicians, pharmacists) ¹⁻⁴**
- ▶ **Vulnerable populations show difficulty in understanding Rx and auxiliary labels. ⁵⁻⁷**
 - Elderly
 - People with low health literacy
 - People with low English proficiency (LEP)

Issues with Rx labels⁸⁻⁹

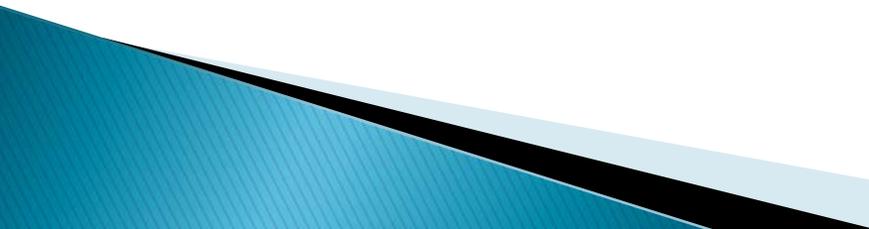
- Difficult to read and/or understand
 - Complex labeling language
 - Unclear administration times
 - Confusing label layout
 - Small font size
 - Auxiliary labels

Impact of Misunderstanding Rx labels

- ▶ Institute of Medicine (IOM) report in 2006 cited Rx labeling as **“the cause of a large proportion of outpatient medication errors and adverse drug events.”** ¹⁰
- ▶ **Misunderstanding Rx label instructions has led to inadvertent patient-initiated errors in med use** ¹¹⁻¹³
 - Under or overdosing
 - Preventable adverse drug reactions
 - Emergency room visits
 - Hospital admissions
 - Morbidity and mortality
 - Economic burden in healthcare system

Impact of Misunderstanding Rx labels

Some statistics¹⁴⁻¹⁵:

- ▶ 63% of patients misunderstand one or more dosage instructions on the prescription label
 - ▶ 12% of emergency room visits are drug related
 - ▶ 1.5 million preventable adverse drug events occur every year
 - ▶ Medication errors and adverse drug reactions result in an estimated annual cost of \$50 billion
- 

Our experience on Rx label

- ▶ ***Our research team has been working to improve prescription (Rx) labels for more than 6 years***

- 1. **‘How do patients read, understand, interpret and use prescription drug labels? An exploratory study examining patient and pharmacist perspectives’¹**
 - *What was desired on a label :*
 - (a) Better content organization of labels
 - (b) Use of bigger fonts
 - (c) Color backgrounds
 - (d) Inclusion of indication and precautions on the labels

Our experience on Rx label

We therefore initiated our next study '**Design and test of preference for a new prescription medication Label**' ¹⁷

to measure preference for newly designed Rx labels compared to the existing labels from different perspectives

How was label redesigned?

▶ **Content, convenience, and cosmetic appearance (3Cs)**

- **Content:**

- Use of simple language (5th grade level)
- A time-table for medication administration
- Indication of medication
- 2008 CA State law requirements for Rx drug labels (section 4076)

- **Convenience:**

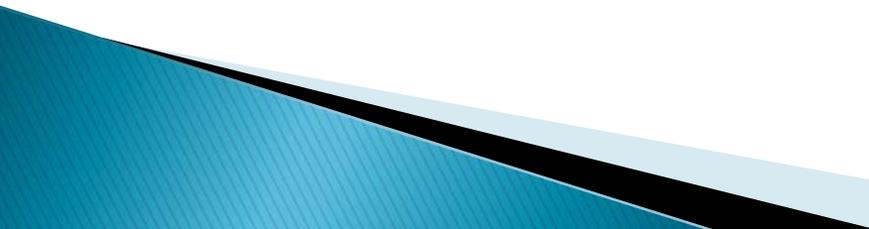
- Bigger font size (patient name, medication name and dosage and directions)
 - Size of label (5.715 x 9.525 cm) fits a 13 dram size bottle
- Delete aux label: Warnings/ Precautions as part of the Rx label

- **Cosmetic appearance**

- Use of color backgrounds and adequate white space

Study Methodology

“Design and test of preference for a new prescription medication Label”

- ▶ Two new labels were designed based on literature and results from our previous study.
 - ▶ A structured interview study design was used to test the preference for a new Rx label from perspective of patients, pharmacists and physicians
 - ▶ 444 patient participants were sampled from 20 community pharmacies and 2 hospital outpatient pharmacy departments
 - ▶ 115 pharmacists and 69 physicians was sampled from professional association meetings held in California
- 

Study Methodology

Test Pharmacy (909)-555- 5555 122 Park Ln. Pomona, CA 91767		RX 0238385-07070									
Prescribed by: Dr. Feelbetter Fill Date: 01/01/2009 JOHN DOE		Description of Pill: OVAL WHITE TABLET Front side: 20 Use Before 09/2010 No Refills - Dr. Auth Required									
LIPITOR- 20mg tabs QTY: 30		Warnings: 1) Avoid grapefruit products while on this medication. 2) Please contact your pharmacist or physician if you experience muscle pain or weakness or if you start any new medications.									
Directions: TAKE 1 TABLET BY MOUTH ONCE EVERY NIGHT FOR CHOLESTEROL.		When to take medication:									
<table border="1"> <tr><td>6-9 am</td><td></td></tr> <tr><td>12-2 pm</td><td></td></tr> <tr><td>5-8 pm</td><td></td></tr> <tr><td>9-11 pm</td><td>✓</td></tr> </table>		6-9 am		12-2 pm		5-8 pm		9-11 pm	✓	CAUTION: FEDERAL LAW PROHIBITS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT	
6-9 am											
12-2 pm											
5-8 pm											
9-11 pm	✓										

Label A

AVOID EATING OR DRINKING GRAPEFRUIT PRODUCTS WITH THIS MEDICATION.	Test pharmacy 775 EAST BOULEVARD POMONA, CA 91767 JOHN DOE 158 W FOOTHILL BLVD POMONA, CA 91767 LIPITOR 20 MG TABLET P-D TAKE 1 TABLET EVERY NIGHT Qty:30 Refills require authorization Store Phone: (999) 621-6708 Rx # 462022 Prescriber: FRANK BURK
TAKE ONLY AT RECOMMENDED DOSE. DON'T TAKE WITH TAO, NIZORAL, SPORANOX, BIAXIN	THIS MEDICATION MAY BE TAKEN WITH OR WITHOUT FOOD.
RPH: A/Ku Orig: 02/11/2009 Date filled: 02/11/2009 Discard after:	This is a WHITE, ELLIPTICAL-shaped, TABLET imprinted with PD 156 on the front and 20 on the back.
NDC: 77522-01-01000 CAUTION: FEDERAL LAW PROHIBITS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT FOR WHOM IT WAS PRESCRIBED.	

Label D

Test Pharmacy (909)-555- 5555 122 Park Ln. Pomona, CA 91767		RX 0238385-07070									
Prescribed by: Dr. Feelbetter Fill Date: 01/01/2009 JOHN DOE		Description of Pill: OVAL WHITE TABLET Front side: 20 Use Before 09/2010 No Refills - Dr. Auth Required									
LIPITOR- 20mg Tabs QTY: 30		Warnings: 1) Avoid grapefruit products while on this medication. 2) Please contact your pharmacist or physician if you experience muscle pain or weakness or if you start any new medications.									
Directions: TAKE 1 TABLET BY MOUTH ONCE EVERY NIGHT FOR CHOLESTEROL.		When to take:									
<table border="1"> <tr><td>6-9 am</td><td></td></tr> <tr><td>12-2 pm</td><td></td></tr> <tr><td>5-8 pm</td><td></td></tr> <tr><td>9-11 pm</td><td>✓</td></tr> </table>		6-9 am		12-2 pm		5-8 pm		9-11 pm	✓	CAUTION: FEDERAL LAW PROHIBITS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT	
6-9 am											
12-2 pm											
5-8 pm											
9-11 pm	✓										

Label B

ELLIPTICAL WHITE TABLET Side 1: PD 156 Side 2: 10	John Smith 788 E FOOTHILL, POMONA, CA 91767 DATE 02/11/09
Check With Your Doctor Before Including Grapefruit Or Grapefruit Juice In Your Diet	LIPITOR 10MG TABLETS NDC PREFIX TAKE 1 TABLET BY MOUTH EVERY NIGHT AT BEDTIME USE BEFORE
This Medicine May Be Taken With Or Without Food	QTY: 90 NO REFILLS - DR. AUTH REQUIRED H. PATEL, MD
Test Pharmacy 9708 E FOOTHILL, POMONA, CA 91767 (909) 624-3013	APPROVED BY:

Label E

New Label A

Test Pharmacy (909)-555- 5555 122 Park Ln. Pomona, CA 91767		RX 0238385-07070	
Prescribed by: Dr. Feelbetter Fill Date: 01/01/2009		<u>Description of Pill:</u> OVAL WHITE TABLET Front side: 20 Use Before 09/2010 No Refills - Dr. Auth Required	
JOHN DOE			
LIPITOR- 20mg tabs		QTY: 30	
Directions: TAKE 1 TABLET BY MOUTH ONCE EVERY NIGHT FOR CHOLESTEROL.			
When to take medication:			
6-9 am			
12-2 pm			
3-6 pm			
9-11 pm			✓
<small>CAUTION: FEDERAL LAW FORBIDS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT</small>			

-Use of color backgrounds and adequate white space
- Bigger font size

Indication included

Table of administration times included

Auxiliary information as part of the Rx label

New Label B (Versus Label A)

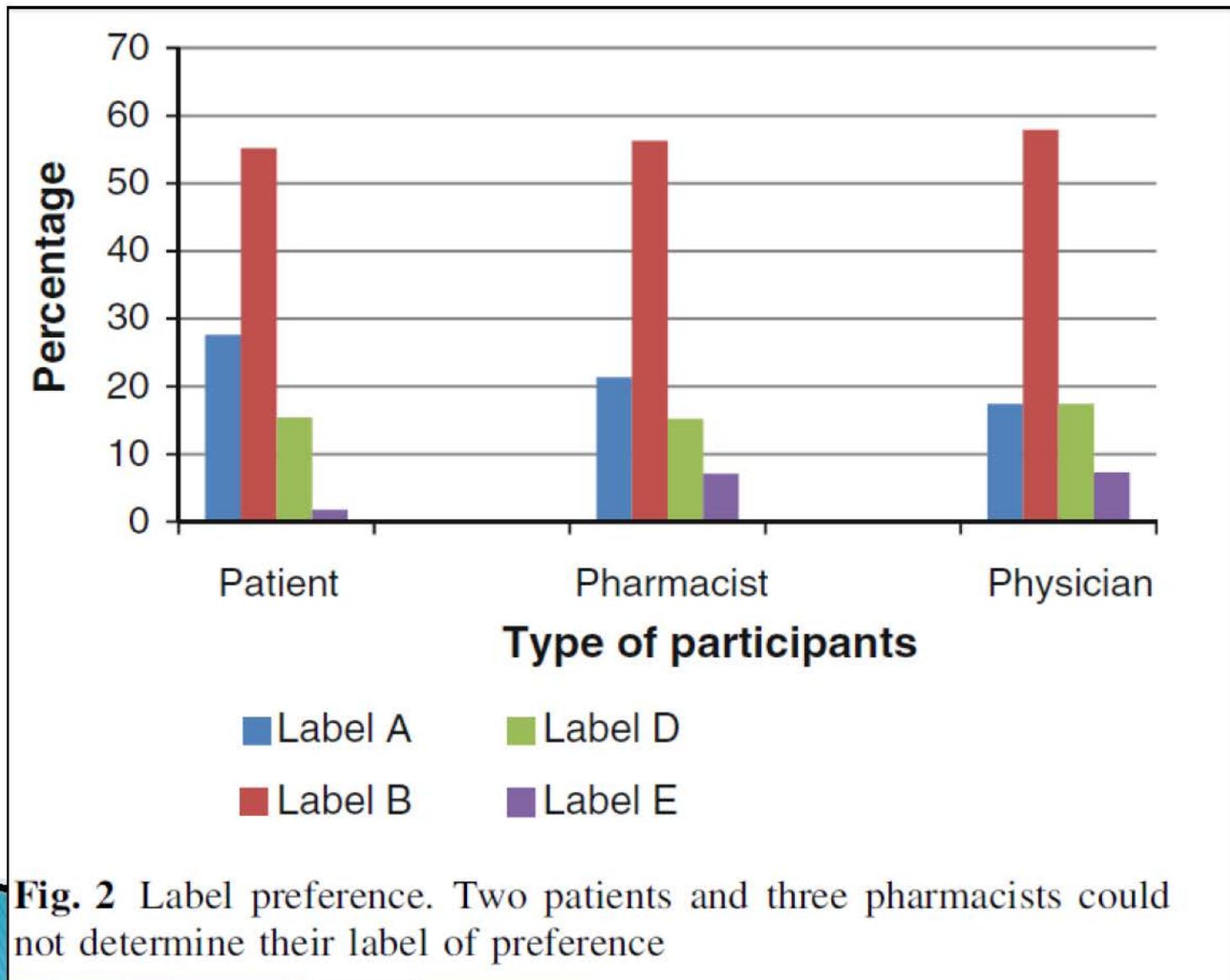
Test Pharmacy (909)-555- 5555 122 Park Ln. Pomona, CA 91767		RX 0238385-07070	
Prescribed by: Dr. Feelbetter Fill Date: 01/01/2009 JOHN DOE		<u>Description of Pill:</u> OVAL WHITE TABLET Front side: 20 Use Before 09/2010 No Refills : Dr. Auth Required	
LIPITOR- 20mg Tabs		QTY: 30	
Directions: TAKE 1 TABLET BY MOUTH ONCE EVERY NIGHT FOR CHOLESTEROL.	When to take:		
	6-9 am		
	12-2 pm		
	5-8 pm		
	9-11 pm		✓
<small>CAUTION: FEDERAL LAW PROHIBITS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT</small>		Warnings: 1) Avoid grapefruit products while on this medication. 2) Please contact your pharmacist or physician if you experience muscle pain or weakness or if you start any new medications.	

More space for directions



Minimized the need to turn the bottle in order to view the directions and table of administration times

Study Findings



2012 USP labeling standards ¹⁸

- ▶ Provide a universal approach to the format, appearance, content and language of instructions for a **'patient-centered Rx label'** used by pharmacists and prescribers.
 - **High- contrast print**
 - **Familiar fonts and large font size for critical information** (e.g. 12-point Times Roman or Arial)
 - **Punctuated like a sentence** (e.g. initial capital followed by lower-case words)
 - **Horizontal text only**
 - **Highlighting, bolding, and other typographical cues**
 - **Include indication of the medication**
 - **Emphasize patient-centric information or information that facilitates adherence** (e.g. refill ordering)
 - **Avoid vague instructions for dosing intervals**
 - **Minimize the need to turn the container to read lines of text**
 - **Limit auxiliary information**

A Currently Existing Rx label



Local Pharmacy

123 MAIN STREET
ANYTOWN USA, 11111

(800) 555 5555

JANE SMITH

456 MAIN STREET ANYTOWN, USA 11111 DATE FILLED: 01/23/13

SIMVASTATIN 20 MG TABLET

TAKE ONE TABLET BY MOUTH IN THE EVENING

RX # 0238385-07070

USE BEFORE: 01/23/14

QTY: 30
REFILLS: 3

C. JONES, MD

Round red tablet MFG: Merck
Side 1: MSD 726 Side 2: 20

RPh: SLF



CAUTION: FEDERAL LAW PROHIBITS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT

What can you tell from them?

Take two tablets twice daily⁴



What can you tell from them?

1.



2.



3.



What can you tell from them? ⁵

Reading Confusion Into Drug Warnings

When researchers asked consumers to interpret prescription warning stickers, these are among the responses they gave:



"Chew pill and crush before swallowing."

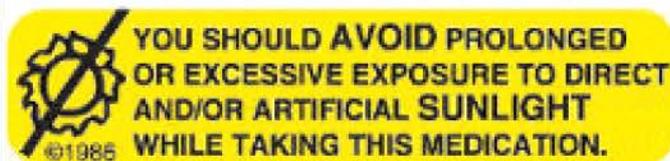
"Chew it up so it will dissolve, don't swallow whole or you might choke."



"Use extreme caution in how you take it."

"Medicine will make you feel dizzy."

"Take only if you need it."



"Don't take medicine if you've been in the sunlight too long."

"Don't leave medicine in the sun."

A Newly Designed Rx label

No separate auxiliary labels and abstract icons

- Familiar font and large font size (12-point Times Roman)
 - Highlighting
 - Bolding

Test Pharmacy (909)-555-5555 123 Main Street, Anytown, USA 11111		RX 0238385-07070	
JANE SMITH 456 MAIN STREET ANYTOWN, USA 11111		Round red tablet Front side: MSD 726 Mfg: Merck Prescribed by: C. Jones, MD Fill Date: 01/23/2013	
Simvastatin 20 mg (Generic for: Zocor)		Use Before: 01/23/2014	
QTY: 30 tabs 3 Refills		----- Warnings:	
Directions: Take 1 tablet by mouth in the evening for lowering cholesterol.	When to take:		1) Avoid grapefruit products. 2) Contact your pharmacist or physician if you experience muscle pain or weakness. 3) Avoid pregnancy or breast-feeding.
	6-11 am		
	12-2 pm		
	5- 8 pm	✓	
	9- 11 pm		
CAUTION: FEDERAL LAW PROHIBITS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT			

Punctuated like a sentence

Indication included

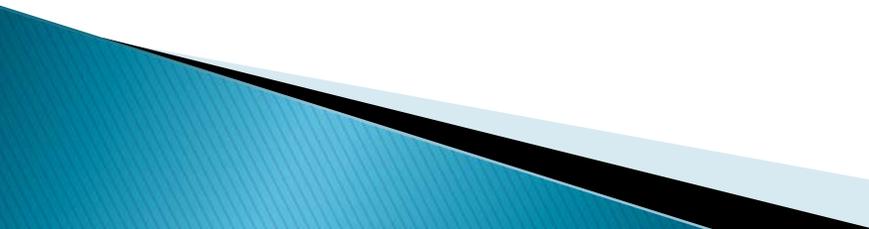
Horizontal text only for the whole Rx label

The need to turn the container is minimized

Table of administration times provides clear instructions for dosing intervals

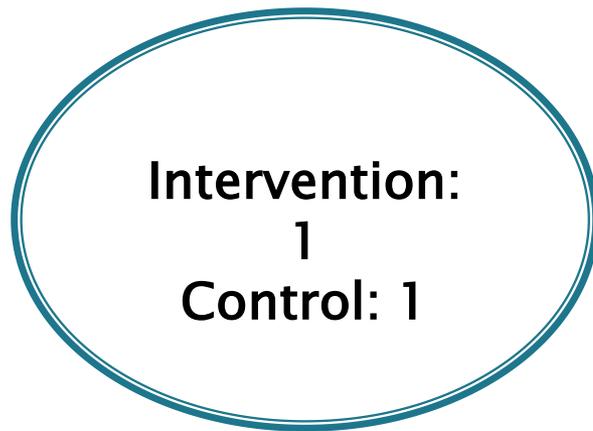
Current Study – Rx Label Comprehension

Study purposes:

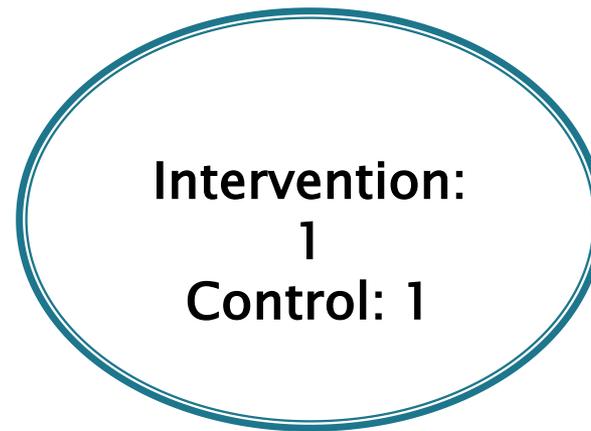
- ▶ To determine the effect of an educational intervention on change in Rx label comprehension among older adults who use Rx medications
 - ▶ To compare change in comprehension with 2 Rx labels:
 - (1) Currently existing label
 - (2) Redesigned patient-centered label
- 

Study Design

- ▶ A multisite, randomized-controlled, multi-arm trial



Current Rx
Label



Redesigned Rx
Label

- ▶ The study was approved by the Institution Review Board at WesternU, CA, USA

Sampling and Setting

- ▶ **Conducted at 5 community senior centers in Southern CA**
 - *Redesigned* Rx label: Irvine, Pomona, LaVerne
 - *Current* Rx label: Montclair, Ontario
- ▶ **Inclusion criteria:**
 - Age \geq 55 years, \geq 2 Rx medications, able to read, speak, and understand English
- ▶ **Exclusion criteria:**
 - Significant vision, hearing, or cognitive impairment

Data collection

- ▶ Recruited participants were assessed for Rx label comprehension at the beginning and the end of the 1-month study after educational intervention
- ▶ **Modified LaRue Medical Literacy Tool (MLT)**
 - Has established reliability and face/content validity
 - Contains 25 open-ended free-text and multiple choice questions central to the appropriate use of Rx medications
 - ✓ *Medication name*
 - ✓ *Indication of the medication*
 - ✓ *Time and direction to take the medication,*
 - ✓ *Original and remaining number of pills in the bottle*
 - ✓ *Number of refills available*
 - ✓ *Expiration date*
 - ✓ *Precautions/warnings on how to take the medication*

▶ Modified LaRue Medical Literacy Tool (MLT)

Simvastatin (example):

1. **How many** tablets of Simvastatin are you going to take in a day?

Your answer: _____

2. **When** will you take Simvastatin during a day?

Your answer: _____

3. **How many times** can you refill this prescription for Simvastatin?

Your answer: _____

4. **What is the reason** you would take Simvastatin (i.e. what is Simvastatin used for)?

Your answer: _____

5. **In how many days** you will run out of these Simvastatin tablets?

Your answer: _____

- ▶ 5 Rx labels: simvastatin, metformin, glipizide, lisinopril, and hydrocodone/acetaminophen
- ▶ Score range of 0 to 25; participant scored 1 point for a correct answer, 0 point for an incorrect answer

Educational Intervention

- ▶ 1 on 1; ~ 10 minutes long
- ▶ Simple, focused training on the Rx labels for 4 health conditions: hypertension, dyslipidemia, diabetes and chronic pain
 - All the important elements of a sample Rx label
 - Sample Rx labels with Q&A for self-assessment/reinforcement
- ▶ Tri-fold educational brochures
 - Adapted from the Agency for Healthcare Research and Quality (AHRQ)
 - Self-paced learning at participant's own time

Study Results– Demographics

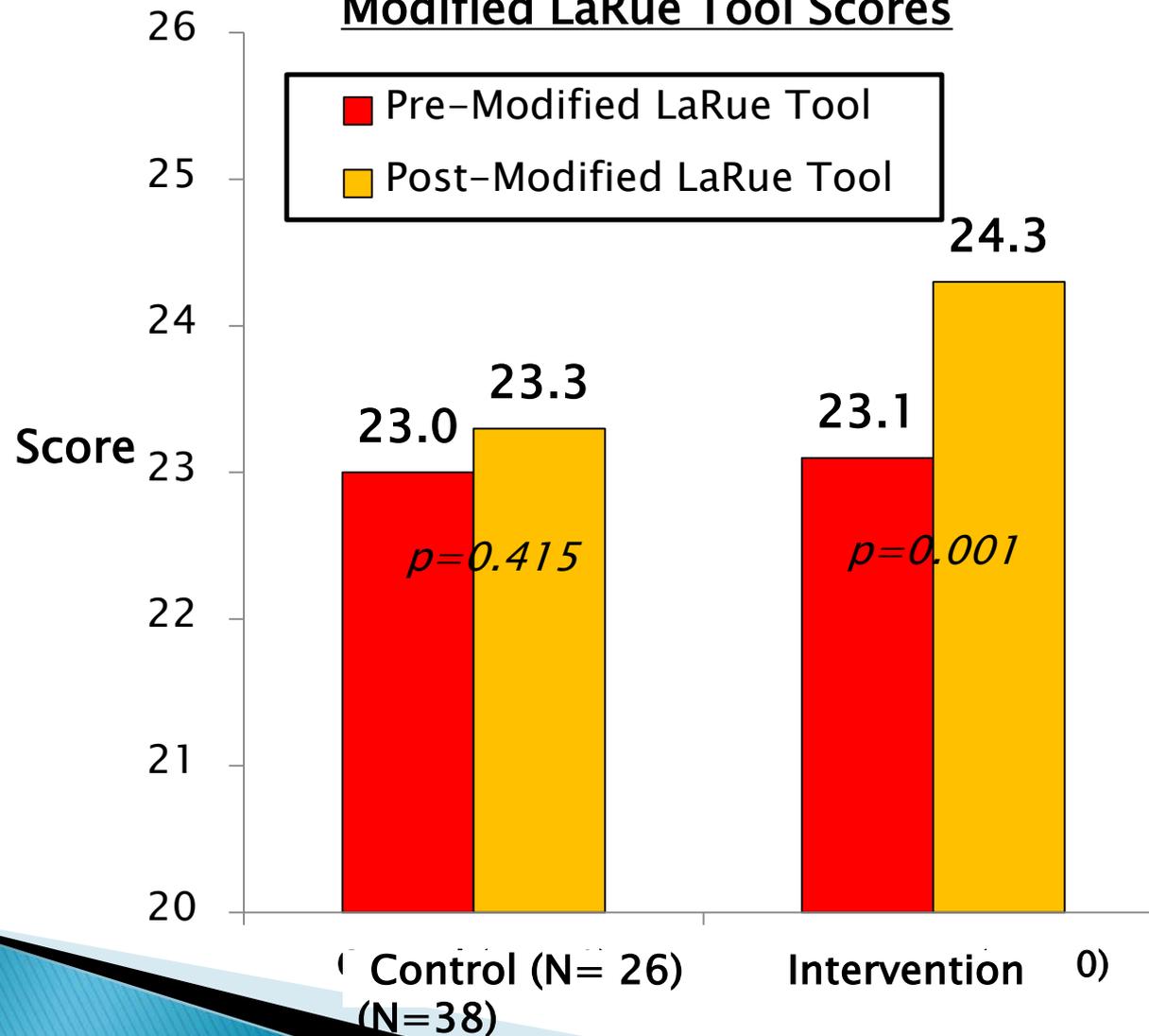
Data are reported as mean \pm SD

or N (%)

	Current, Control (N= 12)	Current, Intervention (N= 16)	Redesigned, Control (N= 26)	Redesigned, Intervention (N= 38)
Age (yrs)	74.2 \pm 9.3	74.7 \pm 8.0	77.5 \pm 9.2	76.0 \pm 8.9
Males	1 (8.3)	8 (50.0)	14 (53.8)	16 (42.1)
Ethnicity				
<i>Caucasian</i>	7 (58.3)	7 (43.8)	16 (61.5)	24 (63.2)
<i>Hispanic/ Latino</i>	2 (16.7)	5 (31.3)	5 (19.2)	3 (7.9)
Education level				
<i>High school diploma or below</i>	2 (16.6)	7 (46.2)	9 (34.6)	9 (23.7)
<i>Some college</i>	5 (41.7)	5 (31.3)	7 (26.9)	13 (34.2)
<i>Bachelor's or above</i>	5 (41.7)	4 (25.1)	10 (38.4)	15 (39.5)
Annual Household Income (\$)				
< 25000	7 (58.3)	10 (62.5)	10 (52.6)	13 (34.2)
Number of Rx meds	3.8 \pm 1.7	5.1 \pm 2.0	5.1 \pm 2.2	5.5 \pm 4.4

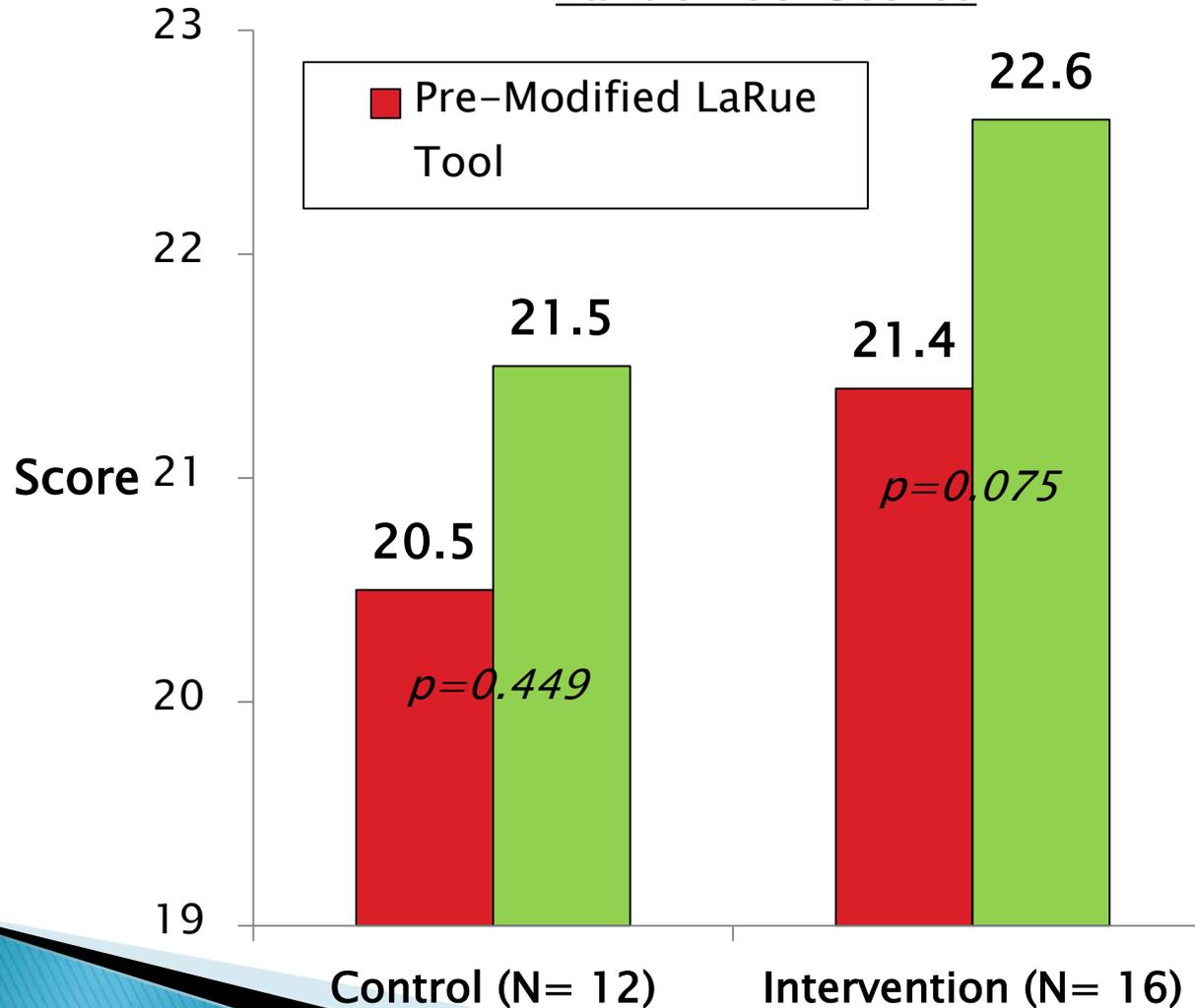
Study Results (Cont'd)– Redesigned Rx Label

Figure 1: Comparison of Pre- and Post-Modified LaRue Tool Scores



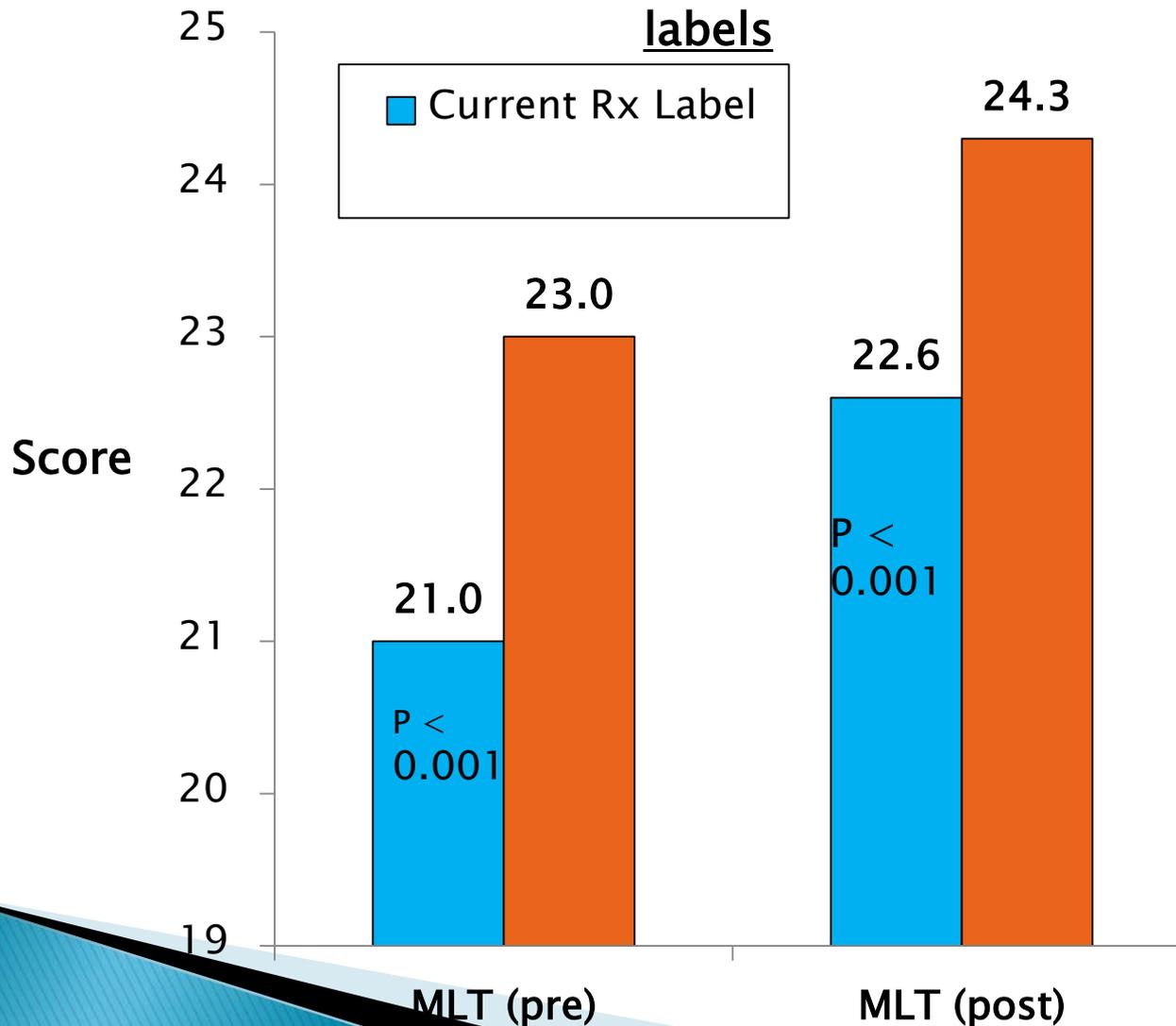
Study Results (Cont'd)– Current Rx Label

Figure 2: Comparison of Pre- and Post-Modified LaRue Tool Scores



Study Results (Cont'd)

Figure 3: Comparison of Modified LaRue Tool (MLT) scores between current and redesigned Rx



Correlation between comprehension and functional Health Literacy

Study sample	Outcomes	Pearson's correlation coefficient*
Redesigned Label (N= 64)	MLR pre-score x STOFHLA pre-score	0.62
	MLR post-score x STOFHLA post-score	0.52
Current Label (N=28)	MLR pre-score x STOFHLA pre-score	0.42
	MLR post-score x STOFHLA post-score	0.38

*All p-values <0.05

Key Messages

- Rx labels need to be simple, easy to use and understand, given that they are a routine part of self-care.
- Certain populations consistently find it difficult to read and understand existing Rx labels, leading to adverse health outcomes and economic burden on the health system.
- The redesigned Rx label was **avored** over current label by all stakeholders
- Simple education **significantly improved** Rx label comprehension in our sample of older adults for patients using our redesigned Rx labels
- Participants showed **better Rx label comprehension** with the redesigned Rx label than with the current Rx label both before and after educational intervention

How about Cost?

- Label change in surface area: 1.7% to 100% => **0 – 2 cents**
- Vial change in size: 13 to 60 drams => **0 – 29.2 cents**
- Amount of ink used: 1.7% to 100% => **0 – 4.0 cents**
- Cost of label change = **0 – 35.2 cents**

- Additional annual cost for a community pharmacy filling:
 - 100 prescriptions/day = $(100 \times 5 \times 52) \times (0 - 35.2) =$ **\$0 – 9,152**
 - 200–500 prescriptions/day = **\$0 – (18,304–45,760)**

- ▶ Cost *MAY* increase if label area is increased.

Cross Cutting Issues

- ▶ A. Manufacturer's name should be listed – not necessarily in the main area of the label
 - ▶ B. Brand name of Generic Equivalent should be included under Drug Name
 - ▶ C. Purpose/Condition SHOULD be a general requirement – 91% of 143 participants in our research indicated they would want it for helping manage medications by category, distinguishing between medications, and reducing confusion.
 - Also helps pharmacists counsel in most cases
 - Does not have to be clinical indication – just lay language
 - Privacy is an issue but it can be left to consumers to opt out
- We asked a panel of experts to modify indications into lay language

<ul style="list-style-type: none"> • Unstable angina (UA) • non-ST-elevation (NSTEMI) • ST-elevation myocardial infarction (STEMI) • DVT 	<ul style="list-style-type: none"> • For prevention/ treatment of blood clots (same for all)
<ul style="list-style-type: none"> • Type 2 diabetes mellitus (NIDDM) 	<ul style="list-style-type: none"> • For controlling high blood sugar
<ul style="list-style-type: none"> • Schizophrenia • acute manic or mixed episodes • adjunct for bipolar disorder 	<ul style="list-style-type: none"> • To improve your mood (same for all)
<p>-Anemia associated with HIV infection (zidovudine) therapy and CRF, reduction of allogeneic blood transfusion for elective, noncardiac, nonvascular surgery, anemia due to concurrent chemotherapy in patients with metastatic cancer receiving chemo for a minimum of 2 months</p>	<p>for low blood count/ To increase blood production (same for all)</p>

Cross Cutting Issues (contd.)

- ▶ D. Fine as is
 - ▶ E. Translations on labels
 - Table of administration times
 - Name of drug and directions translated
 - – use of technology
- 

Our experience on Rx label

- ▶ *Access to multilingual prescription labels and verbal translation services in California*
- ▶ Our 2010 study revealed 68% of 552 CA pharmacies that were interviewed indicated they provide multilingual labels.
- ▶ Issues:
 - Literacy in one's own language
 - Pharmacists' lack of understanding in language
 - Unreliable translations
 - Pictograms are ethnically nuanced

Accuracy of Computer-Generated, Spanish-Language Medicine Labels

[Iman Sharif](#), MD, MPH^a and [Julia Tse](#), Ba^b Pediatrics, Jun 20, 2011.

OBJECTIVE

We evaluated the accuracy of translated, Spanish-language medicine labels among pharmacies in a borough with a large Spanish-speaking population.

METHODS

A cross-sectional, telephone survey of all pharmacies in the Bronx, New York, was performed. Selected pharmacies were visited to learn about the computer software being used to generate Spanish medicine labels. Outcomes included the proportion of pharmacies providing Spanish medicine labels, frequency of computerized translation, and description of Spanish medicine labels produced.

RESULTS

Of 316 pharmacies, 286 (91%) participated. Overall, 209 (73%) provided medicine labels in Spanish. Independent pharmacies were significantly more likely to provide Spanish labels than were hospital or chain pharmacies (88% vs 57% vs 32%; $P < .0001$). Pharmacies that provided Spanish labels mostly commonly (86%) used computer programs to do so; 11% used lay staff members, and 3% used a professional interpreter. We identified 14 different computer programs used to generate Spanish labels, with 70% of pharmacies using 1 of 3 major programs. We evaluated 76 medicine labels generated by 13 different computer programs. Overall, 32 Spanish labels (43%) included incomplete translations (a mixture of English and Spanish), and 6 additional labels contained misspellings or grammar errors, which resulted in an overall error rate of 50%.

CONCLUSIONS

Although pharmacies were likely to provide medicine labels translated into Spanish, the quality of the translations was inconsistent and potentially hazardous. Unless regulations and funding support the technological advances needed to ensure the safety of such labeling, we risk perpetuating health disparities for populations with limited English proficiency.

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8. Moisan J et al. Non-compliance with drug treatment and reading difficulties with regard to prescription labeling among seniors. *J Gerontol* 2002; 48: 44–51.
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10. Cline CM et al. Non-compliance and knowledge of prescribed medication in elderly patients with heart failure. *Eur J Heart Fail* 1999; 1: 145–149.
11. Wolf MS, Davis TC, Shrank W, Rapp DN, Bass PF III, Connor UM, et al. To err is human: patient misinterpretations of prescription drug label instructions. *Patient Educ Couns.* 2007;67: 293–300.
12. Zed PJ, Abu-Laban RB, Balen RM, Loewen PS, Hohl CM, Brubacher JR, et al. Incidence, severity and preventability of medication-related visits to the emergency department: a prospective study. *CMAJ.* 2008;178:1563–9.
13. U.S. Pharmacopeial Convention. *USP-NF General Chapter <17> Prescription Container Labeling.* 2012.
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Global Expertise
Trusted Standards
Improved Health

Prescription Container Labeling Standards

Donna Bohannon, R.Ph, CPPS
Scientific Liaison

USP Nomenclature, Safety, and Labeling Expert Committee
July 31 2014

USP Headquarters, Rockville, Maryland



Need for Standards

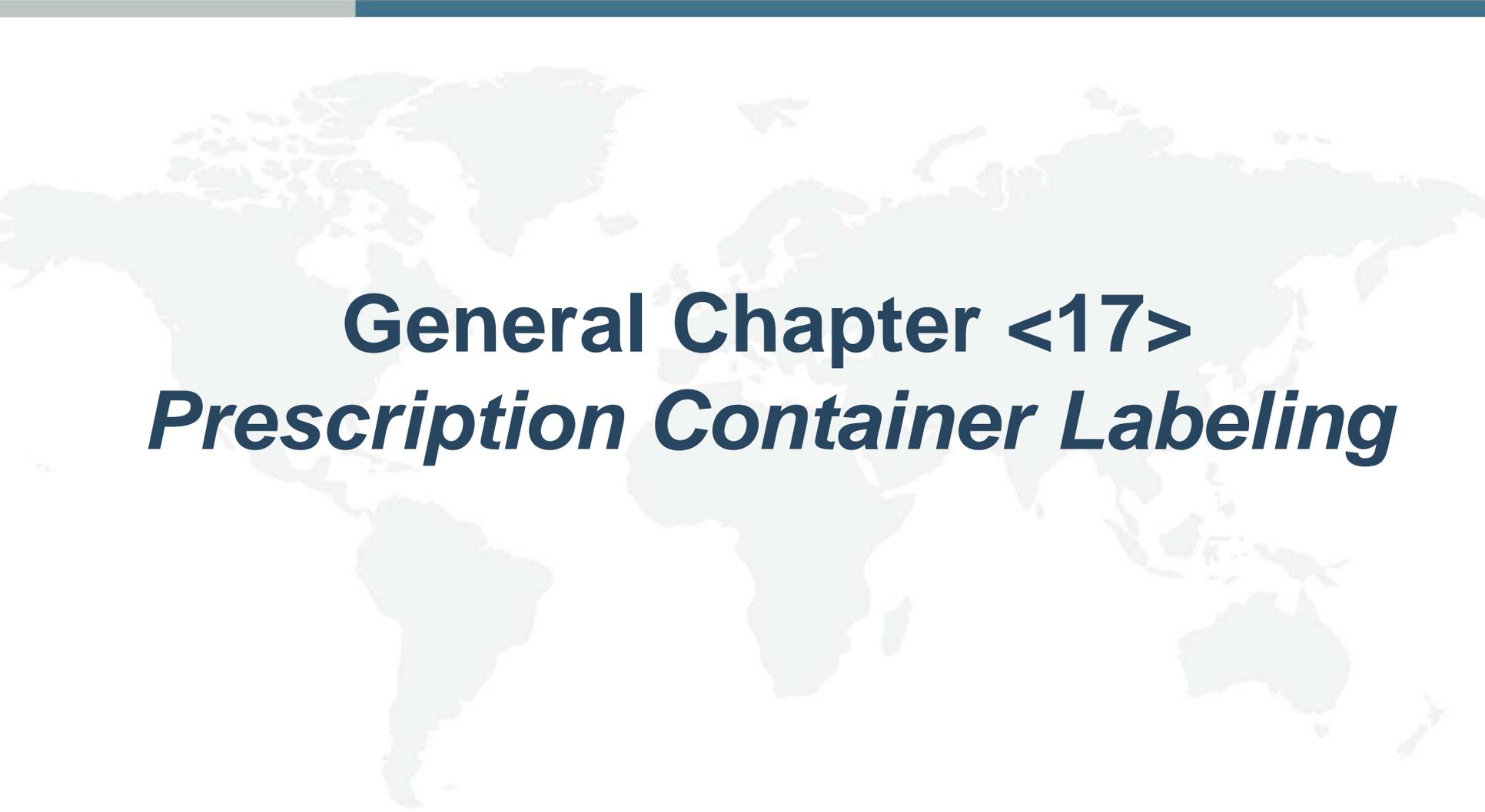
- Medication misuse results in more than one million adverse drug events per year. (IOM 2007)
- The patient's best source (and often only source) of information is the prescription container label.
- Prescription container labels must fulfill professional obligations of prescribers and pharmacists by providing all pertinent information on safe medication use.

USP Expert Panel Convened

- Determine optimal prescription label content and format to promote safe medication use by critically reviewing factors that improve or distract from patient understanding of prescription medication instructions
- Create universal prescription label standards for format/appearance and content/language
- Co-chairs: Gerald McEvoy, Pharm D and Joanne Schwartzberg, MD

USP Expert Panel Members

- Cynthia Brach (AHRQ Health Policy Researcher)
- Sandra Leal, Pharm.D., CDE (Community Pharmacy Practitioner/IOM Bilingual Advisor)
- Linda Lloyd M.Ed. (HRSA Health Literacy Expert)
- Melissa Madigan, Pharm.D., J.D. (Policy - NABP)
- Dan Morrow, Ph.D. (Academia/Researcher)
- Ruth Parker, M.D. (Health Literacy Expert/Practitioner)
- Cynthia Raehl, Pharm.D., FASHP, FCCP (Academia/Practitioner)
- William Shrank, M.D., MSHS (Academia/Practitioner)
- Patricia Sokol, RN, J.D., (AMA - Medication Safety Expert)
- Darren Townzen, R.Ph., MBA (Community Pharmacy/NCPDP)
- Jeanne Tuttle, R.Ph. (Health System Practitioner/Researcher)
- Joan E. Kapusnik-Uner, Pharm.D., FCSHP (Data Industry)
- Michelle Weist, Pharm.D., BCPS (Health System Practitioner/CPOE Expert)
- Michael Wolf, Ph.D., MPH (Health Literacy Researcher)



General Chapter <17> ***Prescription Container Labeling***

Patient Centered

- Patient-directed information must be organized in a way that best reflects how most patients seek out and understand medication instructions.
- Prescription container labeling should feature only the most important patient information needed for safe and effective understanding and use.

Patient Centered continued

USP Standard

- Critical Information at the top of the label
 - Minimum 12 point font
 - Patient name
 - Drug name and strength
 - Brand **and** generic
 - Explicit instructions
- Placement of less critical information

California Regulation

- Clustered items occupy 50% of the label space
 - Patient name
 - Drug name and strength
 - Brand **or** generic
 - Directions for use
 - Condition or purpose

Simplify Language

USP Standard

- Clear
- Concise
- No medical jargon
- Sentence case

California Regulations

- Case not specified

Instructions for Use

USP Standard

- Use explicit text to describe dosage/interval instructions
- Separate dose from timing
- Use numbers for dose (1)
- Specifics for time periods
- Consistent use of the same terms
- **Avoid vague instructions**

California Regulation

- Use explicit text to describe dosage/interval instructions
- Separate dose from timing
- Use numbers for dose (1)
- Specifics for time periods
- Consistent use of the same terms
- **Fifteen specific phrases**

Purpose for Use

USP Standard

- Prescriber discretion
- Patient acceptance
- Plain language
 - (e.g., “high blood pressure” instead of “hypertension”)

California Regulation

- One of four required elements
- Prescriber discretion

Limited English Proficiency

USP Standard

- Patient's preferred language
- Instructions in English as well as preferred language
- High quality translation process

California Regulation

- Patient's language
- Translations for five languages available on the Website
- Interpretive service

Improve Readability

USP Standard

- Optimize typography:
 - High-contrast print
 - Simple, uncondensed fonts
 - Sentence case
 - Large font size

California Regulation

- Large font size

Improve Readability continued

USP Standard

- Generally
 - Limit coloring
 - White space
 - Eliminate truncation
 - Horizontal text

California Regulation

- For required or primary items
 - Highlight in boldface or color
 - White space

Visual Impairment

- Follow patient-centered prescription container label standards
- Provide alternative access to label information
- Enhance communications on available options
- Provide service or direct patient to alternative access
- Follow best practices for alternative access format

Contact Information

USP: <http://www.usp.org/>

USP: Medication Safety & Labeling:
<http://www.usp.org/usp-healthcare-professionals/medication-safety-labeling>

Donna Bohannon, R.Ph., CPPS USP Scientific
Liaison Nomenclature, Safety and Labeling
Expert Committee
1-301-230-3252 / DZB@usp.org



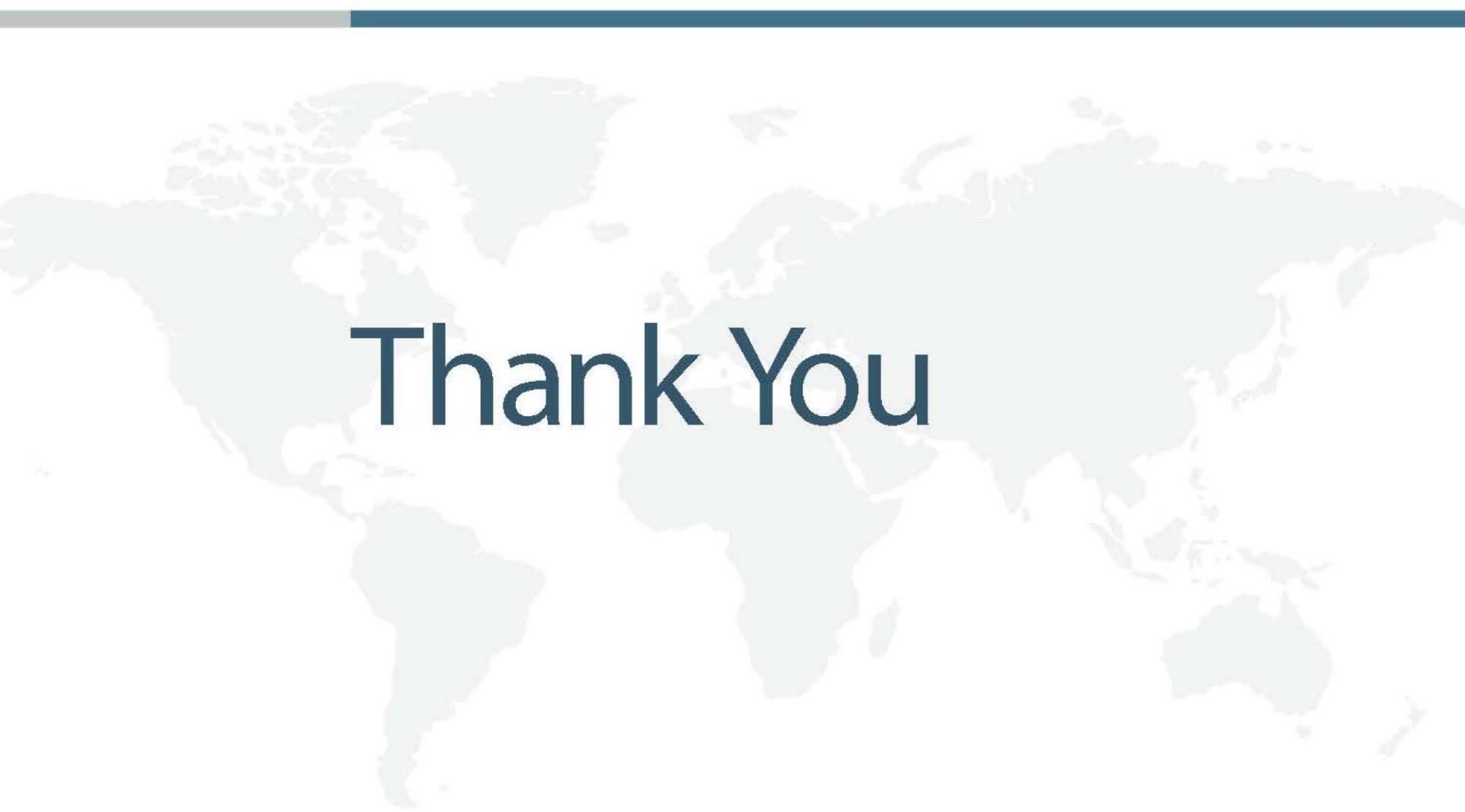
Global Expertise
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A light gray world map is centered in the background of the slide, showing the continents of North America, South America, Europe, Africa, Asia, and Australia.

Questions



Global Expertise
Trusted Standards
Improved Health

A light gray world map is centered in the background of the slide, showing the continents of North America, South America, Europe, Africa, Asia, and Australia.

Thank You

Brief Overview

- Revisiting the Evidence of Need
- Target 1: Directions for Use
- Target 2: Language Concordance
- Recommendations

Problem:

Variable, Poor Quality Rx Information



Risk of improper use and non-adherence

Risk for Safety, Non-Adherence

- Many adults misunderstand R_x labeling and make dosing errors
- 75% can't fully identify R_x indication for use = non-adherence, poorer clinical outcomes
- (Persell et al Am J Med, 2010, Lenahan et al, J Health Comm 2013)



Risk for Safety, Non-Adherence

- Many adults misunderstand R_x labeling and make dosing errors
 - 75% can't identify R_x indication for use = non-adherence, poorer clinical outcomes (Persell et al Am J Med, 2010, Lenahan et al, J Health Comm 2013)
 - 52% misinterpret auxiliary warning information (Davis et al JGIM 2006)
 - 54% demonstrate improper dosing on common 'sigs' (Wolf, Davis et al. Ann Intern Med 2006)
 - Misunderstanding and improper dosing linked to non-adherence, 20% greater risk of readmission (Farber J Asthma 2003; Lindquist et al. JGIM, 2012; Serper et al., under review, 2014)



Risk for Safety, Non-Adherence

- Many adults misunderstand Rx labeling and make dosing errors

- 75% can't identify Rx indication for use = non-adherence, poorer clinical outcomes

(Persell et al Am J Med, 2010, Lenahan et al, J Health Comm 2013)

- 52% misinterpret auxiliary warning information

Variable, Poor Quality Rx Labeling is One Major Root Cause

- 54% demonstrate improper dosing, common 'signs'

(Wolf, Davis et al J Intern Med 2006)

- Misunderstanding and improper dosing linked to non-adherence, 20% greater risk of readmission

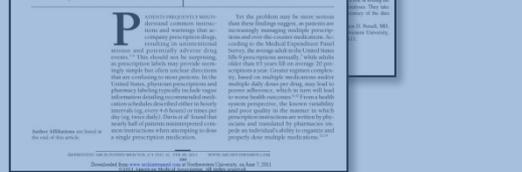
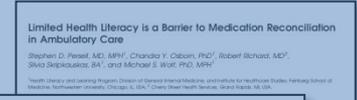
(Farber J Asthma 2003; Lindquist et al. JGIM, 2012; Serper et al., under review, 2014)

- 43 to 85% over-complicate multi-drug regimens

(Wolf et al. Arch Intern Med 2011; Lindquist et al, Pat Ed Counsel 2014)

- Regimen complexity linked to misunderstanding, non-adherence, hospitalization, outcomes

(Gazmararian et al JGIM 2006; Choudhry et al, Arch Intern Med 2011; Neri et al Am J Nephrol 2011; Paquin et al Exp Op Drug Saf 2013)



California Requirements



- **Emphasize** (via font size, color, bold, white space)
 - patient name
 - drug name, dosage
 - directions for use
 - indication, if given
- Above should comprise 50% of label
- Universal Medication Schedule (UMS) recommended, **'when appropriate'**
- Translations or interpreter services minimally required (not specified to label translation)

Evidence-Based Solutions

An Evidence Base



Description of standards for the enhanced Rx container label prototype.^a

Proposed standard	Description
1. Use explicit text to describe dosage/interval in instructions.	Dosage/usage instructions will more clearly separate dose from interval, and provide the explicit frequency of the drug (i.e. “take 4 tablets each day. Take 2 tablets in the morning, and 2 tablets in the evening” vs. “take two tablets by mouth twice daily”). These explicit dose/use instructions will be standardized by the pharmacy to avoid physician variability for the same dose frequency.
2. Use a recognizable visual aid to convey dosage/use instructions.	A matrix will be used to visually identify and support the explicit text dosage/usage instructions, following a familiar format to cue patients (pill sorter box; morning (7 am–9 am); noon (11 am–1 pm); evening (4 pm–6 pm); and night (8 pm–10 pm)). A tablet icon will be used to identify the appropriate dose.
3. Organize label in a patient-centered manner.	Patient-directed information will be organized following the schema patients impart to understand medicine instructions. Patient-directed content will be at the top of the label, while provider-directed content will be placed at the bottom of the label. Drug name and specific dosage/usage instructions will be placed in greatest prominence.
4. When possible, include indication for use.	On the front side of the container label, a box will include “Take for _____”. While Rx approval status and confidentiality may limit inclusion of indications for use, prior studies suggest this is very helpful to patients.
5. Simplify language, avoiding unfamiliar words/medical jargon.	Language on the label, but particularly dosage/usage instructions, will avoid the use of medical jargon, and common terms and sentences will be used only. While readability formulas and software are not recommended for short excerpts of text such as what is included on Rx labels, we will follow the principles established by the Suitability Assessment of Materials by Doak, Doak, and Root [48] for maintaining simple language and will have feedback from non-enrolled patients participating in a pilot test of materials as well.
6. Improve typography, use larger, sans serif font.	A standard for minimum font size (12 pt) will be set for patient name, drug name, and specific dosage–usage instructions (both in text and in matrix). Health literacy and adult education researchers recommend the use of sans-serif font (i.e. Arial) to more clearly present print text information to new adult learners. Patient information on front and back labels will be 12 pt font. Use of all capital letters will be avoided; the first letter of words in text will be capitalized only.
7. When applicable, use numeric vs. alphabet characters.	Presenting numbers instead of the text equivalent (i.e. 2 vs. two) was more helpful to patients for understanding and more rapidly processing dosage/usage instructions.
8. Use typographic cues (bolding and highlighting) for patient content only.	Bolding and highlighting will be used for patient-centered information only. Drug name and dose will be highlighted, dosage/usage instructions bolded.
9. Use horizontal text only.	Several national pharmacy chains place text for warning and instruction messages vertical to the Rx label; requiring the patient to turn the container to read. This may create further difficulty among older adults. We will only include horizontal text on the label.

^a Presented at the Institute of Medicine Health Literacy Roundtable, October 12, 2007.

Target 1: Directions for use

Standardizing Instructions

Universal Medication Schedule (UMS) proposed 2006

- Eliminate prescribing and dispensing variability
- Help patients organize and consolidate multi-drug regimens
- Use recognizable 'pill box' schema - morning, noon, evening, bedtime
- Explicit time intervals better interpreted vs. times per day, hourly intervals, or even explicit times
- Use graphic aid to reinforce dosing schedule (?)

Universal Medication Schedule (UMS)

The Enhanced Rx Label

<p>Do not drink alcoholic beverages while taking this medicine</p> <p>Carry or wear medical identification stating you are taking this medicine</p> <p>You should avoid prolonged or excessive exposure to direct and/or artificial sunlight while taking this medicine</p>	<p>Michael Wolf 04/29/71</p> <p>Glyburide 5mg</p> <p>Take for Diabetes</p>	<p>Rx# 1234567 9/8/2009</p> <p>You have 11 refills 180 pills</p> <p>Discard after 9/8/2010</p> <p>Provider: RUTH PARKER.MD Emory Medical Center (414) 123-4587</p> <p>Pharmacy:NOVA Scripts Central 11445 Sunset Blvd. Reston, VA (713) 123-4567</p>						
	<p>Take:</p> <p>2 pills in the morning 2 pills in the evening</p>	<p>NDC # 1234567</p>						
	<table border="1"> <thead> <tr> <th>Morning 7-9 AM</th> <th>Noon 11-1 PM</th> <th>Evening 4-6 PM</th> <th>Bedtime 9-11 PM</th> </tr> </thead> <tbody> <tr> <td>2</td> <td></td> <td>2</td> <td></td> </tr> </tbody> </table>		Morning 7-9 AM	Noon 11-1 PM	Evening 4-6 PM	Bedtime 9-11 PM	2	
Morning 7-9 AM	Noon 11-1 PM	Evening 4-6 PM	Bedtime 9-11 PM					
2		2						

2.5"

4.625"

Take

Take

Take

Take

1 pill at noon
1 pill in the evening

1 pill in the morning
1 pill at noon
1 pill in the evening
1 pill at bedtime



Noon: 11-1 pm



Evening: 4-6 pm



Bedtime: 9-11 pm

6-8 am

Add the following:

▲(17) PRESCRIPTION CONTAINER LABELING

PRESCRIPTION CONTAINER LABEL STANDARDS TO PROMOTE PATIENT UNDERSTANDING

Organize the prescription label in a patient-centered manner: Information shall be organized in a way that best reflects how most patients seek out and understand medication instructions. Prescription instructions shall be written in plain language and shall be clear, concise, and easy to understand. The information shall be organized in a way that best reflects how most patients seek out and understand medication instructions.

Emphasize instructions to patients: Prominent for patients' safe and effective use of the medication, the label shall specify clear directions for use.

The prescription directions shall be written in plain language and shall be clear, concise, and easy to understand. The information shall be organized in a way that best reflects how most patients seek out and understand medication instructions.

Other less critical but name and phone number information, expiration quantity, physical description (information) should not be included.

Such less critical information from dosing instructions in another less prominent location, which can impair understanding.

Simplify language: Language shall be simplified, concise, and standardized. Do not use Latin terms or medical terminology unless necessary to simplify short prescription labels. Instead, use plain language that has been shown to be understood by patients from samples of diverse backgrounds.

Use of readability formulas to simplify short prescription labels. Instead, use plain language that has been shown to be understood by patients from samples of diverse backgrounds.

Give explicit instructions: The timing of each dose number of dosage units time periods (each day, bedtime), instructions should be explicit. Do not use abbreviations. Example: write "Take 2 in the evening" rather than "Take 1 tablet in the evening" if the prescription is based on dosing interval daily, or hourly intervals should be avoided because patient interpretation through instructions that a.m. and 10 p.m.) may be more difficult to understand than explicit instructions such as "in the morning, lunch, or at bedtime." Clear instructions should help avoid patient misunderstanding.

Whenever available, use the patient's preferred language. If the patient's preferred language is not the English language, the label should be written in the patient's preferred language.

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Whenever available, use the patient's preferred language. If the patient's preferred language is not the English language, the label should be written in the patient's preferred language.

Universal Medication Schedule White Paper

Senate Bill No. 472
CHAPTER 470

An act to add Section 4076.5 to the Business and Professions Code, relating to pharmacy.

[Approved by Governor October 11, 2007. Filed with Secretary of State October 11, 2007.]

LEGISLATIVE COUNSEL'S DIGEST

SB 472, Corbett. Prescription drugs: labeling requirements. Existing law, the Pharmacy Law, provides for the licensure and regulation of the practice of pharmacy by the California State Board of Pharmacy in the Department of Consumer Affairs. Existing law prohibits a pharmacist from dispensing a prescription, except in a container that meets certain labeling requirements.

This bill would require the board to promulgate regulations that require, on or before January 1, 2011, a standardized, patient-centered, prescription drug label on all prescription medication dispensed to patients in California. The bill would require the board to hold special public meetings statewide in order to seek information from certain groups, and would require the

April 2013

National Council for Prescription Drug Programs
9240 East Raintree Drive



(c) When developing the requirements for prescription drug labels, the board shall consider all of the following factors:

(1) Medical literacy research that points to increased understandability of labels.

(2) Improved directions for use.

SECTION 1. This act shall be known and may be cited as the California Patient Medication Safety Act.

SEC. 2. The Legislature hereby finds and declares all of the following:

(a) Health care costs and spending in California are rising dramatically and are expected to continue to increase.

Pertinent Studies

- Unfunded efficacy trials (Davis et al JGIM 2009; Wolf et al Med Care 2011; Sahm Eur J Clin Pharmacol 2012)
- AHRQ/NIH: Pharmacy-based RCT (English, Spanish)
- Cal Endowment: UMS language translation
(Spanish, Korean, Vietnamese, Chinese, Russian)
- NCI: UMS sigs at point of prescribing via EHR (Epic)
- AHRQ CERT: UMS EHR-generated medication list (Cerner)
- NINR: 2 RN-assisted regimen consolidation trials for diabetes
- Merck: UMS strategy including texting at prescribing (Centricity)
- CHCF: Expansion of UMS to non-pill, non-standard sigs
- CHCF: Evaluation of SB 472 R_x labeling regulation

Pertinent Studies

- **Davis et al. JGIM 2009 (N=359, 3 sites)**
 - UMS intervals or specific times > hourly intervals or # times daily
 - UMS intervals > specific times

Pertinent Studies

- **Davis et al. JGIM 2009 (N=359, 3 sites)**
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- **Wolf et al. Med Care 2011 (N=500, 2 sites)**
 - UMS w/o graphic > UMS w/ graphic or standard
 - literacy disparities reduced

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 - UMS ~ standard
 - lower literate patients: UMS > standard

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- **Sahm et al. EJCP 2012 (N=94, 1 site)**
 - UMS ~ standard
 - lower literate patients: UMS > standard
- **Bailey et al. JGIM 2013 (N=202, 2 sites)**
 - translated UMS > standard (all languages)
 - improves multi-R_x regimen consolidation

Pertinent Studies

AHRQ/NIH Clinical Trial [R01HS017687; R01HS016435]

Sites: 8 FQHCs in DC area served by 1 central fill pharmacy

Sample: 845 English/Spanish-speaking patients w/ diabetes & hypertension[†]

Study arms: 1) Enhanced usual care vs. 2) patient-centered label w/ UMS*

Outcomes: 1) Demonstrated R_x use; 2) consolidation; 3) adherence (self-report, pill count); 4) intermediary clinical outcomes (HbA1c via chart)

Follow-Up: Baseline, 3 and 9 months (chart pull at 6 months)

[†]85.4%, 85.8% cooperation rates *simple 1:1 randomization

THE WALL STREET JOURNAL.

WOLF, MICHAEL 09/01/2009 Rx# 6607815
AMOXICILLIN 500MG CAP RANBAXY DOB: 03/29/71
You have 2 refills
40 pills
Discard After 09/01/2010
DR RUTH PARKER, MD

Take:
2 PILLS IN THE MORNING
2 PILLS IN THE EVENING

Morning 7-9 AM	Noon 11-1 PM	Evening 4-6 PM	Bedtime 9-11 PM
2		2	

NOVA SCRIPTSCENTRAL
6400 Arlington Blvd Ste. 120
Falls Church, VA, 22042
(703)532-4158
NDC# 63304-0655-05
Rx Only HN

Intervention

WOLF, MICHAEL 09/01/2009 Rx# 6607815
AMOXICILLIN 500MG CAP RANBAXY DOB: 03/29/71

You have 2 refills
 pills
 Discard After 09/01/2010
 RUTH PARKER, MD

Take:
 2 PILLS IN THE
 2 PILLS IN THE

Morning 7-9 AM	Noon 11-1 PM	Evening 4-6 PM
2		2

TEST, PATIENT
 AMOXICILLIN 500MG CAP RANBAXY

Take:
 2 PILLS IN THE MORNING
 2 PILLS IN THE EVENING

Morning 7-9 AM	Noon 11-1 PM	Evening 4-6 PM
2		2

VA SCRIPTSCENTRAL
 6400 Arlington Blvd Ste. 120
 Falls Church, VA. 22042
 (703)532-0158

NDC# 63304-0655-05
 Rx Only HN

ENHANCED 'UMS' LABEL

WOLF, MICHAEL DOB: 03/29/1971 RX # 6607815
 09/01/09

TAKE TWO CAPSULES BY MOUTH TWICE DAILY

Finish all unless otherwise directed

Report rash or allergic reaction.

May interfere with bi control pills.

AMOXICILLIN 500MG CAP (RANBAXY) #40

2 Refill(s) Remain By 09/01/2010
 QTY: 40 CAP Discard After: 09/01/2010

Dr: PARKER, RUTH MD

NOVA SCRIPTSCENTRAL (703)532-0158
 6400 Arlington Blvd Ste. 120 Falls Church, VA. 22042

NDC: 63304-0655

STANDARD LABEL

Beyond Structured, Codified Sig

ENHANCED DOSAGE INSTRUCTIONS FOR PHARMACY TRANSCRIPTION

ENGLISH	SPANISH
Take 1 pill at bedtime	Tome 1 pastilla a la hora de acostarse
Take 2 pills at bedtime	Tome 2 pastillas a la hora de acostarse
Take 3 pills at bedtime	Tome 3 pastillas a la hora de acostarse
Take 1 pill in the morning	Tome 1 pastilla por la mañana
Take 2 pills in the morning	Tome 2 pastillas por la mañana
Take 3 pills in the morning	Tome 3 pastillas por la mañana
Take 1 pill in the morning, and 1 pill at bedtime	Tome 1 pastilla por la mañana, y 1 pastilla a la hora de acostarse
Take 2 pills in the morning, and 2 pills at bedtime	Tome 2 pastillas por la mañana, y 2 pastillas a la hora de acostarse
Take 3 pills in the morning, and 3 pills at bedtime	Tome 3 pastillas por la mañana, y 3 pastillas a la hora de acostarse
Take 1 pill in the morning, 1 pill at noon, and 1 pill in the evening	Tome 1 pastilla por la mañana, 1 pastilla al mediodía , y 1 pastilla a la hora de acostarse
Take 1 pill in the morning, 1 pill at noon, 1 pill in the evening, and 1 pill at bedtime	Tome 1 pastilla por la mañana, 1 pastilla al mediodía , 1 pastilla al atardecer , y 1 pastilla a la hora de acostarse

General Findings

- **Demonstrated Use:** 2-fold improvement (ARR 1.98, 95% CI 1.02-3.85) (greater benefit among English speaking patients) by 9 months
- **Adherence (via pill count):** non-significant trend among English-speaking patients, improvement among Spanish-speaking patients (ARR 1.72, 95% CI 1.02 – 2.85) at 3 months only
- **Disproportionate Benefit from UMS:** Greatest improvement for:
Demonstrated Use: patients taking >5 medications, lower literate
Adherence: Spanish-speaking patients taking >5 medications, lower literate

Target 2: Language concordance

Lost in Translation...

- Evidence of need for proper translations **strong**
 - ✓ Services are inconsistent and/or highly inadequate (Muzyk JAPHA 2004; Bradshaw Pediatrics 2007; Bailey Med Care 2008; Sharif Pediatrics 2010)
 - ✓ Lack of adequate services a cause of non-adherence and error (Westberg JAPHA 2005; Leyva Ambul Peds 2005)
 - ✓ A matter of equity (Wilson JGIM 2007; Sleath JAPHA 2009)

'ConcordantRx'

- CA Endowment-sponsored project
- Developed UMS directions in 5 languages (Spanish, Chinese, Russian, Korean, Vietnamese)
- Efficacy Trial among 200+ consumers (SF, Chicago)
- ConcordantRx labels improved:
 - proper use by 25%
 - regimen consolidation by 32%

Evaluation of Language Concordant, Patient-Centered Drug Label Instructions

Stacy Cooper Bailey, PhD, MPH¹, Urmimala Sarkar, MD, MPH^{2,3}, Alice Hm Chen, MD, MPH,
Dean Schillinger, MD^{2,3}, and Michael S. Wolf, PhD, MPH⁴

¹Health Literacy and Learning Program, Division of General Internal Medicine, Keck School of Medicine of Northwestern University, Chicago, IL, USA; ²Division of General Internal Medicine, San Francisco General Hospital, University of California at San Francisco, San Francisco, CA, USA; ³University of California at San Francisco Center for Vulnerable Populations, San Francisco General Hospital, San Francisco, CA, USA

BACKGROUND: Despite federal laws requiring language access in healthcare settings, most US pharmacies are unable to provide prescription (Rx) medication instructions to limited English proficient (LEP) patients in their native language.

OBJECTIVE: To evaluate the efficacy of health literacy-informed, multilingual Rx instructions (the ConcordantRx instructions) to improve Rx understanding, regimen dosing and regimen consolidation in comparison to standard, language-concordant Rx instructions.

DESIGN: Randomized, experimental evaluation.
PARTICIPANTS: Two hundred and two LEP adults speaking five non-English languages (Chinese, Korean, Russian, Spanish, Vietnamese), recruited from nine clinics and community organizations in San Francisco and Chicago.

INTERVENTION: Subjects were randomized to review Rx bottles with either ConcordantRx or standard instructions.

MAIN MEASURES: Proper demonstration of common prescription label instructions for single and multi-drug medication regimens. Regimen consolidation was assessed by determining how many times per day subjects would take medicine for a multi-drug regimen.

KEY RESULTS: Subjects receiving the ConcordantRx instructions demonstrated significantly greater Rx understanding, regimen dosing and regimen consolidation in comparison to those receiving standard instructions (incidence rate ratio [IRR]: 1.25, 95% confidence interval [CI]: 1.04-1.48, P=0.007 for Rx understanding, IRR: 1.19, 95% CI: 1.03-1.39, P=0.02 for regimen dosing and IRR: 0.76, 95% CI: 0.64-0.90, P=0.001 for regimen consolidation). In most cases, instruction type was the sole, independent predictor of outcomes in multivariate models controlling for relevant covariates.

CONCLUSIONS: There is a need for standardized, multilingual Rx instructions that can be implemented in pharmacy practices to promote safe medication use among LEP patients. The ConcordantRx instructions represent an important step towards achieving this goal.

KEY WORDS: health literacy; prescription; medication; drug labeling; limited English proficiency
J Gen Intern Med
DOI: 10.1007/s11066-012-0105-3
© Society of General Internal Medicine 2012

INTRODUCTION

Approximately 20% of the United States population speaks a language other than English at home, and nearly 1 in 11 has limited English proficiency (LEP), defined as the ability to speak English less than 'very well'.¹ Despite laws requiring language access in healthcare settings, research on pharmacy practice indicates that language barriers persist.²⁻⁴ Interpreters are rarely available to assist pharmacists in counseling LEP adults, half of pharmacies provide limited or no translation services for prescription (Rx) labels, and other print materials are seldom available in non-English languages.^{5,6} When Rx information is translated, it is often inaccurate or written at a reading level that is too difficult for many to understand.^{7,8}

Such language barriers constitute a serious patient safety concern.⁹ The 2006 Institute of Medicine report *Prescribing Medication Errors* reported that poor comprehension of Rx instructions is a root cause of adverse drug events and other medication errors.⁹ Recently, studies among LEP adults have linked Rx misunderstanding to higher rates of adverse drug reactions, unsafe medication management and poor adherence.¹⁰⁻¹⁴

Interventions are needed to improve comprehension of medication instructions among LEP adults and to promote language access in pharmacy. Lessons learned in the development of health literacy-informed, English-language instructions can guide this process. Wolf and colleagues previously tested the efficacy of patient-centered Rx instructions among English-speaking patients and found that more explicit instructions significantly improved comprehension, particularly among low literate patients.¹⁵ While language proficiency is a distinctly different risk factor, it is closely associated with health literacy.¹⁶ Therefore, our team developed a set of multilingual Rx

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Revised February 2, 2012
Accepted February 10, 2012

Recommendations

1. Provide explicit guidance towards improved directions for use - consider UMS
 - not 'when appropriate'
 - pill form only (for now)
 - no graphic requirement
2. Require the provision of written language translations on prescription container labels
 - require proof of a valid means for accurate written translations
 - offer ConcordantRx instructions as one option for pharmacies who want them

Considerations

- Work with CA Medical Society/Board on standardizing 'sigs' and providing indication
- Take a pragmatic view of what you are asking for (space considerations, inclusion of English and translated instructions, room for indication)
- Expand regulatory requirements beyond container label - coordinate a system of Rx information
- Recognize that action on evidence can only improve upon the current, problematic practices

NORTHWESTERN UNIVERSITY

HeLP

Health Literacy & Learning Program



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**Patient-Centered Prescription
Label Forum
California Board of Pharmacy
Sacramento, CA
July 31, 2014**



**Linda Neuhauser, DrPH, MPH
Clinical Professor
School of Public Health
University of California, Berkeley**

My Background

- **Clinical Professor of Community Health and Human Development**
- **Focus on translating scientific findings to health communication for diverse groups**
- **Head the UC Berkeley Health Research for Action center:
<http://www.healthresearchforaction.org>**
- **Founding member of FDA Risk Communication Advisory Committee (2008)**

Medications & Patient Communication

- Increase in adverse drug events (ADEs)
- Majority of ADEs related to poor communication
- Half of patients take medications incorrectly
- Patients forget/misunderstand half of verbal instructions
- Medication adherence related to communication
- Vulnerable populations: low health literacy and limited English proficient (LEP)

– “perfect storm”

Medications & Patient Communication

(2)

- **> 20% of CA consumers are LEP**
- **Vulnerable populations increasing in CA:**
 - **Increase in minority populations**
 - **ACA enrollment**
 - **Increase in Medicaid enrollment (25%)**
 - **Population is aging**
 - **Shorter clinical encounters**

Policy Trends

2007: Joint Commission Report “What did the Doctor Say?” (patient safety)

- FDAAA law (increased communication authority)
- FDA established Risk Communication Advisory Committee

2009: FDA Safe Use Initiative (prevent ADEs)

2010: Affordable Care Act

- More FDA authority over labeling to support patient decision-making (Sec 3507)

Incentives: Linguistic Labeling

- **Decrease patient morbidity and mortality**
- **Decrease ADEs**
- **Decrease hospital readmissions**
- **Decrease CA healthcare costs**
- **Improve medication adherence**
- **Increase revenue for pharmacies**
- **California as a model**

“Inevitable”

Challenges: Linguistic Labeling

- **Few existing models (NY SafeRx)**
- **Liability concerns (see NY legislation)**
- **Decisions about translations & updates**
- **Revamping pharmacy processes**
- **Training pharmacists and techs**
- **Researching impacts: patients & pharmacies (NY Academy of Medicine)**
- **Addressing issues over time**

NY Legislation: Liability

“Covered pharmacies shall not be liable for injuries resulting from the actions of third-party contractors taken pursuant to and within the scope of the contract with the covered pharmacy as long as the covered pharmacy entered into such contract reasonably in and in good faith to comply with this section, and was not negligent with regard to the alleged misconduct of the third-party contractor.”

2012 New York Consolidated Laws

EDN – Education

Title 8 – The Professions

Article 137 – (6800 – 6830) Pharmacy

6829 – Interpretation and translation requirements for prescription drugs and standardized medication labeling

(Section 5)

Thanks



Linda Neuhauser

lindan@berkeley.edu

Remarks to CA BOP in regards to Patient Centered Labeling

Donna Horn, RPh, DPh
Director Patient Safety- Community Pharmacy
Institute for Safe Medication Practices
July 31, 2014

Label Purpose

- Patients' best source (and often only source) of prescription medications is the prescription container label
- Obligated to include most essential information needed to understand
 - how to take safely and appropriately to adhere to the prescribed medication regimen

ISMP supports efforts of the CA BOP

- Specifically, we support
 - Condition or purpose on label
 - Physical description of the dispensed medication
 - Recommend that color and odor be added for liquids
 - Use of standardized dosing
 - Frequency based on: morning, noon, evening, bedtime
 - Provide and facilitate the use of the patient's native language
 - Web site translations

Look of the Label

- Agree to minimum of 12 point font
 - For patient-centered elements including the patient directions (per current research and guidelines)

Items to Consider

- Prohibiting the term “as directed”
- Pharmacy name, address, phone, etc., should be at the bottom of the label
 - Uppermost should be patient name and date of birth
- Print brand and generic name if medication is written for brand and dispensed generically
- Directions must use metric dosing

More to Consider

- Avoid the use of all potentially dangerous abbreviations and dose expressions
 - Spell out the word Units
 - Properly spaced commas, i.e., 5,000
- PWL in a consistent location
- Horizontal text only

USP and Others' Recommended Guidelines

- Bolding,
- Justification(left-justified)
- Sentence case and spacing
- Contrast
- Black print
- Non-glossy paper

Thank You

- Please refer to the ISMP website for more information and references

<http://www.ismp.org/tools/guidelines/labelFormats/comments/default.asp>

Attachment 3

Top 100 Most Prescribed, Top-Selling Drugs

<http://www.medscape.com/viewarticle/829246>

August 01, 2014

There has been little change in top-prescribed and top-selling prescription drugs in the United States, according to the latest data from research firm IMS Health.

Hypothyroid medication levothyroxine (*Synthroid*, AbbVie) continues to be the nation's most prescribed drug, and the antipsychotic aripiprazole (*Abilify*, Otsuka Pharmaceutical) continues to have the highest sales.

The data reflect a rolling 12 months of history (July 2013 - June 2014) on the top 100 drugs by total sales and total prescriptions in the United States.

Following levothyroxine (with 22.6 million prescriptions) as the most prescribed drug in the United States were the cholesterol-lowering drug rosuvastatin (*Crestor*, AstraZeneca), at about 22.5 million prescriptions; the proton pump inhibitor esomeprazole (*Nexium*, AstraZeneca), at roughly 18.6 million prescriptions; and the asthma medications albuterol (*Ventolin HFA*, GlaxoSmithKline), at 17.5 million prescriptions, and fluticasone propionate/salmeterol (*Advair Diskus*, GlaxoSmithKline), at 15 million prescriptions.

Rounding out the top 10 most prescribed drugs for the period (in order) were the antihypertensive valsartan (*Diovan*, Novartis), the insulin glargine injection (*Lantus Solostar*, sanofi-aventis), the antidepressant duloxetine (*Cymbalta*, Eli Lilly), the attention-deficit drug lisdexamfetamine dimesylate (*Vyvanse*, Shire), and the antiepileptic pregabalin (*Lyrica*, Pfizer).

After aripiprazole, which had sales of \$7.2 billion for the period of July 2013 through June 2014, the next best selling drugs for the period were the arthritis drug adalimumab (*Humira*, AbbVie, \$6.3 billion), esomeprazole (*Nexium*, \$6.3 billion), rosuvastatin (*Crestor*, nearly \$5.6 billion), and the arthritis drug etanercept (*Enbrel*, Amgen, nearly \$5.1 billion).

Rounding out the top 10 in sales were Advair Diskus (\$5.0 billion), the antiviral drug sofosbuvir (*Sovaldi*, Gilead, \$4.4 billion), the arthritis drug infliximab (*Remicade*, Centocor; \$4.3 billion), the insulin glargine injection (*Lantus Solostar*, sanofi-aventis, \$3.8 billion), and the neutropenia drug pegfilgrastim (*Neulasta*, Amgen; nearly \$3.7 billion).

Rank	Drug (Brand Name)	Total Prescriptions to June 2014
1	Synthroid	22,664,826
2	Crestor	22,557,735
3	Nexium	18,656,464
4	Ventolin HFA	17,556,646
5	Advair Diskus	15,003,169
6	Diovan	11,401,503

7	Lantus Solostar	10,154,739
8	Cymbalta	10,065,788
9	Vyvanse	10,019,178
10	Lyrica	9,684,884
11	Spiriva Handihaler	9,518,849
12	Lantus	9,358,961
13	Celebrex	8,815,391
14	Abilify	8,777,842
15	Januvia	8,758,309
16	Namenda	7,640,319
17	Viagra	7,584,152
18	Cialis	7,555,933
19	Zetia	7,411,629
20	Nasonex	7,304,210
21	Suboxone	7,011,882
22	Symbicort	6,948,403
23	Bystolic	6,722,578
24	Flovent HFA	5,623,533
25	Oxycontin	5,559,330
26	Levemir	5,554,827
27	Xarelto	5,014,364
28	Nuvaring	5,011,966
29	Dexilant	4,866,178
30	Thyroid	4,834,481
31	Benicar	4,725,628
32	Voltaren Gel	4,709,766
33	Proventil HFA	4,494,004
34	Tamiflu	4,149,835
35	Novolog	4,044,310
36	Novolog Flexpen	4,006,690
37	Premarin	3,984,357
38	Vesicare	3,873,046

39	Humalog	3,858,256
40	Benicar HCT	3,633,026
41	Lumigan	3,283,060
42	Afluria	3,242,605
43	Lo Loestrin Fe	3,154,488
44	Janumet	3,089,749
45	Ortho-Tri-Cy Lo 28	3,053,738
46	Toprol-XL	3,044,003
47	Pristiq	3,023,546
48	Combivent Respimat	2,994,490
49	Vytorin	2,988,460
50	Travatan Z	2,919,358
51	Focalin XR	2,866,278
52	Pataday	2,757,094
53	Humalog Kwikpen	2,626,530
54	Lunesta	2,590,519
55	Avodart	2,527,583
56	Pradaxa	2,442,678
57	Seroquel XR	2,405,130
58	Strattera	2,387,756
59	Minastrin 24 Fe	2,353,282
60	Evista	2,232,555
61	Chantix	2,151,879
62	Zostavax	2,145,562
63	Humira	1,923,427
64	Victoza 3-Pak	1,902,995
65	Exelon	1,877,942
66	Exforge	1,838,730
67	Combigan	1,821,491
68	Dulera	1,790,677
69	Onglyza	1,784,018
70	Welchol	1,778,218

71	Premarin Vaginal	1,718,405
72	Enbrel	1,627,480
73	Xopenex HFA	1,588,895
74	Ranexa	1,567,961
75	Truvada	1,532,734
76	Alphagan P	1,503,194
77	Viibryd	1,447,730
78	Tradjenta	1,443,791
79	Effient	1,434,572
80	Azor	1,433,045
81	Norvir	1,384,306
82	Actonel	1,339,615
83	Namenda XR	1,319,963
84	Amitiza	1,309,980
85	Aggrenox	1,286,826
86	Lotemax	1,276,480
87	Patanol	1,274,050
88	Levitra	1,273,311
89	Advair HFA	1,272,551
90	Uloric	1,244,536
91	Detrol La	1,225,506
92	Asmanex Twisthaler	1,219,112
93	Lipitor	1,212,376
94	Atripla	1,183,636
95	Prempro Low Dose	1,162,513
96	Latuda	1,123,396
7	Novolog Flxpen Mix 70/30	1,119,855
98	Invokana	1,106,268
99	Epiduo	1,103,330
100	Humulin N	1,071,673

Table 2. Top 100 Drugs by Sales

Rank	Drug (Brand Name)	Sales Through June 2014
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1	Abilify	\$7,240,043,661
2	Humira	\$6,310,742,887
3	Nexium	\$6,303,738,580
4	Crestor	\$5,672,991,435
5	Enbrel	\$5,097,263,350
6	Advair Diskus	\$5,064,138,456
7	Sovaldi	\$4,469,558,675
8	Remicade	\$4,342,356,359
9	Lantus Solostar	\$3,829,943,226
10	Neulasta	\$3,688,450,342
11	Copaxone	\$3,677,307,402
12	Rituxan	\$3,361,247,463
13	Spiriva Handihaler	\$3,270,501,346
14	Januvia	\$3,124,826,108
15	Lantus	\$3,011,654,746
16	Atripla	\$2,898,264,003
17	Cymbalta	\$2,839,722,673
18	Avastin	\$2,784,813,413
19	Lyrica	\$2,782,036,977
20	Oxycontin	\$2,524,152,087
21	Celebrex	\$2,435,800,107
22	Epogen	\$2,378,212,523
23	Truvada	\$2,351,681,656
24	Diovan	\$2,177,824,165
25	Levemir	\$2,121,663,090
26	Gleevec	\$2,087,891,457
27	Herceptin	\$2,032,270,434
28	Vyvanse	\$1,940,313,035
29	Lucentis	\$1,932,528,073
30	Zetia	\$1,930,143,528
31	Tecfidera	\$1,908,407,807
32	Symbicort	\$1,901,446,790

33	Namenda	\$1,774,338,290
34	Novolog Flexpen	\$1,720,294,797
35	Xarelto	\$1,546,602,955
36	Novolog	\$1,466,291,783
37	Humalog	\$1,418,795,789
38	Suboxone	\$1,388,999,843
39	Tysabri	\$1,315,848,323
40	Viagra	\$1,274,239,087
41	Seroquel XR	\$1,266,841,322
42	Victoza 3-Pak	\$1,263,623,179
43	Cialis	\$1,241,580,547
44	Stelara	\$1,221,329,301
45	Alimta	\$1,215,044,019
46	Nasonex	\$1,190,958,069
47	Avonex	\$1,146,712,504
48	Gilenya	\$1,143,648,903
49	Humalog Kwikpen	\$1,140,418,800
50	Flovent HFA	\$1,091,998,384
51	Prezista	\$1,079,469,740
52	Janumet	\$1,071,110,813
53	Renvela	\$1,063,062,816
54	Isentress	\$1,045,929,798
55	Procrit	\$1,028,448,101
56	Orencia	\$1,017,584,725
57	Dexilant	\$1,010,512,519
58	Vesicare	\$1,001,127,504
59	Stribild	\$962,264,200
60	Olysio	\$943,547,154
61	Synthroid	\$927,886,999
62	Neupogen	\$922,013,084
63	Avonex Pen	\$920,097,484
64	Reyataz	\$918,922,508

65	Zytiga	\$918,603,420
66	Xolair	\$902,375,287
67	Invega Sustenna	\$891,518,099
68	Benicar	\$884,750,288
69	Combivent Respimat	\$881,992,234
70	Pradaxa	\$879,463,846
71	Sensipar	\$878,283,696
72	Xgeva	\$844,140,641
73	Vytorin	\$828,020,808
74	Betaseron	\$824,758,830
75	Aranesp	\$824,531,232
76	Prevnar 13	\$818,701,788
77	Latuda	\$803,311,039
78	Afinitor	\$800,598,342
79	Lunesta	\$778,412,409
80	Ventolin HFA	\$771,201,081
81	Complera	\$756,268,942
82	Synagis	\$754,510,179
83	Bystolic	\$736,654,176
84	Zyvox	\$733,964,492
85	Gardasil	\$717,881,961
86	Sandostatin Lar	\$715,506,378
87	Benicar HCT	\$699,679,537
88	Treanda	\$692,288,820
89	Pristiq	\$687,192,710
90	Zostavax	\$674,280,328
91	Erbitux	\$669,382,439
92	Cimzia	\$660,599,949
93	Strattera	\$658,818,959
94	Cubicin	\$655,269,663
95	Xeloda	\$652,443,257
96	Tarceva	\$638,909,500

97	Evista	\$638,155,000
98	Velcade	\$636,704,153
99	Sprycel	\$635,192,399
100	Abraxane	\$634,678,206

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Drug Abuse: Antipsychotics in Nursing Homes

These dangerous medications are prescribed at an alarming rate without the patient's consent

by Jan Goodwin, AARP Bulletin, July/ August 2014



Antipsychotics may trigger serious side effects in patients with Alzheimer's disease. — Dung Hoang

En español | When Patricia Thomas, 79, went into a Ventura, Calif., nursing home with a broken pelvis, the only prescriptions she used were for blood pressure and cholesterol, and an inhaler for her pulmonary disease. By the time she was discharged 18 days later, she "wasn't my mother anymore," says Kathi Levine, 57, of Carpinteria, Calif. "She was withdrawn, slumped in a wheelchair with her head down, chewing on her hand, her speech garbled." Within weeks, she was dead.

Thomas, a former executive assistant, had been given so many heavy-duty medications, including illegally administered antipsychotics, by the Ventura Convalescent Hospital in November of 2010 that she could no longer function. If one drug caused sleeplessness and anxiety, she was given a different medication to counteract those side effects. If yet another drug induced agitation or the urge to constantly move, she was medicated again for that.

"Yes, my mom had Alzheimer's, but she wasn't out of it when she went into the nursing home. She could dress and feed herself, walk on her own. You could have a conversation with her," says Levine. "My mother went into Ventura for physical therapy. Instead, she was drugged up to make her submissive. I believe that my mother died because profit and greed were more important than people."

A Ventura County Superior Court judge agreed that Levine had a legitimate complaint against the nursing home. In May, attorneys from the law firm Johnson Moore in Thousand Oaks, Calif., joined by lawyers from AARP Foundation, agreed to a settlement in an unprecedented class-action suit against the facility for using powerful and dangerous drugs without the informed consent of residents or family members. "It is the first case of its kind in the country, and hopefully we can replicate this nationwide," says attorney Kelly Bagby, senior counsel for AARP Foundation Litigation.

A national problem

Tragically, what happened to Patricia Thomas is not an isolated incident. According to Charlene Harrington, professor of nursing and sociology at the University of California, San Francisco, as many as 1 in 5 patients in the nation's 15,500 nursing homes are given antipsychotic drugs that are not only unnecessary, but also extremely dangerous for older patients. The problem, experts say, stems from inadequate training and chronic understaffing, as well as an aggressive push by pharmaceutical companies to market their products.

"The misuse of antipsychotic drugs as chemical restraints is one of the most common and long-standing, but preventable, practices causing serious harm to nursing home residents today," says Toby Edelman, an attorney at the Center for Medicare Advocacy in Washington, D.C. "When nursing facilities divert funds from the care of residents to corporate overhead and profits, the human toll is enormous."

Kickbacks to doctors

Last November, in what the U.S. Department of Justice called "one of the largest health care fraud settlements in U.S. history," Johnson & Johnson and its subsidiaries were fined more than \$2.2 billion to resolve criminal and civil charges because of their aggressive marketing of drugs, including antipsychotics, to nursing homes, when they knew the drugs had not been approved by the U.S. Food and Drug Administration (FDA) as safe and effective for a general elderly population. The corporation also allegedly paid kickbacks to physicians, as well as to Omnicare, the nation's largest long-term-care pharmacy provider. Omnicare pharmacists were recommending Johnson & Johnson's drugs, including the antipsychotic Risperdal, for use by nursing home residents.

Back in 2009, Eli Lilly did the same thing with its antipsychotic Zyprexa, marketing to older people in nursing homes and assisted living facilities, federal prosecutors charged. In a settlement, the company agreed to pay \$1.4 billion. "This case should serve as still another warning to all those who break the law in order to improve their profits," Patrick Doyle, special agent in charge of the Office of Inspector General for the U.S. Department of Health and Human Services in Philadelphia, said at the time.

A report released in March by the inspector general of Health and Human Services charged that one-third of Medicare patients in nursing homes suffered harm, much of which was preventable. "Too many nursing homes fail to comply with federal regulations designed to prevent overmedication, giving patients antipsychotic drugs in ways that violate federal standards for unnecessary drug use," Inspector General Daniel Levinson said. "Government, taxpayers, nursing home residents, as well as their families and caregivers, should be outraged — and seek solutions."

Antipsychotic drugs are intended for people with severe mental illness, such as patients with schizophrenia or bipolar disorder. As such, they carry the FDA's black-box warning that they are not intended for frail older people or patients with Alzheimer's or dementia. In those populations, these drugs can trigger agitation, anxiety, confusion, disorientation and even death. "They can dull a patient's memory, sap their personalities and crush their spirits," according to a report from the California Advocates for Nursing Home Reform.

Kept in the dark

What's more, the law requires "informed consent" by a patient or, if that is no longer possible, by his or her family before such drugs are administered. Yet advocates say that, all too frequently, this doesn't happen. Levine, for example, says she didn't know about all her mother's medications until she transferred her mom to another facility. "When I saw the list of what she'd been given, I freaked out. I was upset and angry, in tears," she recalls.

How can such things happen? One explanation is that many facilities don't have enough properly trained staff: Most of the patient care in nursing homes falls to certified nursing assistants (CNAs) who need as little as 75 hours of on-the-job training to get certified. "Yet if you want a license to be a hairdresser, you need 1,500 hours of training," Harrington points out.

What's more, CNAs are paid low wages so many of them work long hours. "They are totally exhausted, with extremely heavy workloads," she says. That leads to high employee turnover and caregivers who don't know their patients well enough to recognize their needs.

Compounding the problem, many nursing home patients require a high level of care. Some are incontinent, and an estimated 60 to 70 percent have some form of dementia. There should be one CNA for every seven patients, but in some cases, the ratio is 1 to 15 — or even more, Harrington says. There also tend to be too few physicians actually present in nursing homes. "These facilities are highly medicalized, but doctors are rarely there," says Tony Chicotel, staff attorney for California Advocates for Nursing Home Reform. He says that because of their low rate of reimbursement from Medicare, nursing homes are too often seen as a place where few top doctors practice.

The result of all this can be so-called behavior problems among patients — which is the explanation nursing homes cite for giving patients unnecessary antipsychotic drugs, according to the U.S. Centers for Medicare and Medicaid Services (CMS). And pharmaceutical companies have been aggressively marketing their products as an easy and effective way to control these issues.

"There was a push by drug manufacturers, claiming these medications work for seniors when they knew, in fact, that it doubled their risk of death," Chicotel says.

CMS, which oversees the nursing homes that receive funding from federal programs, says it has been working to correct deficiencies in nursing facilities, including the inappropriate use of medications. The agency achieved the goal of reducing the inappropriate use of antipsychotic drugs by 15 percent over a recent two-year period, and hopes to get to a 30 percent reduction in the next few years, according to spokesman Thomas Hamilton. But Edelman points out that initial goal was reached more than a year late, and some 300,000 patients are still receiving the drugs inappropriately. Hamilton acknowledges that more needs to be done, but lack of funding from Congress is making even the most preliminary work difficult.

Fortunately, a growing number of nursing homes have begun to look for more effective — and more humane — ways to care for patients. Better training for caregivers is key: According to Cheryl Phillips, M.D., a geriatrician at LeadingAge, an organization representing nonprofit services for older people,

nursing home staff can be trained to deal with behavior issues thoughtfully and creatively, without resorting to drugs.

She cites an example of a male patient who was spending his days in a noisy nursing home activity room. One day, he grew more and more agitated and tripped an aide with his cane. To calm him down, the staff took him to his private quarters. Over the following days, his behavior in the activity room became increasingly aggressive; he began randomly hitting caregivers and fellow patients. Each time, he was taken away to spend time in his room.

"The staff initially thought he had become violent and needed an antipsychotic," Phillips recalls. "But they ultimately realized that the cacophony in the activity room was stressing him out. Caregivers inadvertently rewarded him by giving him quiet time in his room, which is what he wanted. When they did it repetitively, they reinforced his aggressive behavior." Once the staff discussed the problem and began finding peaceful activities for the patient, the problem was solved — no drugs needed.

Putting patients first

Another success story is the Beatitudes facility in Phoenix, which dramatically changed its way of handling patients with dementia based on Tom Kitwood's book *Dementia Care Reconsidered: The Person Comes First*. "What happens here is not for our systems, our convenience, but for the people we care for," says Tena Alonzo, the director of education and research at Beatitudes. "People with dementia have disturbances in their sleep/wake cycle, so we let them be comfortable and decide when they want to sleep or eat, or not. Or how they want to spend their time," she says. As a result, patients stop resisting care, and the facility runs more smoothly.

The Beatitudes' philosophy is now being taught to a growing number of nursing homes around the country. "We've created a softer, gentler approach, acknowledging that we are not in charge of a person's life — they are. In allowing them to retain their dignity, and adopt a comfort level of care, we've had better outcomes," says Alonzo. That paradigm shift has not increased operating expenses, or required a higher staff-to-resident ratio. "We discovered that better care was better business," Alonzo says.

For Kathi Levine and her mother, these encouraging developments are coming too late. "I want our lawsuits to impact nursing homes all over the country," Levine says. "We need to protect our family members. They don't have a voice, they can't speak for themselves. So we need to speak out for them and help other people know what to look for. I want to make sure that what happened to my family doesn't happen to anyone else."

Jan Goodwin is an award-winning author and investigative journalist for national publications.

How to steal \$80 million in prescription drugs

AFTER \$400 MILLION IN HEISTS, BIG PHARMA FIGHTS BACK

By Russell Brandom on May 5, 2014



Last month, three Florida men were charged with one of the largest heists in Connecticut history, a March 2010 theft of more than \$80 million in goods from a warehouse in Enfield.

The thieves climbed onto the roof with ladders, cut through the soft tar, then rappelled down with climbing gear to disable the alarm system from within. Once they had access, they loaded 49 pallets onto a single tractor trailer and drove off before anyone knew they'd been there. It was more than 18 months before law enforcement officers caught up with the goods, cached in a storage unit in Florida.

A different kind of heist

But the haul wasn't gold or electronics or even painkillers. It was medications, pills used in the treatment of depression, schizophrenia, and breast cancer. It was a different kind of heist, one that law enforcement was struggling to control. In July 2009, the same group of thieves had taken down a GlaxoSmithKline warehouse in Chesterfield, Virginia, walking away with \$4.3 million in emphysema medication. That year saw 50 major pharma heists for nearly \$200 million in drugs, more than quadruple the figure for bank robberies. But in the five years since, insiders say something's changed, and the golden age of the pharmaceutical heist may finally be finished.

2009 saw 50 major pharma heists for nearly \$200 million in drugs

The thefts first came on to the industry's radar around 2007, as skyrocketing medication costs made pharmaceutical warehouses a particularly attractive target. Most companies were still inexperienced with physical security, but the surge in high-profile thefts got their attention fast. Even worse than the initial loss was when the stolen pills were resold back to pharmacies, often landing back on shelves in dangerously damaged form. If a medication hadn't been properly refrigerated in transit, patients could end up using spoiled medicine, with potentially severe consequences.

Faced with disaster, companies had no choice but to tighten up security from every angle — and for the last five years, that's just what they've been doing. If the Connecticut heist had happened today, the attackers would have faced a battery of new obstacles, starting with the pallets themselves. Most shipments of drugs now come with concealed GPS units, which let law enforcement recover shipments hours after the initial theft. Beyond GPS, some companies have begun labeling each pill with a miniscule serial number, allowing investigators to trace stolen medications after the fact. By all indications, the new measures worked. The Pharmaceutical Cargo Security Coalition (PCSC), a trans-corporate group founded in the wake of the wave of heists, says that major thefts cost the industry less than \$6 million in 2013, just 3 percent of what the industry faced in 2009.

Major thefts cost the industry less than \$6 million in 2013

Reselling has also become more difficult. In 2011, a landmark *Fortune* investigation by Katherine Eban found illicit pills showing up in mainstream supermarkets like Kroger, revealing how stolen and often spoiled pharmaceuticals can trickle back into the supply chain through middlemen. Part of the allure of prescription drugs was that they were easier to fence than jewelry or electronics. All you needed was an unscrupulous wholesaler, who would sell the shipment to a slightly less unscrupulous wholesaler, who would sell it back onto mainstream shelves. But a host of new laws like the Safe Doses Act, the Drug Assurances and Safety Act, and the Drug Supply Chain Security Act have raised the penalties for wholesalers caught trafficking in stolen pills, making medication harder to fence.

"They go where there's money to be made."

For Tom Hauck, an FBI agent specializing in pharma theft, the most important threshold is whether pharmaceutical theft is easier and more lucrative than other kinds of crime. "Some of them, in their past lives, were drug traffickers," Hauck says. "It all comes down to profit. They go where there's money to be made." In the past, that drove thieves to pharmaceutical warehouses, but as the defenses ramp up, they move on to an easier score, whether it's stored tobacco or other kinds of cargo in transit. But for now, medications seem to be well-protected enough to avoid criminal attention.

That's not to say big-time pharmaceutical theft has disappeared entirely — it's just moved overseas. Italian law enforcement officials are already struggling with the organized and persistent theft of cancer drugs, as local crime rings catch onto the potentially lucrative racket. The European version of the heists are more serious in many ways, targeting hospitals instead of warehouses and often reselling counterfeit versions of the drugs, but experts say law enforcement is looking to the same tricks to fight it. "The methodologies mirror what's been happening in the US," says Chuck Forsaith, head of PCSC. "And the victims have been responding with the same tactics."

This Graphic of Counterfeit, Poison-Laced Pills Is Horrifying

Rat poison, wall paint, antifreeze, paint thinner and a few other ingredients that have slipped into the \$75 billion a year market for counterfeit pills

Time Magazine
June 4, 2014

Today the world celebrates, Anti-Counterfeiting Day, and by world, we mean a little-known [coalition](#) of regulators and lawyers celebrating their quiet battle against counterfeit drug makers.

Here's a reason for the non-observant to join the festivities: Some [\\$75 billion worth](#) of counterfeit drugs hit the global market each year. These pills often have brand names etched on the outside and chemical imbalances on the inside that are at best, ineffective, and at worst, toxic.

Just how toxic? The Partnership for Safe Medicines, a not-for-profit association of pharmaceutical organizations, has a [graphic](#) just in time for the holidays. It shows the full sweep of contaminants that health officials have discovered in fake pills over the years.



Source:

Partnership for Safe Medicines

Uranium, of course, is a worst case scenario. Actual contamination rates are hard to measure in an industry that dodges scrutiny for a living. A rough survey by the World Health Organization [found](#) that 73% of counterfeit medications contained either the wrong ingredient, the wrong dosage, or no active ingredient, while 8% were laced with impurities and contaminants. Only 15% contained the right dose and the right ingredient. Some sobering figures to contemplate on World Anti—Counterfeit Day, or any day an unaccredited website offers pills at rock-bottom prices.

California pharmacies resist push to translate drug labels

By [Sammy Caiola](#)
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Published: Thursday, Jul. 24, 2014 - 12:00 am

When Chek Lun Wong picks up his [prescription medication](#) for hepatitis B at his local Walmart, he doesn't understand a word.

"I give them the prescription and my license and they give it to me. I don't read the bottle," said Wong. "I usually just ignore it if I don't understand it."

The 63-year-old Wong, who told his story with the help of a Chinese translator at the Paul Hom Asian Clinic in East Sacramento last weekend, is one of thousands in the capital region and the state who struggle to take their medication correctly because of a [language barrier](#) – an issue that some health advocates want rectified at a California State Board of Pharmacy meeting later this month.

On Saturday at the free medical clinic on Folsom Boulevard, Wong waited among a steady stream of Chinese and Vietnamese patients, most of whom spoke little to no English, to get the prescription for his next refill and to listen to instructions on their use from a Chinese-speaking volunteer. Kai Ming Tan, one of the many UC Davis students who staff the clinic, often writes out directions for Wong in Chinese characters.

When Wong goes to the pharmacy to pick up his prescription bottle, labeled in English, he will rely on this information to take the drug.

"Patients need things written down," said Tan. "If a medical student is presenting, (the patients) can't keep it in their head. They need something written down so they have something if they go home and forget what I said."

Currently, the California State Board of Pharmacy requires pharmacies to provide an interpreter for non-English speakers free of charge, either in person or by phone, when requested at the pharmacy counter. The board itself is required to provide written translations of basic instructions in Spanish, Korean, Russian, Chinese and Vietnamese, in addition to English, on its website. But most pharmacists will not – and are not required to – print translated labels on the bottles themselves.

At its July 31 meeting, the board will consider, among other potential changes, requiring pharmacies to do just that.

Most pharmacists believe the system in place is working, said Jon Roth, chief executive officer of the Sacramento-based California Pharmacists Association. Limited-English speakers can use a

telephonic translation service to get instructions on prescription drug use, which the pharmacist calls when the customer arrives. The customer hears the instructions and can also request a fax of the translation.

Roth said most pharmacists would not feel comfortable dispensing medication in a language they do not understand, especially considering that the pharmacist would be held liable for any potential mistake in the translation.

“We think the potential for error outweighs the potential gain for a patient receiving medication in a translated form,” said Roth. “We don’t think mandating a translation is patient-centric. We think that’s counter to patient care because the pharmacists cannot validate what they are handing over to the patient.”

According to the latest [census data](#), more than one of every four Sacramento-area residents – 573,000 of about 2 million people over the age of 4 – speaks a language other than English at home. Statewide, 44 percent of California’s 38 million residents speak a foreign language at home.

Senate Bill 204, authored by Senator Ellen Corbett, D-San Leandro, in February 2013 and sponsored by the California Pan-Ethnic Health Network, initially fought for printed translations on pill bottles. But after meeting “quite a bit of resistance” from pharmacists and prescribers, the senator and supporters decided to delete the translation requirements from the bill and reassess the issue, said Sarah de Guia, director of [government affairs](#) for CPEHN. She said they will attend the July 31 board meeting in order to “figure out how to move this forward, hopefully with more support in the future.”

While the pharmacy board has the authority to update translation standards at its meeting, Dr. Sergio Aguilar-Gaxiola, director of the UC Davis Center for Reducing [Health Disparities](#), said legislation likely will be necessary to make what he considers a long overdue change.

“It’s not enough to explain something in a language that is potentially not understood – I would not consider that [quality care](#),” he said. “I know it is expensive and it is complicated, but it is more expensive not to provide the right treatment in a way that patients will comply with. They will potentially be in harm’s way, which will require them to use [emergency services](#), which is also expensive.”

The Board of Pharmacy regulates about 6,500 community pharmacies statewide and 500 hospitals, in addition to 140,000 entities holding pharmacy licenses including mail-order pharmacies, drug wholesalers and clinics, said Virginia Herold, executive officer of the board.

Roth said a translated label requirement would disrupt the workflow of the pharmacies and that they would incur “greater waste and higher costs” from the need to switch to larger bottles to accommodate the translated languages.

A 2009 survey administered by the board found that bilingual wording was among the top five customer suggestions for making the label easier to read, along with larger print, highlighted directions, easier wording and doing nothing.

Sara Gaeta, a 64-year-old Sacramento resident who speaks only Spanish, said the directions on her over-the-counter cold medicine are written in English, so she takes them to her daughter – a certified nurse at Sutter Medical Center in East Sacramento – to translate.

Gaeta, a native of Veracruz, Mexico, said she would support having customers' labels tailored to their preferred language.

“There are a lot of families that don't understand English,” said Gaeta, through a translator. “That can be a problem for those of us who don't know the language well. It would be great if they were in Spanish, because it would benefit us all considering the large Latino population here.”

In addition to the translation component, the pharmacy board will address other potential changes to label requirements at its July 31 meeting, including the need to distinguish between generic and brand-name medication and stating how the drug treats a diagnosis, rather than just the diagnosis itself, said Herold.

The most recent change to the regulations, issued June 26, increased the font size of the labels from 10-point to 12-point type. Some pharmacists opposed the change, arguing that the larger font would mean larger bottles, which could prove detrimental to patients who might move their medication to smaller bottles and lose the instructions entirely, said Herold.

For the July 31 meeting, the pharmacy board will bring in a panel of national experts, including the director of the New York Board of Pharmacy, which approved label translations in the spring of 2013. The panel presentation will be followed by a public discussion.

“I hesitate to guess what the board is going to do, but there's certainly a group of people that are very interested in doing that (requiring translations),” she said. “The reality is if somebody hands you something in a language you can't read, you've got to find a way to figure out what it says.”

But, Herold added, “If pharmacists really are the last check between the prescriber and the patient, that is a pretty weighty responsibility.”

Read more here: <http://www.sacbee.com/2014/07/23/6578090/california-pharmacies-resist-push.html#storylink=cpy>

Bilingual drug labels: Pharmacists speak out

Julianne Stein, Content Channel Manager

Publish Date: AUG 11, 2014

Feelings have run high since *Drug Topics* posted "[Should states require bilingual drug labels?](#)" on July 31. Both on [Facebook](#) and at www.DrugTopics.com, reader comments have been intense. As this issue appears to have struck a nerve with pharmacists — who, after all, are closer to the practical realities of dealing with bilingual patients than, say, California lawmakers or regulators might be — we thought we'd fill you in on what some of your fellow pharms are saying.

It'll keep patients marginalized

Speaking of California officials, one reader posted the following comment: "Do the CSBOP inspectors speak all those languages? In the greater scheme of things, it's less expensive to get non-English-speakers to learn English and become constructive members of our English-speaking society than to keep them marginalized in the non-English-speaking society where so many so-called progressives would have them remain. New York made a bad choice, now it looks like California might be headed in the same direction. Sad."

To which two readers responded, "Agree 100%!" and "This is the United States of America...we speak English!"

More on California's proposed changes: [California considering patient-centered Rx labels](#)

Charge for it

Also posting at the website, **Dr. JCalvillo** made the point that the "last thing pharmacy needs is more mandates that cost us money or increase our liability. As pharmacists, we do this anyway. If they make it mandatory, then I suggest all pharmacies charge for this service, because it's going to cost us in the long run."

Grandpa learned

Voicing a sentiment undoubtedly felt by many, **MichaelSherry** wrote, "I say no to bilingual labels. My grandfather was from Holland. No one posted signs in Dutch. He had to learn English, as should all other immigrants."

Required for citizenship

From **Mr. JKramer**: "Speaking English should be a requirement for citizenship. It should be up to the pharmacist to decide whether to provide bilingual labeling. Enough already!"

Did they come here to live?

From an anonymous commenter: "Amen! So many people come to this country and expect us to cater to them. Some of them even have the nerve to say that some of my techs shouldn't be working in the pharmacy because they can't speak Spanish. Luckily, I have Spanish-speaking

techs to put them in their place. It's getting out of control! Everyone should learn English when they come to this country to live, so they can communicate. We shouldn't have to change everything for those that are too lazy to learn the language of this country."

I spoke Italian ...

FrancisPisano said: "This is the United States of America. We speak English. If a person speaks only their native tongue, maybe it is time for them to learn English. I spoke Italian before speaking English, but I quickly learned that if I was going to accomplish anything in America, I had to speak English!"

Eat a banana

An anonymous commenter made a good point: "Different languages have different alphabets and other characters that may not print on an English-programmed printer. That's a problem. Also, just here in the Western hemisphere, there are probably 20 to 30 different dialects of Spanish alone. The phrase 'eat a banana' might just get your face slapped by certain Spanish speakers. That really needs to be considered by the California legislators if they're trying to reach the least common denominator."

What does Europe do?

Mr. DKarant agreed, saying, "This is the United States, and we should be all speaking the same language," and added, "But we still must effectively communicate with those who have needs who walk into our pharmacies. So, my question is, how do the pharmacies in Europe address this? Is there any special legislated labeling of multilingual content for pharmacists to use in England, France, Germany, Italy, or elsewhere? Is there a European model that would be good for us to consider?"

P.C. gone wild

Another anonymous commenter pronounced the issue ridiculous, and said, "It's a California thing. Political correctness running wild."

Where are the pharmacist groups?

DougBennett asked, "At what point in time does a patient become responsible for his/her care? The patient is better off having a friend or relative translate, someone who can easily be reached by the patient at any time."

He added, "Where are APHA and CPHA? They should be all over this. We already spend more time on eligibility, formulary, and authorizations than on patient care. Every year we are asked to do more for less."

It's a setup

A very practical concern was expressed by **Dr. DLevasseur**: "How can a pharmacist who speaks one language ensure accuracy in other languages? You can imagine seeing it all over the news. 'Pharmacist incorrectly translates prescription label, resulting in injury/death.' This pharmacist would then likely lose his/her job and/or license, all because of a labeling requirement for a language he/she cannot read."

In a nice piece of tit for tat, this writer added, "I want the CSBOP to write their regulations in all the languages they expect pharmacy labels to be written."

How 'bout handouts?

Another commenter asked: "What is wrong with drug information handouts in different languages?"

Our folks learned

And yet another commenter echoed thoughts expressed earlier. “My father is a first-generation American, and he always told us that we are in America and we speak English. Previous generations of immigrants wanted to learn English and knew they would have to learn it. Now, we make it too easy for immigrants NOT to learn English.

“When New York was talking about doing this a few years back, I remember reading an article about a woman upset and afraid to give medication to her ‘child’ because she could not read the label. Later in the article, we find out that she has been in America for 14 years and has a 14-year-old child. Why can't her child read English after being schooled in America, and why can't she read basic words after 14 years in this country?”

Try fitting 30 languages on a label

And **RobertDeBus** said, “I basically agree, the patient is responsible. English should be required. However, I had many patients from Somalia (Arabic), Mexico (Spanish), and SE Asia (??), and a couple of Russian and Bosnian patients. Communication was always a problem. As I understand it, in parts of California, there are up to 30 different languages spoken. Impossible to do all of them on a label. Supplying a sheet with a translation should be OPTIONAL. Would help patient care. But a requirement? NO.”

Facebook posters also had opinions to share.

Been doing it

Said **Rick McCoy**, “We've done it for YEARS and didn't need a law.”

Don't dispense in an unfamiliar language

Jeff Pierce wrote, “A pharmacist should NEVER dispense a prescription if he or she cannot understand the language of the words on the label. This potential requirement does nothing to encourage immigrants to assimilate to learn the English language or American culture. Enough already.”

It's about healthcare

Responding to the latter, **SarahBeth Joachim** said, “Jeff, it said ‘bilingual.’ I think most Rx's can print a label in a different language if needed. We did in Arizona. While assimilating, it takes time. If someone can't read English well, it is more likely there will be noncompliance or even death from misunderstanding. Any healthcare professional should want the patient to be able to read — or even a family member. It's about healthcare, not politics.”

So there you have it. To some *Drug Topics* readers, it IS about politics. To others, it's about healthcare. What do you think? Post your own comment at www.DrugTopics.com or e-mail us at drugtopics@advanstar.com, for sharing with your colleagues.

Drug Topics

Voice of the Pharmacist

Published on *Drug Topics* (<http://drugtopics.modernmedicine.com>)

Electronic prescriptions: Return to sender

[The Cynical Pharmacist](#)

Publish Date: JUN 10,2014

Life doesn't come with an instruction manual. Fortunately, everything I buy at IKEA does. In the pharmacy world, our assembly instructions come in the form of a prescription. Its singular purpose, the reason for its very existence, is to communicate to the pharmacist the prescribers' intentions. What do we do if the communication system is broken?

Years ago, prescriptions were handwritten. If we couldn't read something, we'd call the office for clarification. Today we have electronic prescribing (e-Rxs), the savior of healthcare. It exists to reduce errors.

When I was first asked about the pure awesomeness of this new technology, the offices and software companies were taken aback by my response: "We do not have fewer errors, we have more legible errors." Now I can clearly see the mistake that was made on the prescription. Pharmacists used to know the handwriting of their local prescribers. We knew what their hieroglyphics meant and often didn't need to call. Today, the errors are so bad that many e-scripts we receive cannot be filled as sent.

Whose fault?

Who is to blame? The offices. This is either a training error, which falls on the e-script service/provider that was selected, or a lack-of-learning error. This means that, despite repeated calls from pharmacies all over town, the offices are not changing their habits and continue to repeat the same mistakes.

If you go to a restaurant and order a steak medium rare and receive it well done, what do you do? You send it back. You could ask the waiter to bring you the chef, but it doesn't expedite your receipt of a new, properly cooked filet. Did the waiter enter the order incorrectly? Did the chef not cook it correctly? Either way, you aren't likely to leave a big tip.

In the pharmacy world, even though we are not at fault for not being able to fill your prescription, we will be the ones to get yelled at.

It's the same with a prescriber's office. Did the prescriber enter the order incorrectly? Did the assistant not check the order and enter it incorrectly? I don't know. What is important is that the order is correct and I am able to fill patients' prescriptions without wasting my time or any more of theirs. The prescribers get off without ever knowing what they did wrong.

What's the fix?

How do we fix this? We need a Return-to-Sender button. We need a way to directly communicate with the offices.

Pharmacists have long been relegated to the refill line at many offices. This means that we have to leave a message and wait for an answer. Many times we will receive a phone call asking why we called. This is a waste of time. We need to be able to reply to the offices with a note of what needs to be fixed.

The other problem is with the software itself. Prescribers should not be allowed to make selections that do not match each other.

If the prescriber wants metoprolol, the computer should prompt her to then choose succinate or tartrate. Once that selection is made, the strength options should be given for the chosen salt. This way, the prescriber cannot select metoprolol tartrate 200 mg. This will also result in fewer errors from prescribers selecting what they think they want as opposed to what they really want. And it will stop my local prescribers from writing gabapentin 200 mg.

I also have a suggestion that prescribers be given default quantities on unit-of-use products. This way we won't receive prescriptions for 15 g or 30 g of mupirocin ointment when it's only available in a 22-g size. And how many prescriptions have you received that told you to dispense 3.1415 tablets?

Short-term fixes

This issue has caused more divisiveness between professions than any other in recent memory. We as pharmacists have allowed this to happen.

There is a mindset among prescribers that it is the pharmacist's job to fix everything. It is not. If the order is entered incorrectly every time, how is that our fault? If the assembly instructions are incomplete, can the end user really be to blame for how a product was assembled?

We have to go to the source. The only way for this to happen is for us to have a direct link to the point of entry.

On my Facebook page, the community is quite helpful with idea-sharing. We offer fixes that seem to work for others around the country.

Some pharmacies print the e-script, circle the errors, then fax it to the offices.

Some call, leave messages, and then hand the incorrect copy to the patient to have him or her deal directly with the prescribing office. These are short-term fixes, not permanent solutions.

Solve the problem at its source

Here is my proposal. We need to talk with the e-script providers. We need to discuss their training methods, their software, their programming, and the ability for pharmacies to return problem prescriptions.

Prescribers should not be able to select drugs, strengths, directions, and dosage forms that do not all match.

We need a voice on this problem. Our local, state, and national organizations seem to be absent, or at least silent, on this issue. Instead of forcing a broken technology down the collective throat of us in healthcare, let's get together and fix it. Let's put right what once went wrong.

Pharmacists are tired of complaining about the problems with electronic prescriptions. We are tired of fighting with offices to make them correct their errors. We are tired of wasting our time and the patients' time and the offices' time fixing something that never should have been sent. Call me. Let's fix this.

Empowering patients with limited health literacy

By: [Julia Talsma, Content Channel Director](#)<http://drugtopics.modernmedicine.com/drug-topics/news/empowering-patients-limited-health-literacy?page=0,0>

MAY 10, 2014

By: [Julia Talsma, Content Channel Director](#)

A patient with severe cardiovascular disease (CVD) was taking a number of prescribed medications, including nitroglycerin sublingual tablets and ranolazine. To assess the management of the patient's CVD during a complete medication review, Salvatore J. Giorgianni, Jr., PharmD, BSc, CMHE, asked him how often he had to use the nitro-sublingual medication. The patient replied that he needed to use nitroglycerin more frequently, about twice to three times weekly. Concerned that the patient was having so many angina attacks while taking ranolazine, Giorgianni questioned him further and discovered that he had misunderstood the label, which directed, "Take one a day for chest pain." The patient was taking the preventative agent ranolazine only when he felt chest pain and not once daily, as intended.

"We often get caught up with imprecise language in preparing prescription labels, and imprecision can lead to confusion in patients with low literacy or who simply are confused by all that is happening to them," said Giorgianni in the white paper "Health literacy, medication adherence, and pharmacist interventions," recently released by Pharmacist Partners. Giorgianni works for a compounding pharmacy in Florida and is an advisor to Pharmacist Partners, a Clinical Knowledge Organization specializing in enhanced medication compliance among patients through its partnerships with drug manufacturers.

In sharing the white paper with *Drug Topics* (it can be downloaded from the website www.pharmacistpartners.com), the company expanded upon the root causes of low and limited health literacy in the U.S. population and offered solutions for pharmacists seeking to increase medication adherence through interventions personalized to specific patients.

Scope of the problem

The 2003 [National Assessment of Adult Literacy](#) (NAAL), a federally funded census of adult literacy, was launched to determine the change in levels of English literacy in the United States between 1992 and 2003. More than 19,000 adults were surveyed at the national and state level, including 1,200 prison inmates.

The results demonstrated that 93 million U.S. residents (43%) have basic or below basic literacy. These participants could read short text and find a single piece of information identical to information contained in a question. They could not find and interpret information that was in dense or lengthy text with no organizational headings, could not understand multiple text sections, could not find and interpret information from complex tables and graphs, and had difficulty finding numbers in text. They also had limited quantitative reasoning skills.

In 1992, the [National Adult Literacy Survey](#) (NALS), an earlier project to assess adult literacy in the United States, found that 77 million people (more than a third of American adults) had trouble with some basic tasks for their healthcare, “such as following directions on a prescription drug label or adhering to a childhood immunization schedule using a standard chart,” said Lisa Van Brackle, PhD, MSW. The primary author of the white paper, she has more than 20 years of experience in the design and implementation of social programs for disadvantaged populations.

Of the participants in the NALS, 25% were immigrants with limited access to employment and education, and 26% had physical, mental, or health conditions. One-third were elderly, defined as older than 65 years of age. Among those who scored at the lowest literacy level (level 1), 40% were in poverty, 50% were unemployed, and only 30% were employed full-time.

The main groups in the nation with limited literacy include U.S. residents with limited access to education, immigrants for whom English is not the first language, and older adults. These are the same groups that show limited health literacy, noted Van Brackle, who has managed programs for TV411, a television based, multimedia project of the Adult Literacy Media Alliance and provided training to adult literacy instructors for the Literacy Assistance Center.

Implications of limited health literacy

The NAAL data were analyzed, and a [report](#) published in 2006 by Mark Kutner of the National Center for Education Statistics and colleagues concluded that almost “90% of adults have difficulty using the everyday health information that is routinely available in our healthcare facilities, retail outlets, media, and communities.” In addition, they found that about three-quarters of U.S. adults with long-term illnesses have limited literacy and difficulty understanding their disease states and what to do about symptoms.

In 1999, Catharine Selden of the National Library of Medicine and colleagues, reported in an article titled “[Health Literacy: January 1990 – January 1999](#),” that literacy and functional health literacy are closely associated. Those individuals with low functional health literacy have difficulty reading and understanding prescription labels, appointment reminders, and other health materials that providers expect functionally literate patients to comprehend.

Low and limited health literacy carries a large cost to society. In 2003, costs associated with health literacy reached between \$106 and \$236 billion annually. When adjusted for inflation, the annual U.S. costs range from \$134 to \$299 billion, according to Lynn Nielsen-Bohlman, of the [Institute of Medicine](#), and colleagues.

Interventions for improved medication adherence

Health literacy interventions should focus on improving communication between the patient and the provider.

Information designed to increase understanding of what constitutes good health includes written information found in both the healthcare setting and community venues such as health fairs, public libraries, and governmental agencies. Information about good health can be presented during a

doctor or pharmacy visit. It is also available through various media channels, including television, radio, and the internet.

“Interventions that make accommodations for low literacy by, for example, increasing awareness of information about health or healthy behaviors, using videos, illustrated, or other materials developed with a mindfulness of low literacy, and verbal teaching using simplified language have proven to be effective,” Van Brackle said in the white paper.

Use of simpler language, shorter sentences, good syntax, and understandable graphics go a long way in conveying health information to individuals with low health literacy.

In her work at New York City’s Literacy Assistance Center, Van Brackle secured a contract to provide health literacy training to clinical and support staff of New York City’s Health and Hospital Corp. The goal was to elevate awareness of health literacy issues and their prevalence among the patient population, and to start a dialogue on how to address them.

The year-long program, which Van Brackle directed six years ago, offered a variety of sessions for all segments of the healthcare system, including physicians, nurses, nursing assistants, social workers, medical informatics practitioners, and support staff not directly involved in patient care.

“We included all different workers, including transport workers who look very much like the patient population,” Van Brackle told *Drug Topics*. “When patients are in a facility and they are scared and don’t know what to do, they are going to go to someone who looks like them. So we wanted to provide some kind of support — not just to healthcare professionals who also need help — but also to these other individuals, so they would be in a position of helping patients without diminishing them or ignoring them.”

Strategies that work

Van Brackle noted some effective strategies for use with families of patients being treated in the emergency department.

Family members are often afraid and can’t hear what the healthcare provider is saying at first, she said. So it is important to acknowledge their emotions and to speak slowly. If the family member doesn’t speak the same language as the healthcare professional, the healthcare worker may have a tendency to speak louder instead of more slowly.

After distilling what is happening and what needs to be done for the patient, the healthcare professional should ask the family member, “What did you hear?” and wait for the family member to summarize what was said. The healthcare professional then needs to ask, “What are you going to do next? What steps are you going to take?”

Helpful aids for patients in the healthcare setting include forms and documents written at a sixth-grade level, as well as hospital signage that is understandable and easy to navigate.

Some hospitals assign a nurse or community health worker to help patients with low or limited literacy. These staffers attend appointments to acquaint themselves with management of the patient’s condition(s), provide patients with phone reminders to pick up prescriptions at the

pharmacy, and help with follow-up. Because costs are associated with this model, it is not a widely used practice among health systems, Van Brackle noted.

Other helpful tools to support patient medication adherence include pillboxes individualized for the different days of the week as well as for times of day. These are particularly helpful for patients with complex drug regimens.

“There is a movement to also use pictures on prescription bottles. Graphics can show that you should take the medication on an empty stomach. If you need to take it at the beginning of the day, the graphic will be the sunshine,” said Van Brackle.

Improved adult learning

Individuals with low or limited health literacy can have significant deficits connected with medication adherence. Patients can misinterpret prescriptions; they can have trouble identifying medications; they can experience difficulty understanding how to take medicine; and they can have poorer short-term memory.

To improve the odds that patients will understand and adhere to their medication regimens, the principles of [William Glasser’s](#) work on adult learning have stood the test of time.

Glasser’s work has demonstrated that “adults maximize learning through hearing, seeing, and doing, with a combination of these three elements giving optimal results. Glasser’s work [has remained] the industry standard ... for over five decades,” according to Khrys Kantarze, BS, MS, a certified training and development professional, and vice president of talent management at Pharmacist Partners.

Pharmacists can greatly improve their communications pertaining to medication adherence by understanding adult learning processes and bearing in mind the rate of retention that corresponds to each method.

Adults who read new information will retain 10%. Those who hear new information will retain 20%. Individuals who see new information will retain 30%. However, if pharmacists and patients discuss new information, patients will retain 70%. The best results are seen with adults who experience new information (80% retention rate) and with adults who can show or teach it to someone else (95%), said Kantarze.

“In the healthcare setting, the trainer will demonstrate something, so the trainee will retain 30% of that information. Then the trainer will have the trainee do what is called ‘return demonstration.’ The trainee will show the trainer that he or she can do it, which is experience, so you have an 80% retention rate,” she said.

In the pharmacy, return demonstration also can be easily employed, taking only about five minutes. For example, if the subject is insulin administration, the pharmacist can demonstrate how to draw up insulin through a dummy syringe, and then the patient can demonstrate the task to the pharmacist.

“The corporate offices could [initiate] this, and lead their pharmacists this way,” Kantarze said.

In the pharmacy that Kantarze uses, she witnessed a Hispanic mother picking up her prescriptions. Her 8-year-old child, who spoke English, accompanied her and acted as the translator. The pharmacy technician interacted with the child.

“Of course, the pharmacy technician said to the child, ‘Do you have any questions [about the medication]?’ ” Kantarze said. “And, of course, the answer was no. Using Glasser’s adult learning principles, I would have done this instead: ‘Let me explain this medication to you, and then you explain it to your mother and have your mother explain it back to you. Then you tell me [what she said].’”

The two- to three-minute encounter

Pharmacists are in the best position to conduct an open dialogue with patients to assess their literacy levels, discuss their medications, help them understand the need for the medication, and motivate them over the course of the treatment, said Giorgianni.

When a patient comes in with a new prescription, the pharmacist should consider three questions:

- What is the patient taking this medication for?
- What can the pharmacist tell the patient to expect with this medication?
- Why is it important for the patient to do this?

“This two- to three-minute encounter is what I always have with a person who is picking up his/her medications for the first time,” Giorgianni said. He also has a conversation with patients after reviewing multiple refills that may raise a red flag, including, for example, those individuals who have been prescribed a Zithromax Z-Pak (azithromycin five-day course), for the 15th time. This could be problematic because of the increased risk of antibiotic resistance. If pharmacists see a problem, they should do their due diligence, he said.

While language barriers to medication adherence can be difficult, it is not impossible to overcome them. In the United States, the Hispanic/Latino community has reached more than 50 million and is expected to more than double by 2050, representing 30% of U.S. population. Pharmacists need to take the time to counsel patients who may not speak English or who have limited English proficiency, said Giorgianni.

Personnel. A best practice for community pharmacies includes hiring personnel who reflect the community, such as those who speak the same language as some of the patients using the pharmacy and who understand the culture of those patients. These staff members can help with translation if it is needed, he said.

Family members. Pharmacists can also interact with family members, whose participation is common among members of the Latino population, Giorgianni noted. In a tight-knit community, family members can be extremely supportive as well as helpful in matters of translation. Pharmacists can also ask the patient to have a family member call the pharmacy when the patient returns home. This could help with the patient counseling, he said.

Physical environment. Another best practice for community pharmacies would be to create a physical environment that encourages communication, such as a specific area for private counseling.

Visual aids. For patients with impaired hearing, the pharmacist can use graphically dense material to help explain the patient’s condition and its management, or use a teletypewriter to accommodate

these patients. Brochures printed in different languages, such as Spanish, can help describe certain disease states.

A culture of encouragement

“The onus is to create an environment in your pharmacy practice and culture that encourages communication between pharmacists and patients,” Giorgianni said.

“With this white paper, I hope the message comes across that the working pharmacist can counsel patients effectively in three minutes. If you are cautious about whom you counsel and how you counsel, those can be extremely productive three-minute conversations,” he said.

For the owners and managers of community pharmacies, the best approach is to encourage and reward pharmacists for patient counseling focused on improved medication adherence. Not only will this “enhance adherence and compliance; it will enhance the patients’ perspective of community pharmacies as health places as opposed to hybrid retail places,” Giorgianni said.

Falsified medicines found to be riddled with bacteria

http://www.securindustry.com/pharmaceuticals/falsified-medicines-found-to-be-riddled-with-bacteria/s40/a2072/#.U7Q_8n_n9aQ

Some falsified medicines have high levels of microbial contamination and could pose a significant danger to patients, says a new study.

The findings come as no major surprise for anyone who has seen pictures of the conditions in which many fake drugs are produced, but are notable as they represent one of the first systematic of microbial contamination levels in counterfeits intercepted in western markets.



Falsified drugs are potentially harmful in all manner of ways, and can cause patient harm because they have no active ingredient and are ineffective, have the wrong dose of active or are contaminated with harmful materials.

The researchers behind the study - from the regulatory authorities in Austria and Canada - tested falsified and unapproved medicines seized in their respective countries for microbial contamination and - where possible - compared them to their genuine counterparts.

The legitimate products had no appreciable contamination, while 23 per cent of the illegal products in Canada and 6 per cent in Austria had contamination levels exceeding the limits laid down in the US and European Pharmacopoeias. The contamination represents a "potential threat to consumer health," they note.

The contaminating organisms were mostly *Bacillus* species, some of which can be harmful to humans although no major pathogenic strains were discovered in this study. The work is published in the journal *BMC Pharmacology and Toxicology*.

"We recommend the risk-based inclusion of microbiological quality studies in the surveillance of the illegal pharmaceutical market," conclude the authors.

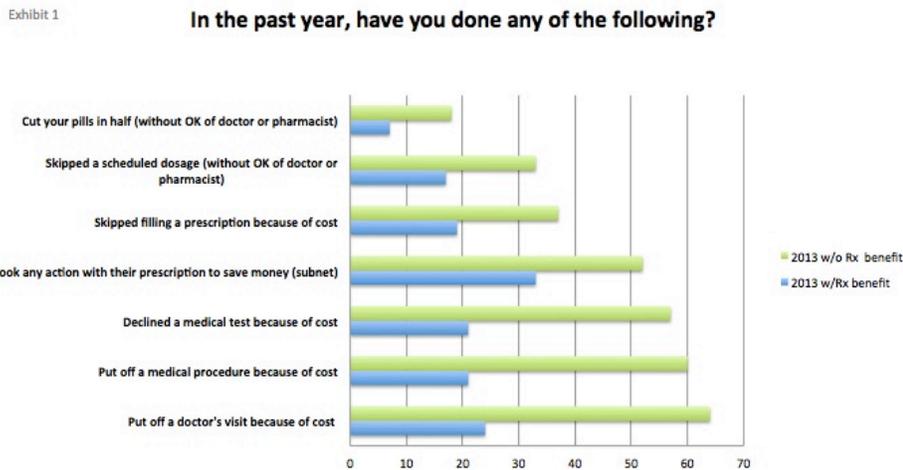
Our national poll of more than 1,000 Americans shows many skeptical about generics

Ginger Skinner, Consumer Reports Best Buy Drugs

Americans take a lot of medicine. More than 4 in 10 (44 percent) regularly take a prescription drug, and among those, the average number they take is 4.5 medicines— 16 percent take 7 or more, according to the 2013 Consumer Reports Best Buy Drugs Prescription Drug Tracking Poll of 1,136 U.S. adults.

The national telephone poll found that the high costs all those medicines too often can lead to risky behaviors and force families to choose between the medications they need and paying other bills. More than half (57 percent) of those we surveyed reported taking steps in the past year – some of them potentially dangerous – to curb costs. In addition, 30 percent failed to comply with prescriptions from their doctor. Other measures to save money included not filling a prescription (17 percent), skipping a scheduled dose (14 percent), and taking an expired medication (14 percent). People who didn't have insurance coverage were hit the hardest—they were far more likely to have skipped filling prescriptions and refused, tests, treatments and doctors visits because they couldn't afford them. (See Table 1. and Table 2 below.)

Americans' personal finances were affected in other ways, too. Three in 10 (29 percent) reported cutting back on entertainment and dining out, 19 percent spent less on groceries, and 15 percent put off paying other bills in order to afford their prescription drugs.

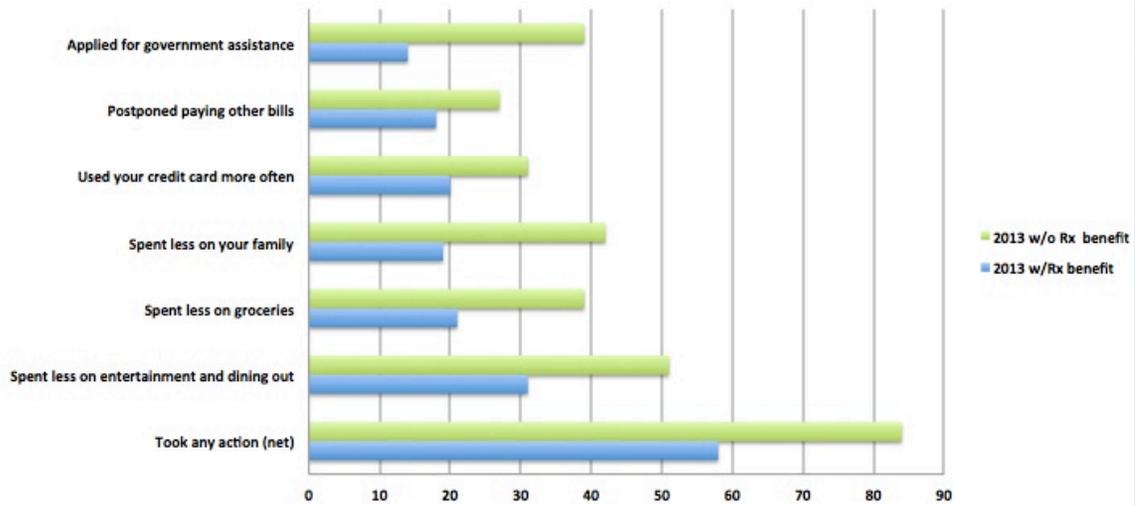


SOURCE: Consumer Reports Best Buy Drugs Prescription Drug Tracking Poll of 1,136 U.S. adults who currently take a prescription drug.

Table 1

Exhibit 2

During the past year, have you done any of the following in order to pay for medications?



SOURCE: Consumer Reports Best Buy Drugs Prescription Drug Tracking Poll of 1,136 U.S. adults who currently take a prescription drug.

Table 2

Doubts about generics prevalent

Despite struggling to pay for prescriptions, Americans remain skeptical about generic drugs. Nearly a fourth of those aware of **generic drugs** (23 percent) said they are not as effective as brand-name medications, 13 percent said they’re not as safe, and 21 percent said they don’t trust generics as much as brand-name drugs. Even so, when asked if they were willing to switch from a brand-name to a generic drug, nearly two-thirds (64 percent) said they were “very willing.”

Drug ads lead to higher costs

One reason for Americans’ reluctance to trust generics could be related to the marketing of brand-name drugs. Overall, 18 percent of Americans currently taking a medicine have asked their doctor to prescribe a drug they learned about from an advertisement, and among them, 63 percent said their **doctor complied**. Moreover, 57 percent of those taking a medicine have accepted free drug samples from their doctor. **Free drug samples** are often a promotional tactic used by drug manufacturers as a way to get consumers acquainted with newer and usually more expensive drugs.

Patients and doctors reluctant to discuss costs

Despite the difficulties consumers face paying for medicines, some are still uncomfortable discussing costs with their doctor or pharmacist. Just half had spoken with their doctor about switching prescriptions, and of those,

slightly more than a third (38 percent) mentioned a reason related to cost, including wanting a less expensive medication or one covered by insurance. Almost no one (5 percent) found out about the cost of their medication at the doctor's office. Instead, most (61 percent) find out about the cost when they pick up their prescription from the pharmacy.

One encouraging finding: roughly 9 in 10 consumers aware of generics said they were willing to change to a generic. However, though generic drugs can provide huge savings, sometimes priced as much as 95 percent less than brand-name medication, four out of 10 respondents said their doctor sometimes or never recommends generics over brand-name drugs.

What you can do

With consumers spending upwards of \$1,000 a year on prescription drugs, keeping money in your pocket while getting treatment for what ails you is no easy feat. So it's crucial that you be assertive and tell your doctor that cost, as well as effectiveness, matters.

Ask about generics, stopping drugs you no longer need, and whether it's safe to split your pills in half.

Following these **surprising tips** can help lighten financial your burden and keep money in your wallet. And make sure you get the right insurance, with the drug coverage that works best for you. Our **advice** on navigating the new health law and picking a good insurance plan can help.

Finally, check out our **Best Buy Drug reports**. We rate nearly two dozen common drug classes, including those used to treat **allergies, diabetes, heartburn, high blood pressure, high cholesterol, migraines, and sleep problems** on how well the drugs work, their risk of side effects, and price.

Prescription Drugs News: Study Finds Latino Seniors Are Less Likely to Have Prescription Drug Coverage Than White Seniors

By Scharon Harding (staff@latinpost.com)

First Posted: May 27, 2014 10:59 AM EDT

<http://www.latinpost.com/articles/13515/20140527/prescription-drugs-news-study-finds-latino-seniors-less-drug-coverage.htm>

A record 4.02 billion prescriptions were filled in 2011, costing almost \$320 billion. In 2010, 3.99 billion prescriptions were filled with a total cost of \$308.6 billion.

Latino senior citizens are 35 percent less likely to have prescription drug coverage than white citizens, according to a study released in the Health Affairs journal by University of Rochester School of Medicine and Dentistry.

The May report makes its conclusion despite the Medicare Prescription Drug Plan and the availability of insurance premium payment assistance. It is estimated that 65 percent of Latinos without prescription coverage are eligible to receive [support](#) in paying their premiums.

"These results indicate that disparities in prescription drug coverage exist between Hispanic and white Medicare beneficiaries, despite the existence of a potentially universal entitlement program," Brian McGarry, a [graduate student](#) in the Department of Public [Health Sciences](#) at the University of Rochester School of Medicine and Dentistry and co-author of the study, said via University of Rochester's [Newsroom page](#).

The study suggests that the complicated process and the [financial](#) know-how needed to apply for premium assistance could be the reason for this statistic, although it does note that there is ample information available in Spanish. Another possibility is a lack of outreach in educating the Latino community.

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"This study suggests that, in spite of the overall [success](#) of the Part D [program](#), future policies need to focus on the disproportionately low enrollment of vulnerable populations," McGarry said.

The same sort of issues have been brought up regarding Latinos and the [Affordable](#) Care Act.

"With all that is known about the adverse health and economic effects associated with a lack of prescription drug coverage, the authors point out that -- with a rapidly growing population of Hispanic seniors -- addressing this disparity is a critical public health priority."

The study was co-authored by McGarry, Robert Strawderman, Sc.D., the chair of the University of Rochester Department of Biostatistics and Computational Biology, and Yue Li, Ph.D., an associate professor in the Department Public Health Sciences and considered [data](#) from the 2011 [National Health and Aging Trends Study](#). The Agency for Healthcare Research and Quality, the National Institute for Aging and the National Institute on Minority Health and Health Disparities funded the study.

Rx for a medical near-miss

<http://articles.latimes.com/2013/jun/03/opinion/la-oe-margolius-prescription-drugs-20130603>

Op-Ed

The California Senate is considering a bill to require pharmacies to dispense medicine with translated instructions in other languages.

June 03, 2013 | By David Margolius

Los Angeles Times

The Legislature is considering a bill -- SB 204 -- that, if passed, would... (William Thomas Cain / Getty...)As the saying goes, "With great power comes great responsibility." That applies to physicians when prescribing medications, but it also should apply to pharmacies when they're dispensing medications.

In December, after seven years of exams, lectures and rounds, I received my medical license. Finally, I had the power to prescribe medications without the co-signature of my supervisor. "Be careful," she advised, "remember the story of 'once.'"

The story of "once" is a cautionary tale that — best as I am able to tell from Google — was adapted from a Spanish soap opera.

In one version, a doctor prescribes a patient a 30-day supply of a medication. Three days later, the patient returns for a refill. "How can this be?" the doctor wonders. The Spanish-speaking patient responds, "I took the pills exactly as the bottle said to: '11 daily.'" The doctor scrutinized the pill bottle: "Take once daily." But "once" read and pronounced "ohn-say" means 11 in Spanish. The patient had taken 11 pills daily, just as the bottle label said — in Spanish.

The patient lives in that story, but in other versions he is hospitalized or even dies. Shortly after I received my license, I had my own version.

Mr. P is a 65-year-old gentleman originally from Mexico. He speaks English well enough to have a light conversation but would be classified as limited English proficient, or LEP. That means he speaks English less than "very well," and he is not unique: 40% of Californians speak a language other than English at home, and more than 6 million Californians are LEP.

He has diabetes, high cholesterol, high blood pressure and coronary artery disease, and takes 10 medications daily. He is a perfect candidate to be one of 150,000 Californians who are sickened or killed each year because of medication errors.

I had hoped to help him. He was taking one blood pressure medication twice a day, so I changed it to the once-a-day formulation. I wrote "Tome 1 pastilla en la noche" on a sticker and stuck it to the bottle to avoid any "once" pitfalls. I felt that this was part of my responsibility as a prescriber of medications.

Three months later, Mr. P ended up in the hospital. He had begun to feel lightheaded a week before, and then he fell. His heart rate in the emergency room was dangerously low. After an extensive evaluation and ultimately a visit to his home by a nurse, we discovered that he had resumed taking his blood pressure medication twice a day, despite being given the new once-a-day formulation. He in effect had doubled the dosage I had prescribed.

The directions I wrote out may have worked, but then he received his first refill and a new pill bottle. Although many pharmacies in California (including some but not all large chains) print non-English directions on pill bottles, his did not.

The Legislature is considering a bill — SB 204 — that would help; it's moved to the Assembly after passage by the state Senate. If it becomes law, pharmacies will be required to print standard medication instructions translated into languages other than English on pill bottles. The instructions are already available in Spanish, Chinese, Vietnamese, Korean and Russian on the Board of Pharmacy's website. With this law, they would be printed on the bottles themselves. (New York has a similar law.)

I, with my power to prescribe, almost killed my patient. Pharmacies, with their power to dispense and advise, could have helped keep him out of the hospital. The Legislature should make this procedure the law.

David Margolius, an internal medicine resident at UC San Francisco, testified before the state Senate Committee of Business and Professions in April in support of SB 204.

Standing Up to Pain

LA Times

<http://www.latimes.com/brandpublishing/healthplus/la-ss-standing-up-to-pain-20120315-story.html>



Chronic pain can be a debilitating force in a person's life. But treatments are available.

Pain took center stage during season 11 of ABC's "Dancing with the Stars," when Jennifer Grey almost didn't perform during the finale due to a severe back injury.

The actress, who shot to fame in the 1987 flick "Dirty Dancing," ruptured a disc during her final freestyles and turned to her longtime physician, Dr. Robert Bray, the first California neurosurgeon to devote his practice to minimally invasive spine surgery. Following an outpatient procedure, the then 50-year-old actress returned to the prime time show to beat out competitors a fraction of her age and take home the coveted mirror-ball trophy. "She went from disabled to winning the mirror ball," Bray said.

Diagnosis

As many as eight out of 10 people will be affected by debilitating pain in their lifetime. "It's the leading cause of disability for work in the United States, other than the common cold," Bray said.

Fortunately, most of these cases are temporary inflammation, which the body uses to jump start the immune system, and can be managed with rest or over-the-counter drugs. "A heating pad, ice packs, physical therapy can help," said Dr. Rostam Khoshsar, a pain management specialist at the Presbyterian Intercommunity Hospital in Whittier.

But about 3% of people affected by pain end up with chronic pain syndrome, which is pain that lasts longer than six months and interferes with lifestyle.

Grey is one of the thousands of patients treated at the L.A.-based DISC Sports and Spine Center, founded by Bray in 2006. The center, which is the official medical provider of the U.S. Olympic Team and Los Angeles Kings, takes a multidisciplinary approach to pain with a team of providers — acupuncturists, chiropractors, pain management specialists, rehab therapists and surgeons — functioning as an integrated group.

“When a patient is truly affected by chronic disabling pain, they need to seek a level of expertise where they will be fully evaluated,” Bray said.

At DISC, which has offices in Marina del Rey, Beverly Hills and Orange County, specialists use different techniques, including a scans and X-rays, to hunt down the cause of a patient’s pain.

“The most important thing, in my opinion, is getting an accurate idea of the cause,” Bray said. “Too many people are just treated with narcotics without a diagnosis.”

Treatment

When it comes to treatments, Bray’s philosophy is to try the most conservative options first, including prescribed exercise and rehabilitation programs, counseling with a psychologist to help with stress and pain management, as well as injections and anti-inflammatory drugs.

Khoshsar turns to new technology to treat patients, including radio frequency treatments, epidural injections and a spinal cord stimulator. Acting like a pacemaker for the spine, the stimulator releases electrical impulses to block pain. “I’ve done over 150 cases with a very high success rate,” he said, adding that the procedure can be used to treat abdominal pain, endometriosis and migraines.

Even the most minimally invasive surgeries are often last on the treatment list. “We created this entire structure to try to avoid surgery,” Bray said of D.I.S.C.

If a patient is still in severe pain post-surgery, Khoshsar said a spinal pump is another option. “It’s implanted in the body and delivers medication to the spinal cord where it needs to go without side effects of oral narcotics.”

Despite the variety of potential treatments, patients often need a dose of reality.

“Chronic pain patients have to live with a certain degree of realism — they’re going to live with some pain,” Bray said. “We shoot for an improvement in their lifestyle, not necessarily pain-free perfect.”

—**Jamie Wetherbe**, *Brand Publishing Writer*

Substitution errors: Surveys describe harm from differences between prescriptions and drugs dispensed

<https://www.avma.org/News/JAVMANews/Pages/140901a.aspx>

JAVMA NEWS By Greg Cima

Posted Aug. 20, 2014

Updated Sept. 4, 2014

Ten percent of veterinarians responding to recent polls said they have had patients harmed when outside pharmacies made substitutions in filling prescriptions.

Surveys conducted by five veterinary medical associations together indicate about one-third of respondents knew of occasions when pharmacies dispensed drugs to clients that were different from those that were prescribed or were different in dosage, and they did so without consulting the prescribing veterinarian. Most of those changes occurred without any known harm.

The Oregon, Idaho, Iowa, and Washington veterinary medical associations conducted their surveys in 2012, and the Southern California VMA conducted its survey in 2013. They received responses from 707 veterinarians.

Those veterinarians provided examples—included in reports from the VMAs—such as replacement of a prescribed insulin product with one less effective in dogs, a recommendation that a client administer aspirin to a cat rather than pay for a prescription nonsteroidal anti-inflammatory drug, and reduction of a dog's thyroid medication dosage that seemed high to the pharmacist in comparison with the dosage for humans.

Glenn Kolb, executive director of the Oregon VMA, which conducted the first survey, said veterinarians had been asking the association how to respond when they find out about substitutions. While he acknowledged that pharmacists need to counsel clients, it seems to him that some have altered prescriptions for animals on the basis of uses in human medicine.

Jennifer Davis, PharmD, president of the Oregon State Pharmacy Association, noted that a pharmacist can work with hundreds of patients in a typical week. While the Oregon VMA asked veterinarians whether they had encountered a change in a prescription at some point, she noted that the survey did not ask how many times such problems occurred.

"The error rate based on those thousands of interactions is exceptionally low," she wrote in a message. "None-the-less, we accept that every error is significant and continually work on processes and knowledge that can minimize the likelihood of an error."

Study and response in Oregon

Dr. Laird M. Goodman, owner of Murrayhill Veterinary Hospital in Beaverton, Ore., said a client told him she cut an epileptic dog's phenobarbital dosage in half on advice from a pharmacist who thought the dosage was high. The dog's seizures returned and could not be controlled, leading to a decision to administer euthanasia.

He also has seen alterations to patients' thyroid medication prescriptions.

“In the good old days, they would at least call us and say, ‘Hey, are you sure you want to give this high of a dose?’” Dr. Goodman said. “And we would advise the pharmacist that dogs take a higher dose than people.”

Gary Miner, RPh, compliance director for the Oregon Board of Pharmacy, expects that changes without consultation occur no more often in veterinary medicine than in human medicine, where they are rare. Over the past few years as the board has raised awareness among pharmacists about the need for consultation on veterinary prescriptions, he said, “They’re probably more cautious about filling veterinary prescriptions than they are the human prescriptions,” although he hopes pharmacists provide the same due diligence for both.

Prior to the surveys, the Oregon Board of Pharmacy and the state’s two pharmacy schools had been in talks about increasing pharmacy students’ education on veterinary pharmacy. Fiona Karbowicz, RPh, a consultant to the Oregon pharmacy board, said veterinary pharmacy has not been a substantial part of pharmacists’ education, yet pharmacists are filling increasing numbers of veterinary prescriptions.

“We saw the need to get more education out there in a variety of different ways,” she said.

Oregon’s pharmacy board has advocated that pharmacists and pharmacy technicians be mindful when filling veterinary prescriptions, and the board has given pharmacy students and pharmacist associations presentations that included information on veterinary prescriptions, Karbowicz said. The board also requires that pharmacies dispensing veterinary drugs have references such as Plumb’s Veterinary Drug Handbook or the Merck Veterinary Manual.

The Oregon State Pharmacy Association also has worked to improve the “critical link in patient care” between veterinarians and pharmacists by providing continuing education on veterinary pharmacy, Dr. Davis said. And she noted that an increasing number of U.S. pharmacists are completing residency training in veterinary pharmacies.

“We do need to work on opening stronger communications between pharmacists and veterinarians,” Dr. Davis said. “Pharmacists take their responsibility as the last check in drug review and distribution seriously but need to follow up with veterinarians if they have questions.

“We hope that veterinarians will be equally open to working with pharmacists as they fulfill their professional responsibilities.”

Kolb said representatives from the Oregon VMA and state pharmacy board have talked about the issue over the past two years, and the OVMA has developed information sheets for veterinarians to give to clients when writing prescriptions to be filled by outside pharmacies. He thinks changes in the absence of consultation are less common than before the OVMA conducted its survey.

Accidents, intent, and generics

Miner suspects that some of the Oregon VMA survey respondents who reported knowing of unauthorized changes were referring to instances when clients received generic rather than name-brand drugs.

If a veterinarian writes “no substitution” or “dispense as written,” a pharmacist cannot provide an equivalent without the veterinarian’s authorization.

He also said the Oregon VMA did not give details that would have let the board investigate incidents reported in the survey.

The board has been receiving more reports of errors since the survey, Miner said, although most are related to accidental changes rather than deliberate substitutions. Such mistakes are unfortunate but normal occurrences in pharmacies, he said.

Karbowicz said a 2013 investigation found, for example, that an Oregon pharmacy made a decimal point-related error rather than an intentional substitution in filling a prescription for a pet's thyroid medication at 0.05 mg rather than the prescribed dose of 0.5 mg, although the former would be a more typical dose for humans. The board imposed a \$1,000 fine.

"We are initiating an investigation for each and every call that we get," she said.

But Karbowicz, who previously worked in retail pharmacy, expects almost no pharmacist would intentionally dispense medication differing from a prescription without consulting the prescriber.

"I'm very appreciative of the surveys because they have brought the conversation forward," she said. "And the conversation clearly showed that education and more awareness was needed around the whole topic, especially as it's just grown over the past, maybe 10 years, or so."

But she said the survey results need to be substantiated, and the limited data available are not alarming.

Concern among VMAs

Candace Joy, executive vice president of the Washington State VMA, said her association's survey, patterned after the Oregon VMA's, indicated it is commonplace, in her words, "to have pharmacists switching drugs, altering dosages, changing quantities without any authorization from the prescribing veterinarian." Her organization presented their survey findings to the Washington State Pharmacy Quality Assurance Commission.

The results, described in a January 2013 report, showed that most pharmacists call the prescribing veterinarian when they have questions or concerns. But they also show "an alarming trend in recurring problems by pharmacists unfamiliar with veterinary pharmacology and physiology" as well as problems related to an inadequate supply of veterinary drugs.

"Pharmacists are not specifically trained in veterinary pharmacology and physiology and are making the assumption that animals respond to drugs similarly to humans," the report states. "Cats and dogs are not small humans and species variability in the metabolism of drugs is significant."

Given the survey results from Oregon and Washington, Joy said such changes in veterinary prescriptions are a national issue.

"If it's happening this much in our two states, I know that it's happening everywhere," she said.

Dr. Peter Weinstein, executive director of the Southern California VMA, which also based its survey on Oregon's, wants veterinarians to follow up on filled prescriptions and ensure that clients are receiving the intended products. He also advocates that veterinarians have working relationships with pharmacies.

He said that, as more clients receive prescriptions from pharmacists, organized veterinary medicine should find a way to benefit pets, pet owners, and veterinarians.

"I think that there has to be a way that we can all benefit from this and not end up in a contentious battle," he said.
"It's just going to change the way we think about conducting our businesses."

Correction:An earlier version of this article included an inaccurate statement that pet owners in Oregon could, by requesting generic alternatives, override a veterinarian's orders against substitutions.

Attachment 4

FORTY-THIRD ANNUAL REPORT

of the

**RESEARCH ADVISORY PANEL
OF CALIFORNIA**

2013



PREPARED FOR THE

LEGISLATURE AND GOVERNOR

RESEARCH ADVISORY PANEL OF CALIFORNIA

**455 Golden Gate Avenue - Suite 11000
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2013 PANEL MEMBERS

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Appointed by Attorney General

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This report represents a consensus among Panel members acting as individual experts. It does not represent policies or positions of the appointing agencies nor have those agencies been consulted by the Panel during its function or during the preparation of this report.

SUMMARY OF 2013 PANEL ACTIVITIES

During 2013 the Panel reviewed thirty-two research study submissions. Twenty-eight were approved by the Panel. Among twenty-eight approved studies, ten studies were Academic research studies, nine studies were Substance Abuse Treatment research protocols, and nine studies were Clinical Drug Trial research protocols.

Thirteen research studies were completed or, in a few cases, terminated in 2013, and they were closed on the Panel's records.

At the end of 2013, the Panel was monitoring eighty-nine active research projects. Note Appendices A, B, and C for specific listings.

As part of the Panel's supervisory responsibility, ongoing projects are monitored by means of annual reports, Significant Adverse Event (SAE) reports and site visits. Approval may be withdrawn if the study deviates significantly from the approved protocol.

Table 1 is a list of the studies approved by the Panel in 2013 and Table 2 is a list of the studies closed by the Panel in 2013.

SELECTED RESEARCH FINDINGS

Below are brief summary reports of several Panel approved projects which are of interest and indicative of the types of controlled substance research projects currently ongoing in California:

Alkermes has submitted Annual Progress Report titled "A Phase II Randomized, Multicenter, Safety, Tolerability, and Dose-Ranging Study of Samidorphan, A Component of ALKS3831, in Adults with Schizophrenia Treated with Olanzapine" (ALKS3831-302)

ALKS3831 is composed of two active substance: olanzapine and samidorphan and is under investigation for the treatment of schizophrenia. Olanzapine is FDA-approved for the treatment of schizophrenia and bipolar disorder and is not a controlled substance by the Drug Enforcement Agency (DEA). Samidorphan is a new chemical entity, under development by Alkermes for the treatment of reward disorders. Samidorphan was classified as a Schedule II substance by the DEA under the Controlled Substances Act ("CSA") (CSCN 9668).

To date, over 600 subjects have been exposed to samidorphan, either as a single agent, a co-formulation with buprenorphine or co-administered with olanzapine. Samidorphan is prepared from the uncontrolled substance naltrexone and retains the structural features of naltrexone that result in μ -opioid receptor antagonist activity. This activity likely underlies the effect of samidorphan to block subjective and physiological effects of opioid drugs, as seen in clinical and nonclinical studies. No evidence of withdrawal has been observed after discontinuing samidorphan.

ALKS3831-302 is a Phase II, randomized, placebo-controlled multicenter study, which is being conducted in 2 parts: Part A and Part B. Part A begins with screening and includes a 1-week olanzapine lead-in period followed by a 12 week double-blind, placebo-controlled treatment period where subjects receive samidorphan or placebo (in addition to the olanzapine prescribed on Study Day 1). Part B includes an additional 12-week treatment period where all subjects receive active olanzapine + samidorphan (ie, ALKS3831). At the end of Part B, samidorphan dosing stops, but olanzapine dosing continues uninterrupted through a 4-week follow-up period, which includes 2 safety visits.

Due to the blinded nature of the study, no efficacy results are available at this time. No subjects have died during the course of the study and there were no serious adverse events during the report period.

Dr. Friedbert Weiss, PhD, and colleagues at the Scripps Research Institutes, La Jolla, CA have provided the Panel with the following summary of research titled "Ethanol Seeking and Relapse: Therapeutic Potential of Transdermal Cannabidiol"

Drug addiction is a chronically relapsing disorder. Susceptibility to relapse can be traced to multiple factors including craving elicited by drug-related clues, heightened anxiety and hypersensitivity to stress, as well as drug-induced impairments in impulse control. Thus, treatment drugs that target more than a single factor or vulnerability state for relapse are likely to offer significant clinical advantages. Our findings suggest that cannabidiol (CBD), the main non-psychoactive and non-addictive component of the cannabis sativa plant, may provide such a profile of actions. A factor limiting the therapeutic potential of CBD is the drug's low oral bioavailability in man due to a major first-pass effect. This limitation can be overcome by transdermal administration, which eliminates the first-pass effect and reduces variability in bioavailability. In collaboration with our coinvestigator, Dr. Stinchcomb, we therefore developed a transdermal CBD formulation (tCBD) suitable for behavioral testing in rats, consisting of a fast drying CBD gel applied to a shaved area of skin.

The effects of tCBD were examined in animal models of relapse (cue and stress),

anxiety, and impulsivity. Rats with a history of ethanol or cocaine self-administration were treated with tCBD (15mg/kg) at 24h intervals for 7 days.

tCBD significantly reduced cue-induced reinstatement of ethanol and cocaine seeking, as well as stress-induced reinstatement by yohimbine or electric footshock, without producing tolerance. Remarkably, both stress- and cue-induced reinstatement remained fully attenuated as late as 138 days after termination of tCBD treatment. In tests of anxiety (using the elevated plus maze), all rats showed significantly reduced anxiety-like behavior. To study tCBD's effects on impulse control, rats were subjected to a 7d ethanol intragastric intoxication procedure during which they were treated at 24h intervals with tCBD (15mg/kg). In subsequent delay discounting tests, rats with an intoxication history showed significantly reduced preference for large delayed reward indicative of heightened impulsivity. This profile of high impulsivity was fully reversed in tCBD-treated rats. In tests of nonspecific behavioral effects, tCBD neither with reinstatement motivated by a palatable sweet solution, nor altered spontaneous locomotor activity.

Although presently limited to a single dose, the results are consistent with the hypothesis that tCBD has therapeutic potential for multiple vulnerability states underlying relapse risk. Particularly significant was the observation that cue- and stress-induced ethanol seeking remained effectively reduced as late as =5 months (138 days) post-treatment. This observation, paired with the finding that tCBD attenuates impulsivity in rats with a severe ethanol intoxication history, is of substantial interest both from a medication development and neurobiological perspective in that it is suggestive of diverse neuroregulatory actions that restore normal function to brain circuitries regulating reward, incentive motivation, impulsivity, stress and anxiety.

Dr. Walter Ling, M.D. and colleagues at University of California, Los Angeles have provided the Panel with the following summary of research titled "Analgesic Response to Opioid Analgesics in Buprenorphine-Maintained Individuals"

The extensive and detrimental effects of unrelieved pain are well described, with negative physiological and psychological consequences (see Brennan et al., 2007; Leykin et al., 2007). Fortunately, opiates and synthetic opioids provide powerful and effective treatment for pain. Recent national indicators show that rates of prescription opioid abuse have risen dramatically over the past decade (McCabe et al., 2008; NIDA, 2008; SAMHSA, 2009), presenting a pressing need to effectively and safely manage pain in opioid-dependent patients. To effectively treat pain and maximize health outcomes in patients at high risk for poor pain management, clinicians need a more comprehensive understanding of the effects of ongoing opioid use on pain outcomes.

Patients treated with opioids, including buprenorphine, for extended periods may develop physical dependence, and opioid-induced hyperalgesia. Managing acute pain in these patients has been hampered by misunderstanding and misinformation, and by a genuine lack of systematically gathered controlled study data. Many physicians believe that the ceiling effect of buprenorphine makes it a poor analgesic and that patients maintained on buprenorphine will not benefit from the analgesic effects of added opioids, although anecdotal reports from physician experience and observational—largely uncontrolled—data suggest otherwise. There is a dearth of data to provide guidance for clinicians for an evidence-based approach to providing meaningful analgesia using opioids in treating acute pain in buprenorphine-maintained patients.

The favorable clinical safety profile gives buprenorphine considerable latitude in practice settings and in method of medication dispensing and prescribing. Clinicians may have taken advantage of buprenorphine's off-label use to treat a variety of painful conditions. This practice in itself is within the scope of usual and customary clinical practice, but because, at least in the United States, analgesia is not the primary approved indication for buprenorphine, relevant and critical information of such use is rarely available to clinicians.

This project intends to provide information on analgesic responses to single doses of various opioid analgesics, including buprenorphine, in study participants maintained on buprenorphine. Study findings will provide needed data for an empirically based approach to using opioids in managing acute pain in buprenorphine-maintained patients. The study will also collect data related to mu receptor blockade of buprenorphine when combined w additional opioids.

The aim of this study is to examine the effects of opioid analgesics on acute pain in participants maintained on buprenorphine+naloxone (Suboxone) for opioid use disorders.

Study design is a single-blind examination of the analgesic effects of a single dose of seven test medications provided in an experimental pain paradigm using a cold pressor test (CPT). Test medication conditions include buprenorphine, morphine, hydromorphone, hydrocodone, oxycodone, and two placebo conditions to match test medication formulations (oral tablet, sublingual tablet). Each medication condition will be tested on separate days (seven total days, completing within 12 weeks), with random assignment to order of study medications.

Participants will be 12 males, age 20-50, who are currently prescribed buprenorphine maintenance treatment and are under the care of a physician not associated with the study. Presence of buprenorphine and buprenorphine metabolites will be confirmed in baseline urine toxicology tests. Participants must not require regular daily use of any other medications for pain or have any other condition that could interfere with participation, study procedures, or the interpretation of study findings.

After screening, eligible participants will be scheduled for 7 days of testing with test days at least 3 days apart to provide a sufficient medication wash-out period. Pain testing will utilize cold pressor tests (CPT), in which the participant submerges his arm and hand in a bath of ice cold water to determine pain threshold and tolerance. Participants will be given a practice trial to provide familiarity with the test and reduce test anxiety. Two CPTs will occur on each test day, and pre- and post-CPT assessments will be administered. Blood samples will be taken on each test day to measure blood levels of buprenorphine. Daily procedures include: (1) A baseline CPT (BL-CPT), (2) Administration of the test medication (active drug or placebo), (3) CPT administered at the time of maximum drug effect (Tmax-CPT) specific to medication (range 30-120 minutes), (4) Pupillometry conducted at baseline (before BL-CPT), and at time of maximum drug effect (before Tmax-CPT). Each participant will be discharged after clinical determination of the participant's safety and well-being.

TABLE 1
RESEARCH STUDIES
APPROVED IN 2013

<u>PI / Sponsor</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
Michael Fischbach, Ph.D. Dept of Anesthesia, UCSF San Francisco, CA	Engineering a human gut bacteria to produce dimethyltryptamine
George Koob, Ph.D. The Scripps Research Institute La Jolla, CA	Prescription Opioid Addiction: Neurobiological Mechanisms
Walter Ling, M.D. Integrated Substance Abuse Programs, UCLA Los Angeles, CA	Analgesic Response to Opioid Analgesics in Buprenorphine-Maintained Individuals
Robert Malenka, M.D. School of Medicine Stanford University Palo Alto, CA	The Role of Oxytocin in the Pathogenesis of Autism
Florian Rader, M.D. Cedars-Sinai Med Center Los Angeles, CA	Mechanisms and Modulation of Cocaine Effects on Blood Flow to the Heart
Richard Reznicek, M.D. Harbor-UCLA Los Angeles, CA	Panel approved research

Table 1 Cont.

PI / Sponsor

Title of Study / Clinical Drug
Trial Protocol

Paolo Sassone-Corsi, Ph.D.
Center for Epigenetics
UC Irvine
Irvine, CA

The Role of Liver CB1 Receptor in Regulation
of the Circadian Metabolism

Ronald Victor, M.D.
Cedars-Sinai Med Center
Los Angeles, CA

Effects of Cocaine on Blood Flow to the Heart

Friedbert Weiss, Ph.D.
The Scripps Research Institute
La Jolla, CA

Ethanol Seeking and Relapse: Therapeutic
Potential of Transdermal Cannabidiol"

Roya Yumul, MD, PhD
Cedars-Sinai Med Center
Los Angeles, CA

Intraoperative ketamine and methadone for
laminectomy: effect on recovery,
postoperative pain, and opioid requirements

AcelRx
Redwood City, CA

A Multicenter, Randomized, Double-Blind,
Placebo-Controlled Trial to Evaluate the
Efficacy and Safety of the Sufentanil
NanoTab® PCA System/15 mcg for the
Treatment of Post-Operative Pain in Patients
after Knee or Hip Replacement Surgery
(IAP311)

Alkermes, Inc.
Waltham, MA

A Phase 2, Randomized, Multicenter, Safety,
Tolerability, and Dose-Ranging Study of
Samidorphan, A Component of ALKS 383, in
Adults with Schizophrenia Treated with
Olanzapine
(ALK3831-302)

Table 1 Cont.

<u>PI / Sponsor</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
CNS Therapeutics / CRO: Pacific-Link Consulting	A Controlled, Two-Arm Parallel Group, Randomized Withdrawal Study to Assess the Safety and Efficacy of Hydromorphone HCl Delivered by intrathecal Administration a Programmable Implantable Pump (HYD201US)
CNS Therapeutics / CRO: Pacific-Link Consulting	A Phase 3 Open-Label, Single-Arm Study To Assess The Safety of Hydromorphone HCl Delivered by Intrathecal Administration (HYD202US)
Forest Research Institute Jersey City, NJ	A Randomized, Double-Blind, Placebo- and Active-Controlled Study to Evaluate the Safety and Efficacy of GRT6005 in Patients with Moderate tot Severe Chronic Pain Due to Osteoarthritis of the Knee (GRT-MD-101)
GW Pharmaceuticals Mill Valley, CA	Panel approved research
MAPS Santa Cruz, CA	A Placebo-Controlled, Randomized, Blinded, Dose Finding Phase 2 Pilot Safety Study of MDMA-Assisted Therapy for Social Anxiety in Autistic Adults (MAA-1)

Table 1 Cont.

PI / Sponsor

Title of Study / Clinical Drug
Trial Protocol

Teva Pharmaceuticals
Frazer, PA

A 12-week, Randomized, Double-Blind,
Placebo-Controlled, R-Withdrawal Study to
Evaluate the Efficacy & Safety of
Hydrocodone Bitartrate ER Tabs (CEP-33237)
at 30-90mg q12 hrs for Relief of Moderate to
Severe Pain in Patients with Chronic Low
Back Pain Who Require Opioid Treatment for
an Extended Period of Time
(C33237/3103)

Teva Pharmaceuticals /
CRO: RPS
Upper Darby, PA

A 6 months, Open-Label, Extension Study to
Evaluate the Safety of Hydrocodone Bitartrate
ER tabs (CEP-33237) at 15mg-90mg q12h for
Relief of Moderate to Severe Pain in Patients
with Chronic Low Back Pain Who Require
Opioid Treatment for an Extended Period of
Time
(C33237/3104)

NIDA
Rockville, MD

Achieving Cannabis Cessation-Evaluating
N-Acetylcysteine Treatment (ACCENT)
(CTN-0053)

Courtney Kelly, M.S.
UCLA
Los Angeles, CA

Effects of Naltrexone on Methamphetamine
Cue-Induced Brain Activity in
Methamphetamine Dependence

<u>PI / Sponsor</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
US WorldMeds, LLC Louisville, KY	A Phase 3, Randomized, Multicenter, Double-Blind, Placebo-Controlled, Efficacy, Safety, and Dose-Response Study of Lofexidine in the Treatment of Opioid Withdrawal (Days 1-7) Followed by Open-Label, Variable Dose Lofexidine Treatment (Days 8-14) (USWM-LX1-300)
Keith Heinzerling, M.D. UCLA Los Angeles, CA	Randomized Trial of Ibudilast for Methamphetamine Dependence
Lara Ray, Ph.D. UCLA Los Angeles, CA	Effects of Naltrexone on Alcohol-Dependent Asian Americans
Lara Ray, Ph.D. UCLA Los Angeles, CA	Effects of Ibudilast on Non-treatment Seeking Patients Who Meet Criteria for Alcohol Abuse or Dependence
Lara Ray, Ph.D. UCLA Los Angeles, CA	Effects of Ivermectin on Non-Treatment Seeking Patients Who Meet Criteria for Alcohol Abuse or Dependence
NIDA Rockville, MD	Accelerated Development of Addictive Pharmacotherapy (ADAPT) (CNS Protocol 0054)

Table 1 Cont.

PI / Sponsor

Title of Study / Clinical Drug
Trial Protocol

Teva Pharmaceuticals
Frazer, PA

A 12 week, Multicenter, Randomized,
Double-Blind, Placebo-Controlled, Parallel-
Group Study to Evaluate the Efficacy & Safety
of 1-week IM Injection of TV-1380
(150mg/wk or 300mg/wk) as a Treatment for
Facilitation of Abstinence in
Cocaine-Dependent Subjects
(TV1380-COA-20)

TABLE 2

RESEARCH STUDIES CLOSED IN 2013

Sponsor / PI

Title of Study / Clinical Drug
Trial Protocol

Valerie Gruber, Ph.D.
UCSF / SF General Hospital
San Francisco, CA

Investigation of Age Differences in
Analgesic, Cognitive, and subjective effects
of Oxycodone, Hydrocodone, and
Acetaminophen

Reese Jones, M.D.
Drug Dependence Research Ct.
UCSF
San Francisco, CA

Phase I Study of Interactions between Oral
Naltrexone and Bupripion and Intravenous
Methamphetamine in Mathamphetamine
Experienced Volunteers

Edith London, Ph.D.
UCLA
Los Angeles, CA

A Study to Assess the Cardiovascular,
Cognitive, and Subjective Effects of
Atomoxetine in Combination with
Intravenous Amphetamine

Richard Reznichak, M.D.
Harbor-UCLA Medical Center
Torrance, CA

Panel approved research

Acel Rx
Redwood City, CA

A Multicenter, Randomized, Double-Blind,
Placebo-Controlled Trial to Evaluate the
Efficacy and Safety of the Sufentanil
NanoTab® PCA System/15 mcg for the
Treatment of Post-Operative Pain in
Patients after Knee or Hip Replacement
Surgery
(IAP311)

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug
Trial Protocol

Alkermes, Inc.
Waltham, MA

A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate ALKS 5461 in Subjects with Major Depressive Disorder and Inadequate Responses to Antidepressant Therapy (ALKS5461-202)

Noven / CRO: PRA
Lenexa, KS

A Randomized, DB, PC, Cross-Over, Lab Classroom Study to Evaluate the Safety & Efficacy of d-Amphetamine Transdermal Drug Delivery System (d-ATS) Compared to Placebo in Children & Adolescents w ADHD (N25-006)

Noven Pharmaceuticals
New York, NY

An Investigational Study to Evaluate the Usability of Reformulated Methylphenidate Transdermal System in Children, Adolescents and Adults with ADHD and Caregivers (N17-030)

Purdue / CRO: PRA
Raleigh, NC

A Randomized, Double-Blind, Placebo-Controlled, Multicenter Trial with an Enriched Study Design to Assess the Efficacy & Safety of Oxycodone/Naloxone C-R Tabs (OXN) Compared to Placebo in Opioid-experienced Subjects with Moderate to Severe Pain due to Chronic Low Back Pain who Require A-T-C Opioid Therapy (ONU3701)

Sponsor / PI

Title of Study / Clinical Drug
Trial Protocol

Shire / CRO: INC Research
Cincinnati, OH

A Phase 3 Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, 25-week, DO Study to Eval the Efficacy, Safety, & Tolerability of SPD489 Low Dose Range 40 80 100mg & Hi Dose Range 120 140 160mg as Adj Treatment to Establish Mt Doses of Antipsychotic Medications on Neg Symptoms in Clinically Stable Adults with Persistant Predominant Neg Symptoms of Schizophrenia (SPD489-335)

Shire / CRO: INC Research
Cincinnati, OH

A Phase 3 LT, Open-Label, Multicenter, 52-week Flex-D Safety Study of SPD489 as Adj Treatment of Establish Maintenanant Dose of Antipsychotic Medications on Neg Symptoms in Clinically Stable Adults with Persistent Pred Neg Symptoms of Schizophrenia (SPD489-336)

Shire / CRO: INC Research
Cincinnati, OH

A Phase 3 Multicenter, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled 12-wk, Forc-D Tat Study to Evaluate the Efficacy, Safety, & Tolerability of SPD489 40 100 or 160mg as Adj Treatment to Establish Maintenanant Dose of Antipsychotic Medications on Neg Symptoms in Clinically Stable Adults with Persistent Pred Neg Symptoms of Schizophrenia (SPD489-338)

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug
Trial Protocol

Shire Pharmaceuticals
Wayne, PA

A Phase 3b, Double-blind, Randomized,
Active-controlled, Parallel-group Study to
Compare the Time to Response of
Lisdexamfetamine to Atomoxetine in
Children & Adolescents aged 6-17 with
ADHD who have had an Inadequate
Response to Methylphenidate Therapy
(SPD489-317)

APPENDIX A

CURRENTLY OPEN (*through December 31, 2013*)
SCHEDULE I AND SCHEDULE II
NON-HUMAN AND ACADEMIC HUMAN
RESEARCH STUDIES

<u>Principal Investigator</u>	<u>Title of Study</u>
Mark A. Agius, M.D. UC. Davis Davis, CA	Cannabis for Spasticity in MS: Placebo- Controlled Study
Philip E. Bickler, MD, PhD Dept of Anesthesia, UCSF San Francisco, CA	Detecting Apnea in Healthy Volunteers Receiving Opiate or Sedative Medications
John R. Cashman, Ph.D. Human BioMolecular Research Institute San Diego, CA	Molecular Evolution of Human Cocaine Catalysis
Kent S. Chu, Ph.D. YJ Bio-Products Cordova, CA	Immunochromatographic Test Device for THC and LSD
Laura Colin Biostride, Inc. Redwood City, CA	Panel Approved Research
Michael Fischbach UCSF San Francisco, CA	Engineering a human gut bacteria to produce dimethyltryptamine
Mark A. Geyer, Ph.D. Dept of Psychiatry, UCSD La Jolla, CA	Behavioral and Cytofluorimetric Studies of Psychoactive Drugs in Rats

Appendix A Cont.

Principal Investigator

Title of Study

Kanthi Hettiarachchi, Ph.D.
SRI International
Menlo Park, CA

Analysis of Controlled Substances

Thomas S. Kilduff, Ph.D.
SRI International
Menlo Park, CA

Neurobiological Studies of
Gammahydroxybutyrate (GHB)

George Koob, Ph.D.
The Scripps Research Institute
La Jolla, CA

Prescription Opioid Addiction: Neurobiological
Mechanisms

Adam Leventhal, Ph.D.
USC Keck School of Medicine
Alhambra, CA

Influence of Genes and Emotions on
medication Effects

Daniel Levin, Ph.D.
NORAC Pharma
Azusa, CA

Panel Approved Research

Daniel Levin, Ph.D.
NORAC Pharma
Azusa, CA

Panel Approved Research

Daniel Levin, Ph.D.
NORAC Pharma
Azusa, CA

Panel Approved Research

Marie Lin, Ph.D. R.Ph.
Lin-Zhi International, Inc.
Sunnyvale, CA

Lin-Zhi Immunoassay Development Study

<u>Principal Investigator</u>	<u>Title of Study</u>
Walter Ling, M.D. Integrated Substance Abuse Programs, UCLA Los Angeles, CA	Analgesic Response to Opioid Analgesics in Buprenorphine-Maintained Individuals.
Sean Mackey, MD, PhD Stanford University Palo Alto, CA	Neural and Immune Effects of Short-term Opioid Use in Chronic Pain Patients
Robert Malenka, M.D. School of Medicine Stanford University Palo Alto, CA	The Role of Oxytocin in the Pathogenesis of Avtism
Sean D. McAllister, Ph.D. CPMC Research Institute San Francisco, CA	Panel Approved Research Project
Ardis Moe, Ph.D. UCLA Center for AIDS Research Los Angeles, CA	Phase III, Placebo-Controlled, Double-Blind Crossover Study of Slow-Release Methylphenidate (Concerta™) for Treatment of HIV Dementia
Florian Rader, M.D. Cedars-Sinai Med Center Los Angeles, CA	Mechanisms and Modulation of Cocaine Effects on Blood Blow to the Heart
Richard Reznichek, M.D. Harbor-UCLA Los Angeles, CA	Panel approved research

Appendix A Cont.

Principal Investigator

Title of Study

Rajkumar J. Sevak, Ph.D.
UCLA
Los Angeles, CA

Human Methamphetamine
Self-Administration in a Progressive-Ratio
Paradigm

Rajkumar J. Sevak, Ph.D.
UCLA
Los Angeles, CA

Safety and Initial Efficacy of
Lisdexamfetamine for Modifying the
Behavioral Effects of Intravenous
Methamphetamine in Humans

Matthew L. Springer, Ph.D.
UCSF
San Francisco, CA

Assessment of Impairment of Vascular
Function in Rats by Environmental Exposure
to Marijuana Second Hand Smoke

Raymond Stevens, Ph.D.
The Scripps Research Institute
La Jolla, CA

Structure Determination of the Hallucinogens
LSD and Psilocin Bound to the Serotonin
Receptor 5-HT_{2B}

Paolo Sassone-Corsi, Ph.D.
Center for Epigenetics
UC Irvine
Irvine, CA

The Role of Liver CB1 Receptor in Regulation
of the Circadian Metabolism

Michael Taffe, Ph.D.
The Scripps Research Institute
La Jolla, CA

Behavioral Toxicities of amphetamine and
cathinone stimulant drugs

Michael Taffe, Ph.D.
The Scripps Research Institute
La Jolla, CA

Behavioral toxicities of amphetamine and
cathinone stimulant drugs

<u>Principal Investigator</u>	<u>Title of Study</u>
Michael Taffe, Ph.D. The Scripps Research Institute La Jolla, CA	Behavioral and Physiological Toxicities of Cannabinoids: Effects of Cannabidiol
Stephen Van Dien, Ph.D. Genomatica, Inc. San Diego, CA	Panel Approved Research Project
Ronald Victor, M.D. Cedars-Sinai Med Center Los Angeles, CA	Effects of Cocaine on Blood Flow to the Heart
Friedbert Weiss, Ph.D. The Scripps Research Institute La Jolla, CA	Ethanol Seeking and Relapse: Therapeutic Potential of Transdermal Cannabidiol"
Jennifer L. Whistler, Ph.D. Ernest Gallo Clinic & Research Ct. Emeryville, CA	Endocytosis and Opioid Receptors
Timothy Wigal, Ph.D. UC Irvine Irvine, CA	Brain Dopamine Function in Adults with Attention Deficit/Hyperactivity Disorder (ADHD)
Barth Wilsey, M.D. UC Davis Medical Center Sacramento, CA	The Effect of Vaporized Cannabis on Neuropathic Pain in Spinal Cord Injury
Roya Yumul, MD, PhD Cedars-Sinai Med Center Los Angeles, CA	Intraoperative ketamine and methadone for laminectomy: effect on recovery, postoperative pain, and opioid requirements

APPENDIX B

CURRENTLY OPEN (*through December 31, 2013*)
SCHEDULE II CLINICAL DRUG TRIAL STUDIES

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
AcelRx Redwood City, CA	A Multicenter, Randomized, Open-Label, Parrell-Group Trial to Compare the Efficacy & Safety of the Sufentanil Nano Tab PCA System 15 mcg to Intravenous Patient-Controlled Analgesia with Morphine for the Treatment of Post-Operative Pain (IAP309)
AcelRx Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab for the Management of Acute Pain Following Bunionectomy Alone or with Hammertoe Repair (SAP202)
AcelRx Redwood City, CA	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab PCA System/15 mcg for the Treatment of Post-Operative in Patients after Open Abdominal Surgery (IAP310)

Appendix B Cont.

Sponsor

Description or Title
of Clinical Drug Trial Protocol

AcelRx
Redwood City, CA

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of the Sufentanil NanoTab® PCA System/15 mcg for the Treatment of Post-Operative Pain in Patients after Knee or Hip Replacement Surgery (IAP311)

Alkermes, Inc.
Waltham, MA

A Phase 2, Randomized, Multicenter, Safety, Tolerability, and Dose-Ranging Study of Samidorphan, A Component of ALKS 383, in Adults with Schizophrenia Treated with Olanzapine (ALK3831-302)

Astra Zenica / CRO - Quintiles
Overland Park, KS

A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of NKTR-118 in Relieving Opioid-Induced Constipation (OIC) in Patients with Cancer-Related Pain (D3820C00006)

Astra Zenica / CRO - Quintiles
Overland Park, KS

A Randomized, Double-Blind, Placebo-Controlled 12-Week Extension Study to Assess the Safety and Tolerability of NKTR-118 in Patients with Non-Cancer-Related Pain and Opioid-Induced Constipation (OIC) (D3820C00007)

Appendix B Cont.

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
Astra Zenica / CRO - Quintiles Overland Park, KS	An Open-Label 52 week Study to Assess the Long-Term Safety of NKTR-118 in Opioid-Induced Constipation (OIC) in Patients with Non-Cancer-Related Pain (D3820C00008)
Astra Zenica / CRO - Quintiles Overland Park, KS	An Open-label, Parallel-group, Phase I Study to Compare the Pharmacokinetics of NKTR-118 Following a Single-Oral Dose in Subjects with Renal Impairment and Subjects with Normal Renal Function (D3820C00009)
CNS Therapeutics / CRO: Pacific-Link Consulting	A Controlled, Two-Arm Parallel Group, Randomized Withdrawal Study to Assess the Safety and Efficacy of Hydromorphone HCl Delivered by intrathecal Administration a Programmable Implantable Pump (HYD201US)
CNS Therapeutics / CRO: Pacific-Link Consulting	A Phase 3 Open-Label, Single-Arm Study To Assess The Safety of Hydromorphone HCl Delivered by Intrathecal Administration (HYD202US)
Forest Research Institute Jersey City, NJ	A Randomized, Double-Blind, Placebo- and Active-Controlled Study to Evaluate the Safety and Efficacy of GRT6005 in Patients with Moderate tot Severe Chronic Pain Due to Osteoarthritis of the Knee (GRT-MD-101)

Appendix B Cont.

Sponsor

Description or Title
of Clinical Drug Trial Protocol

GW Pharmaceuticals
Mill Valley, CA

Panel approved research

GW Pharmaceuticals
Mill Valley, CA

Panel approved research

GW Pharmaceuticals
Milly Valley, CA

Panel Approved Research Project

GW Pharmaceuticals
Mill Valley, CA

Panel Approved Research Project

INTRuST Clinical Consortium
La Jolla, CA

Randomized Controlled Trial of Galantamine,
Methylphenidate, and Placebo for the
Treatment of Cognitive Symptoms in Patients
with Mild Traumatic Brain Injury (mTBI)
and/or Posttraumatic Stress Disorder (PISD)
("Cognitive REmediation After Trauma
Exposure" Trial = CREATE Trial")

MAPS
Santa Cruz, CA

A Placebo-Controlled, Randomized, Blinded,
Dose Finding Phase 2 Pilot Safety Study of
MDMA-Assisted Therapy for Social Anxiety in
Autistic Adults
(MAA-1)

Sponsor

Description or Title
of Clinical Drug Trial Protocol

Mitsubishi / CRO-Quintiles
Overland Park, KS

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Fixed-Dose, Parallel-Group, Multicenter, Efficacy, and Safety Study of MT-9938 for Treatment of Uremic Pruritus in Subjects with End-Stage Renal Disease Receiving Hemodialysis (MT-9938-01)

Nektar
San Francisco, CA

A Phase 2, Enriched-Enrollment, Randomized-Withdrawal, DB, PC, MC Study to Assess the Efficacy, Tolerability, & Safety of NKTR-181 in Opioid-Naïve Subjects w Mod to Sev Chr Pain Due to Osteoarthritis of the Knee (12-181-04)

Pfizer Inc.
New York, NY

An Investigational Study to Evaluate the Usability of Reformulated Methylphenidate Transdermal System in Children, Adolescents and Adults with ADHD and Caregivers (B4531002)

Purdue / CRO-INC Research
Raleigh, NC

A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study with an Open-Label Run-in to Assess the Efficacy & Safety of Hydrocodone Bitartrate (HYD) Tablets 20 to 120 mg Once-day in Subjects with Moderate to Severe Chronic Low Back Pain (HYD3002)

Appendix B Cont.

Sponsor

Description or Title
of Clinical Drug Trial Protocol

Purdue / CRO-INC Research
Raleigh, NC

A Randomized, Double-blind, Placebo-controlled, Multicenter Trial with an Enriched Study Design to Assess the Efficacy and Safety of Oxycodone/Naloxone Controlled-release Tablets (OXN) Compared to Placebo in Opioid-experienced Subjects with Moderate to Severe Pain due to Chronic Low Back Pain who Require Around-the-clock Opioid Therapy (ONU3701)

Purdue / CRO-Quintiles
Overland Park, KS

A Randomized, Double-blind, Double-dummy, Placebo-controlled, Active-controlled, Parallel-group, Multicenter Trial of Oxycodone Naloxone Controlled-release Tablets (OXN) to Assess the Analgesic Efficacy (Compared to Placebo) and the Management of Opioid-induced Constipation (Compared to Oxycodone Controlled-release Tablets (OXY) in Opioid-experienced Subjects with Uncontrolled Moderate to Severe Chronic Low Back Pain and a History of Opioid-induced Constipation who Require Around-the-clock Opioid Therapy (ONU3704)

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
Purdue / CRO-Quintiles Overland Park, KS	A Randomized, Double-Blind, DD, Placebo-controlled, AC, Parallel-Group, Multicenter Trial of OXN to Assess the Analgesic Efficacy (Compare to Placebo) and the management of Opioid-induced Const (Compare to OXY) in Opioid-exp Sub with Cont Moderate to Severe Chronic Low Back Pain and a History of Opioid-induced Const with Req ATC Opioid Therapy (ONU3705)
Purdue / CRO-INC Research Raleigh, NC	An Open-label, Multicenter Study to Assess the Long-Term Safety of Hydrocodone Bitartrate (HYD) Tablets 20 to 120 mg Once-daily in Subjects with Moderate to Severe Chronic Non-malignant and Non-neuropathic Pain (HYD3003)
Purdue / CRO-PRA Charlottesville, VA	An Open-label, Extension Study to Assess the Long-Term Safety of Twice Daily Oxycodone Hydrochloride Controlled-release Tablets in Opioid Experienced Children Who Completed the OTR3001 Study (OTR3002)

Appendix B Cont.

Sponsor

Description or Title
of Clinical Drug Trial Protocol

QrxPharma / CRO-INC
Austin, TX

A Double-Blind, Randomized, Placebo, & Active-Controlled, Parallel-Group Study to Evaluate the Safety, Tolerability & Efficacy of Q8011 Compared to OxyContin & Placebo in Patients with Moderate to Severe Chronic Hip or Knew with Pain Due to Osteoarthritis (Q8011-201)

Shire / CRO - ICON
Brentwood, TN

Phase 3, Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled, Flexible Dose Titration, Efficacy and Safety Study of SPD489 in Combination with an Antidepressant in the Treatment of Adults with Major Depressive Disorder with Inadequate Response to Prospective Treatment with an Antidepressant (SPD489-323)

Shire Pharmaceuticals
Wayne, PA

A Phase 2, Multicenter, Double-blind, Parallel-group, Randomized, Placebo-controlled, Forced-dose Titration, Dose-ranging Efficacy and Safety Study of SPD489 in Combination with an Antidepressant in the Treatment of Adults with Major Depressive Disorder with Inadequate Response to Prospective Treatment with an Antidepressant (SPD 489-209)

Sponsor

Description or Title
of Clinical Drug Trial Protocol

Shire / CRO-Premier
Research Group
Alexander, NC

A Phase 3, Multicenter, Randomized,
Double-Blind, Parallel-Group,
Placebo-Controlled, Dose-Optimization Study
to Evaluate the Efficacy, Safety, and
Tolerability of SPD489 in Adults Aged 18-55
Years with Moderate to Severe Binge Eating
Disorder
(SPD489-344)

Shire / CRO-ICON
Brentwood, TN

Phase 3, Open-label, Multicenter, 12-month
Extension Safety and Tolerability Study of
SPD489 in Combination with an
Antidepressant in the Treatment of Adults
with Major Depressive Disorder with
Residual Symptoms or Inadequate Response
Following Treatment with an Antidepressant
(SPD489-329)

Shire / CRO-Premier
Research Group
Alexander, NC

A Phase 3, Multicenter, Randomized,
Double-Blind, Parallel-Group,
Placebo-Controlled, Dose-Optimization Study
to Evaluate the Efficacy, Safety, and
Tolerability of SPD489 in Adults Aged 18-55
Years with Moderate to Severe Binge Eating
Disorder
(SPD489-343)

Appendix B Cont.

Sponsor

Description or Title
of Clinical Drug Trial Protocol

Shire Pharmaceuticals
Wayne, PA

A Phase 3b, Double-Blind, Randomized, Active-Controlled, Parallel-Group Study to Compare the Time to Response of Lisdexamfetamine to Atomoxetine in Children and Adolescents Aged 6-17 with ADHD who have had an Inadequate Response to Methylphenidate Therapy (SPD489-317)

Sunovion / CRO: INC Research
Seattle, WA

A Randomized, Double-Blind, Parallel-Group, Multicenter Efficacy and Safety Study of SEP-225289 Versus Placebo in Adults with ADHD (SEP360-20)

Teva Pharmaceuticals
Frazer, PA

A 12-week, Randomized, Double-Blind, Placebo-Controlled, R-Withdrawal Study to Evaluate the Efficacy & Safety of Hydrocodone Bitartrate ER Tabs (CEP-33237) at 30-90mg q12 hrs for Relief of Moderate to Severe Pain in Patients with Chronic Low Back Pain Who Require Opioid Treatment for an Extended Period of Time (C33237/3103)

Teva Pharmaceuticals /
CRO: RPS
Upper Darby, PA

A 6 months, Open-Label, Extension Study to Evaluate the Safety of Hydrocodone Bitartrate ER tabs (CEP-33237) at 15mg-90mg q12h for Relief of Moderate to Severe Pain in Patients with Chronic Low Back Pain Who Require Opioid Treatment for an Extended Period of Time (C33237/3104)

APPENDIX C

CURRENTLY OPEN (*December 31, 2013*)
RESEARCH STUDIES
ON THE TREATMENT OF CONTROLLED SUBSTANCE ABUSE

<u>Investigator or Sponsor</u>	<u>Description or Title of Research Study</u>
Gantt P. Galloway, Pharm.D. APRL/CPMC Research Institute San Francisco, CA	A Dose Ranging Study of Modafinil for Methamphetamine Dependence
Liza Gorgon NIDA Bethesda, MD	Phase 2, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Trial of Nepicastat for Cocaine Dependence (CS#1031)
Walter Ling, M.D. UCLA ISAP Los Angeles, CA	Sustained-Release Methylphenidate for management of Methamphetamine Dependence
Edythe London, Ph.D. Semel Institute, UCLA Los Angeles, CA	Safety and Initial Efficacy of Buspirone for Methamphetamine Dependence
Steven Shoptaw, Ph.D. UCLA. Los Angeles, CA	Phase I Safety Interaction Trial of Ibudilast with Methamphetamine

Appendix C Cont.

Investigator or Sponsor

Description or Title
of Research Study

Steven Shoptaw, Ph.D.
UCLA.
Los Angeles, CA

Varenicline for Methamphetamine
Dependence

Douglas Winship
Catalyst
Coral Gables, FI

Vigabatrin for Treatment of Cocaine
Dependence: A Phase II Study Multi-Center
Drug Trial

APPENDIX D

SECTIONS CONCERNING THE RESEARCH ADVISORY PANEL FROM THE CALIFORNIA HEALTH AND SAFETY CODE

§ 11213. Persons who, under applicable federal laws or regulations, are lawfully entitled to use controlled substances for the purpose of research, instruction, or analysis, may lawfully obtain and use for such purposes such substances as are defined as controlled substances in this division, upon approval for use of such controlled substances in bona fide research, instruction, or analysis by the Research Advisory Panel established pursuant to § 11480 and § 11481.

Such research, instruction, or analysis shall be carried on only under the auspices of the head of a research project which has been approved by the Research Advisory Panel pursuant to § 11480 or § 11481. Complete records of receipts, stocks at hand, and use of these controlled substances shall be kept.

§ 11480. The Legislature finds that there is a need to encourage further research into the nature and effects of marijuana and hallucinogenic drugs and to coordinate research efforts on such subjects.

There is a Research Advisory Panel which consists of a representative of the State Department of Health Services, a representative of the California State Board of Pharmacy, a representative of the Attorney General, a representative of the University of California who shall be a pharmacologist, a physician, or a person holding a doctorate degree in the health sciences, a representative of a private university in this State who shall be a pharmacologist, a physician, or a person holding a doctorate degree in the health sciences, a representative of a statewide professional medical society in this state who shall be engaged in the private practice of medicine and shall be experienced in treating controlled substance dependency, a representative appointed by and serving at the pleasure of the Governor who shall have experience in drug abuse, cancer, or controlled substance research and who is either a registered nurse, licensed pursuant to Chapter 6 (commencing with § 2700) of Division 2 of the Business and Professions Code, or other health professional. The Governor shall annually designate the private university and the professional medical society represented on the Panel. Members of the Panel shall be appointed by the heads of the entities to be represented, and they shall serve at the pleasure of the appointing power.

The Panel shall annually select a chairman from among its members.

Appendix D Cont.

§ 11480. Cont.

The Panel may hold hearings on, and in other ways study, research projects concerning marijuana or hallucinogenic drugs in this state. Members of the Panel shall serve without compensation, but shall be reimbursed for any actual and necessary expenses incurred in connection with the performance of their duties.

The Panel may approve research projects, which have been registered by the Attorney General, into the nature and effects of marijuana or hallucinogenic drugs, and shall inform the Attorney General of the head of the approved research projects which are entitled to receive quantities of marijuana pursuant to § 11478.

The Panel may withdraw approval of a research project at any time, and when approval is withdrawn shall notify the head of the research project to return any quantities of marijuana to the Attorney General.

The Panel shall report annually to the Legislature and the Governor those research projects approved by the Panel, the nature of each research project, and, where available, the conclusions of the research project.

§ 11481. The Research Advisory Panel may hold hearings on, and in other ways study, research projects concerning the treatment of abuse of controlled substances.

The Panel may approve research projects, which have been registered by the Attorney General, concerning the treatment of abuse of controlled substances and shall inform the chief of such approval. The Panel may withdraw approval of a research project at any time and when approval is withdrawn shall so notify the chief.

The Panel shall, annually and in the manner determined by the Panel, report to the Legislature and the Governor those research projects approved by the Panel, the nature of each research project, and where available, the conclusions of the research project.

§ 11603. The Attorney General, with the approval of the Research Advisory Panel, may authorize persons engaged in research on the use and effects of controlled substances to withhold the names and other identifying characteristics of individuals who are the subjects of the research. Persons who obtain this authorization are not compelled in any civil, criminal, administrative, legislative, or other proceedings to identify the individuals who are the subjects of research for which the authorization was obtained.

§ 11604. The Attorney General, with the approval of the Research Advisory Panel, may authorize the possession and distribution of controlled substances by persons engaged in research. Persons who obtain this authorization are exempt from state prosecution for possession and distribution of controlled substances to the extent of the authorization.

§ 24172. Experimental subject's bill of rights; contents

As used in the chapter, "experimental subject's bill of rights," means a list of the rights of a subject in a medical experiment, written in a language in which the subject is fluent. Except as otherwise provided in § 24175, this list shall include, but not be limited to the subject's right to:

- (a) Be informed of the nature and purpose of the experiment.
- (b) Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
- (c) Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.
- (d) Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
- (e) Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
- (f) Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
- (g) Be given an opportunity to ask any questions concerning the experiment or the procedures involved.
- (h) Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

Appendix D Cont.

§ 24172. Cont.

- (i) Be given a copy of the signed and dated written consent form as provided for by § 24173 or § 24178.
- (j) Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

§ 24173. Informed consent

As used in this chapter, "informed consent" means the authorization given pursuant to § 24175 to have a medical experiment performed after each of the following conditions have been satisfied:

- (a) The subject or subject's conservator or guardian, or other representative, as specified in § 24175, is provided with a copy of the experimental subject's bill of rights, prior to consenting to participate in any medical experiment, containing all the information required by § 24172, and the copy is signed and dated by the subject or the subject's conservator or guardian, or other representative, as specified in § 24175.
- (b) A written consent form is signed and dated by the subject or the subject's conservator or guardian, or other representative, as specified in § 24175.
- (c) The subject or subject's conservator or guardian, or other representative, as specified in § 24175, is informed both verbally and within the written consent form, in nontechnical terms and in a language in which the subject or the subject's conservator or guardian, or other representative, as specified in § 24175, is fluent, of the following facts of the proposed medical experiment, which might influence the decision to undergo the experiment, including, but not limited to:
 - (1) An explanation of the procedures to be followed in the medical experiment and any drug or device to be utilized, including the purposes of the procedures, drugs, or devices. If a placebo is to be administered or dispensed to a portion of the subjects involved in a medical experiment, all subjects of the experiment shall be informed of that fact; however, they need not be informed as to whether they will actually be administered or dispensed a placebo.

§ 24173. Cont.

(2) A description of any attendant discomfort and risks to the subject reasonably to be expected.

(3) An explanation of any benefits to the subject reasonably to be expected, if applicable.

(4) A disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.

(5) An estimate of the expected recovery time of the subject after the experiment.

(6) An offer to answer any inquiries concerning the experiment or the procedures involved.

(7) An instruction to the subject that he or she is free to withdraw his or her prior consent to the medical experiment and discontinue participation in the medical experiment at any time, without prejudice to the subject.

(8) The name, institutional affiliation, if any, and address of the person or persons actually performing and primarily responsible for the conduct of the experiment.

(9) The name of the sponsor or funding source, if any, or manufacturer if the experiment involves a drug or device, and the organization, if any, under whose general aegis the experiment is being conducted.

(10) The name, address, and phone number of an impartial third party, not associated with the experiment, to whom the subject may address complaints about the experiment.

(11) The material financial stake or interest, if any, that the investigator or research institution has in the outcome of the medical experiment. For purposes of this section, "material" means ten thousand dollars (\$10,000) or more in securities or other assets valued at the date of disclosure, or in relevant cumulative salary or other income, regardless of when it is earned or expected to be earned.

Appendix D Cont.

§ 24173. Cont.

(d) The written consent form is signed and dated by any person other than the subject or the conservator or guardian, or other representative of the subject, as specified in § 24175, who can attest that the requirements for informed consent to the medical experiment have been satisfied.

(e) Consent is voluntary and freely given by the human subject or the conservator or guardian, or other representative, as specified by § 24175, without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence.