



**California State Board of Pharmacy**  
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BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY  
DEPARTMENT OF CONSUMER AFFAIRS  
GOVERNOR EDMUND G. BROWN JR.

## NOTICE OF MEETING and AGENDA Communication and Public Education Committee

**Date:** October 7, 2013  
**Time:** 12:30 - 3:00 p.m.

**Contact:** Laura Hendricks  
(916) 574-7918

**Place:** Department of Consumer Affairs  
First Floor Hearing Room  
1625 N. Market Boulevard  
Sacramento, CA 95834

This committee meeting is open to the public and will be held in a barrier-free facility in accordance with the Americans with Disabilities Act. Any person with a disability who requires a disability-related modification or accommodation in order to participate in the public meeting may make a request for such modification or accommodation by contacting Laura Hendricks at (916) 574-7918, by emailing [laura.hendricks@dca.ca.gov](mailto:laura.hendricks@dca.ca.gov) or by sending a written request to the board at the above address. Providing your request at least five working days before the meeting will help ensure availability of the requested accommodation.

Opportunities are provided for public comment on each agenda item. A quorum of the board may be present at committee meetings. Board members who are not on the committee may observe, but may not participate as a committee member or vote.

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*Note: Pharmacists and pharmacy technicians who attend the full committee meeting can be awarded two hours of continuing education, in accordance with the Board's CE policy. A maximum of four CE hours can be earned each year by attending the meetings of two different Board committees.*

### Call to Order

**12:30 p.m.**

1. Review and Discussion of the 42<sup>nd</sup> Annual Report of the Research Advisory Panel of California
2. Discussion and Action on Requests from California Pharmacies for Exemption from 16 California Code of Regulations Section 1707.6(e) to Use Their Own Notice of Interpreter Availability Posters
3. Update on the Status of the Updated Emergency Contraception Fact Sheet, as Required by 16 California Code of Regulations Section 1746
4. Assessment of California's Patient-Centered Labeling Requirements as Required by 16 California Code of Regulations Section 1707.5(e)
5. Update on the Committee's Goals for 2012-2017 to Fulfill the Board's Strategic Plan
6. Update on *The Script*
7. Public Outreach Activities Conducted by the Board
8. Public Comment for Items Not on the Agenda\*

*\*(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.**

Meeting materials will be available from the board's website by October 3, 2013.



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BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY

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GOVERNOR EDMUND G. BROWN JR.

**Date: October 7, 2013**

**To: Communication and Public Education Committee**

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**I. Review and Discussion of the 42<sup>nd</sup> Annual Report of the Research Advisory Panel of California**

**Attachment 1**

The California Health and Safety Code establishes the Research Advisory Panel of California to oversee research involving use of controlled substances. Section 11213 provides that:

Persons who, under applicable federal laws or regulations, are lawfully entitled to use controlled substances for the purposes 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 Sections 11480 and 11481.

Patrick R. Finley, Pharm.D., is the board's appointment to the seven member advisory panel. A copy of the 42<sup>nd</sup> Annual Report of the Research Advisory Panel of California (July, 2012) is provided in Attachment 1 providing a summary of the panel's approved studies and 2012 activities.

**II. Discussion and Action on Requests from California Pharmacies for Exemption from 16 California Code of Regulations Section 1707.6(e) to Use Their Own Notice of Interpreter Availability Posters**

**Attachment 2**

Board regulation requires pharmacies to prominently post the "Notice to Consumers" required by 16 CCR Section 1707.6. In addition, Section 1707.6(c) requires every pharmacy to post or provide a "point to your language" notice so that consumers are aware that interpreter services will be provided to them at no cost. That subdivision specifies that the pharmacy shall use the standardized notice provided by the Board unless the pharmacy has received prior approval of another format or display methodology. The board has delegated to the Communication and Public Education Committee the authority to act on all requests to use another format or display methodology of these posters<sup>1</sup>.

Board regulation requires that the phrase "point to your language" appear in twelve specific languages: Arabic, Armenian, Cambodian, Cantonese, Farsi, Hmong, Korean, Mandarin, Russian, Spanish, Tagalog and Vietnamese. The poster shall be a minimum 8 ½" x 11" and is required to be kept within easy reach of each counter in the pharmacy where drugs are dispensed or furnished, and positioned so that a consumer can easily point to and touch the statement identifying the language in which he or she requests assistance.

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<sup>1</sup> Authorized by the Board at the February 2013 Board Meeting.

At this meeting, the committee will consider requests to use another format or display methodology of the “point to your language” poster. A copy of each request is provided in Attachment 2. To aid the board in reviewing future requests for approval, staff developed a Request for Waiver form for the purpose of gathering relevant information for the committee to consider with a request for using another format or display methodology. A copy of this request form is also provided in Attachment 2.

### **Request #1: Costco Wholesale**

The committee considered a request from Costco Wholesale (Costco) at its July 2013 meeting, and the committee determined additional information was required to consider the request. Attachment 2 contains Costco’s letter requesting approval of an alternative “point to your language” poster, a picture depicting how this poster would be displayed at each of Costco’s pharmacy counters, and a copy of the proposed “point to your language” poster.

**Alternative Poster:** Costco states their poster would be printed in color on 8 1/2 “ x 11” paper.

**Location of Poster:** Costco indicates each pharmacy will place the poster in a document easel in an area clearly visible and within reach of the consumer at both the prescription drop-off counter and the patient counseling counter. Costco asserts each pharmacy has sufficient counter space for the poster/easel (see photo sample of placement).

**Languages:** Costco’s “point to your language” poster contains the twelve language specified in the board’s regulation, as well as eight additional languages: Thai, Italian, Hindi, German, French, Portuguese, Polish and Japanese.

**Number of Locations:** As of September 30, 2013, the board issued 119 pharmacy permits to Costco pharmacies in California, and 2 permits to out-of-state Costco pharmacies.

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### **Request #2: Walmart Stores, Inc. (for Walmart and Sam’s Club pharmacies)**

The committee first considered a request from Walmart Stores, Inc. at the July 2013 committee meeting. Additional information is provided today for the committee’s consideration. A copy of Walmart’s letter requesting the board’s approval for Walmart and Sam’s Club Pharmacies as well as copies of the posters (one with a header for Walmart, and an identical poster with a header for Sam’s Club) are provided in Attachment 2.

**Scope:** Walmart Stores, Inc. is requesting approval of the alternative format of the “point to your language” notice for all Walmart and Sam’s Club pharmacies currently licensed by the board, as well as for those that may be licensed by the board in the future.

**Alternative Poster:** The notices will be printed in color on 8 1/2 “ x 11” paper (samples provided).

**Location of Poster:** The notices will be placed at both the prescription drop-off and prescription pick-up counters, within reach of the consumer at all Walmart and all Sam’s Club community pharmacies.

**Languages:** Walmart’s “point to your language” poster contains the twelve languages specified in Board regulation, as well as the four additional languages: Portuguese, Polish, French (Canadian), German and Italian. In addition, Walmart’s notice also includes both “simplified” and “traditional” Cantonese and Mandarin. Walmart Stores Inc. utilizes a “point to your language” poster at all Walmart and Sam’s Club pharmacies nationwide. Following the adoption of California’s rule, two additional languages were added to their existing posters (which already contained ten of California’s twelve languages). The languages specified on the notices reflect Walmart’s nationwide demographic data.

**Number of Locations:** As of September 30, 2013, the board issued the following permits to Wal-Mart and Sam’s Club pharmacies:

Wal-Mart: 244 pharmacies in California, 1 out-of-state pharmacy  
Sam’s Club: 30 pharmacies in California, no out-of-state pharmacies

**III. Update on the Status of the Updated Emergency Contraception Fact Sheet, as Required by 16 California Code of Regulations Section 1746**

**Attachment 3**

The board is in the process of receiving bids to have the Emergency Contraception Fact Sheet translated into six languages: Chinese, Korean, Russian, Spanish, Tagalog and Vietnamese. These are the same six languages in which the board makes available its “Notice to Consumers” posters (upon request, or download). When available, the Fact Sheets will be available upon request, and will also be available for download from the board’s web site.

#### IV. Assessment of California's Patient-Centered Labeling Requirements as Required by 16 California Code of Regulations Section 1707.5(e)

Attachments 4 - 9

Title 16 CCR Section 1707.5 specifies requirements for patient-centered labels for prescription drug containers. When the board promulgated these requirements, it 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.

##### **Background:**

Business and Professions Code Section 4076.5 required the board to consider the following factors when developing requirements for the patient-centered prescription label requirements:

- Medical literacy research that points to increased understandability of labels.
- Improved directions for use
- Improved font types and sizes
- Placement of information that is patient-centered
- The needs of patients with limited English proficiency
- The needs of senior citizens
- Technology requirements necessary to implement the standards.

The patient-centered label requirements went into effect on January 1, 2011, and since that time the board has worked to secure compliance by educating licensees, conducting surveys, distributing notices, and reviewing pharmacies' compliance with requirements. Major milestones:

1. Finalized regulations to update the "Notice to Consumers" poster.
2. Finalized a new "Notice to Consumers" poster and video format of the poster to explain to the public essential information about pharmacy services and taking medications and distribute these to California pharmacies.
3. Finalized regulations to require "Point to Your Language" consumer notices in pharmacies; finalized the notice itself, and distributed it to California pharmacies.
4. Conducted onsite surveys of pharmacies for compliance with label requirements.

In April 2013, this committee initiated the review of the patient-centered prescription label requirements. At this meeting, the committee will continue this discussion, and develop recommendations for the board's consideration on possible modifications to the regulation.

##### **a. United States Pharmacopeia Guidelines for Prescription Drug Labels**

In November 2012, the U.S. Pharmacopeial Convention (USP) published guidelines for prescription container labeling (**Attachment 4**). The guidelines provide a universal approach to the format, appearance, content and language of instructions for medicines in containers dispensed by pharmacies. Review of the material in USP's guidelines would be one source of information useful for comparison of the board's regulations with guidelines for premium presentation and focus on patient needs. It is important to note that USP's guidelines already

closely resemble the board's existing regulation requirements for patient-centered prescription container labels, specifically:

- Organize the prescription label in a patient-centered way. Feature the information patients most often seek out or need to understand about taking the medication safely.
  - Emphasize: directions
  - At the top of the label place: patient's name
  - Drug name (spell out full brand AND generic name)
  - Strength
  - Explicit and clear directions for use in simple language
- Prescription directions should follow a standard format so the patient can expect where to find information.
- Less critical information can be placed elsewhere and in a matter where it will not "supersede" critical patient information, and away from where it can be confused with dosing instructions
- Use language that is clear, simplified, concise and familiar, and in a standardized manner. Use common terms and full sentences. Do not use unfamiliar words, Latin terms or medical jargon
- Use simplified, standardized sentences that have been developed to ensure ease understanding the directions (by seeking comment from diverse consumers)
- Separate dose from the timing of each dose to clearly explain how many pills to take and specify if there is an appropriate time to take them (morning, noon, evening, bedtime).
- Do not use alphabetic characters for numbers (not in CA's) e.g., "nine" instead of "9".
- Use standardized directions whenever possible.
- Avoid ambiguous terms such as "take as directed" (not in CA's) unless clear and unambiguous supplemental instructions and counseling are provided
- Include purpose on the label unless patient does not want it, and if used, use "purpose for use" language such as for blood pressure rather than hypertension.
- Limit auxiliary information, and only if evidence based. (not in CA's)
- Use icons only if vetted with the general public (not in CA's)
- Address limited English proficiency.
- Labels should be designed so they are easy to read. Optimize typography by using:
  - High contrast print (black print on white background)
  - Large font sizes in simple, uncondensed fonts in at least 11 point if Arial, or 12 point if Times New Roman)
  - Optimize use of white space between lines (25-30 percent of font size)
  - Horizontal placement of lettering only
  - Sentence case
  - Highlighting, bolding and other typographical cues should enhance patient-centered information, but limit the number of colors used for highlighting
- Address visual impairment (not in CA's)

Regarding addressing limited English speaking/reading patients, USP encourages directions for use in the patient's language as well as in English. Translations should be developed using high quality translation processes (CA's translated directions would fit this criterion).

## **b. Medical Literacy Research**

The National Council for Prescription Drug Programs developed the “Universal Medication Schedule White Paper” (draft April 2013, **Attachment 5**). This document supports the standardized directions in the board’s regulation at 16 CCR Section 1707.5. The goal of the universal medication schedule is to increase patient understanding and adherence to medication instructions by standardizing the phrasing of directions, thereby improving health outcomes.

The hope is to secure the use of directions for use in a Universal Medication Schedule into e-prescribing systems. Staff will continue to identify additional medical literacy research for the committee’s consideration.

## **c. Surveys**

The board has conducted surveys to assess California’s patient-centered label requirements. Survey results are provided in **Attachment 6**.

### **1. Survey of Patient-Centered Labels in Use in California Pharmacies**

The first survey was conducted in 2012 and was used to measure pharmacies’ compliance with the patient-centered label requirements. It included components related to the 10- and 12-point fonts used on labels and how pharmacies have been complying with the interpreter requirements. Over the course of approximately seven months, board inspectors collected prescription labels used in California 767 pharmacies to determine compliance with the patient-centered label requirements. In general, nearly 70 percent of the labels in use as found by the board’s inspectors are printed in 12-point font; 15 percent use both 10 and 12 point font on the labels; and about 15 percent are printed in 10 point.

### **2. Survey of Pharmacies’ Compliance with Interpreter Availability**

During the inspections described in the above survey, the board’s inspectors also inquired how pharmacies are complying with the requirements for the availability of interpreters to provide services to limited English speaking patients.

### **3. Consumer Satisfaction with Prescription Labels**

The board conducted a survey in 2012 to determine if consumers were satisfied with their prescription labels and how they could be improved. Several consumer groups including AARP, Consumers Union, and California Pan Ethnic Health Network (CPEHN) distributed the survey electronically. The survey was also translated into Chinese and Spanish by the board and distributed by CPEHN to the appropriate audiences. Further, surveys were distributed and collected in person at local Senior Scam Stopper seminars (public protection fairs) sponsored by the Contractors State License Board. The board received a total of 1204 completed surveys.

#### 4. Survey of Pharmacies that Translate Labels

The board is currently surveying pharmacies to determine if they are providing consumers with translated labels, and if they are using the translation 'directions for use' that are on the board's website. A copy of the survey questions are provided in **Attachment 7**.

#### **d. Language Assistance and Translations of Directions for Use**

##### Notice to Consumers Poster

Following the implementation of the patient-centered prescription label requirements, the board promulgated a regulation to amend its Notice to Consumers poster. Following approval of the regulation, the new Notice to Consumers poster was designed, printed and subsequently distributed to all board licensed pharmacies in late May 2013.

This poster has also been printed in six additional languages: Chinese, Korean, Russian, Spanish, Tagalog, and Vietnamese – which are available upon request from the board. These translated posters are also available for download from the board's website.

Pharmacies may also request board approval of another format or display methodology.

##### Interpreter Availability Poster ("Point to Your Language")

As part of the patient-centered prescription label requirements, the board developed a "Point to Your Language" poster, which is required to be posted in pharmacies at or adjacent to the pharmacy counter so that consumers can point to a language to receive interpreter services. The board's regulation requires that the "point to your language" text be printed in 12 languages: Arabic, Cambodian, Farsi, Korean, Russian, Tagalog, Armenian, Cantonese, Hmong, Mandarin, Spanish and Vietnamese.

Pharmacies may request approval of another format or display methodology from the board.

##### Translated Directions for Use

The California Endowment, in an effort to support quality labels for those who do not read English, funded a project with national patient literacy researchers to develop and vet translations of the standardized directions for use that are posted on the board's website for use where appropriate on patient-centered prescription labels. These translations are in: Chinese, Korean, Russian, Spanish and Vietnamese.

#### **e. At This Meeting – Recommendations for Improving Requirements for California's patient-centered labels**

In reviewing the patient-centered prescription label requirements, discussion should be focused on the components in Senate Bill 472 (Corbett), the enabling legislation (Business and Professions Code Section 4076.5):

- Medical literacy research that points to increased understandability of labels.
- Improved directions for use
- Improved font types and sizes
- Placement of information that is patient-centered
- The needs of patients with limited English proficiency
- The needs of senior citizens
- Technology requirements necessary to implement the standards.

***For Discussion:***

**1. Placement of information that is “patient-centered” (i.e., patient name, name/strength of the drug, directions for use, and condition or purpose [if indicated]).**

**(a) Do we have the right patient-centered elements? Do we need to modify what is considered “patient centered”?**

***Possible considerations:***

**(i) Patient Name**

**(ii) Name and Strength of the Drug:** *Currently the regulation provides that “name of the drug and strength of the drug” must be on the label in the patient-centered area. The regulation goes on to specify that “name of the drug” means either the manufacturer’s trade name of the drug or the generic name and the name of the manufacturer. At one point, the board considered whether to include manufacturer in the patient-centered area of the label.*

***Should the board move manufacturer to another part of the label?***

- O USP suggests that: Drug name be spelled out fully (brand AND generic name) – no abbreviations.*
- O NABP (Attachment 8) suggests that if a prescription is written for a brand name and a generic drug is dispensed then “generic for [brand name]” appear on the label.*
- O NABP suggests inclusion of suffixes (CD, SR, XL, XR, etc.)*

**(iii) Directions for use of the drug**

*There is support in NABP, USP, and in the NCPDP White Paper to emphasizing use of the standardized directions for use. These directions are listed in the regulation, but are noted as “When applicable, directions for use shall use one of the following phrases:”.*

*Work may need to be done with the Medical Board and other prescribing boards to secure the wider use of standardized phrases. New research by Mike Wolf points to substantial improvement in patient comprehension of using such standardized directions (Attachment 9)*

**(iv) Purpose on the label:** Currently the board's regulation provides as one of the patient-centered elements: "The condition or purpose for which the drug is prescribed if the condition or purpose is indicated on the prescription."

Mandating purpose on the label is a consideration the board deferred until this reevaluation of the regulation. The board has long-standing policy in supporting inclusion of purpose on the label as a key patient safety element. Knowing why a medication is being taken aids patient understanding about drug therapy, provides important information to patient caregivers, and can prevent medication errors when a pharmacy is dispensing.

**2. Font-size requirements. Is 10, 12 or another font / typeface appropriate?**

**Much of the discussion in promulgating the regulation initially centered on whether the patient-centered elements should be printed in 10 point or 12 point. As a compromise, the regulation requires that each element in the patient-centered area shall be printed in at least a 10-point sans serif typeface or, if requested by the consumer, at least a 12-point typeface.**

**Should the board alter this requirement?**

**(i) USP provides that:**

Labels should be designed so they are easy to read. Optimize typography by using:

- High contrast print (black print on white background)
- Large font sizes in simple, uncondensed fonts in at least 11 point if Arial, or 12 point if Times New Roman)
- Optimize use of white space between lines (25-30 percent of font size)
- Horizontal placement of lettering only
- Sentence case
- Highlighting, bolding and other typographical cues should enhance patient-centered information, but limit the number of colors used for highlighting

**(ii) NABP provides that:**

- Label with emphasis (highlighted or bolded) in a sans serif (such as "arial"), minimum 12-point font and in "sentence case." Field size and font size may be increased in the best interest of patient care. Critical information text should never be truncated.

**(iii) Results of board inspections of over 750 pharmacies indicate that about 70 percent of the pharmacies inspected were printing directly into 12 point font, 15 percent were printing with a combination of 10 and 12 point fonts, and 15 percent starting with 10 point.**

**(iv) Senior groups and other consumer advocates strongly seek the minimum font size of 12 point. Currently on the Governor's desk is a proposal to require 12-point font on all labels for the patient-centered elements. This proposal, if signed, would take effect in 2016.**

**3. Use of bold text, highlighting, color and/or white space to add emphasis or set off the patient-centered items.**

*California's label requirements seem to meet the existing standards for use of type font enhancers such as bolding, highlighting and white space. Staff are unable to suggest additional changes here.*

**4. Standardized directions for use.**

*Standardized directions for use is described above under patient-centered elements. If this to be implement, more work and education needs to be done to promote and achieve wider use of these directions by pharmacies. Perhaps collaboration with prescribers will assist in this area.*

**5. Translated directions for use are available on the board's website. Should the board require use of them to aid patients with limited or no English proficiency understand the information on the prescription label?**

*The regulation requires that an oral interpreter be available to assist limited-English speaking patients. Is this sufficient?*

- (i) Should the board support translations of labels?
- (ii) Should translations be only of directions for use or the whole patient-centered portion of the label?
- (iii) Should the board support translations of labels only if there is wider use of standardized directions for use?
- (iv) Should the board support translations of labels if there is also a requirement for an English version of the directions on the label as well. Should the English translation appear in the patient-centered dedicated area, or somewhere else on the label?
- (v) Should the board support translations of labels only if there is a liability exemption for pharmacies?
- (vi) Currently labels on all medication provided to patients in California have to be in the board's patient-centered format. Should all practitioners who dispense medication to patients be required to translate the labels if pharmacies are so required?

**6. Should the board consider technology standards to enhance the patient-centered requirement?**

*Are there impediments to improving prescription container labels?*

**Additional Questions for Discussion:**

- 1. Should the board amend the regulation to require Purpose on the label?
- 2. Should the board amend the regulation to prohibit anything other than the patient-centered elements in the dedicated space? For example, currently some labels print a patient's address in the patient-centered label directly below the patient's name, but in a smaller font than 10 or 12 point. Should this be specifically prohibited?

**3. Should the board emphasize the description of the medication on the label as another patient-centered element? Should the board require at some point in the future that a picture of any pill appear on the label as an alternative to a verbal description?**

Title 16, California Code of Regulations Section 1746 authorizes pharmacists to provide emergency contraception without a prescription to patients of any age. Pursuant to a protocol developed by the Medical Board of California, a fact sheet was to be developed and made available to patients at the time of the pharmacist consultation.

In accordance with Business and Professions Code Section 4052.3(e), the Board developed the standardized fact sheet that a pharmacist is required to provide a patient when dispensing emergency contraception.

The board is in the process of acquiring bids to have this Fact Sheet translated into the following languages: Chinese, Korean, Russian, Spanish, Tagalog and Vietnamese. These six languages mirror those for which the "Notice to Consumers" poster is translated. The translations of the EC Fact Sheet will be available on the board's web site for download and available upon request.

**V. Update on the Committee's Goals for 2012-2017 to Fulfill the Board's Strategic Plan**

Staff will bring to the committee meeting information related to setting Committee goals for the Board's Strategic Plan.

**VI. Update on *The Script***

The next issue of *The Script* is being finalized and should be available on the board's website in October. *The Script* includes information regarding disciplinary actions taken by the Board, answers questions to frequently asked questions, and contains an article about the Joint Forum to Promote Appropriate Prescribing and Dispensing held earlier this year in South San Francisco.

**VII. Public Outreach Activities Conducted by the Board**

Staff will bring to the committee meeting information related to public outreach activities conducted during the months of July, August, and September.

**VIII. Public Comment for Items Not on the Agenda**

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).

# Attachment 1

**FORTY-SECOND ANNUAL REPORT**

**of the**

**RESEARCH ADVISORY PANEL  
OF CALIFORNIA**

**2012**



**PREPARED FOR THE**

**LEGISLATURE AND GOVERNOR**

**RESEARCH ADVISORY PANEL OF CALIFORNIA**

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## MEMBERS

### RESEARCH ADVISORY PANEL OF CALIFORNIA

Edward P. O'Brien, J.D.  
Panel Chairman  
Appointed by Attorney General

Y. Jennifer Ahn, Pharm.D.  
Executive Officer

Patrick R. Finley, Pharm.D.  
Appointed by the State Board of Pharmacy

Andrew S. Kayser, MD, PhD  
Appointed by the University of California at San Francisco  
Designated University of California

John E. Mendelson, M.D.  
Appointed by the California Medical Association  
Designated professional medical society

Michele T. Pato, M.D.  
Appointed by the University of Southern California  
Designated private university

Laurence R. Upjohn, Pharm.D.  
Appointed by the Department of Public Health

**RAPC Website : [www.ag.ca.gov/research](http://www.ag.ca.gov/research)**

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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 2012 PANEL ACTIVITIES

During 2012 the Panel reviewed twenty-five research study submissions. Twenty-four were approved by the Panel. Among approved studies, four studies were Academic research studies, two studies were Substance Abuse Treatment research protocols, and eighteen studies were Clinical Drug Trial research protocols.

Forty-three research studies were completed in 2012, and they were closed on the Panel's records.

At the end of 2012, the Panel was monitoring one hundred-twenty 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 2012 and Table 2 is a list of the studies closed by the Panel in 2012.



TABLE 1

RESEARCH STUDIES  
APPROVED IN 2012

<u>PI / Sponsor</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
Jack Berger, M.D. LAC + USC Medical Center Los Angeles, CA	Prospective, Double-Blinded, and Randomized Control Trial of Multimodal Pain Relief with Intravenous Magnesium, Lidocaine and Ketorolac in Patients with Opiate Refractory, Post-Operative Pain
Philip E. Bickler, MD, PhD Dept of Anesthesia, UCSF San Francisco	Detecting Apnea in Healthy Volunteers Receiving Opiate or Sedative Medications
Raymond Stevens, Ph.D. The Scripps Research Institute La Jolla, CA	Structure Determination of the Hallucinogens LSD and Psylocin Bound to the Serotonin Receptor 5-HT2B
Michael A. Taffe, Ph.D. The Scripps Research Institute La Jolla, CA	Behavioral and Physiological Toxicities of Cannabinoids: Effects of Cannabidiol
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 (ALK5461-202)

Collegium / CRO-INC Research  
Raleigh, NC

A Phase 3, Multi-Center, Randomized,  
Double-Blind, Placebo-Controlled, Safety,  
Tolerability, and Efficacy Study of Oxycodone  
DETERx™ Versus Placebo in  
Opioid-Experienced and Opioid-Naive  
Subjects with Moderate-to-Severe Chronic  
Low Back Pain  
(CO-OXYDET-08)

GW Pharmaceuticals  
Mill Valley, CA

Panel Approved Resesarch

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)

NextWave Pharmaceuticals  
Chapel Hill, NC

A Multicenter, Dose-Optimized,  
Double-Blind, Randomized,  
Placebo-Controlled Study to Evaluate the  
Efficacy of NWP09 in Pediatric Patients with  
Attention Deficit Hyperactivity Disorder  
(ADHD) in a Laboratory Classroom  
(NWP09-ADHD-300)

Table 1 Cont.

<u>PI / Sponsor</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
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)
Pfizer, Inc. New York, NY	A MC, 12-week, DB, PC, Rand. Withdrawal Study to Determine The Efficacy & Safety of ALO-02 (Oxycodone HCl & Naltrexone HCl) ER Caps in Subjects w Mod to Sev Chr. Low Back Pain (B4531002)
QRxPharma / CRO-INC Research Austin, TX	A DB, Rand, P, & AC, PG Study to Evaluate the Safety, Tolerability & Efficacy of Q8011 Compd to OxyContin & Placebo in Pts w Mod to Sev Chr. Hip or Kneww Pain Due to Osteoarthritis (Q8011-201)
Roxane / CRO-Quintiles Durham, NC	A Multicenter, Open-Label, Safety & PK Study of Oral Codeine Sulfate Adm of Pediatric Subjects 2 yrs old thru 17 yrs old w Post-Procedural Pain (Code-OS+T-(2-17)-SPK-1)

Shire / CRO-Premier  
Research Group  
Bluff City, TN

A Phase 3, Multicenter, Open-Label,  
12-Month Extension Safety and Tolerability  
Study of SPD489 in the Treatment of Adults  
with Binge Eating Disorder  
(SPD489-345)

Shire / CRO-Premier  
Research Group  
Philadelphia, PA

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 Pharmaceuticals  
New York, NY

A Phase I, Rand, DB, PC Study to Evaluate  
the Safety, Tolerability, & PK of Single &  
Multiple-Doses of SPD489 in Japanese &  
Caucasian Healthy Adult Subjects  
(SPD489-121)

Shire / CRO-Premier  
Research Group  
Alexander, NC

A Phase 4, Rando, DB, MC, PG, AC,  
Forced-dose Titration, Safety & Efficacy  
Study of SPD489 (Vyvanse) Compared w  
OROS-MPH (Concerta) w a Placebo  
Reference Arm, in Adolescents Aged 13-17  
Years w ADHD  
(SPD489-406)

Shire / CRO-Premier  
Research Group  
Alexander, NC

A Phase 4, Rando, DB, MC, PG, AC,  
Dose-optimization Safety & Efficacy Study of  
SPD489 (Vyvanse) Compared w OROS-MPH  
(concerta) w a Placebo Reference Arm, in  
Adolescents Aged 13-17 Years w ADHD  
(SPD489-405)

Table 1 Cont.

<u>PI / Sponsor</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
Shire / CRO-Premier Research Group Philadelphia, PA	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)
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 Attention Deficit Hyperactivity Disorder (ADHD) (SEP360-201)
Liza Gorgon NIDA Bethesda, MD	Phase 2, Double-Blind, Placebo-Controlled, Parallel-Group, Multi-Center Trial of Nepicastat for Cocaine Dependence (CS# 1031)
Edythe London, Ph.D. Semel Institute, UCLA Los Angeles, CA	Safety and Initial Efficacy of Buspirone for Methamphetamine Dependence



**TABLE 2**

**RESEARCH STUDIES CLOSED IN 2012**

<u>Sponsor / PI</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
Hussein Al-Shamma, Ph.D. Arena Pharmaceuticals San Diego, CA	Evaluation of lorcaserin for abuse liability using the Drug Discrimination Test in the Rat
Danilyn Angeles, Ph.D. Loma Linda Univeristy Medical Ct. Loma Linda, CA	A Double-blind randomized Clinical Trial on the Use of Pre-emptive Morphine Infusion in Asphyxiated Term and Near-Term Infants
Mariusz Banaszczyk, Ph.D. Biosite Diagnostics San Marcos, CA	Development of In-vitro Immunoassays for the Detection of Abused Substances
Selena Barrett, Ph.D. Ernest Gallo Clinic & Research Ct. Emeryville, CA	The role of cannabinoids and ibogaine in the treatment of alcoholism and drug addiction
Marthias Behrends, M.D. Dept. of Anesthesia, UCSF San Francisco, CA	A Randomized, Parallel, Double-Blind Efficacy and Safety Study of Biphentin™ Methylphenidate Hydrochloride Extended Release Capsules Compared to Placebo in Children and Adolescents 6 to 18 years with Attention Deficit Hyperactivity Disorder

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug  
Trial Protocol

Jack Berger, Ph.D.  
LAC + USC Medical Center  
Los Angeles, CA

Prospective, Double-Blinded, and  
Randomized Control Trial of Multimodal  
Pain Relief with Intravenous Magnesium,  
Lidocaine and Ketorolac in Patients with  
Opiate Refractory, Post-Operative Pain

Nancy Buckley, Ph.D.  
Biological Sciences Dept  
CA State Polytechnic University

Effects of delta-9-tetrahydrocannabinol on  
Candida albicans infection

Peggy Compton, RN, Ph.D.  
UCLA School of Nursing  
Los Angeles, CA

Pain, Opioids, and Pro-inflammatory  
Immune Responses

Keith Flower, M.D.  
APRL/CPMC Research Institute  
San Francisco, CA

A Pilot Trial of Naltrexone for  
Methamphetamine Addiction - Role of the  
A118G SNP

Keith Heinzerling, MD, PhD  
UCLA Geffen School of Medicine  
Los Angeles, CA

Pilot Trial of Bupropion versus Placebo  
for Methamphetamine Abuse in  
Adolescents

Scott Irwin, MD, PhD  
San Diego Hospice and  
Institute for Palliative Medicine  
San Diego, CA

An Open label Trial of Oral Ketamine for  
the Rapid Treatment of Depression in  
Hospice Patients

<u>Sponsor / PI</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
Daniel Levin, Ph.D. Norac Pharma Azusa, CA	Evaluation of Cannabinoids derived from the Natural Product Marijuana
Walter Ling, M.D. UCLA Geffen School of Medicine Los Angeles, CA	Optimizing Outcomes Using Suboxone for Opiate Dependence
Edythe London, Ph.D. UCLA Geffen School of Medicine Los Angeles, CA	A Study to Assess the Cardiovascular, Cognitive, and Subjective Effects of Atomoxetine in Combination with Oral Methamphetamine
James McCracken, M.D. APRL/CPMC Research Institute San Francisco, CA	An 8-Wk, Rndmzd, Dbl-Blind Comparison of Twice-Daily Guanfacine, Once-Daily d-Methylphenidate ER (Focalin XR) and the Combination, with a 12 Month Open-Lbl Extension for the Treatment of ADHD in Pediatric Subjects Aged 7 to 14 years
John E. Mendelson, M.D. APRL/CPMC Research Institute San Francisco, CA	Bioavailability and Urinary Excretion of Oral L-Methamphetamine

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug  
Trial Protocol

John E. Mendelson, M.D.  
APRL/CPMC Research Institute  
San Francisco, CA

The Effects of MDMA on Sleep  
Architecture, Water Homeostasis, and  
Cognitive Function

Loren Parsons, Ph.D.  
The Scripps Research Institute  
La Jolla, CA

Cognitive and Neurochemical Effects of  
 $\Delta^9$ -tetrahydrocannabinol and related  
cannabinoids in rodents

Lara Ray, Ph.D.  
UCLA  
Los Angeles, CA

Genetics of Naltrexone in  
Methamphetamine Users

Rajesh Venugopal  
NIDA, The EMMES Corp.  
Rockville, MD

Cocaine Use Reduction with  
Buprenorphine (CURB)  
(CTN-0048)

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

Cocaine and Sympathetic Nerve Activity  
in Humans - "Cocaine and the Heart"

Mark Wallace, M.D.  
Center for Pain Medicine, UCSD  
La Jolla, CA

Efficacy of Inhaled Cannabis for the  
Treatment of Painful Diabetic Peripheral  
Neuropathy

<u>Sponsor / PI</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
<p>Barth Wilsey, M.D. UC Davis Medical Center Sacramento, CA</p>	<p>The Analgesic Effect of Vaporized Cannabis on Neuropathic Pain</p>
<p>Titan Pharmaceuticals, Inc. S. San Francisco, CA</p>	<p>A Randomized, Placebo and Active-Controlled, Multi-Center Study of Probuphine in Patients with Opioid Dependence (PRO-806)</p>
<p>Titan Pharmaceuticals, Inc. S. San Francisco, CA</p>	<p>A Phase 3, Six-Month, Open-Label Re-Treatment Study of Probuphine in Opioid Addiction (PRO-811)</p>
<p>Astra Zenica / CRO-Quintiles Overland Park, KS</p>	<p>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)</p>

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug  
Trial Protocol

BRC Operations  
Ultimo, NSW

International Study to Predict Optimized  
Treatment in Attention  
Deficit/Hyperactivity Disorder

Cephalon, Inc.  
Fort Washington, PA

A 12 wk, Rand, Dbl-Blind, P-C. Study to  
Eval. the Efficacy & Safety of  
Hydrocodone Bitartrate ER Tabs  
(CEP-33237) at 15-90mg q12 hrs for  
Relief of Mod to Sev Pain in Pts w/ OA or  
Low Back Pain Who Require Opioid Tx  
for an Ext. Period of Time  
(C33237/3079)

Cephalon, Inc.  
Fort Washington, PA

A 12-Month, Open-Label Study to  
Evaluate the Long-Term Safety of  
Hydrocodone Bitartrate Extended-Release  
Tablets (CEP-33237) at 15 to 90mg Every  
12 Hours in Patients Who Require Opioid  
Treatment for an Extended Period of Time  
(Cephalon C33237/3080)

GW Pharmaceuticals  
Mill Valley, CA

Panel Approved Research

<u>Sponsor / PI</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
Janssen / J&J Titusville, NJ	A Rand, DB, Parallel Arm, Clinical Trial to Compare the Clin Effectiveness of Tapentadol ER vs Oxycodone CR in Subjects w Mod to Sev Chronic Low Back Pain (R331333PAI4003)
Johnson & Johnson PRD Malvern, PA	Single-Dose, Open-Lbl. Ran. Two-Way Crossover Study to Assess the BE of Tapentadol Given as Two 50mg ER TRF Tabs Relative to One 100mg ER TRF Tab in Healthy Japanese Male Subjects (PAI 1063)
Johnson & Johnson PRD Titusville, NJ	A Randomized-Withdrawal, Placebo-Controlled, Study Evaluating the Efficacy, Safety, and Tolerability, of Tapentadol Extended-Release (ER) in Subjects with Chronic, Painful Diabetic Peripheral Neuropathy (DPN) (PAI 3027)
Johnson & Johnson PRD Malvern, PA	A Single-Dose, Open-Lbl, Ran. Two-Way Crossover Study to Assess the BE of Tapentadol Given as Two 25mg ER Tamper-Resistant Form (TRF) Tabs Relative to One 50mg ER TRF Tab in Healthy Japanese male Subjects (PAI 1062)

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug  
Trial Protocol

Johnson & Johnson PRD  
Malvern, PA

A Single-Dose, Open-Label, Rand. 4-Way  
Crossover Study to Assess the  
Dose-Proportionality of the PK of  
Tapentadol, Given as Tamper-Resistant  
Tabs, in Healthy Japanese & Korean Male  
Subjects  
(PAI 1064)

Mallinckrodt  
Hazelwood, MD

A Phase 3 MC, R, DB, PC, PG Evaluation  
of the Safety & Analgesia Efficacy of  
COV795 (Oxycodone HCl /  
Acetaminophen) ER Tablets in Mod to  
Sev Post-Operative Bunionectomy Pain  
Followed by an Open Label Extension  
(COV15000182US)

Mallinckrodt / CRO-INC Research  
Middleton, WI

An Open Label Safety Study of COV795  
in Subjects with Osteoarthritis or Chronic  
Low Back Pain  
(COV15000181US)

Mundipharma / CRO-Parex  
Woburn, MA

A Confirmatory, Placebo-Controlled,  
Rand, D-B, Single-Dummy, Parallel Gr,  
Ratio-Finding Study in Constipated Pain  
Pts to Establish an Optimal  
Hydromorphone-naloxone ratio w an  
Improved Bowel Funct & a Comp Analg  
Eff Comp to H-morphone alone  
(HMX3501)

<u>Sponsor / PI</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
NextWave Pharmaceuticals Chapel Hill, NC	A Multicenter, Dose-Optimized, Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy of NWP09 in Pediatric Patients with Attention Deficit Hyperactivity Disorder (ADHD) in a Laboratory Classroom (NWP09-ADHD-300)
Novartis Pharmaceuticals East Hanover, NJ	A 6-Month, Open-Label Extension to a 40-Week, Randomized, Double-Blind, Placebo-Controlled, Multicenter Efficacy and Safety Study of Ratain LA in the Treatment of Adult Patients with Childhood-Onset ADHD (CRIT124D2302E1)
Novartis Pharmaceuticals East Hanover, NJ	A 40-Week, Randomized, Double-Blind, Placebo controlled, Multicenter Efficacy and Safety Study of Ritalin® LA in the Treatment of Adult Patients with Childhood-Onset ADHD (CRIT124D2302)
Purdue / CRO-PRA International Lenexa, KS	An Open-label, MC Study of the Safety of Twice Daily Oxycodone HCl CR Tabs in Opioid Experienced Children from Ages 6 to 16 Years Old, Inclusive, w/ Mod to Sev Malignant and/or Nonmalignant Pain Requiring Opioid Analgesics (OTR3001)

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug  
Trial Protocol

Purdue / CRO-PRA International  
Lenexa, KS

An Open-label Study to Characterize the  
PK and Safety of Oxycodone HCl q12h  
CR (ORF) Tabs in Pediatric Pts Aged 6 to  
16 years inclusive, Who Require Opioid  
Analgesia  
(OTR 1020)

Rhodes / CRO-NuTec Inc.  
Boston, MA

A Random, Dbl-Blind Study of the Time  
Course of Response of Biphentin®  
Methylphenidate HCl ER Caps As  
Compared to Placebo in Children 6-12  
y.o. w/ ADHD in an Analog Classroom  
Setting  
(RP-BP-EF001)

Rhodes / CRO-NuTec Inc.  
Boston, MA

A Randomized, Parallel, Double-Blind  
Efficacy and Safety Study of Biphentin™  
Methylphenidate Hydrochloride Extended  
Release Capsules Compared to Placebo in  
Children and Adolescents 6 to 18 years  
with Attention Deficit Hyperactivity  
Disorder  
(RP-BP-EF002)

Roxane / CRO-Quintile  
Durham, NC

A Multicenter, Open-Label, Safety & PK  
Study of Oral Codeine Sulfate Adm of  
Pediatric Subjects 2 yrs old thru 17 yrs old  
w Post-Procedural Pain  
(Code-OS+T-(2-17)-SPK-1)

<u>Sponsor / PI</u>	<u>Title of Study / Clinical Drug Trial Protocol</u>
Roxane / CRO-Quintile Durham, NC	A MC, Open Label, Safety & PK Study of Oral Morphine Sulfate Admin. In Pediatric Subjects 2 yrs old thru 17 y.o. w/ Postoperative Pain (MORP-OS+T-(2-17)-SPK-1)
Shire Pharmaceuticals Wayne, PA	A Phase 1, R, DB, PC Study to Assess the Safety, Tolerability, PK, & PD of Ascending, Multiple Oral Doses of SPD489 in Clinically Stable Adults w Schizophrenia (SPD489-119)
Shire / CRO-Premium Research Bluff City, TN	A Phase 2 Multicenter, Randomized, Double-blind, Parallel-group, Placebo-controlled, Forced-dose Titration Study to Evaluate the Efficacy, Safe, and Tolerability of SPD489 in Adults Aged 18-55 Years with Binge Eating Disorder (SPD489-208)

Table 2 Cont.

Sponsor / PI

Title of Study / Clinical Drug  
Trial Protocol

Shire /Hampshire Intn'l  
Hampshire, UK

A Phase III, Db-Blind, Placebo-Cont.  
Randomized Withdrawal, M-C,  
Extension, Safety & Efficacy study of  
LDX in Children & Adoles. Aged 6-17 w/  
ADHD  
(SPD489-326)

Shire Pharmaceuticals  
New York, NY

A Phase I, Rand, DB, PC Study to  
Evaluate the Safety, Tolerability, & PK of  
Single & Multiple-Doses of SPD489 in  
Japanese & Caucasian Healthy Adult  
Subjects  
(SPD489-121)

Shire / CRO-INC Research  
Raleigh, NC

A Phase 2, MC, Rand, DB, PC,  
Parallel-gr. Study to Evaluate the  
Efficacy, Safety & Tolerability of SPD489  
in Adults w Clin. Signif. Persistent  
Executive Function Impairments (EFI) &  
Partial or Full Remission of Rec. Major  
Depressive Disorder  
(SPD489-205)

Zogenix Inc.  
Emeryville, CA

A Long-Term Open-Label Safety Study of  
Hydrocodone Bitartrate  
Controlled-Release Capsules with  
Flexible Dosing to Treat Subjects with  
Moderate to Severe Pain  
(Zx002-0802)

APPENDIX A

CURRENTLY OPEN (*through December 31, 2012*)  
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
Mark A. Geyer, Ph.D. Dept of Psychiatry, UCSD La Jolla, CA	Behavioral and Cytoflourimetric Studies of Psychoactive Drugs in Rats

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

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

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

Analysis of Controlled Substances

Reese Jones, M.D.  
UCSF  
San Francisco, CA

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

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

Neurobiological Studies of  
Gammahydroxybutyrate (GHB)

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

<u>Principal Investigator</u>	<u>Title of Study</u>
Marie Lin, Ph.D. R.Ph. Lin-Zhi International, Inc. Sunnyvale, CA	Lin-Zhi Immunoassay Development Study
Edythe London, Ph.D. UCLA Los Angeles, CA	A Study to Assess the Cardiovascular, Cognitive, and Subjective Effects of Atomoxetine in Combination with Intravenous Amphetamine
Sean Mackey, MD, PhD Stanford University Palo Alto, CA	Neural and Immune Effects of Short-term Opioid Use in Chronic Pain Patients
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
Richard Reznichak, M.D. Harbor-UCLA Medical Center Torrance, CA	A prospective, randomized, double-blind study comparing the efficacy and safety of intra nasal fentanyl spray to placebo as an analgesic in patients undergoing outpatient cystoscopic procedures
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

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

Human Methamphetamine  
Self-Administration in a Progressive-Ratio  
Paradigm

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<sub>2B</sub>

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

Behavioral and physiological toxicities of  
cannabinoids

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

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

Principal Investigator

Title of Study

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



**APPENDIX B**

CURRENTLY OPEN (*through December 31, 2012*)  
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, 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)
AcelRx Redwood City, CA	A Multicenter, Randomized, Open-Label, Parallel-Group Trial to Compare the Efficacy and Safety of the Sufentanil NanoTab PCA System/15 mcg to Intravenous Patient-Controlled Analgesia with Morphine for the Treatment of Acute Post-Operative Pain (IAP309)
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 (ALK5461-2)

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
Astra Zenica / CRO - Quintiles Overland Park, KS	A Randomized, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Safety of NKTR-118 in Patients with Non-Cancer-Related Pain and Opioid-Induced Constipation (OIC) (D3820C00004)
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)
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)

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
Collegium /CRO-INC Research Raleigh, NC	A Phase 3, Multi-Center, Randomized, Double-Blind, Placebo-Controlled, Safety, Tolerability, and Efficacy Study of Oxycodone DETERx™ Versus Placebo in Opioid-Experienced and Opioid-Naive Subjects with Moderate-to-Severe Chronic Low Back Pain (CO-OXYDET-08)
GW Pharmaceuticals Mill Valley, CA	Panel Approved Research Project
GW Pharmaceuticals Milly Valley, CA	Panel Approved Research Project
GW Pharmaceuticals Milly 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”]
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)

Sponsor

Description or Title  
of Clinical Drug Trial Protocol

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)

Noven / CRO-PRA  
Lenexa, CA

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)

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 MC, R, DB, PC Study w an OL Run-in to  
Assess the Efficacy & Safety of Hydrocodone  
Bitartrate (HYD) Tabs 20 to 120 mg  
Once-day in Subjects w Mod to Sev Chronic  
Low Back Pain  
(HYD3002)

Sponsor

Description or Title  
of Clinical Drug Trial Protocol

Purdue / CRO-PRA  
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)

Sponsor

Description or Title  
of Clinical Drug Trial Protocol

Purdue / CRO-Quintiles  
Overland Park, KS

A Rand, DB, DD, PC, AC, PG, MC Trial of OXN to Asses the Analg Effic (Comp to Plac) & the Magm of Opioid-induc Const (Comp to OXY) in Opioid-exp Sub w Cont Mod to Sev Chr Low Back Pain & a His of Opioid-induc Const w 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)

QrxPharma / CRO-INC  
Austin, TX

A DB, Rand, P, & AC, PG Study to Evaluate the Safety, Tolérability & Efficacy of Q8011 Comped to OxyContin & Placebo in Pts w Mod to Sev Chr. Hip or Kneww Pain Due to Osteoarthritis (Q8011-201)

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
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 (489-322)
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)

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
Shire / CRO-Premier Research Group Alexander, NC	A Phase 4, Rando, DB, MC, PG, AC, Dose-optimization Safety & Efficacy Study of SPD489 (Vyvanse) Compared w OROS-MPH (concerta) w a Placebo Reference Arm, in Adolescents Aged 13-17 Years w ADHD (SPD489-405)
Shire / CRO-Premier Research Group Alexander, NC	A Phase 4, Rando, DB, MC, PG, AC, Forced-dose Titration, Safety & Efficacy Study of SPD489 (Vyvanse) Compared w OROS-MPH (Concerta) w a Placebo Reference Arm, in Adolescents Aged 13-17 Years w ADHD (SPD489-406)
Shire / CRO-Premier Research Group Alexander, NC	A Phase 3, Multicenter, Open-Label, 12-Month Extension Safety and Tolerability Study of SPD489 in the Treatment of Adults with Binge Eating Disorder (SPD489-345)
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)

<u>Sponsor</u>	<u>Description or Title of Clinical Drug Trial Protocol</u>
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)
Shire Pharmaceuticals Wayne, PA	A Phase 3b, Dbl-blind, Randomized, Active-controlled, Parallel-gr Study to Compare the Time to Response of Lisdexamfetamine to Atomoxetine in Children & Adolescents aged 6-17 w ADHD who have had an Inadequate Response to Methylphenidate Therapy (SPD489-317)
Sunovion / CRO-INC Seattle, WA	A Randomized, Double-Blind, Parallel-Group, Multicenter Efficacy and Safety Study of SEP-225289 Versus Placebo in Adults with Attention Deficit Hyperactivity Disorder (ADHD) (SEP360-20)



## APPENDIX C

### CURRENTLY OPEN (*December 31, 2012*) 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, Multi-Center Trial of Nopicastat for Cocaine Dependence (CS#1031)
Keith Heinzerling, MD, MPH UCLA ISAP Los Angeles, CA	Pharmacogenomics and Medication Development for Methamphetamine Dependence
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

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.

# Attachment 2



July 9, 2013

Jan Jamison  
California State Board of Pharmacy  
Public Information Officer  
1625 N Market Blvd N219  
Sacramento, CA 95834

Re: Notice of Interpreter Availability "Point to Your Language" Notice (Section 1707.6(c))

Dear Ms. Jamison:

This letter is a formal request by Costco Wholesale for approval from the Board for an alternative form of notice pursuant to 16 California Code of Regulations Section 1707.6(c). Costco would like to use our own form of notice of interpreter services. A sample of this is included in attachment two. We would be using this in color, on an 8 ½" by 11" easel.

Thank you,

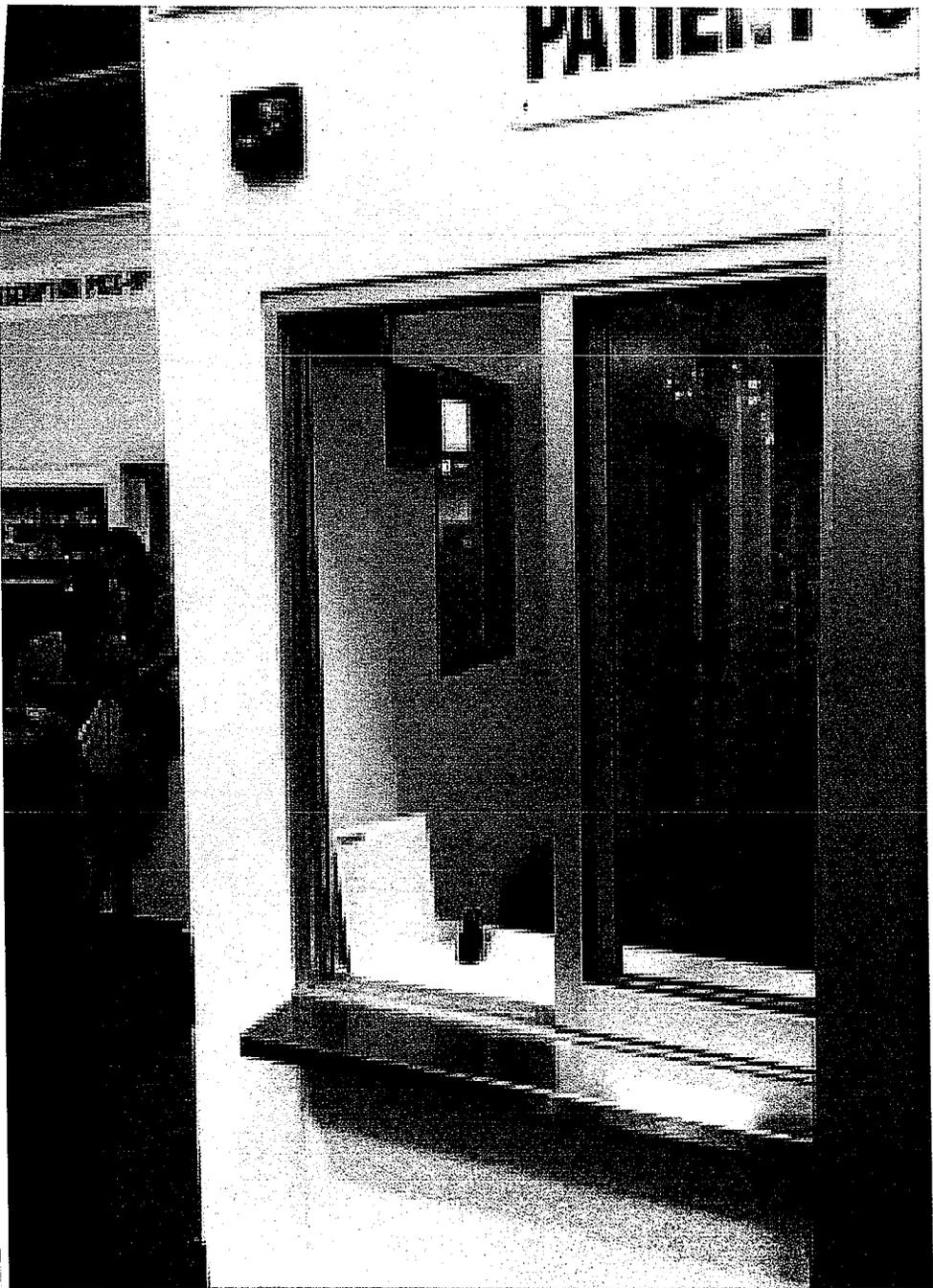
A handwritten signature in black ink, appearing to read "Jon McArthur".

Jon McArthur  
Pharmacy Compliance  
Costco Wholesale  
999 Lake Drive  
Issaquah WA 98027

**English Translation:** Point to your language. An interpreter will be called. The interpreter is provided at no cost to you.

<p><b>Arabic</b> عربي </p> <p>أشر إلى لغتك. وسوف يتم جلب مترجم فوري لك. سيتم تأمين المترجم الفوري مجاناً.</p>	<p><b>Japanese</b> 日本語 </p> <p>あなたの話す言語を指して下さい。 無料で通訳を提供します。</p>
<p><b>Armenian</b> Հայերեն </p> <p>Ցոյց տու՛նք ո՞ր մէկ լեզուն և դիտարկումների մը կանչել և տանք. Թարգմանիչը և տրանսլորուի անվճար.</p>	<p><b>Korean</b> 한국어 </p> <p>귀하께서 사용하는 언어를 지적하시면 해당 언어 통역 서비스를 무료로 제공해 드립니다.</p>
<p><b>Cambodian (Khmer)</b> កម្ពុជា (ខ្មែរ) </p> <p>សូមចង្អុលភាសាអ្នក ។ យើងនឹងហៅអ្នកបកប្រែភាសាមកជូន ។ អ្នកបកប្រែភាសានឹងជួយអ្នកដោយមិនគិតថ្លៃ ។</p>	<p><b>Mandarin</b> 國語 </p> <p>請指認您的語言， 以便為您提供免費的口譯服務。</p>
<p><b>Cantonese</b> 廣東話 </p> <p>請指認您的語言， 以便為您提供免費的傳譯服務。</p>	<p><b>Polish</b> Polski </p> <p>Proszę wskazać swój język i wezwiemy tłumacza. Tłumacza zapewnimy bezpłatnie.</p>
<p><b>Farsi</b> فارسي </p> <p>زبان مورد نظر خود را مشخص کنید. یک مترجم برای شما درخواست خواهد شد. مترجم بصورت رایگان در اختیار شما قرار می گیرد.</p>	<p><b>Portuguese</b> Português </p> <p>Indique o seu idioma. Um intérprete será chamado. A interpretação é fornecida sem qualquer custo para você.</p>
<p><b>French</b> Français </p> <p>Pointez vers votre langue et on appellera un interprète qui vous sera fourni gratuitement.</p>	<p><b>Russian</b> Русский </p> <p>Укажите язык, на котором вы говорите. Вам вызовут переводчика. Услуги переводчика предоставляются бесплатно.</p>
<p><b>German</b> Deutsch </p> <p>Zeigen Sie auf Ihre Sprache. Ein Dolmetscher wird gerufen. Der Dolmetscher ist für Sie kostenlos.</p>	<p><b>Spanish</b> Español </p> <p>Señale su idioma y llamaremos a un intérprete. El servicio es gratuito.</p>
<p><b>Hindi</b> हिंदी </p> <p>अपनी भाषा पर इंगित करें और एक दुभाषिया बुलाया जाएगा। दुभाषिये का प्रबन्ध आप पर बिना किसी खर्च के किया जाता है।</p>	<p><b>Tagalog</b> Tagalog </p> <p>Ituro po ang inyong wika. Isang tagasalin ang ipagkakaloob nang libre sa inyo.</p>
<p><b>Hmong</b> Hmoob </p> <p>Taw rau koj hom lus. Yuav hu rau ib tug neeg txhais lus. Yuav muaj neeg txhais lus yam uas koj tsis tau them dab tsi.</p>	<p><b>Thai</b> ไทย </p> <p>ช่วยชี้ที่ภาษาที่ท่านพูด แล้วเราจะจัดหาสามให้ท่าน การใช้สามไม่ต้องเสียค่าใช้จ่าย</p>
<p><b>Italian</b> Italiano </p> <p>Puntare sulla propria lingua. Un interprete sarà chiamato. Il servizio è gratuito.</p>	<p><b>Vietnamese</b> Tiếng Việt </p> <p>Hãy chỉ vào ngôn ngữ của quý vị. Một thông dịch viên sẽ được gọi đến, quý vị sẽ không phải trả tiền cho thông dịch viên.</p>

PATIENT





## Health and Wellness Practice Compliance

Debbie Mack, R.Ph, CHC  
Sr. Director, Corporate Compliance

702 SW 8<sup>th</sup> Street  
Bentonville, AR 72716  
Phone 479.277.0491  
Fax 479-273-8675  
Debbie.Mack@wal-mart.com

July 26, 2013

California State Board of Pharmacy  
Jan Jamison, Public Information Officer  
1625 N. Market Blvd. N219  
Sacramento, CA 95834  
Phone: 916-574-7957  
Fax: 916-574-8618

**RE: Notice of Interpreter Availability**

Dear Ms. Jamison:

Thank you for considering this request for approval by the California State Board of Pharmacy for Walmart and Sam's Club Pharmacies to use the enclosed sign for the Notice of Interpreter Availability pursuant to 16 California Code of Regulations Section 1707.6(c).

The attached example is for Walmart Pharmacies only. We plan to co-brand the logo to include Walmart and Sam's Club.

Thank you again for considering this request. Should you have any questions or need additional information regarding this matter, please do not hesitate to contact me at 479-277-0491.

Sincerely,

Debbie Mack, R.Ph, CHC  
Walmart Stores, Inc.



Interpreter Services available at no cost to you. Please point to your language.

**Spanish**

Servicios de intérprete disponible sin costo alguno para usted. Por favor señale su idioma.

**Portuguese (Brazilian)**

Serviços de tradutor disponível para você gratuitamente. Favor apontar para o seu idioma.

**Hmong**

Peb yuav muaj tug paab txhais lug rua koj dlawb dlawb. Thov taw rua koj yaam lug.

**German**

Sie können von kostenlosen Dolmetschdiensten Gebrauch machen. Bitte zeigen Sie auf Ihre Sprache.

**Cantonese (Simplified)**

请点击这里以获得免费广东话口译服务

**Mandarin (Traditional)**

請點這裏以獲得免費國語口譯服務

**Korean**

통역 서비스를 무료로 제공합니다.

**Tagalog**

Mga Serbisyo ng Tagasalin nang walang gastos sa iyo. Pakituro sana ang iyong lengguwahe.

**Farsi**

خدمات ترجمه رایگان برای شما موجود است.  
لطفاً به زبان خود اشاره کنید.

**Italian**

Servizi di interpretariato gratuiti. Indicare la lingua.

**Russian**

Вы имеете право на бесплатные услуги переводчика. Пожалуйста просим Вас указать на Ваш язык.

**Polish**

Pacjenci mogą korzystać z bezpłatnych usług tłumacza. Proszę wskazać swój język.

**French (Canadian)**

Services d'interprète disponibles sans frais pour vous. Veuillez indiquer votre langue.

**Vietnamese**

Dịch vụ Thông dịch luôn có sẵn miễn phí cho quý vị. Vui lòng cho biết ngôn ngữ của quý vị.

**Cantonese (Traditional)**

請點這裏以獲得免費廣東話口譯服務

**Mandarin (Simplified)**

请点击这里以获得免费普通话口译服务

**Cambodian/Khmer**

សំណើកម្មវិធីបកប្រែសេរី  
មានជូនដល់លោកអ្នកដោយមិនអស់លុយ។  
សូមចងអុលទៅភាសារបស់លោកអ្នក។

**Arabic**

يمكننا توفير خدمات الترجمة الفورية مجاناً. الرجاء تحديد لغتك

**Armenian**

Կարողանալուք ստանալ անվճար արագ և անվճար և՛ ձեր համայն  
հնչյունները և՛ լեզուները անվճար և՛ առանց ցածր արժեքի:



**CERTIFIED LANGUAGES**  
INTERNATIONAL



Savings Made Simple

Interpreter Services available at no cost to you. Please point to your language.

**Spanish**

Servicios de intérprete disponible sin costo alguno para usted. Por favor señale su idioma.

**Portuguese (Brazilian)**

Serviços de tradutor disponível para você gratuitamente. Favor apontar para o seu idioma.

**Hmong**

Peb yuav muaj tug paab txhais lug rua koj dlawb dlawb. Thov taw rua koj yaam lug.

**German**

Sie können von kostenlosen Dolmetschdiensten Gebrauch machen. Bitte zeigen Sie auf Ihre Sprache.

**Cantonese (Simplified)**

请点击这里以获得免费广东话口译服务

**Mandarin (Traditional)**

請點這裏以獲得免費國語口譯服務

**Korean**

통역 서비스를 무료로 제공합니다.

**Tagalog**

Mga Serbisyo ng Tagasalin nang walang gastos sa iyo. Pakituro sana ang iyong lengguwahe.

**Farsi**

خدمات ترجمه رایگان برای شما موجود است.

لطفاً به زبان خود اشاره کنید.

**Italian**

Servizi di interpretariato gratuiti. Indicare la lingua.

**Russian**

Вы имеете право на бесплатные услуги переводчика. Пожалуйста просим Вас указать на Ваш язык.

**Polish**

Pacjenci mogą korzystać z bezpłatnych usług tłumacza. Proszę wskazać swój język.

**French (Canadian)**

Services d'interprète disponibles sans frais pour vous. Veuillez indiquer votre langue.

**Vietnamese**

Dịch vụ Thông dịch luôn có sẵn miễn phí cho quý vị. Vui lòng cho biết ngôn ngữ của quý vị.

**Cantonese (Traditional)**

請點這裏以獲得免費廣東話口譯服務

**Mandarin (Simplified)**

请点击这里以获得免费普通话口译服务

**Cambodian/Khmer**

សំណើកម្មវិធីបកប្រែសំឡេង  
មានជូនដល់លោកអ្នកដោយមិនគិតថ្លៃ។  
សូមចង្អុលទៅភាសារបស់លោកអ្នក។

**Arabic**

يمكننا توفير خدمات الترجمة الفورية مجاناً. الرجاء تحديد لغتك

**Armenian**

Կարելի է ապահովել անվճար արձագանքային թարգմանչական ծախսերի ազատում և նախընտրել ձեր լեզուն:



CERTIFIED LANGUAGES INTERNATIONAL



**California State Board of Pharmacy**

1625 N. Market Blvd, N219, Sacramento, CA 95834  
Phone: (916) 574-7900  
Fax: (916) 574-8618  
www.pharmacy.ca.gov

BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY  
DEPARTMENT OF CONSUMER AFFAIRS  
GOVERNOR EDMUND G. BROWN JR.

**Request for Approval of Alternate Format or Display Methodology  
“Point To Your Language” Notice (Notice of Interpreter Availability)**

Every pharmacy is required to post or provide a notice of interpreter availability in a place conspicuous to and readable by a consumer, at or adjacent to each counter in the pharmacy where dangerous drugs are dispensed or furnished. Every pharmacy shall use the standardized notice provided by the board unless prior approval has been received to use another format or display methodology. *16 Cal. Code Reg. 1707.6(c).*

Completion of this form is not mandatory. You may submit a written request to the board at the address below. Unless approved by the board in advance, each pharmacy must use the standard notice provided by the board, available on the board’s website:

[http://www.pharmacy.ca.gov/publications/point\\_to\\_your\\_language.pdf](http://www.pharmacy.ca.gov/publications/point_to_your_language.pdf)

**IMPORTANT:** All twelve languages specified in the board’s regulation must be on the “Point To Your Language” notice.

Please send your request, a sample of your proposed notice, and any relevant / additional information to the board at the following address: California State Board of Pharmacy, 1675 North Market Blvd., Suite 219, Sacramento, CA 95834.

Name of Pharmacy: \_\_\_\_\_ License Number: \_\_\_\_\_

Address: \_\_\_\_\_

Contact Person: \_\_\_\_\_ Phone Number: \_\_\_\_\_

E-mail address: \_\_\_\_\_

**Please complete the following:**

**1. What are you requesting? (Check all that apply.)**

Print

- Approval of an alternate printed format of the notice of interpreter availability.
- Approval of a specific display methodology of the printed notice.

Video

- Approval of another video format of the notice of interpreter availability.
- Approval of a specific display methodology of the video notice.

**2. Are all twelve languages required by 16 California Code of Regulations Section 1707.6(c) on your notice?**

YES

NO

**3. Are additional languages (in addition to the twelve languages required by 16 CCR § 1707.6(c)) on your notice?**

YES

NO

a. If YES, what additional languages are listed?

b. How did you determine what additional languages to include?

**4. Did you contract with a translation service to provide translations for your notice?**

YES

NO

a. If YES, is the translation service certified or accredited?

b. If YES, what is the agency or agencies that certified or accredited the translation service?

c. Please provide the name, address and phone number of the translation service you used.

NAME:

ADDRESS:

PHONE NO:

**5. Additional Information:**

# Attachment 3

# Key Facts About Emergency Contraception



Emergency Contraception (EC) is a safe and effective way to prevent pregnancy after sex.

Consider using Emergency Contraception (EC) if:

- You had unprotected sex, or
- You think your contraceptive didn't work.

**What are Emergency Contraceptive pills?**

Emergency Contraceptive pills contain the same medication as regular birth control pills, and help to prevent pregnancy. There are three basic types of Emergency Contraceptive pills:

- Progestin-only pills (Plan B® One-Step, Next Choice®)
- Ulipristate acetate (ella®)
- High doses of regular oral contraceptive pills

**Don't wait! Take EC as soon as possible.**

- It is best to take EC as soon as possible; the sooner you take EC the more effective it is.
- It has been shown to be effective for up to 5 days.
- For more information talk to your pharmacist or doctor.

**When taken as directed Emergency Contraception has been shown to be safe and effective.**

- Emergency Contraception may reduce the risk of pregnancy by up to 89 percent.
- The effectiveness of EC varies based on the type used and when it is taken.
- EC is only recommended as a backup and should not be used as your primary method of birth control.
- Emergency Contraceptive pills do not protect against sexually transmitted infections, including HIV/AIDS.

What EC does:

- Emergency Contraceptive pills prevent pregnancy.
- Emergency Contraceptive pills are not effective after pregnancy has occurred and they will not harm the developing fetus.
- Emergency Contraceptive pills are NOT the same as RU-486 (the abortion pill).
- Using Emergency Contraceptive pills will not affect a woman's ability to become pregnancy in the future.

**Follow-up after taking Emergency Contraceptive pills:**

- If you vomit after taking emergency contraception you may need to take another dose. Before you do, contact a pharmacist or healthcare provider immediately.
- If you do not get a normal period within three weeks, take a pregnancy test.
- It is important to visit your doctor or clinic for a regular birth control method and information about preventing sexually transmitted infections.
- Medical providers or your pharmacist can provide Emergency Contraception for future use if needed.

In California, women and men may receive free family planning services through Family PACT based on income.

If you don't have a doctor or clinic, call (800) 942-1054 to find a Family PACT provider near you.

Under the Affordable Care Act (ACA), Emergency Contraception may be covered with a prescription.



**BE AWARE AND TAKE CARE:**  
Talk to your pharmacist!  
CALIFORNIA STATE BOARD OF PHARMACY

California State Board of Pharmacy  
1625 North Market Blvd., Suite N-219  
Sacramento, CA 95834

www.pharmacy.ca.gov  
(916) 574-7900

# Attachment 4



**FOR IMMEDIATE RELEASE**

**CONTACT: Francine Pierson  
301/816-8588; [fp@usp.org](mailto:fp@usp.org)**

## **First Universal Standards Guiding Content, Appearance of Prescription Container Labels to Promote Patient Understanding of Medication Instructions**

*Nearly Half of Patients Misunderstand One or More Dosage Instructions Pharmacies Across the Country Urged to Adopt "Patient-Centered" Labels*

**Rockville, Md., October 9, 2012** — With medication misuse resulting in more than one million adverse drug events per year in the United States, new standards released today by the U.S. Pharmacopeial Convention (USP) for the first time provide a universal approach to the format, appearance, content and language of instructions for medicines in containers dispensed by pharmacists. Wide variability in prescription container labels exists today across individual prescriptions, pharmacies, retail chains and states. The USP standards provide specific direction on how to organize labels in a "patient-centered" manner that best reflects how most patients seek out and understand medication instructions.

"Lack of universal standards for labeling on dispensed prescription containers is a root cause for patient misunderstanding, non-adherence and medication errors," said Joanne G. Schwartzberg, M.D., director, aging and community health for the American Medical Association and a member of the USP Nomenclature, Safety and Labeling Expert Committee, the group of independent experts responsible for the new standard. "With an aging and increasingly diverse population, and people utilizing a growing number of medications, the risks are more pronounced today than ever. These USP standards will promote patient understanding of their medication instructions, which is absolutely essential to preventing potentially dangerous mistakes and helping to ensure patient health and safety."

Studies have found that 46 percent of patients misunderstood one or more dosage instructions on prescription labels. The problem is particularly troublesome in patients with low or marginal literacy (one study showed patients with low literacy were 34 times more likely to misinterpret prescription warning labels), and in patients receiving multiple medications that are scheduled for administration using unnecessarily complex, non-standardized time periods. However, even patients with adequate literacy often misunderstand common prescription directions and warnings.

The USP effort to create these new standards developed from an Institute of Medicine (IOM)-led initiative to improve health literacy, which is defined as the degree to which people can obtain, process and understand the basic health information and services they need to make appropriate health decisions. According to IOM, 77 million Americans have limited health literacy, and a majority of Americans have difficulty understanding and using currently available health information and services.

Elements of the new USP standards, contained in General Chapter <17> *Prescription Container Labeling*, of the *United States Pharmacopeia* and the *National Formulary*, include:

- **Emphasize instructions and other information important to patients.** Prominently display information that is critical for patients' safe and effective use of the medicine. At the top of the

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Rockville, Maryland  
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**Europe/Middle East/Africa**  
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**USP-India Private Limited**  
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Farlapally Village, Genome Valley  
Shameerpet, Rangareddy District  
Hyderabad 500 078, A.P., India  
+91 40 6448 2200

**USP-China**  
Building 11  
Lane 67 Libing Road  
Zhangjiang Hi-Tech Park  
201203, Shanghai, China  
+86 21 51379600

**USP-Brazil**  
Avenida Cecl, 1600-Jamboré  
Barueri-SP  
06460-120  
Brazil  
+55 11 3245-6400



label specify patient name, drug name (spell out full nonproprietary and brand name) and strength, and clear directions for use in simple language. Less critical information (e.g., pharmacy name, drug quantity) should not supersede critical information and should be placed away from dosing instructions.

- **Improve readability.** Labels should be designed and formatted so they are easy to read. Typography should be optimized by using high contrast print; adequate white space between lines of text (i.e., 25-30 percent of the point size); simple uncondensed familiar fonts (Times Roman or Arial are specifically recommended); and large font size (e.g., minimum 12-point Times Roman or 11-point Arial) for critical information. Older adults, in particular, have difficulty reading small print.
- **Give explicit instructions.** Instructions for use should clearly separate the dose itself from the timing of each dose. Do not use alphabetic characters for numbers. For example, write, “Take 2 tablets in the morning and 2 tablets in the evening” rather than “Take 2 tablets twice daily.” Dosing intervals such as “twice daily,” “3 times daily,” or hourly intervals such as “every 12 hours” should be avoided because such instructions are implicit rather than explicit, may involve numeracy skills, and patient interpretation may vary from prescriber intent. Although instructions worded in terms of specific hourly times (e.g., 8 a.m. and 10 p.m.) may be assumed to be more easily understood, in actual use they are less readily understood and may present greater adherence issues due to individual lifestyle patterns (e.g., shift work) than general timeframes such as “in the morning” or “after breakfast.” Ambiguous directions such as “take as directed” should be avoided without clear supplemental information.
- **Include purpose for use.** If the purpose of the medication is included on the prescription, it should be included on the label unless a patient prefers that it not appear. Confidentiality and FDA approval for intended use (i.e., labeled vs. off-label use) may cause some to constrain its inclusion on labels. Current evidence supports inclusion of purpose-for-use language in clear, simple terms, e.g., “for high blood pressure” rather than “for hypertension.”
- **Address limited English proficiency.** Whenever possible, the directions for use on a prescription container label should be provided in the patient’s preferred language. The drug name shall be in English as well so that emergency personnel can have quick access to the information. Translations should be produced using a high-quality translation process; an example is provided in the standard.
- **Address visual impairment.** Provide alternative access for visually impaired patients (e.g., tactile, auditory, or enhanced visual systems that may employ advanced mechanics or assistive technology).

“Patients’ best—and often only—source of information regarding the medications they have been prescribed is on the prescription container label,” Dr. Schwartzberg noted. Although other written information and oral counseling may be available, the prescription container label must fulfill the professional obligations of the prescriber and pharmacist. These include giving the patient the most essential information needed to understand how to safely and appropriately use the medication and to adhere to the prescribed medication regimen.

USP issued a draft version of this standard for public review and comment by all interested stakeholders—including healthcare practitioners, retailers, software vendors, consumers and others—in December 2011. The final standard will be published in November 2012, and incorporates multiple additions based on comments received, including more detail on producing high-quality translations,



the visual impairment section, and the direction to include both brand and nonproprietary names on labels.

Enforcement of the standard will be the decision of individual state boards of pharmacy, which may choose to adopt it into their regulations—similar to USP standards for sterile and nonsterile pharmaceutical compounding, both of which are widely recognized by states. At its 2012 annual meeting, the National Association of Boards of Pharmacy passed a resolution supporting state boards in requiring a standardized prescription container label.

Examples of prescription container labels that comply with the new USP standard are available at <http://uspgo.to/prescription-container-labeling>. Media inquiries may be directed to [mediarelations@usp.org](mailto:mediarelations@usp.org).

###

**USP – Advancing Public Health Since 1820**

The United States Pharmacopeial Convention (USP) is a scientific, nonprofit, standards-setting organization that advances public health through public standards and related programs that help ensure the quality, safety, and benefit of medicines and foods. USP's standards are relied upon and used worldwide. For more information about USP visit <http://www.usp.org>. FY1317

Add the following:

## (17) PRESCRIPTION CONTAINER LABELING

### INTRODUCTION

Medication misuse has resulted in more than 1 million adverse drug events per year in the United States. Patients' best source (and often only source) of information regarding the medications they have been prescribed is on the prescription container label. Although other written information and oral counseling sometimes may be available, the prescription container label must fulfill the professional obligations of the prescriber and pharmacist. These obligations include giving the patient the most essential information needed to understand how to safely and appropriately use the medication and to adhere to the prescribed medication regimen.

Inadequate understanding of prescription directions for use and auxiliary information on dispensed containers is widespread. Studies have found that 46% of patients misunderstood one or more dosage instructions, and 56% misunderstood one or more auxiliary warnings. The problem of misunderstanding is particularly troublesome in patients with low or marginal literacy and in patients receiving multiple medications that are scheduled for administration using unnecessarily complex, nonstandardized time periods. In one study, patients with low literacy were 34 times more likely to misinterpret prescription medication warning labels. However, even patients with adequate literacy often misunderstand common prescription directions and warnings. In addition, there is great variability in the actual auxiliary warning and supplemental instructional information applied by individual practitioners to the same prescription. The specific evidence to support a given auxiliary statement often is unclear, and patients often ignore such information. The essential need for, and benefit of, auxiliary label information (both text and icons) in improving patient understanding about safe and appropriate use of their medications vs. explicit simplified language alone require further study.

Lack of universal standards for labeling on dispensed prescription containers is a root cause for patient misunderstanding, nonadherence, and medication errors. On May 18, 2007, the USP Safe Medication Use Expert Committee established an Advisory Panel to: 1) determine optimal prescription label content and format to promote safe medication use by critically reviewing factors that promote or distract from patient understanding of prescription medication instructions and 2) create universal prescription label standards for format/appearance and content/language.

In November 2009, the Health Literacy and Prescription Container Labeling Advisory Panel presented its recommendations to the Safe Medication Use Expert Committee, which then requested that USP develop patient-centered label standards for the format, appearance, content, and language of prescription medication instructions to promote patient understanding. These recommendations form the basis of this general chapter.

Note—These standards do not apply when a prescription drug will be administered to a patient by licensed personnel who are acting within their scope of practice.

## 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 container labeling should feature only the most important patient information needed for safe and effective understanding and use.

**Emphasize instructions and other information important to patients:** Prominently display information that is critical for patients' safe and effective use of the medicine. At the top of the label specify the patient's name, drug name (spell out full generic and brand name) and strength, and explicit clear directions for use in simple language.

The prescription directions should follow a standard format so the patient can expect that each element will be in a regimented order each time a prescription is received.

Other less critical but important content (e.g., pharmacy name and phone number, prescriber name, fill date, refill information, expiration date, prescription number, drug quantity, physical description, and evidence-based auxiliary information) should not supersede critical patient information. Such less critical information should be placed away from dosing instructions (e.g., at the bottom of the label or in another less prominent location) because it distracts patients, which can impair their recognition and understanding.

**Simplify language:** Language on the label should be clear, simplified, concise, and familiar, and should be used in a standardized manner. Only common terms and sentences should be used. Do not use unfamiliar words (including Latin terms) or medical jargon.

Use of readability formulas and software is not recommended to simplify short excerpts of text like those on prescription labels. Instead, use simplified, standardized sentences that have been developed to ensure ease of understanding the instructions correctly (by seeking feedback from samples of diverse consumers).

**Give explicit instructions:** Instructions for use (i.e., the SIG or signatur) should clearly separate the dose itself from the timing of each dose in order to explicitly convey the number of dosage units to be taken and when (e.g., specific time periods each day such as morning, noon, evening, and bedtime). Instructions shall include specifics on time periods. Do not use alphabetic characters for numbers. For example, write "Take 2 tablets in the morning and 2 tablets in the evening" rather than "Take two tablets twice daily."

Whenever available, use standardized directions (e.g., write "Take 1 tablet in the morning and 1 tablet in the evening" if the prescription reads b.i.d.). Vague instructions based on dosing intervals such as twice daily or 3 times daily, or hourly intervals such as every 12 hours, generally should be avoided because such instructions are implicit rather than explicit, they may involve numeracy skills, and patient interpretation may vary from prescriber intent. Although instructions that use specific hourly times (e.g., 8 a.m. and 10 p.m.) may seem to be more easily understood than implicit vague instructions, recommending dosing by precise hours of the day is less readily understood and may present greater adherence issues due to individual lifestyle patterns, e.g., shift work, than more general time frames such as in the morning, in the evening, after breakfast, with lunch, or at bedtime. Consistent use of the same terms should help avoid patient confusion.

Ambiguous directions such as "take as directed" should be avoided unless clear and unambiguous supplemental instructions and counseling are provided (e.g., directions for use that will not fit on the prescription container label). A clear statement referring the patient to such supplemental materials should be included on the container label.

**Include purpose for use:** If the purpose of the medication is included on the prescription, it should be included on the prescription container label unless the patient prefers that it not appear. Always ask patients their preference when prescriptions are submitted for filling. Confidentiality and FDA approval for intended use (e.g., labeled vs. off-label use) may limit inclusion of the purpose on labels. Current evidence supports inclusion of purpose-for-use language in clear, simple terms (e.g., "for high blood pressure" rather than "for hypertension").

**Limit auxiliary information:** Auxiliary information on the prescription container label should be evidence-based in simple explicit language that is minimized to avoid distracting patients with nonessential information. Most patients, particularly those with low literacy, pay little attention to auxiliary information. The information should be presented in a standardized manner and should be critical for patient understanding and safe medication use (e.g., warnings and critical administration alerts). Icons are frequently misunderstood by patients. In addition, icons that provide abstract imagery for messages that are difficult to visually depict may be ineffective at improving understanding compared with simplified text alone. Use only icons for which there is adequate evidence, through consumer testing, that they improve patient understanding about correct use. Evidence-based auxiliary information, both text and icons, should be standardized so that it is applied consistently and does not depend on individual practitioner choice.

**Address limited English proficiency:** Whenever possible, the directions for use on a prescription container label should be provided in the patient's preferred language. Otherwise there is a risk of misinterpretation of instructions by patients with limited English proficiency, which could lead to medication errors and adverse health outcomes. Additionally, whenever possible, directions for use should appear in English as well, to facilitate counseling; the drug name shall be in English so that emergency personnel and other intermediaries can have quick access to the information.

Translations of prescription medication labels should be produced using a high-quality translation process. An example of a high-quality translation process is:

- Translation by a trained translator who is a native speaker of the target language
- Review of the translation by a second trained translator and reconciliation of any differences
- Review of the translation by a pharmacist who is a native speaker of the target language and reconciliation of any differences
- Testing of comprehension with target audience

If a high-quality translation process cannot be provided, labels should be printed in English and trained interpreter services used whenever possible to ensure patient comprehension. The use of computer-generated translations should be limited to programs with demonstrated quality because dosage instructions can be inconsistent and potentially hazard-

ous. Standardized translated instructions and technology advances are needed to ensure the accuracy and safety of prescription container labeling for patients with low English proficiency.

**Improve readability:** Labels should be designed and formatted so they are easy to read. Currently no strong evidence supports the superiority in legibility of serif vs. sans serif typefaces, so simple uncondensed fonts of either type can be used.

Optimize typography by using the following techniques:

- High-contrast print (e.g., black print on white background).
  - Simple, uncondensed familiar fonts with sufficient space within letters and between letters (e.g., Times Roman or Arial).
  - Sentence case (i.e., punctuated like a sentence in English: initial capital followed by lower-case words except proper nouns).
  - Large font size (e.g., minimum 12-point Times Roman or 11-point Arial) for critical information. Note that point size is not the actual size of the letter, so 2 fonts with the same nominal point size can have different actual letter sizes. X-height, the height of the lower-case x in typeface, has been used as a more accurate indicator of apparent size than point size. For example, for a given point size, the x-height and apparent size of Arial are actually bigger than those for Times Roman. Do not use type smaller than 10-point Times Roman or equivalent size of another font. Older adults, in particular, have difficulty reading small print.
  - Adequate white space between lines of text (25%–30% of the point size).
  - White space to distinguish sections on the label such as directions for use vs. pharmacy information.
  - Horizontal text only.
- Other measures that can also improve readability:
- If possible, minimize the need to turn the container in order to read lines of text.

- Never truncate or abbreviate critical information.
- Highlighting, bolding, and other typographical cues should preserve readability (e.g., high-contrast print and light color for highlighting) and should emphasize patient-centric information or information that facilitates adherence (e.g., refill ordering).
- Limit the number of colors used for highlighting (e.g., no more than one or two).
- Use of separate lines to distinguish when each dose should be taken.

**Address visual impairment:**

- Provide alternative access for visually impaired patients (e.g., tactile, auditory, or enhanced visual systems that may employ advanced mechanics of assistive technology).

# Attachment 5

# Universal Medication Schedule White Paper

April 2013 DRAFT

National Council for Prescription Drug Programs  
9240 East Raintree Drive  
Scottsdale, AZ 85260

Phone: (480) 477-1000  
Fax (480) 767-1042



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# Universal Medication Schedule White Paper

## Version 1.0

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## 1. EXECUTIVE SUMMARY

Universal Medication Schedule (UMS) is a methodology that simplifies medication administration instructions for the patient and / or their caregiver. The goal of UMS is to increase patient understanding and adherence of their medication instructions, thus resulting in improved health outcomes.

Two considerations were ever present in the development of this paper. One, the reason for moving to UMS is for the patient – to reduce potential errors and improve outcomes. Two, there is a limited ability to measure a hard return on investment. No studies have been done that have isolated the financial impact of UMS.

Currently, prescription administration instructions appear on the label in an inconsistent manner. Depending on the prescriber and the pharmacist, any of the following may be used, either as interpretation of "1 qd" or as a direct representation of what the prescriber communicated to the pharmacist:

- Take one tablet once daily.
- Take 1 tablet 1 time per day.
- Take one tablet each morning.
- Take one tablet every 24 hours.

Administration instructions using UMS are standardized to provide explicit timing with standard intervals (morning, noon, evening, bedtime):

- Take 1 pill in the morning.

The simplification of medication administration instructions should provide many benefits to patients, caregivers and healthcare providers, including increase in adherence and health for the patient, and efficiencies in the prescribing and dispensing of medications.

The authors researched best practices in the industry, the state of health literacy in the United States, prescription label requirements in individual states, recommendations from the National Association of Boards of Pharmacy, federal government requirements, chain pharmacy initiatives and published research concerning medication compliance and medication scheduling.

The authors have also taken into consideration the discussion that will inevitably surround the implementation of UMS into daily workflows of prescribers and pharmacists and attempted to practicably address those associated items.

The use of UMS will benefit the provider and the patient. NCPDP supports the use of UMS in all applicable situations.

## 2. PURPOSE

This paper will introduce the concept of Universal Medication Schedule and discuss how it can be implemented, and ultimately presented to the patient, using NCPDP standards. The Universal Medication Schedule (UMS) is intended as an optimal way to convey prescription directions for use to the patient. NCPDP's electronic prescribing standard, the SCRIPT standard, will support the transmission of the UMS through the use of the Sig segment when an electronic prescription is sent from a prescriber to a pharmacy. The consistent and widespread use of these standards will assist patients in understanding and adhering to their medication regimen. As an example, instructions that indicate "take one pill in the morning and take one pill in the evening" are clearer than "take twice a day".

Understanding how patients use their prescription labels illustrates the need for additional clarity. A study performed by the VA National Center for Patient Safety found that only 56% of veterans surveyed confirmed their name on the prescription label and 55% confirmed the directions prior to each use.

The information contained in this paper will address the concept of "best practice", a history of UMS, a snapshot of health literacy in the United States, and an overview of prescription container label requirements. Also included are the benefits and considerations associated with the implementation of UMS.

The audience for this paper is health care providers; pharmacists; system/software vendors; informaticists; oversight bodies, such as boards of pharmacy and medicine; and patient advocates. NCPDP hopes these stakeholders, and others, acknowledge the importance of health literacy and the role that the UMS can play in improving medication adherence for all patients. In addition, it is envisioned that these stakeholders will eagerly and actively implement UMS into their operations and practices.

### 3. OVERVIEW

Through its collaborative efforts with many organizations that are addressing issues of health literacy and patient safety, NCPDP has determined that the use of the Universal Medication Schedule (UMS) to convey Sig instructions for solid dosage forms has been convincingly shown to significantly improve an individual's ability to understand prescription instructions, properly dose medicines, and organize multi-drug regimens. Early evidence supports initial gains in medication adherence. Given the amount of evidence already available, NCPDP therefore recommends the UMS be adopted as a best practice when appropriate, regardless of dosage form.

"Best practice" is a term that does not yet have a standardized definition or legal set of qualifications related to patient-centered prescription labeling or the UMS concept. Most of the literature on the topic of best practices in the healthcare industry points to a relatively common idea that a best practice is one that has repeatedly demonstrated outcomes superior to any other comparable method. This practice or behavior should persist across settings or populations.

This definition is supported by the work of a number of different organizations. Examples include:

- The Department of Health and Human Services has said that a best practice demonstrates evidence of effectiveness and can be generalized to other populations and settings.<sup>i</sup>
- The National Registry of Evidence-Based Programs and Practices require a demonstration of positive outcomes in at least one experimental study which has been published in a peer-reviewed journal.<sup>ii</sup>
- The California Reducing Disparities Project identifies best practices by those that demonstrate both positive results and community consensus.<sup>iii</sup>
- The National Resource Center defines a Research Validated Best Practice as "a program, activity or strategy that has the highest degree of proven effectiveness supported by objective and comprehensive research and evaluation".<sup>iv</sup>

Despite the lack of official standards, some efforts have been made towards defining best practices in prescription labeling. In 2007, a research team led by faculty from Northwestern University devised the UMS to standardize and simplify medication instructions to support safe and effective prescription drug use. The UMS was reviewed and highlighted by both the Institute of Medicine (IOM) and the U.S. Pharmacopeia (USP) as a health literacy 'best practice', and the state of California passed legislation recommending the use of the UMS with drug labeling. Simply put, the UMS standardizes the prescribing and dispensing of medicine by using health literacy principles and more explicit times to describe when to take medicine (morning, noon, evening, bedtime). This eliminates variability found in the way prescriptions are written by prescribers and transcribed by pharmacists onto prescription container labels.

The *Journal of Young Pharmacists* stated that evidence-based best practices for prescription container labeling exist, and that they include a Universal Medication Schedule. The U.S. Pharmacopeial Convention has released standards surrounding prescription container labeling which include a patient-centered, low health literacy

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perspective. The UMS concept itself was vetted, and a pending recommendation has been issued by the USP Drug Labeling Advisory Panel to incorporate it as recent studies are summarized.

According to the article in the *Journal of Young Pharmacists* in 2010:<sup>v</sup>

"There is evidence available to detail "best practices" for improving dosage or usage instructions written by the prescribing physician and the format and content of prescription medication container labels designed by the dispensing pharmacy.<sup>1</sup>The use of standard and more explicit dosage or usage instructions can improve patients' functional understanding of how and when to take a medicine. Evidences are available for best practices in labeling format and content, such as increasing font size, using clear and simple language, using headers, and placing a more appropriate emphasis on organizing label content around what is most important for patients such as drug name, dose, dosage or usage instructions, patient name, doctor name, quantity, refill information, and provider content such as pharmacy name, logo and national drug code number should be in optimal font size. A complete list of evidence-based, recommended standards for format, content, and instruction is as follows:

- Use explicit text to describe dosage and interval in instructions.
- **Use a universal medication schedule (UMS) to convey and simplify dosage and use instructions.**
- Organize labels in a patient-centered manner.
- According to need, include indication for use.
- Simplify language, avoiding unfamiliar words or medical jargon.
- Improve typography, use larger, sans serif font.
- When applicable, use numeric versus alphabet characters.
- Use typographic cues (bolding and highlighting) for patient content only.
- Use horizontal text only.
- Use a standard icon system for signaling and organizing auxiliary warnings and instructions."

There are increased efforts to simplify language in a variety of settings. Many of these initiatives are related to health care and will likely have profound impact on the US health care system.

- The Department of Health and Human Services' 2010 National Action Plan to Improve Health Literacy, which is grounded on two principles; that all people are entitled to health information that helps them make informed decisions; and, that healthcare must be provided in a way that is easy to understand and promotes health.<sup>vi</sup>
- The Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy (NABP Model Act) identify critical and important information for patients that must appear as well as additional information that may appear

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on all prescription labels.<sup>vii</sup> See "Appendix A. Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy August 2011".

- o The Joint Commission has begun considering certain new "Patient-Centered Communication Standards & EPs" as part of its accreditation process. Among other things, these standards may require hospitals to identify and meet their patients' need for plain language communication. (see, e.g., Standard PC.02.01.21)<sup>viii</sup>
- o Under the "Value Based Purchasing" regulations promulgated by CMS pursuant to the 2010 Patient Protection and Affordable Care Act (ACA), providers' reimbursement levels are adjusted according to the quality of care they provide. Quality is measured in a variety of ways, including patients' subjective assessment of the quality of the communication they receive from providers. This provides an incentive to use plain language for effective communication.<sup>ix, x</sup>
- o HealthyPeople 2020 is the continuation of efforts begun several decades ago to improve the health of all Americans. The project looks at over three dozen different areas of health. Of particular interest is the goal related to health literacy.  
**HC/HIT-1: (Developmental) Improve the health literacy of the population.**
  - o HC/HIT-1.1 Increase the proportion of persons who report their health care provider always gave them easy-to-understand instructions about what to do to take care of their illness or health condition.<sup>xi, xii</sup>
- o The National Patient Safety Foundation indicates that studies show that people who understand health instructions make fewer mistakes when they take their medicine or prepare for a medical procedure. They may also get well sooner or be able to better manage a chronic health condition.<sup>xiii</sup>
- o The VA National Center for Patient Safety (NCPS) conducted a study that identified safety vulnerabilities with prescription labels used at the VA. A key finding was that there was a discrepancy in the placement of information deemed important to the patient as opposed to what the pharmacist felt was important. As a result of their study, a new patient-centric label design will likely be introduced nationally in 2013.<sup>xiv</sup>

Although the above do not establish mandatory requirements for every pharmacist and provider, they make it clear that the importance of plain language has been accepted by policy makers at the highest levels. This is further reflected in an article recently published, which was authored by senior federal policy makers:

"According to the Affordable Care Act of 2010, health literacy is the capacity to obtain, communicate, process, and understand basic health information and services to make appropriate health decisions. An increasing body of research links health literacy with health outcomes. In particular, limited health literacy

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leads to a cascade of suboptimal outcomes, including reduced ability to interpret labels and health messages, *limited ability to take medications appropriately* (emphasis added), lower likelihood of receiving preventive care, more hospitalizations, greater use of emergency care, and—among elderly people—worse overall health status and higher mortality rates.<sup>xv</sup>

Please see “Appendix C. BEST” for more information regarding best practices.

## 4. UMS RESEARCH

In a recent clinical trial led by Northwestern University's Feinberg School of Medicine (PI: Michael Wolf, PhD MPH), the UMS was randomly administered to a cohort of 425 patients from eight community health centers outside of Washington, D.C. – all of whom had Type 2 diabetes and hypertension.<sup>xvi</sup> Patients' ability to correctly demonstrate proper, safe use of their medications significantly increased over nine months compared to a usual-care arm that received medicines with instructions that followed a typical standard from a national pharmacy chain. At three months, those receiving the UMS had significantly greater adherence to their regimen as measured by pill count.

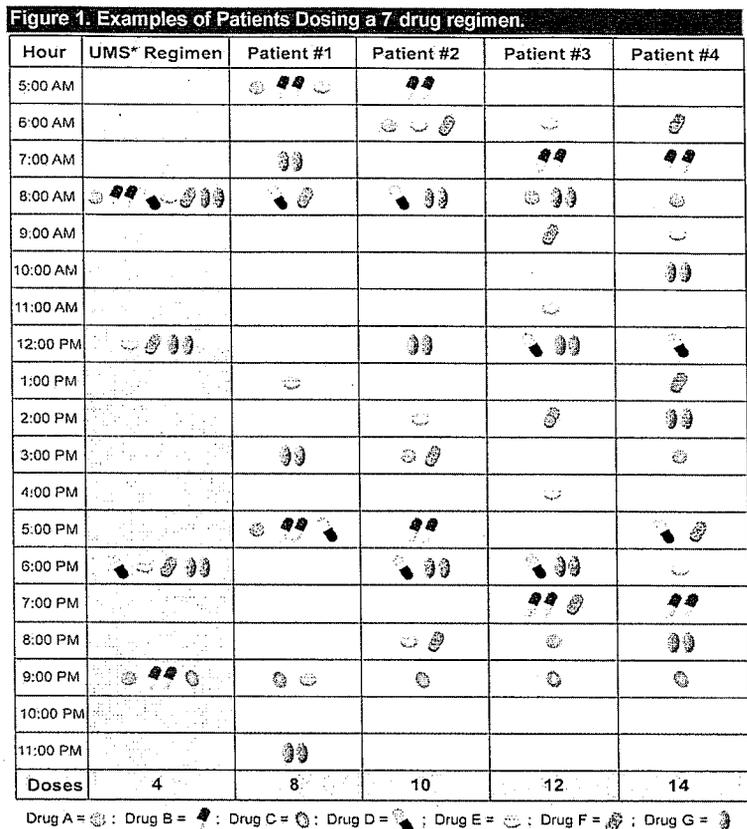
### The Universal Medication Schedule (UMS)

In the context of ambulatory care, patients assume primary responsibility for safely and appropriately administering prescription regimens. Yet the expectations placed on patients by the healthcare system for medication-related tasks are considerable.<sup>21</sup> Multiple steps need to occur for patients to gain the benefits of drug therapy while minimizing the risks of adverse drug events. This includes: 1) having a functional understanding of medications and their proper dosing, 2) consolidating the regimen to the most efficient daily schedule, 3) problem-solving around regimen use as changes occur, and 4) repeating the behaviors over time.

Studies have repeatedly documented that patients have problems performing these routine tasks.<sup>7,12,13,24</sup> This is alarming, as adults are being prescribed increasingly complex medication regimens.<sup>25</sup> Over the past decade, the percentage of Americans who take 5 or more prescription drugs has almost doubled; nearly 40% of older adults use at least 5 prescription medications.<sup>25</sup> While long-term adherence is essential to reap health benefits, all forms of non-adherence - failure to fill new prescriptions, incomplete use, and premature discontinuation - are common.<sup>26-31</sup> Non-adherence has been linked to greater morbidity and mortality from chronic conditions. Complex drug regimens also raise the risk for errors and adverse drug events, of which many are either preventable or ameliorable.<sup>32-37</sup> The 2006 IOM report, *Preventing Medication Errors*, suggests 1.5 million preventable adverse drug events occur annually, with a third occurring in outpatient settings.<sup>21</sup>

In the Veterans Administration study, 446 veterans were asked how many tablets per day they would take when given a prescription with the directions to "Take one tablet daily with meals". Only 42% of the respondents identified the correct answer. The VA NCPS has received numerous reports of medication mishaps caused by a lack of understanding by veterans on how to accurately adhere to the medication regimen as prescribed by their prescriber.

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**Limited Literacy.** Numerous studies have found limited literacy to be significantly associated with patients' poorer recall of medication names and indications, inadequate understanding and demonstrated use of prescription instructions and precautions.<sup>11-13,38-42</sup> The study team at Northwestern recently found that patients also may overcomplicate multi-drug regimens by taking medicine more times a day than necessary.<sup>7</sup> Lower literate patients were at greater risk for not consolidating medications [M=6.1 times/daily (SD=1.8); adequate literacy M=5.8 (SD=1.6) vs. low literacy M=6.5 (SD=2.4), p=0.03; see **Figure 1** for examples]. While studies have been inconclusive as to whether lower literacy is associated with non-adherence,<sup>43-46</sup> the evidence clearly suggests that patients with lower literacy are more likely to misunderstand prescription instructions, putting them at greater risk for poor adherence.<sup>24,47</sup>

**Limited English Proficiency.** Limited English Proficiency (LEP) is common in the US.<sup>48</sup> Research on language access in healthcare indicates serious barriers exist.<sup>48-53</sup> Interpreters are rarely available to aid prescribers and pharmacists in counseling LEP patients on safe prescription use, instructions are frequently unavailable in non-English languages, and multilingual materials are often inaccurate and poorly translated.<sup>54-57</sup> These barriers have been shown to have a deleterious effect on LEP patients' prescription use.<sup>14,15,58</sup> Wilson, *et al.* conducted a survey among 1,200 LEP adults speaking one of 11 languages in California.<sup>15</sup> In this study, more than one-third of LEP

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adults reported confusion about how to take medication, 42% stated that they encountered difficulties interpreting prescription container labels, and 16% reported experiencing an adverse reaction due to this confusion. Similarly, Sleath *et al.* conducted interviews with Spanish-speaking, Latino adults in North Carolina and found that 58% reported difficulty understanding English prescription instructions as a primary barrier to safe use.<sup>59</sup> This study found that less than a third of LEP Latinos consistently received prescription labels, verbal counseling, or print materials in Spanish.

**Health System Barriers.** Individual barriers to proper prescription use, such as limited literacy and LEP, are exacerbated (if not the result of) health system barriers.<sup>60</sup> For instance, multiple studies have shown prescribers often fail to discuss with patients basic information around the safe use of prescribed medicines, let alone other relevant concerns (i.e. cost of medications).<sup>61-65</sup> Furthermore, print prescription information is rarely distributed at the point of prescribing. Evidence also suggests that pharmacists equally fail to counsel patients on safe and appropriate prescription use.<sup>61,63,64</sup> While print materials (prescription labels, warning stickers, Medication Guides, patient leaflets) are provided by pharmacies, these materials are often poorly written and confusing.<sup>66-69</sup> In addition, considerable variability has been identified across this process.<sup>4,5,70</sup> Bailey *et al.* found prescription instructions written by prescribers to be highly variable,<sup>4</sup> and Wolf *et al.* reviewed prescription instructions printed by multiple pharmacies and also found that pharmacy translations often deviated from prescribers' instructions.<sup>5</sup> *An individual's ability to organize and properly dose out multiple medications becomes increasingly complex when factoring in such variability and poor quality in how prescriptions are written by prescribers and translated by pharmacies.*

**Figure 2. Universal Medication Schedule (UMS)**

Take	1 pill in the morning	
Take	1 pill in the morning 1 pill in the evening	 Morning: 6-8 am
Take	1 pill in the morning 1 pill at noon 1 pill in the evening	 Noon: 11-1 pm
Take	1 pill in the morning 1 pill at noon 1 pill in the evening 1 pill at bedtime	 Evening: 4-6 pm  Bedtime: 9-11 pm

The IOM 2008 report *Standardizing Medication Labels* recognized the need for setting standards within prescribing and dispensing practices to promote safe and accurate medication use for patients.<sup>2</sup> Members of the Northwestern research team presented the concept of the universal medication schedule (UMS) in this report. As approximately 90% of prescriptions are taken four times a day or less, the UMS was specifically

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proposed to establish four standard time intervals (morning, noon, evening, bedtime) for the prescribing and dispensing of medicine. This would remove the current variability found in the manner in which prescriptions are written by prescribers and transcribed by pharmacists.<sup>4,5,70</sup> All prescriptions would instruct patients to take their medicine at one or more of these specified times, and this would be described in a single, standardized fashion (**Figure 2**). Beyond standard times, UMS instructions also use simplified text, numeric characters instead of words to detail dose (i.e. 1 instead of 'one'), and 'carriage returns' to place each dose on a separate line to clearly identify every time period a medicine is to be taken.<sup>7</sup>

There is strong evidence supporting the UMS.<sup>2,7,9,10</sup> Among a multi-site sample of 500 primary care patients, Wolf *et al.* found those receiving UMS instructions versus a current standard were 33% more likely to accurately interpret prescription instructions.<sup>10</sup> Lower literate adults were also more likely to correctly comprehend the UMS instructions. These findings were replicated among 94 patients in Cork, Ireland, and also among 203 LEP patients in Chicago and San Francisco.<sup>71,72</sup> Earlier studies also found the use of more explicit time intervals such as those used in the UMS approach improved patient understanding and reduced medication errors.<sup>10,73</sup>

Our team's most recent efficacy trial of the UMS also found that those receiving UMS instructions were significantly more likely to consolidate prescription regimens to fewer times per day compared to those receiving standard instructions.<sup>74</sup> We have early evidence from our ongoing AHRQ/NIH-funded trial (885 English and Spanish-Speaking patients currently enrolled) testing the UMS at the point of pharmacy practice that patients may prefer UMS instructions.<sup>16</sup> *In reviewing the body of evidence on the UMS, The IOM issued favorable findings on the concept, the USP and American College of Physicians Foundation have recommended it as a standard, and the state of California passed legislation stating the UMS as a best practice for drug labeling.*<sup>1-3</sup>

### Limitations of UMS: What is known and not known

At present, repeated studies among diverse patient populations have demonstrated *efficacy* and *effectiveness* to the outcomes of improved comprehension, consolidation of regimens, and early evidence also highlights a two-fold improved rate of adherence as measured by pill count among diabetic patients receiving care at safety net settings (personal correspondence, Michael Wolf, August 2012). Whether or not improvements can be documented towards clinical outcomes is not known, yet that also should not be necessary. The UMS is meant to more clearly state instructions for multi-drug regimens, and benefits to adherence might be expected, however longer-term benefits and improvements in biomarkers are subject to many other barriers to proper self-care behaviors.

What remains to be tested, to complete the UMS concept, is further testing of the UMS for non-pill form drugs (liquids, inhalers, injectables, etc.) This work is under way with support from The California Healthcare Foundation. The current UMS has already been translated from English to Spanish, Chinese, Korean, Vietnamese, and Russian. Further language translations should be explored, for all instructions.

## 5. DISCUSSION

### 5.1 OPERATING ASSUMPTIONS/SCOPE

The focus of this paper is the information presented to the patient as a result of the prescription sent by the prescriber and received by the pharmacy. If UMS is used in the transmission of the electronic prescription, it must be displayed to both the sender and the receiver. The NCPDP Universal Medication Schedule Task Group acknowledges there may be confusion if the patient has additional information (monographs, auxiliary labels, previous prescription containers, etc.) that contain information that does not exactly align with the UMS. There will be a known transition period during implementation where prescribers and pharmacists must be prepared to address any questions or confusion with their patients.

While there does not appear to be any reason to believe that the UMS concept cannot be successfully applied to other dosage forms, research has not yet been published that specifically addresses the use of UMS on non-solid dosage forms and non-daily frequencies.

The simplicity of UMS can be augmented with additional instructions, such as "take with meals". The use of UMS will still require review by providers to handle unique situations, such as non-traditional work/sleep schedules; i.e. those patients who may work overnight.

The UMS offers more explicit patient-centric dosing times and better consolidated regimens and should be incorporated into medication therapy management and counseling. Drug interactions **within** a regimen need to be addressed by the provider.

While UMS is focused on the Sig, the task group recognizes that a transition to UMS should occur in concert with the development of a patient-centric label. Operational issues regarding the size and format of any new label design in addition to the practical aspects of implementing it will need to be addressed.

Legislation enacted in California in 2008 required the California State Board of Pharmacy to develop requirements for patient-centered labels to aid patient adherence to their prescribed medication therapy. Over a period of two years, the board surveyed consumers, pharmacists and others as well as convened hearings to develop the requirements, which took effect in January 2011. These requirements, establishing parameters for the first patient-centered labels in the US, specify that at least 50% of every prescription container label be dedicated exclusively to only the following elements: patient name, drug name and strength, directions for use, and if on the prescription document, the purpose of the medication. This information was deemed most important to patients. The dedicated section must be printed in at least a 10 point, sans serif font, but must be provided to the patient upon request in a 12 point font. The label must present all other required information on the label outside this dedicated space in a manner that does not detract from the patient-centered and clustered information.

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Within one year after implementation, surveys of the labels in use conducted by the Board of Pharmacy during inspections indicated that 60% of all labels were being printed directly in 12 point font, with another 25% of the labels being printed in both 10 point and 12 point fonts, and only 15% being printed (at least initially) in 10 point font.

Other elements of California's requirements establish standardized directions for use to be printed on the label "when appropriate" based on the pharmacist's judgment. These standardized directions, developed by UMS researchers Dr. Mike Wolf and Dr. Stacey Bailey, conform to UMS principles to maximize patient comprehension. The standardized directions have been translated into five languages to permit widespread availability of translations on prescription containers to limited English speaking patients.

### 5.2 BACKGROUND OF LABEL INFORMATION

What is perhaps not widely known or well understood is the process that results in the information printed on a prescription container label.

The information below, based on the *Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy (Model Act)* does not provide greater specificity regarding "Directions for Use", such as how the medication is to be administered, or the timing associated with the medication. As such, there is as much variety in "directions for use" as there are prescribers. See "*Appendix A. Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy August 2011*".

The state of California has added language in support of standardized directions to provide consistent directions for the patient and to enable accurate translation of the directions into the patient's preferred language. See "*APPENDIX B. California Statute*".

Additional requirements can be found in the Federal Food, Drug and Cosmetic Act, Subchapter V, Part A, Sections 352 and 353. Requirements specific to prescriptions containing controlled substances can be found in § 290.2.<sup>xvii</sup>

Laws vary from state to state, but generally, the following information is required on each prescription label.

- **Patient Name\***
- **Directions for use - *directions for use as indicated by the prescriber\****
- **Drug Name\***
- **Drug Strength\***
- "use by" date
- Important information for patients
  - pharmacy name;
  - pharmacy telephone number;
  - prescriber name;
  - "fill date;"
  - prescription number;
  - drug quantity;

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- number of remaining refills;
- written or graphic product description;
- auxiliary information;
- any cautions and other provisions which may be required by federal or state law.

The following additional information for Patients – may appear on the label:

- bar codes;
- pharmacy address; and
- store number.

\* **Items** that are considered critical information by the US Pharmacopeial Convention:

***Emphasize instructions and other information important to patients.*** Prominently display information that is critical for patients' safe and effective use of the medicine. At the top of the label specify the patient's name, drug name (spell out full generic and brand name) and strength, and explicit clear directions for use in simple language.

The prescription directions should follow a standard format so the patient can expect that each element will be in a regimented order each time a prescription is received. Other less critical but important content (e.g., pharmacy name and phone number, prescriber name, fill date, refill information, expiration date, prescription number, drug quantity, physical description, and evidence-based auxiliary information) should not supersede critical patient information. Such less critical information should be placed away from dosing instructions (e.g., at the bottom of the label or in another less prominent location) because it distracts patients, which can impair their recognition and understanding."

***Simplify language.*** Language on the label should be clear, simplified, concise, and familiar and should be used in a standardized manner.

***Give explicit instructions.*** Instructions for use (i.e., the SIG or signatura) should clearly separate the dose itself from the timing of each dose in order to explicitly convey the number of dosage units to be taken and when (e.g., specific time periods each day such as morning, noon, evening, and bedtime). Instructions shall include specifics on time periods. Do not use alphabetic characters for numbers. For example, write, "Take 2 tablets in the morning and 2 tablets in the evening" rather than "Take two tablets twice daily."

***Address limited English proficiency.*** Whenever possible, the directions for use on a prescription container label should be provided in the patient's preferred language.

In November 2012, USP published a new General Chapter <17> Prescription Container Labeling in USP 36–NF 31. <sup>xviii</sup> The standard provides, for the first time, a universal approach to the format, appearance, content and language of instructions for medicines in containers dispensed by pharmacists. The new USP general chapter offers specific

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direction to label manufacturers, pharmacies and prescribers on how prescription labels should be organized in a "patient-centered" manner that reflects how most patients seek out and understand medication instructions.

Patients' best (and often only) source of information regarding the medications they have been prescribed is on the prescription container label. Although other written information and oral counseling sometimes may be available, the prescription container label must fulfill the professional obligations of the prescriber and pharmacist. These obligations include giving the patient the most essential information needed to understand how to use the medication safely and appropriately and to adhere to the prescribed medication regimen.

The USP effort to create these new standards developed from an Institute of Medicine (IOM)-led initiative to improve health literacy, which is defined as the degree to which people can obtain, process and understand the basic health information and services they need to make appropriate health decisions. According to IOM, 77 million Americans have limited health literacy, and a majority of Americans have difficulty understanding and using currently available health information and services. At a 2007 IOM workshop on Standardizing Medication Labels: Confusing Patients Less, USP Chief Executive Officer Roger L. Williams pledged that the organization would initiate work on a standardized prescription container label. The resulting standard was finalized by the USP Nomenclature, Safety, and Labeling Expert Committee, which is chaired by Thomas Reinders, Pharm.D. The standard was developed by experts in patient safety, health literacy, pharmacy, medicine, human factors research and labeling technology. Key areas covered in General Chapter <17> include organizing the label in a patient-friendly way, using explicit language to describe dosages and intervals, improving readability with clear formatting, including "purpose for use" (e.g., "for high blood pressure") and addressing those with visual impairments and those with limited English comprehension.

Enforcement of the standard will be the decision of individual state boards of pharmacy, which may choose to adopt it into their regulations—similar to USP standards for sterile and non-sterile pharmaceutical compounding, both of which are widely recognized by states. At its 2012 annual meeting, the National Association of Boards of Pharmacy passed a resolution supporting state boards in requiring a standardized prescription container label.<sup>xix</sup>

The efforts of USP and NABP are intended to provide a standard patient centered prescription label that will be consistently applied nationally. More information is available at "*Appendix E. NABP Resolution*".

### **5.3 WHAT ARE THE BENEFITS AND CONSIDERATIONS OF USING UMS?**

It is anticipated that the use of UMS will not interfere with existing professional practice or communications.

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### Impact to the patient/caregiver:

- Increases understanding by simplifying the medication regimen.
- Simplifies the use of multiple medications.
- Inherent assumption that simplification and increased understanding will improve adherence and health outcomes.
- Provides additional opportunities for prescribers and pharmacists to communicate with the patient about the patient's regimen.

### Impact to the pharmacist/pharmacy team:

- Improves productivity, accuracy and workflow efficiencies due to standardization.
- Provides additional opportunities for counseling (as a result of staff availability from increased productivity/improved workflows) which may increase patient loyalty.
- Standardized content may ease translations to other languages.
- Increases interoperability when exchanging information across systems.
- Greater patient adherence likely leads to more consistent and regular refill schedule.
- Continued ability to exercise professional judgment when communicating prescriber's instructions or intent to the patient/caregiver. This includes the ability to support medication administration schedules in facilities.
- Greater clarity in the Sig (as received from the prescriber) may reduce the need for additional verification.

### Impact to the Prescriber:

- Reduces calls to the prescriber for clarification based on improved patient understanding of medication.
- While all patients can benefit from the use of UMS, there are care settings that may see greater impact such as federally qualified health centers, community clinics, geriatric practices, etc.
- Increases productivity efficiencies by using UMS rather than adding clarification to Sig.
- Impacts a variety of quality of care programs that affect prescribers including the Physician Quality Reporting System of CMS (Centers for Medicare & Medicaid Services). The measures reported by prescribers can impact reimbursement levels and patient satisfaction scores. As stated above, the Value Based Purchasing Regulations allow for provider reimbursement levels to be adjusted based upon the quality of care provided.
- Offers support for patient engagement measures under Meaningful Use Stage 2 by creating and transmitting prescription instructions using UMS and making that available to patients.
- New reimbursement models in the private sector, such as Accountable Care Organizations (ACO) also consider quality of care and patient outcomes measures when determining reimbursement agreements.
- Increases interoperability when exchanging information across systems.
- System modifications to support UMS or convert existing Sig "favorites" may require additional financial investment.
- May have to change prescribing practices depending on level of system modification that is completed. (i.e., user interface and practice).

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While the industry does not consistently track who actually picks up a prescription, there are various reports indicating that anywhere from 20%-60% of prescriptions are delivered to someone other than the patient. Given this, having easily understandable dosing information included on the prescription is incredibly important. As the industry considers the changing demographics of the American population, it is reasonable to presume that there will be more and more situations where there is an intermediary between the pharmacy and the patient.

With adoption and implementation of UMS, it is possible that EMRs and pharmacy systems will be able to view a patient's chronic medication regimens by day/week/month, rather than by medication. Such a view can assist with patient counseling and medication reconciliation resulting in improved adherence and outcomes.

The National Consumers League has launched a medication adherence campaign, "Script Your Future", to assist patients with managing their medication regimens. The campaign focuses on providing tools to assist patients in remembering to take their medications as instructed. <sup>xx</sup>

### 5.4 FORMAT AND TERMINOLOGY

Implementing UMS forces the industry to revisit discussions and decisions related to the format and terminology used on patient prescription labels. The state of California has been at the forefront of moving to a patient-centric label, requiring many of the elements outlined as part of the Model Act and adding additional requirements.

Patients are comfortable with the term "pill", yet many containers are labeled with "tablet", "tab", "capsule", "cap". While prescriptions may specify the actual dose form, the pharmacist should continue to have the discretion to provide the patient with the information that is most readily understood.

Because everyone processes information differently, there is likely value in adding visual images to the label to improve patient understanding. A study published in 2008 found a significant reduction in medication dosage errors when pictograms were used. <sup>xxi</sup>

"Medication counseling using a plain language, pictogram-based intervention resulted in fewer medication-dosage errors (5.4 percent versus 47.8 percent) and greater adherence, compared to standard medication counseling (38 percent versus 9.3 percent)".

According to the International Pharmaceutical Federation, "pictograms give health professionals a means of communicating medication instructions to people with no common language and/or who may be illiterate. Pictograms may also be used for those who have slight cognitive impairment or difficulties seeing such as the elderly."

The same type of simple imagery could be added to prescription labels. See "Appendix F. Imagery Examples".

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Using icons (and pictograms) is recommended only when proven through testing to improve consumer and patient understanding beyond simple explicit text alone.

Research shows that “not all of the patient-centered icons were effective at improving comprehension beyond the revised text. In particular, a few of the icons provided abstract imagery for messages that were more difficult to visually depict in such a small size. Given the limited space for content on prescription drug containers, it would be helpful to include only those icons that have been shown in consumer testing to significantly improve comprehension beyond simplified text alone.”<sup>xxii</sup>

Another recommendation from the research suggests that patients better understand how to take their medicine when the information is separated with each timing segment on a separate line.

As an example, instead of “Take two tablets three times daily”:

Take 2 pills in the morning,  
2 pills at noon, and  
2 pills in the evening.

### 5.5 TRANSLATION INTO OTHER LANGUAGES

Health literacy, especially among those with limited English proficiency (LEP), is a widely documented issue. Providing oral and/or written information in a patient's primary language is more likely to lead to greater comprehension, especially for those with limited health literacy. Improved comprehension can result in more successful adherence to medication regimens.

According to the 2010 Census,<sup>xxiii</sup> LEP individuals accounted for 25.2 million, or nine percent, of the US population over age 5. This reflects a growth of 80 percent in the prior 20 years. Of all people who speak a language other than English at home, about 66 percent speak Spanish. In 2010, five languages – Spanish, Chinese, Vietnamese, Korean and Tagalog – were spoken by 79 percent of all LEP individuals.

Given that approximately four billion prescriptions are filled each year, nearly 360 million are filled by those with LEP. Using the information presented earlier regarding LEP, it can be extrapolated that for approximately 120 million prescriptions, there is confusion about how to take the medication; that for approximately 50 million prescriptions, there is difficulty in interpreting the container label and over 19 million patients experienced an adverse reaction due to this confusion.

Providing consistent, structured terminology for patient instructions will likely ease translation efforts. Some translations using UMS are available in Chinese, Korean, Russian, Spanish and Vietnamese through the California Board of Pharmacy.<sup>xxiv</sup> More information on translation guidelines can be found in the “Toolkit for Making Written Material Clear and Effective”, as published by CMS.<sup>xxv</sup>

It should be noted that several states have requirements related to translations of prescription labels, and other items. Translations can occur via printed materials or with

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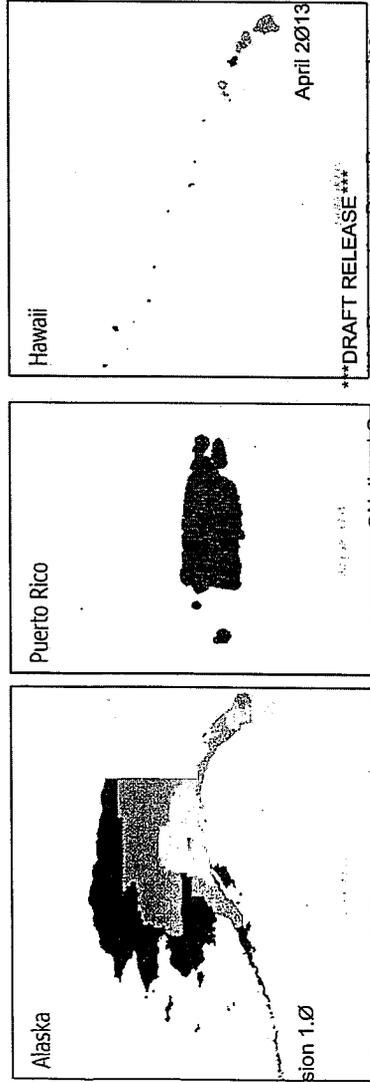
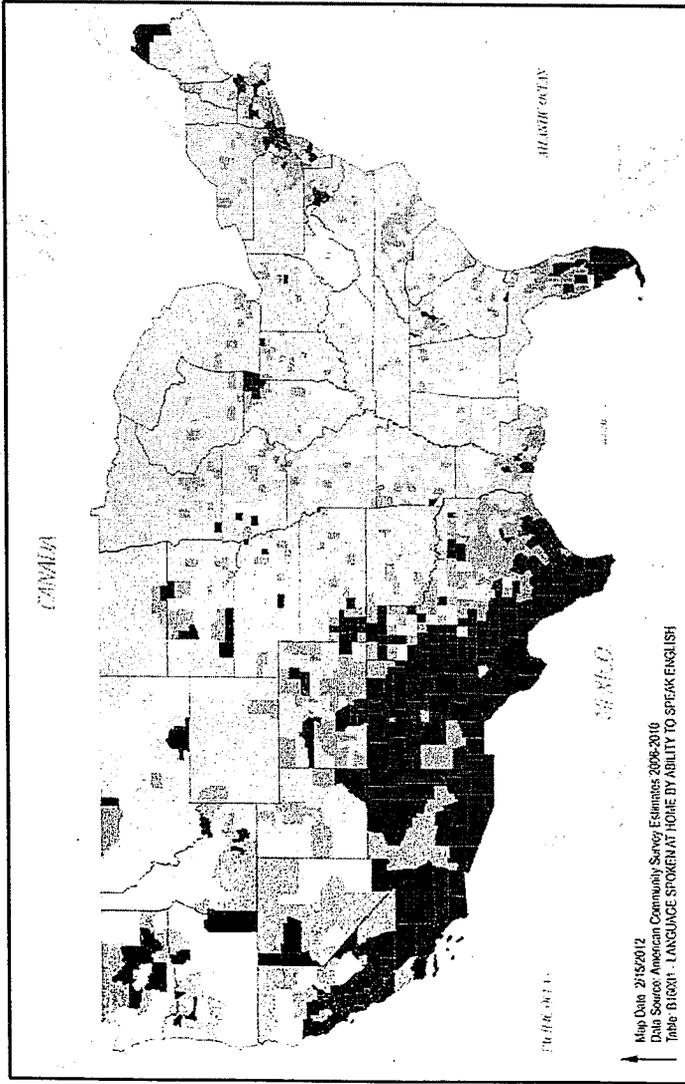
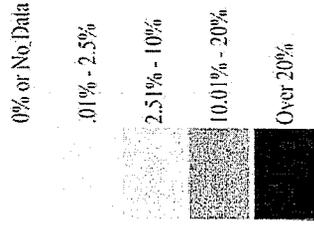
the use of interpreters. New York's requirements, as an example, are specific to pharmacies with a minimum of eight locations. The law requires that pharmacies provide free interpretation and translation services to customers with limited English proficiency (LEP) who request the services or fill a prescription that indicates that the customer is LEP.<sup>xxvi</sup>

The National Conference of State Legislatures has tracked initiatives at the state level to address medication errors.<sup>xxvii</sup>

The map below provides an illustration of the US population who speak a language other than English at home.

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Population Speak Other Language At Home



## **5.6 CHALLENGES IN ADOPTION AND IMPLEMENTATION**

As with any change, adoption and implementation of UMS will present stakeholders with challenges. Among the challenges to be considered are:

- Capacity of industry to implement in light of other activities, i.e. new and existing regulatory requirements, corporate initiatives, etc.
- Timing of implementation by trading partners – how is patient impacted?
- Changes in workflow process.
- Enabling the technology to support consistent execution and delivery.
- Role of professional organizations, state boards (pharmacy, medical, dental, etc.).
- Cost effectiveness.

## **5.7 ADOPTION AND IMPLEMENTATION RECOMMENDATIONS AND CONSIDERATIONS**

Prescribers and dispensers are highly encouraged to begin incorporating UMS into their practices. With the industry's transition to NCPDP SCRIPT version 10.6 for electronic prescribing, the use of UMS can be easily accomplished by leveraging the features that are included.

Adopting the use of UMS concurrently with the adoption of SCRIPT 10.6 will allow users to leverage the efforts already planned to achieve the additional benefit of UMS. If users will be including the Structured Sig in their 10.6 implementation, then incorporating UMS can be readily accomplished. Even if users are not planning to use the Structured Sig, existing Sig strings in EMR or pharmacy management systems can be mapped to UMS.

### **Items to consider when implementing UMS:**

- Community collaboration – ensuring that all community stakeholders (prescribers, pharmacies and payers) understand the timing of the upcoming changes and the implications for all involved.
  - The general consensus among the task group is that the “rip the bandage” approach may be the most effective, as the change would be made overnight, not in phases. This may or may not work for all stakeholders, depending upon their service area, and the readiness of their trading partners.
  - Identify opportunities to share implementation experiences with others.
- Communication plans, for internal (employee) and external (patient/customer/caregiver) recipients.
  - Opportunity to increase professional satisfaction via enhanced patient communication tools.
  - One chain saw great success with the use of counter mats when they introduced a new bottle and label design. The mat allowed for easy, comprehensive reference when pharmacists were counseling patients.
- Other related changes that will be visible to the patient

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- Conversion from APAP to acetaminophen
- Recommendations from USP Chapter 17
- Contractual impacts
  - Review trading partner agreements to determine if:
    - Amendments are needed to support use of UMS.
    - Transition to UMS is included in vendor system support.
    - Notice is required to be given to third party payers.
  - Identify opportunities to share implementation experiences with others.
- Workflow changes – as with any system enhancement, project teams will need to consider associated workflow changes.
  - Patient education opportunities at the prescriber's office or pharmacy.
  - Increased automation of label generation at the point of dispensing.
- Measurement – items that might be measured to demonstrate the impact of implementing and using UMS. Depending on what information is currently measured, isolating the impact of UMS may be difficult.
  - Patient/employee satisfaction scores
  - Call volume/clarification contacts
  - Errors
  - Adherence rates
  - Outcomes; perhaps even re-admission rates
  - Opportunities to improve (identified during implementation)

Throughout its discussions, the task group acknowledged two considerations. One, the reason for moving to UMS is for the patient – to improve outcomes and reduce potential errors. Two, the ability to measure a hard return on investment is limited. No studies have been done that have isolated the financial impact of UMS.

## 6. CONCLUSION

This paper explains the case for the industry to adopt the Universal Medication Schedule (UMS), a methodology that simplifies medication administration instructions for the patient and / or their caregiver, as a best practice. Use of UMS has the potential to improve patient care and increase positive outcomes. A recent study showed that patients receiving UMS instructions were 33% more likely to accurately interpret prescription instructions.

Use of UMS provides many benefits to patients/caregivers, pharmacists and prescribers, including:

- Increase in consistent patient understanding of and adherence to medication regimens.
- Simplification of the dosing regimen when using multiple medications.
- Standardization of dosing regimens will likely result in enhanced pharmacist and prescriber productivity, accuracy and workflow efficiencies.
- Ease of translation to other languages.

The adoption and incorporation of UMS into health care practice presents a significant opportunity for the industry to improve patient safety, promote better quality of care, and ensure more cost effective use of health care resources.

## APPENDIX A. MODEL STATE PHARMACY ACT AND MODEL RULES OF THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY AUGUST 2011

### Section 3. Pharmacy Practice.

- (a) Prescription Drug Order  
A Prescription Drug Order shall contain the following information at a minimum:
- (1) full name, date of birth, and street address of the patient;
  - (2) name, prescribing Practitioner's license designation, address, and, if required by law or rules of the Board, DEA registration number of the prescribing Practitioner;
  - (3) date of issuance;
  - (4) name, strength, dosage form, and quantity of Drug prescribed;
  - (5) directions for use;
  - (6) refills authorized, if any;
  - (7) if a written Prescription Drug Order, prescribing Practitioner's signature;
  - (8) if an electronically transmitted Prescription Drug Order, prescribing Practitioner's electronic or digital signature;
  - (9) if a hard copy Prescription Drug Order generated from electronic media, prescribing Practitioner's electronic or manual signature. For those with electronic signatures, such Prescription Drug Orders shall be applied to paper that utilizes security features that will ensure the Prescription Drug Order is not subject to any form of copying and/or alteration.
- (e) Labeling
- (1) All Drugs Dispensed for use by inpatients of a hospital or other health care facility, whereby the Drug is not in the possession of the ultimate user prior to Administration, shall meet the following requirements:
    - (i) The label of a single-unit package of an individual-dose or unit-dose system of packaging of Drugs shall include:
      - (A) the nonproprietary or proprietary name of the Drug;
      - (B) the route of Administration, if other than oral;
      - (C) the strength and volume, where appropriate, expressed in the metric system whenever possible;
      - (D) the control number and expiration date;
      - (E) identification of the repackager by name or by license number shall be clearly distinguishable from the rest of the label; and
      - (F) special storage conditions, if required.
    - (ii) When a multiple-dose Drug Distribution system is utilized, including Dispensing of single unit packages, the Drugs shall be Dispensed in a container to which is affixed a label containing the following information:
      - (A) identification of the Dispensing Pharmacy;
      - (B) the patient's name;
      - (C) the date of Dispensing;
      - (D) the nonproprietary and/or proprietary name of the Drug Dispensed; and

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- (E) the strength, expressed in the metric system whenever possible.
- (2) All Drugs Dispensed to inpatients for self-administration shall be Labeled in accordance with Subparagraph 4 of this Section (e).
- (3) Whenever any Drugs are added to parenteral solutions, such admixtures shall bear a distinctive label indicating:
- (i) name of solution, lot number, and volume of solution;
  - (ii) patient's name;
  - (iii) infusion rate;
  - (iv) bottle sequence number or other system control number;
  - (v) name and quantity of each additive;
  - (vi) date of preparation;
  - (vii) Beyond-Use Date and time of parenteral admixture; and
  - (viii) ancillary precaution labels.
- (4) All Drugs Dispensed to ambulatory or outpatients shall contain a label affixed to the container in which such Drug is Dispensed including:
- (i) *Critical Information for Patients – Critical information must appear on the label with emphasis (highlighted or bolded), in a sans serif typeface (such as "Arial"), minimum 12-point size, and in "sentence case." Field size and font size may be increased in the best interest of patient care. Critical information text should never be truncated and shall include:*
    - (A) *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.*
    - (B) *directions for use*
      - (-a-) *directions for use as indicated by the prescriber and medication purpose/indication if included on prescription drug order; and*
      - (-b-) *language should be simplified, avoiding unfamiliar words and medical jargon; when applicable, use numeric instead of alphabetic characters.*
    - (C) *drug name*
      - (-a-) *if written for a brand name and a generic drug is dispensed, include phrase "Generic for [brand name];"and*
      - (-b-) *include drug name suffixes, such as CD, SR, XL, XR, etc.*
    - (D) *drug strength*
    - (E) *"use by" date*
      - (-a-) *date after which medication should be used; not expiration date of medication or expiration date of prescription; and*
      - (-b-) *format as – "Use by: MM/DD/YY."*
  - (ii) *Important information for patients – Must appear on the label but should not supersede critical information for patients and shall include:*
    - (A) *pharmacy name;*

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- (B) *pharmacy telephone number;*
  - (C) *prescriber name;*  
(-a-) *format as – “Prescriber: [prescriber name].”*
  - (D) *“fill date;”*  
(-a-) *format as – “Date filled: MM/DD/YY.”*
  - (E) *prescription number;*
  - (F) *drug quantity;*  
(-a-) *format as – “Qty: [number].”*
  - (G) *number of remaining refills;*  
(-a-) *format as – “Refills: [number remaining]” or “No refills,”*  
*using whole numbers only and managing partial fills*  
*through the pharmacy recordkeeping system;*
  - (H) *written or graphic product description;*
  - (I) *auxiliary information;*
  - (J) *any cautions and other provisions which may be required by*  
*federal or state law.*
- (iii) *The following additional information for Patients – may appear on the label:*
- (A) *bar codes;*
  - (B) *pharmacy address; and*
  - (C) *store number.*
- (5) No radiopharmaceutical may be Dispensed unless a label is affixed to the immediate container bearing the following information:
- (i) the standard radiation symbol;
  - (ii) the words “Caution – Radioactive Material”; and
  - (iii) the prescription number.
- (6) No radiopharmaceutical may be Dispensed unless a label is affixed to the outer or Delivery container bearing the following information:
- (i) the standard radiation symbol;
  - (ii) the words “Caution – Radioactive Material”;
  - (iii) the radionuclide and chemical form;
  - (iv) the activity and date and time of assay;
  - (v) the volume, if in liquid form;
  - (vi) the requested activity and the calibrated activity;
  - (vii) the prescription number;
  - (viii) patient name or space for patient name. Where the patient’s name is not available at the time of Dispensing, a 72-hour exemption is allowed to obtain the name of the patient. No later than 72 hours after Dispensing the radiopharmaceutical, the patient’s name shall become a part of the Prescription Drug Order to be retained for a period of three years;
  - (ix) the name and address of the nuclear Pharmacy;
  - (x) the name of the Practitioner; and
  - (xi) the lot number of the prescription.
- (i) Patient Counseling
- (1) Upon receipt of a Prescription Drug Order and following a review of the patient’s record, a Pharmacist shall personally initiate discussion of matters which will enhance or optimize Drug therapy with each patient or

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caregiver of such patient. Such discussion shall be in Person, whenever practicable, or by telephone and shall include appropriate elements of Patient Counseling. Such elements may include the following:

- (i) the name and description of the Drug;
  - (ii) the dosage form, dose, route of Administration, and duration of Drug therapy;
  - (iii) intended use of the Drug and expected action;
  - (iv) special directions and precautions for preparation, Administration, and use by the patient;
  - (v) common severe side or adverse effects or interactions and therapeutic contraindications that may be encountered, including their avoidance, and the action required if they occur;
  - (vi) techniques for self-monitoring Drug therapy;
  - (vii) proper storage and appropriate disposal method(s) of unwanted or unused medication;
  - (viii) prescription refill information;
  - (ix) action to be taken in the event of a missed dose; and
  - (x) Pharmacist comments relevant to the individual's Drug therapy, including any other information peculiar to the specific patient or Drug.
- (2) Alternative forms of patient information shall be used to supplement Patient Counseling when appropriate. Examples include written information leaflets, pictogram labels, video programs, etc.
  - (3) A Pharmacist providing telepharmacy services across state lines shall:
    - (i) identify himself or herself to patients as a "licensed Pharmacist"; and
    - (ii) notify patients of the State in which he or she is currently licensed to Practice Pharmacy and registered to Practice Telepharmacy across state lines.
  - (4) Patient Counseling, as described above and defined in this Act, shall not be required for inpatients of a hospital or institution where other licensed health care professionals are authorized to Administer the Drug(s).  
A Pharmacist shall not be required to counsel a patient or caregiver when the patient or caregiver refuses such consultation.

### **Section 3(e)(4)(i)(B)(-a)-. Comment.**

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.

### **Section 3(e)(4)(ii). Comment**

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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.

### Section 3(e)(4)(ii)(A). Comment

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

### Section 3(e)(4)(ii)(B). Comment

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.

### Section 3(e)(4)(ii)(D). Comment

"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.

### Section 3(e)(4)(ii)(I). Comment

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

### Section 3(e)(4)(i), (ii), and (iii). Comment

Boards of pharmacy may consider utilizing these suggested labeling formats provided below.

Pharmacy Name:	Date Filled: MM/DD/YY	Cautions:
Phone:	Rx No.:	
<b>Purpose:</b>		Description:
<b>Patient Q. Name</b>		
Prescriber:		
<b>Take 1 tablet in the morning and 2 tablets at bedtime.</b>		
<b>Drug Name and Strength</b>		
Generic for:	Qty:	
<b>Discard after: MM/DD/YY</b>	Refills:	

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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:
---	---

### Section 3(i). Comment

The intent of this Section is to require that the Pharmacist personally initiate counseling for all new Prescriptions and to exercise his or her professional judgment for refills. Situations may arise, however, where the prescriber specifically indicates that a patient should not be counseled. In such circumstances, it is the responsibility of the Pharmacist to provide the best patient care through appropriate communication with the prescriber and to document the reason(s) for not providing counseling to the patient.

## APPENDIX B. CALIFORNIA STATUTE

### 4076.5. Standardized, Patient-Centered Prescription Labels; Requirements

(a) The board shall promulgate regulations that require, on or before January 1, 2011, a standardized, patient-centered, prescription drug label on all prescription medicine dispensed to patients in California.

(b) To ensure maximum public comment, the board shall hold public meetings statewide that are separate from its normally scheduled hearings in order to seek information from groups representing consumers, seniors, pharmacists or the practice of pharmacy, other health care professionals, and other interested parties.

(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.
- (3) Improved font types and sizes.
- (4) Placement of information that is patient-centered.
- (5) The needs of patients with limited English proficiency.
- (6) The needs of senior citizens.
- (7) Technology requirements necessary to implement the standards.

(d) The board may exempt from the requirements of regulations promulgated pursuant to subdivision (a) prescriptions dispensed to a patient in a health facility, as defined in Section 1250 of the Health and Safety Code, if the prescriptions are administered by a licensed health care professional. Prescriptions dispensed to a patient in a health facility that will not be administered by a licensed health care professional or that are provided to the patient upon discharge from the facility shall be subject to the requirements of this section and the regulations promulgated pursuant to subdivision (a). Nothing in this subdivision shall alter or diminish existing statutory and regulatory informed consent, patients' rights, or pharmaceutical labeling and storage requirements, including, but not limited to, the requirements of Section 1418.9 of the Health and Safety Code or Section 72357, 72527, or 72528 of Title 22 of the California Code of Regulations.

(e) (1) The board may exempt from the requirements of regulations promulgated pursuant to subdivision (a) a prescription dispensed to a patient if all of the following apply:

- (A) The drugs are dispensed by a JCAHO-accredited home infusion or specialty pharmacy.
- (B) The patient receives health-professional-directed education prior to the beginning of therapy by a nurse or pharmacist.
- (C) The patient receives weekly or more frequent follow-up contacts by a nurse or pharmacist.
- (D) Care is provided under a formal plan of care based upon a physician and surgeon's orders.

(2) For purposes of paragraph (1), home infusion and specialty therapies include parenteral therapy or other forms of administration that require regular laboratory and patient monitoring.

(f) (1) On or before January 1, 2010, the board shall report to the Legislature on its progress under this section as of the time of the report.

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(2) On or before January 1, 2013, the board shall report to the Legislature the status of implementation of the prescription drug label requirements adopted pursuant to this section.

### **1707.5. Patient-Centered Labels for Prescription Drug Containers; Requirements**

(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.

(C) The directions for the use of the drug.

(D) The condition or purpose for which the drug was prescribed if the condition or purpose is indicated on the prescription.

(2) For added emphasis, the label shall also highlight in bold typeface or color, or use blank space to set off the items listed in subdivision (a)(1).

(3) The remaining required elements for the label specified in section 4076 of the Business and Professions Code, as well as any other items of information appearing on the label or the container, shall be printed so as not to interfere with the legibility or emphasis of the primary elements specified in paragraph (1) of subdivision (a). These additional elements may appear in any style, font, and size typeface.

(4) When applicable, directions for use shall use one of the following phrases:

(A) Take 1 [insert appropriate dosage form] at bedtime

(B) Take 2 [insert appropriate dosage form] at bedtime

(C) Take 3 [insert appropriate dosage form] at bedtime

(D) Take 1 [insert appropriate dosage form] in the morning

(E) Take 2 [insert appropriate dosage form] in the morning

(F) Take 3 [insert appropriate dosage form] in the morning

(G) Take 1 [insert appropriate dosage form] in the morning, and Take 1 [insert appropriate dosage form] at bedtime

(H) Take 2 [insert appropriate dosage form] in the morning, and Take 2 [insert appropriate dosage form] at bedtime

(I) Take 3 [insert appropriate dosage form] in the morning, and Take 3 [insert appropriate dosage form] at bedtime

(J) Take 1 [insert appropriate dosage form] in the morning, 1 [insert appropriate dosage form] at noon, and 1 [insert appropriate dosage form] in the evening

(K) Take 2 [insert appropriate dosage form] in the morning, 2 [insert appropriate dosage form] at noon, and 2 [insert appropriate dosage form] in the evening

(L) Take 3 [insert appropriate dosage form] in the morning, 3 [insert appropriate dosage form] at noon, and 3 [insert appropriate dosage form] in the evening

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(M) Take 1 [insert appropriate dosage form] in the morning, 1 [insert appropriate dosage form] at noon, 1 [insert appropriate dosage form] in the evening, and 1 [insert appropriate dosage form] at bedtime

(N) Take 2 [insert appropriate dosage form] in the morning, 2 [insert appropriate dosage form] at noon, 2 [insert appropriate dosage form] in the evening, and 2 [insert appropriate dosage form] at bedtime

(O) Take 3 [insert appropriate dosage form] in the morning, 3 [insert appropriate dosage form] at noon, 3 [insert appropriate dosage form] in the evening, and 3 [insert appropriate dosage form] at bedtime

(P) If you have pain, take \_\_\_ [insert appropriate dosage form] at a time. Wait at least \_\_\_ hours before taking again. Do not take more than \_\_\_ [appropriate dosage form] in one day

(b) By October 2011, and updated as necessary, the board shall publish on its Web site translation of the directions for use listed in subdivision (a)(4) into at least five languages other than English, to facilitate the use thereof by California pharmacies.

(c) Beginning in October 2011 the board shall collect and publish on its Web site examples of labels conforming to these requirements, to aid pharmacies in label design and compliance.

(d) The pharmacy shall have policies and procedures in place to help patients with limited or no English proficiency understand the information on the label as specified in subdivision (a) in the patient's language. The pharmacy's policies and procedures shall be specified in writing and shall include, at minimum, the selected means to identify the patient's language and to provide interpretive services in the patient's language. If interpretive services in such language are available, during all hours that the pharmacy is open, either in person by pharmacy staff or by use of a third-party interpretive service available by telephone at or adjacent to the pharmacy counter.

(e) The board shall re-evaluate the requirements of this section by December 2013 to ensure optimal conformance with Business and Professions Code section 4076.5.

(f) As used in this section, "appropriate dosage form" includes pill, caplet, capsule or tablet.

Authority cited: Sections 4005 and 4076.5, Business and Professions Code. Reference: Sections 4005, 4076, and 4076.5, Business and Professions Code.

## APPENDIX C. BEST PRACTICE RESEARCH

### SUPPORTING EVIDENCE

**MALLENBAKER.NET:** <http://www.mallenbaker.net/csr/post.php?id=429>

- "In my view, Best Practice must surely be able to demonstrate a superior outcome achieved because of the way the thing has been done."

**WIKIPEDIA:** [http://en.wikipedia.org/wiki/Best\\_practice](http://en.wikipedia.org/wiki/Best_practice)

- In recent years, public agencies and NGOs have been exploring and adopting best practices when delivering health and human services. In these settings, the use of the terms "promising practices", "best practices", and "evidence-based practices" is common and often confusing as there is not a general consensus on what constitutes promising practices or best practices.
- **DHHS:** A general working definition used by the U.S. Department of Health and Human Services (HHS) in referring to a promising practice is defined as one with at least preliminary evidence of effectiveness in small-scale interventions or for which there is potential for generating data that will be useful for making decisions about taking the intervention to scale and generalizing the results to diverse populations and settings. (Reference: U.S. Department of Health and Human Services, Administration for Children and Families Program Announcement, 2003).
  - Since evidence of effectiveness, potential for taking the intervention to scale and generalizing the results to other populations and settings are key factors for best practices, the manner in which a method or intervention becomes a best practice can take some time and effort.
- **NREPP:** The National Registry of Evidence-Based Programs and Practices (NREPP) (External Link: <http://nrepp.samhsa.gov>) is a searchable online registry of interventions supporting substance abuse prevention and mental health treatment that have been reviewed and rated by independent reviewers
  - Minimum requirements include:
    - demonstration of one or more positive outcomes among individuals, communities, or populations
    - evidence of these outcomes has been demonstrated in at least one study using an experimental or quasi-experimental design
    - the results of these studies have been published in a peer-reviewed journal or other professional publication, or documented in a comprehensive evaluation report
    - implementation materials, training and support resources, and quality assurance procedures have been developed and are ready for use by the public.
- **CDRP:** There is existing controversy about the lack of culturally appropriate evidence-based best practices and the need to utilize a research-based approach to validate interventions. Some communities have deployed practices over a long period of time that have produced positive outcomes as well as a general community consensus to be successful. The California Reducing Disparities Project (CRDP) is working to identify such practices. (External Link:

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[http://www.dmh.ca.gov/Multicultural\\_Services/CRDP.asp](http://www.dmh.ca.gov/Multicultural_Services/CRDP.asp)) CRDP intends to improve access, quality of care, and increase positive outcomes for racial, ethnic and cultural communities.

**FEDERAL REGISTER:** <http://www.gpo.gov/fdsys/pkg/FR-2003-07-09/pdf/03-17395.pdf>

- Federal Register referenced above in Wikipedia article

### **THE HEALTH TELEVISION SYSTEM:**

<http://www.healthtvsystem.com/pressrm/docs/1167076048.PDF>

- Comments from The Joint Commission and ISMP, two standards-setting organizations, represented:
  - Standards are just starting point
  - Standards don't go into sufficient detail to actually get the job done
  - Even if guidelines are prescriptive, they're on a patient by patient basis
  - When there's a variation, there's a rationale, and we all learn
- Interpretations: HEALTH OUTCOMES
  - The development of Best Practice Guidelines as relates to Patient Education will benefit from an understanding of and agreement on terminology and expectations.
  - The interpretations and definitions of health outcomes resulted in refining and honing criteria for Patient Education Best Practice Guidelines that will help in meeting patient specific educational needs and expectations.
  - Depending on patient population, outcomes can relate to:
    - Quality-of-life indicators
    - Functional indicators
    - Morbidity
    - These indicators incorporate subsets: e.g. medication compliance
    - Intent of education is to inform rather than persuade
    - Therapy/recovery strategy will be negotiated with patient
    - Patient's expectations of outcomes may be very different from those of the healthcare providers/educators
    - Outcome is based on patient's objectives, and the desired benefit that the patient wants to achieve
    - Focus must be on patient's perception of and satisfaction with the outcome (i.e. the healthcare provider may think the patient is doing just fine)
    - The healthcare provider's outcome expectations and obligations often focus on: 'You must take'/'You must do' instead of patients' wants and needs

### **NATIONAL RESOURCE CENTER:**

[http://www.acf.hhs.gov/programs/ocs/ccf/about\\_ccf/qbk\\_pdf/pp\\_gbk.pdf](http://www.acf.hhs.gov/programs/ocs/ccf/about_ccf/qbk_pdf/pp_gbk.pdf)

Research Validated	A program, activity or strategy that has the highest degree of proven effectiveness supported by objective and comprehensive research and
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Best Practice	evaluation.
Field Tested Best Practice	A program, activity or strategy that has been shown to work effectively and produce successful outcomes and is supported to some degree by subjective and objective data sources.
Promising Practice	A program, activity or strategy that has worked within one organization and shows promise during its early stages for becoming a best practice with long term sustainable impact. A promising practice must have some objective basis for claiming effectiveness and must have the potential for replication among other organizations.

<b>Criteria for Differentiating Types of Practices</b>	
Research Validated Best Practice	<ul style="list-style-type: none"> <li>■ Proven effectiveness in addressing a common problem.</li> <li>■ Proven effectiveness in more than one organization and in more than one context.</li> <li>■ Replicability on a broad scale.</li> <li>■ Conclusive data from comparison to objective benchmarks with positive results.</li> <li>■ Conclusive data from a comprehensive and objective evaluation by an external, qualified source (most often an academic institution or individual with the appropriate academic credentials).</li> </ul>
Field Tested Best Practice	<ul style="list-style-type: none"> <li>■ Effectiveness in addressing a common problem.</li> <li>■ Effectiveness in more than one organization and in more than one context.</li> <li>■ Replicability on a limited scale.</li> <li>■ Supporting data from comparison to objective benchmarks with positive results.</li> <li>■ Supporting data from an internal assessment or external evaluation.</li> </ul>
Promising Practice	<ul style="list-style-type: none"> <li>■ Suggested effectiveness in addressing a common problem.</li> <li>■ Successful use in one organization and context.</li> <li>■ Potential for replicability.</li> <li>■ Limited supporting data from comparison to objective benchmarks with positive results.</li> <li>■ Limited supporting data from internal assessment.</li> </ul>

**JOURNAL OF YOUNG PHARMACISTS:**

<http://www.jyoungpharm.in/article.asp?issn=0975-1483;year=2010;volume=2;issue=1;spage=107;epage=111;aulast=Jeetu>

- There is evidence available to detail "best practices" for improving dosage or usage instructions written by the prescribing physician and the format and content of prescription medication container labels designed by the dispensing pharmacy.
- A complete list of evidence-based, recommended standards for format, content, and instruction is as follows:
  - Use explicit text to describe dosage and interval in instructions.
  - Use a universal medication schedule (UMS) to convey and simplify dosage and use instructions.
  - Organize labels in a patient-centered manner.
  - According to need, include indication for use.
  - Simplify language, avoiding unfamiliar words or medical jargon.
  - Improve typography, use larger, sans serif font.
  - When applicable, use numeric versus alphabet characters.
  - Use typographic cues (bolding and highlighting) for patient content only.
  - Use horizontal text only.
  - Use a standard icon system for signaling and organizing auxiliary warnings and instructions.

**US PHARMACOPEIA:**

<http://us.vocuspr.com/ViewAttachmentStrict.aspx?EID=bK0ke822q8svy24Psob15hb/gmKMwnuDvYOUhHwyiw=>

<http://www.usp.org/usp-nf/notices/retired-compendial-notices/usp-seeks-comments-proposed-general-chapter-prescription-container-labeling>

- The new standards, developed by the U.S. Pharmacopeial Convention (USP)—the nonprofit scientific organization that sets FDA-enforceable standards for the quality, purity and strength of medicines in the United States—are the result of a broad effort led by the Institute of Medicine (IOM) to improve health literacy in the United States by bringing together government, industry, associations and other groups to advance practical strategies that can be implemented to maximize patient comprehension of health information.
- Generally, the new standards propose that prescription container labels generated by pharmacies:
  - Are organized in a patient-centered manner—Organized in a way that best reflects how most patients understand medication instructions, featuring the most important information for safe and effective understanding and use.
  - Emphasize instructions and other important information to patients—Prominently display information that is critical to patient's safe and effective use of the medicine, such as, patient's name, drug name and strength, and clear directions for use. Less critical but important content (e.g., pharmacy name and number) should not supersede critical patient information.

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- Give explicit instructions—Instructions should clearly separate the dose itself from the timing of each dose and use numeric characters (e.g., “Take 2 tablets in the morning and 2 tablets in the evening” rather than “Take two tablets twice daily”).
- Include purpose for use—The medication’s purpose should be included on the label unless the patient prefers that it not appear. When included, use clear, simple terms (e.g., “for high blood pressure” rather than “for hypertension”).
- Improve readability—The label type should use high-contrast print (e.g. black print on white background); large font size (e.g., minimum 12-point Times New Roman or 11-point Arial); and horizontal text only.
- Limit auxiliary information—Labels, stickers, or other supplemental information should be expressed in simple and explicit language that is minimized to avoid distracting patients with nonessential information.

**FDA/NCPDP:** <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM266631.pdf>

5	<p><b>Recommendation: Patient-Centered Pharmacy Warning Labels</b></p> <ul style="list-style-type: none"><li>• Employ general health literacy and plain language principles on the warning label to promote patient readability and understanding.</li><li>• Patient-centered labels should reflect strategies (simple, clear language; font type and size) that promote optimal readability of critical information, consistent with recommendations by health literacy experts, plain language experts, and other organizations that have addressed patient-centered approaches to labeling in order to maximize readability and patient comprehension.</li></ul>
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## APPENDIX D. TARGET CLEARRX IMPLEMENTATION

### ClearRx: The Future of Pharmacy

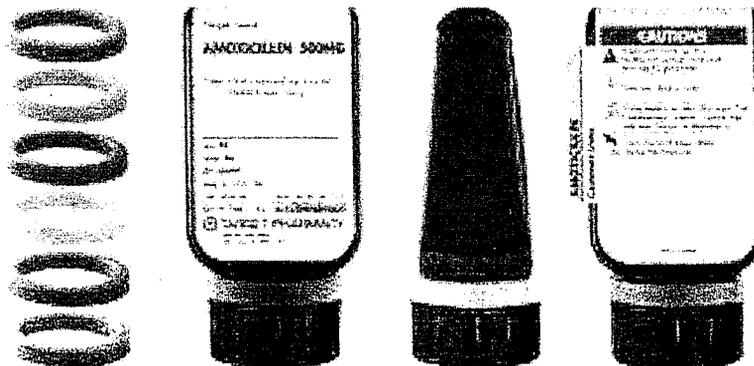
*Target Introduces Innovation with Safety and Design for Guests*

**Minneapolis, MN (May 1, 2005)** — Target® introduced today ClearRx™, an innovative prescription distribution and communication system. ClearRx is a pharmacy concept that offers improvements in medication packaging and design, prescription and health information and patient communication.

"Improved consumer understanding and increased quality of care were driving forces behind this new system. Each year in the United States, as many as 3 billion prescriptions are administered which create significant opportunities for error," said Dr. Linda Rosenstock, dean of the University of California, Los Angeles School of Public Health. "An improved prescription distribution and communication system like ClearRx is a real step forward in helping patients better understand and more easily use the medications their physicians prescribe."

A recent survey commissioned by Target and conducted by Harris Interactive® revealed that nearly six out of 10 U.S. adults have taken prescription medication incorrectly. The same survey found the following reasons for why adults rarely or never read their prescription information sheets: the language is standard and does not vary from prescription to prescription, and information is too wordy, overwhelming, complex and incomprehensible.

"ClearRx makes it easier for people to understand how to take their medication," says Deborah Adler, ClearRx innovator and principal designer. "By rethinking the prescription bottle and label, we have created a new system that we think minimizes confusion for the consumer, such as misreading a dosage or taking another family member's medication. Ultimately, we hope that ClearRx will allow people to feel more confident and secure when it comes to filling their prescriptions and taking their medication."



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### FEATURES OF CLEARRX

In an effort to address the growing concern of medication errors, ClearRx was designed to offer the following benefits:

**Re-designed Bottle** — The new shape, which can easily be gripped and opened, places all the vital information right in the palm of the hand.

**Easy-to-Read Label** — Designed for readability and ease-of-use, this label sits flat across the front panel of the bottle so the bottle does not have to be turned to read the pertinent information. Type and easy-to-read fonts make information clearer to identify. In addition, prescription information is re-organized with the most important information—including drug name and prescribing instructions—at the top of the label accompanied by doctor name and prescription number.

**Removable Information Card** — Tucked securely on the back of the bottle in a permanent sleeve, this newly created information card summarizes the most common uses and side effects associated with the medication. This innovative card is ideal for quick reference and includes reader-friendly fonts and more comprehensive text.

**Color-Coded Ring** — For multi-member households, color-coded rings on the neck of the bottle help clearly identify each person's medication at-a-glance.

**Re-Designed Warning Icons** — Newly located on the flat back surface of the ClearRx bottle — these re-designed icons make important medical warnings clearer and easier to understand.

"This introduction allows us the opportunity to impact our guests in a meaningful and relevant way," remarked Mary Kelly, vice president, health & beauty and pharmacy, Target. "Great Design is so much a part of our DNA at Target. We brought this same belief of improving people's lives through great design to Target Pharmacy in a logical way with the introduction of ClearRx."

ClearRx will be available exclusively at Target Pharmacies nationwide starting this month.

#### Methodology

Harris Interactive® conducted the survey for Target by telephone between December 17 and 20, 2004 among a nationwide cross section of 1,033 U.S. adults aged 18 and older, of who 132 say they rarely or never read the prescription information card that comes with the prescription. Figures for age, sex, race, education, number of adults, number of voice/telephone lines in the household, region and size of place were weighted where necessary to align them with their actual proportions in the population.

In theory, with a probability sample of this size, one can say with 95 percent certainty that the results for the overall sample have a sampling error of plus or minus 3 percentage points. Sampling error for the adults who rarely or never read the prescription information card results is plus or minus 9 percentage points.

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## APPENDIX E. NABP RESOLUTION

<http://www.nabp.net/news/uniform-outpatient-pharmacy-prescription-container-labels-designed-for-patient-safety-resolution-108/>

Uniform Outpatient Pharmacy Prescription Container Labels Designed for Patient Safety  
(Resolution 108-1-12)  
May 25, 2012 01:14 PM

Topics: Resolutions

Resolution No. 108-1-12

Title: Uniform Outpatient Pharmacy Prescription Container Labels Designed for Patient Safety

Action: Pass

Whereas, medication misuse has resulted in more than one million adverse drug events per year in the United States; and

Whereas, patients' best source (and often only source) of information regarding the medications they have been prescribed is on the prescription container label; and

Whereas, other written information and oral counseling should be available, the prescription container label must fulfill the professional obligations of the prescriber and pharmacist; and

Whereas, these obligations include giving the patient the most essential information needed to understand how to safely and appropriately use the medication and to adhere to the prescribed medication regimen; and

**Whereas, the purpose of the prescription label is for the patient, not the regulator or auditor; as such, the only information needed on the label is information the patient needs to take the medication correctly; and**

Whereas, the National Association of Boards of Pharmacy (NABP), US Pharmacopeial Convention and the Institute for Safe Medication Practices have researched, identified, and agreed upon elements that do need to be on the patient prescription container label to ensure patient safety; and

**Whereas, the elimination of data elements not required for patient safety will increase readability and understanding by allocating more white space, increasing the ability to use larger font size, providing more space so as not to truncate medication names or directions, and affording space for a description of the medication on the patient's medication container label; and**

Whereas, these various labeling standards could potentially create a risk for patient confusion due to various jurisdictions requiring differing label formats, thus defeating the goal of a uniform, patient centered label;

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THEREFORE BE IT RESOLVED that NABP support the state boards of pharmacy in their efforts to require a standardized prescription container label recommended by the 2008-2009 NABP Task Force on Uniform Prescription Labeling Requirements, the elements of which are found in the *Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy*.

(Resolution passed at the NABP 108<sup>th</sup> Annual Meeting, Philadelphia, PA)

## APPENDIX F. IMAGERY EXAMPLES

From FIP website (<http://www.fip.org/pictograms>)

Pictograms give health professionals a means of communicating medication instructions to people with no common language and / or who may be illiterate. Pictograms may also be used for those who have slight cognitive impairment or difficulties seeing such as the elderly. To help improve communication, various formats of the medication instructions can be printed (see below):

- A label with customizable size
- A medication information sheet for one medication
- A prescription calendar that combines all medicines
- A storyboard of a medication

Medication instructions included:

- Medication name
- Route and quantity of medicines per dose
- Frequency

Optional instructions to include on information sheets:

- The picture of the medication
- Reason(s) for use
- Precautions
- Side effects (up to 2)

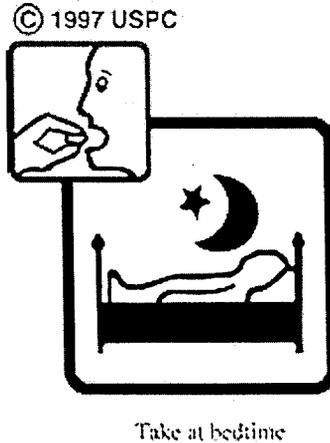
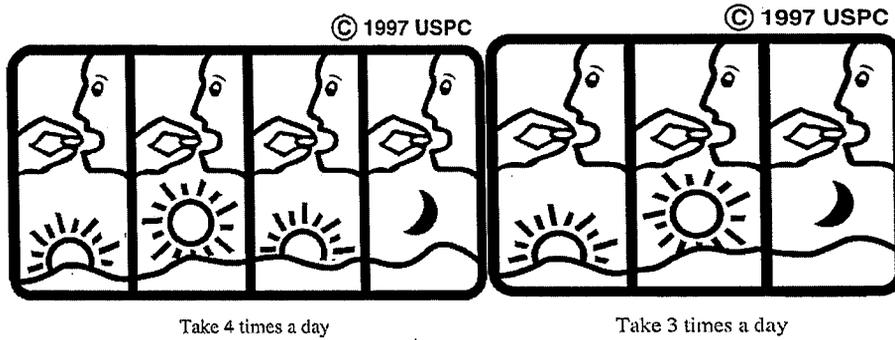
<b>Penicillin</b>		<b>Administrator</b>		
RX# 2341		2011/08/12		
<b>REF # B4B6 7AAE FD90 6B06</b>				
				
10.m		12.00		
GIVE USING MEDICATION SPOON THREE TIMES DAILY. TAKE WITH WATER.				
Quantity: 5			Refills:2	

The same type of simple imagery could be added to prescription labels:

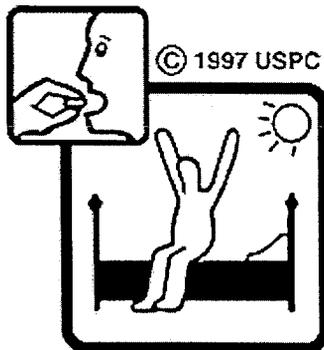
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	Morning:	6-8 am
	Noon:	11-1 pm
	Evening:	4-6 pm
	Bedtime:	9-11 pm

The US Pharmacopeial provided the following sample pictograms:



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Take in the morning

Breakfast	Lunch	Dinner	Bedtime
1		1	

Copyright © Polyglot Systems, Inc.

once daily	X			
twice a day	X		X	
three times a day	X	X	X	
four times a day	X	X	X	X
evening			X	
bedtime				X

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## 14 ENDNOTES

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Add the following:

## ◊ (17) PRESCRIPTION CONTAINER LABELING

### INTRODUCTION

Medication misuse has resulted in more than 1 million adverse drug events per year in the United States. Patients' best source (and often only source) of information regarding the medications they have been prescribed is on the prescription container label. Although other written information and oral counseling sometimes may be available, the prescription container label must fulfill the professional obligations of the prescriber and pharmacist. These obligations include giving the patient the most essential information needed to understand how to safely and appropriately use the medication and to adhere to the prescribed medication regimen.

Inadequate understanding of prescription directions for use and auxiliary information on dispensed containers is widespread. Studies have found that 46% of patients misunderstood one or more dosage instructions, and 56% misunderstood one or more auxiliary warnings. The problem of misunderstanding is particularly troublesome in patients with low or marginal literacy and in patients receiving multiple medications that are scheduled for administration using unnecessarily complex, nonstandardized time periods. In one study, patients with low literacy were 34 times more likely to misinterpret prescription medication warning labels. However, even patients with adequate literacy often misunderstand common prescription directions and warnings. In addition, there is great variability in the actual auxiliary warning and supplemental instructional information applied by individual practitioners to the same prescription. The specific evidence to support a given auxiliary statement often is unclear, and patients often ignore such information. The essential need for, and benefit of, auxiliary label information (both text and icons) in improving patient understanding about safe and appropriate use of their medications vs. explicit simplified language alone require further study.

Lack of universal standards for labeling on dispensed prescription containers is a root cause for patient misunderstanding, nonadherence, and medication errors. On May 18, 2007, the USP Safe Medication Use Expert Committee established an Advisory Panel to: 1) determine optimal prescription label content and format to promote safe medication use by critically reviewing factors that promote or distract from patient understanding of prescription medication instructions and 2) create universal prescription label standards for format/appearance and content/language.

In November 2009, the Health Literacy and Prescription Container Labeling Advisory Panel presented its recommendations to the Safe Medication Use Expert Committee, which then requested that USP develop patient-centered label standards for the format, appearance, content, and language of prescription medication instructions to promote patient understanding. These recommendations form the basis of this general chapter.

Note—These standards do not apply when a prescription drug will be administered to a patient by licensed personnel who are acting within their scope of practice.

### 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 container labeling should feature only the most important patient information needed for safe and effective understanding and use.

Emphasize instructions and other information important to patients: Prominently display information that is critical for patients' safe and effective use of the medicine. At the top of the label specify the patient's name, drug name (spell out full generic and brand name) and strength, and explicit clear directions for use in simple language.

The prescription directions should follow a standard format so the patient can expect that each element will be in a regimented order each time a prescription is received.

Other less critical but important content (e.g., pharmacy name and phone number, prescriber name, fill date, refill information, expiration date, prescription number, drug quantity, physical description, and evidence-based auxiliary information) should not supersede critical patient information. Such less critical information should be placed away from dosing instructions (e.g., at the bottom of the label or in another less prominent location) because it distracts patients, which can impair their recognition and understanding.

Simplify language: Language on the label should be clear, simplified, concise, and familiar, and should be used in a standardized manner. Only common terms and sentences should be used. Do not use unfamiliar words (including Latin terms) or medical jargon.

Use of readability formulas and software is not recommended to simplify short excerpts of text like those on prescription labels. Instead, use simplified, standardized sentences that have been developed to ensure ease of understanding the instructions correctly (by seeking feedback from samples of diverse consumers).

Give explicit instructions: Instructions for use (i.e., the SIG or signatur) should clearly separate the dose itself from the timing of each dose in order to explicitly convey the number of dosage units to be taken and when (e.g., specific time periods each day such as morning, noon, evening, and bedtime). Instructions shall include specifics on time periods. Do not use alphabetic characters for numbers. For example, write "Take 2 tablets in the morning and 2 tablets in the evening" rather than "Take two tablets twice daily".

Whenever available, use standardized directions (e.g., write "Take 1 tablet in the morning and 1 tablet in the evening" if the prescription reads b.i.d.). Vague instructions based on dosing intervals such as twice daily or 3 times daily, or hourly intervals such as every 12 hours, generally should be avoided because such instructions are implicit rather than explicit, they may involve numeracy skills, and patient interpretation may vary from prescriber intent. Although instructions that use specific hourly times (e.g., 8 a.m. and 10 p.m.) may seem to be more easily understood than implicit vague instructions, recommending dosing by precise hours of the day is less readily understood and may present greater adherence issues due to individual lifestyle patterns, e.g., shift work, than more general time frames such as in the morning, in the evening, after breakfast, with lunch, or at bedtime. Consistent use of the same terms should help avoid patient confusion.

Ambiguous directions such as "take as directed" should be avoided unless clear and unambiguous supplemental instructions and counseling are provided (e.g., directions for use that will not fit on the prescription container label). A clear statement referring the patient to such supplemental materials should be included on the container label.

**Include purpose for use:** If the purpose of the medication is included on the prescription, it should be included on the prescription container label unless the patient prefers that it not appear. Always ask patients their preference when prescriptions are submitted for filling. Confidentiality and FDA approval for intended use (e.g., labeled vs. off-label use) may limit inclusion of the purpose on labels. Current evidence supports inclusion of purpose-for-use language in clear, simple terms (e.g., "for high blood pressure" rather than "for hypertension").

**Limit auxiliary information:** Auxiliary information on the prescription container label should be evidence-based in simple explicit language that is minimized to avoid distracting patients with nonessential information. Most patients, particularly those with low literacy, pay little attention to auxiliary information. The information should be presented in a standardized manner and should be critical for patient understanding and safe medication use (e.g., warnings and critical administration alerts). Icons are frequently misunderstood by patients. In addition, icons that provide abstract imagery for messages that are difficult to visually depict may be ineffective at improving understanding compared with simplified text alone. Use only icons for which there is adequate evidence, through consumer testing, that they improve patient understanding about correct use. Evidence-based auxiliary information, both text and icons, should be standardized so that it is applied consistently and does not depend on individual practitioner choice.

**Address limited English proficiency:** Whenever possible, the directions for use on a prescription container label should be provided in the patient's preferred language. Otherwise there is a risk of misinterpretation of instructions by patients with limited English proficiency, which could lead to medication errors and adverse health outcomes. Additionally, whenever possible, directions for use should appear in English as well, to facilitate counseling; the drug name shall be in English so that emergency personnel and other intermediaries can have quick access to the information.

Translations of prescription medication labels should be produced using a high-quality translation process. An example of a high-quality translation process is:

- Translation by a trained translator who is a native speaker of the target language
- Review of the translation by a second trained translator and reconciliation of any differences
- Review of the translation by a pharmacist who is a native speaker of the target language and reconciliation of any differences
- Testing of comprehension with target audience

If a high-quality translation process cannot be provided, labels should be printed in English and trained interpreter services used whenever possible to ensure patient comprehension. The use of computer-generated translations should be limited to programs with demonstrated quality because dosage instructions can be inconsistent and potentially hazard-

ous. Standardized translated instructions and technology advances are needed to ensure the accuracy and safety of prescription container labeling for patients with low English proficiency.

**Improve readability:** Labels should be designed and formatted so they are easy to read. Currently no strong evidence supports the superiority in legibility of serif vs. sans serif typefaces, so simple uncondensed fonts of either type can be used.

Optimize typography by using the following techniques:

- High-contrast print (e.g., black print on white background).
- Simple, uncondensed familiar fonts with sufficient space within letters and between letters (e.g., Times Roman or Arial).
- Sentence case (i.e., punctuated like a sentence in English: initial capital followed by lower-case words except proper nouns).
- Large font size (e.g., minimum 12-point Times Roman or 11-point Arial) for critical information. Note that point size is not the actual size of the letter, so 2 fonts with the same nominal point size can have different actual letter sizes. X-height, the height of the lower-case x in typeface, has been used as a more accurate indicator of apparent size than point size. For example, for a given point size, the x-height and apparent size of Arial are actually bigger than those for Times Roman. Do not use type smaller than 10-point Times Roman or equivalent size of another font. Older adults, in particular, have difficulty reading small print.
- Adequate white space between lines of text (25%–30% of the point size).
- White space to distinguish sections on the label such as directions for use vs. pharmacy information.
- Horizontal text only.
- Other measures that can also improve readability:
- If possible, minimize the need to turn the container in order to read lines of text.
- Never truncate or abbreviate critical information.
- Highlighting, bolding, and other typographical cues should preserve readability (e.g., high-contrast print and light color for highlighting) and should emphasize patient-centric information or information that facilitates adherence (e.g., refill ordering).
- Limit the number of colors used for highlighting (e.g., no more than one or two).
- Use of separate lines to distinguish when each dose should be taken.

**Address visual impairment:**

- Provide alternative access for visually impaired patients (e.g., tactile, auditory, or enhanced visual systems that may employ advanced mechanics of assistive technology).

# Attachment 6

Summary

**Patient-Centered Labeling Inspections**      **DATE: April - August 2012**

This survey is intended to be used during inspections of all pharmacies. Unless otherwise indicated, please use tally marks. Sections 1-4 should always be completed. Section 5 will only be used if the pharmacy is compliant and indicated as such in section 4.

<b>1</b>	<b>Number of Inspections</b>	<b>767</b>
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<b>2</b>	<b>Patient-Centered Label (B&amp;P 4076[a] &amp; CCR 1707.5[a][1][A] - [D])</b>			
		<b>Chain Store</b>	<b>Community</b>	<b>Clinic</b>
	Compliant	355	339	1
	Noncompliant	13	67	7
	Corrections issued	13	49	7

<b>3</b>	<b>The label is usually printed in...</b>	<b>Chain Store</b>	<b>Community</b>	<b>Clinic</b>
	10-point font is the default	40	73	0
	12-point font is the default	280	161	1
	Both 10-point & 12-point font appear on the label	47	138	0

Please tally the number in sections 2 and 3 of the survey. This survey is designed to measure compliance with the patient-centered labeling requirements (section 2). Section 3 is designed to identify if pharmacies are defaulting to the larger or smaller font, or using a combination of sizes on the patient-centered elements.

<b>4</b>	<b>Interpretative Services (CCR 1707.5[d])</b>			
		<b>Chain Store</b>	<b>Community</b>	<b>Clinic</b>
	Compliant (all 12 languages available)	349	253	0
	Noncompliant	23	150	1
	Corrections issued	23	146	1

<b>5</b>	<b>If compliant, interpretative services provided by</b>	<b>Chain Store</b>	<b>Community</b>	<b>Clinic</b>
	Staff only	17	2	0
	Telephone (e.g. language line)	68	51	0
	Combination of staff and telephone	260	199	43
	Other, please specify	0	1	0

Please tally the number of pharmacies compliant and non-compliant in Section 4. Complete Section 5 section only if the pharmacy is compliant with the interpretative services provisions.

Other: Internal system with video conference - UC Davis

**California State Board of Pharmacy  
Patient-Centered Prescription Label Survey**

**Objective**

To secure public comments from California consumers regarding the new patient-centered prescription labels pursuant to Senate Bill 472 (Chapter 470, Statutes of 2007).

**Methodology**

The consumer survey soliciting feedback regarding the readability of the new prescription drug container labels was widely distributed. An electronic version of the survey was sent to several consumer groups, who in turn distributed the survey to their ListServe contacts. The survey was also translated into Chinese and Spanish and distributed by The California Pan Ethnic Health Network (CPEHN) to the appropriate audiences. Surveys have also been collected at local Senior Scam Stopper seminars sponsored by the Contractors State Licensing Board.

**Results**

A total of 1204 surveys were received. Respondents did not always provide answers to all of the questions. Results are summarized below:

**Responses to Yes/No Questions**

<b>English: 1142 Surveys Received</b>	<b>YES</b>	<b>NO</b>
1. Are your prescription container labels easy to read?	693	502
2. Are the directions for taking the medicine easy to understand?	245	959
3. Do you know why you take each of your medicines?	1049	149
4. Would you like the general reason why you take the medicine to appear on the label (for pain, for infection, etc.)?	963	232
<b>Chinese: 46 Surveys Received</b>	<b>YES</b>	<b>NO</b>
1. Are your prescription container labels easy to read?	40	5
2. Are the directions for taking the medicine easy to understand?	45	1
3. Do you know why you take each of your medicines?	42	4
4. Would you like the general reason why you take the medicine to appear on the label (for pain, for infection, etc.)?	30	4

<b>Spanish: 16 Surveys Received</b>	<b>YES</b>	<b>NO</b>
1. Are your prescription container labels easy to read?	6	10
2. Are the directions for taking the medicine easy to understand?	7	9
3. Do you know why you take each of your medicines?	7	9
4. Would you like the general reason why you take the medicine to appear on the label (for pain, for infection, etc.)?	16	0

**Top responses to open-ended questions:**

**When asked what information on the label was most important, the top responses were:**

1. Directions for use/clear dosing instructions: 539 of 1098 responses = 49%
2. Name of drug (including generic and brand name): 403 of 1098 responses = 36%
3. Side effects/warnings/interactions/contraindications: 68 of 1098 responses = 6%

**When asked what changes would make the labels better, the top responses were:**

1. Larger font: 318 of 1180 responses = 26%
2. State purpose for taking med: 84 of 1180 responses 7%
3. Include brand name as well as generic name: 52 of 1180 responses = 4%

**When asked how the information could be improved:**

1. Include clear directions/dosing instructions: 123 of 574 responses = 21%
2. Larger font: 43 of 574 = 7%
3. Include purpose for taking the med: 27 of 574 = 4%

# Attachment 7

Results of Translation Surveys  
Conducted by Board Inspectors

Under tabulation – will be shared at the  
Committee Meeting

# Attachment 8



## Report of the Task Force on Uniform Prescription Labeling Requirements

### Members Present:

Michael J. Romano (PA), *chair*; Barry J. Boudreaux (NV); Karen DiStefano (RI); Patricia Donato (NY); Virginia Herold (CA); Ronald Huether (SD); William Prather (GA); Leo H. Ross (VA)

### Others Present:

Karen M. Ryle, *executive committee liaison*; Carmen Catizone, Melissa Madigan, Larissa Doucette, *NABP staff*

### Guests:

Colleen Brennan, *United States Pharmacopeia*; Darren K. Townzen, *National Council for Prescription Drug Programs*

The Task Force on Uniform Prescription Labeling Requirements met December 6, 2008 at the JW Marriott Starr Pass Hotel, Tucson, AZ.

This task force was established in response to Resolution 104-3-08, Task Force on Uniform Prescription Labeling Requirements, which was approved by the NABP membership at the Association's 104<sup>th</sup> Annual Meeting in May 2008.

### Review of the Task Force Charge

Task force members reviewed their charge and accepted it as follows:

1. Evaluate current state and federal laws and regulations addressing prescription label format and content.
2. Review the results of the findings of both state and federal studies regarding prescription labeling.
3. Study the feasibility of implementing standardized state requirements for prescription label format and content and for patient medication information.
4. Recommend revisions, if necessary, to the Model State Pharmacy Act and Model Rules of the National Association of Boards of Pharmacy (*Model Act*) addressing these issues so as to increase readability and comprehension of labels by patients.

**Recommendation 1: Endorse and disseminate statement on prescription labeling.**

The task force recommends that the NABP Executive Committee endorse the following statement on the issue of prescription labeling and disseminate it to all interested stakeholders:

The purpose of the prescription label is to provide critical information to the patient so that he or she may use the medication appropriately and comply with the medication regimen. The label should be patient-centered. The label should not be used as an audit mechanism by third-party payers, nor should it be used for promotional purposes by dispensing pharmacies. Further, the label should not be used as a sole means to determine compliance with pharmacy laws and regulations by pharmacy regulators.

The prescription label cannot and should not replace critical pharmacist care responsibilities, such as appropriately identifying the patient at the time of dispensing and providing patient counseling.

**Background:**

Upon review and discussion of the issue of prescription labeling and concerns related to patients' understanding of such labeling, the task force determined it is important to clearly identify for what purposes prescription labels should and should not be used. As stated above, members felt that labels should be used solely to provide patients with important information about medication use. They agreed that prescription labels should not replace critical pharmacist care responsibilities. Identified were two such primary responsibilities: patient identification and patient counseling. On these issues, the task force stated the following:

1. Patient Identification – Patient data elements, such as address, are important identifiers but do not warrant inclusion on the label; instead, such information should be contained in other patient identification systems upon which a pharmacist relies to ensure that the patient receives his or her medication and to avoid confusion among patients with similar names or whose names may bear suffixes such as “Jr” or “Sr” within a family group.
2. Patient Counseling – The single most effective component to increase and improve patient compliance and avoid medication errors, as documented in numerous studies, is appropriate patient counseling. The prescription label is designed to supplement this critical pharmacist responsibility and not replace it in any way. Pharmacists cannot avoid their legal and professional responsibilities by deferring counseling activities to the prescription label. Further, boards of pharmacy cannot regulate counseling activities through the prescription label.

**Recommendation 2: Amend the NABP Model Act language addressing prescription drug labeling.**

The task force recommends that NABP Executive Committee approve amendments to the *Model Act* that will ensure prescription labels are organized in a patient-centered manner and that mandate the following data elements appear on the prescription label. The task force has consciously removed some data elements historically included on prescription labels to make room for the most critical patient information.

- A. Critical Information for Patients – Critical information must appear on the label with emphasis (highlighted or bolded), in a sans serif (such as “arial”), minimum 12-point

font, and in “sentence case.” Field size and font size may be increased in the best interest of patient care. Critical information text should never be truncated.

- a. Patient name.
    - i. Legal name of the patient. If patient is an animal, include the last name of the owner, name of the animal, and animal species.
  - b. Directions for use.
    - i. The directions for use as indicated by the prescriber and medication purpose/indication if included on prescription drug order.
      1. 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.
      2. It is understood that prescription drug orders often do not include the indication for use.
    - ii. Language should be simplified, avoiding unfamiliar words and medical jargon; when applicable, use numeric instead of alphabetic characters.
  - c. Drug name.
    - i. Name of the drug.
    - ii. If written for a brand name and a generic drug is dispensed, include phrase “Generic for [brand name].”
    - iii. If a fixed combination generic product is dispensed, use the United States Pharmacopeia (USP) publication of Pharmacy Equivalent Names (PEN) abbreviation. If no PEN has been officially issued by the USP, label the medication *secundum artem*.
    - iv. Include drug name suffixes, such as CD, SR, XL, XR, etc.
  - d. Drug strength.
    - i. Strength of the drug.
  - e. “Use by” date.
    - i. Date by which medication should be used; not expiration date of medication or expiration date of prescription.
    - ii. Format as: “Use by: MM/DD/YY.”
- B. Important Information for Patients – Must appear on the label but should not supersede Critical Information for Patients.
- a. Pharmacy name.
    - i. Name of the dispensing pharmacy. Boards of pharmacy should recognize that some pharmacies “do business as” a name other than the corporate name.
  - b. Pharmacy telephone number.
    - i. 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.

Report of the Task Force on Uniform Prescription Labeling Requirements

- c. Prescriber name.
  - i. Name of the prescriber.
  - ii. Format – “Prescriber: [prescriber name].”
- d. “Fill date.”
  - i. Date the prescription is dispensed, which will change with each subsequent refill. Format – “Date filled: MM/DD/YY.”
  - ii. The “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.
  - iii. The term “fill date” should be defined in the *Model Act*.
- e. Prescription number.
  - i. Identifies the number of the pharmacy record under which the prescription information is recorded.
- f. Drug quantity.
  - i. Quantity of drug dispensed.
  - ii. Format – “Qty: [number].”
- g. Number of refills.
  - i. Number of remaining refills.
  - ii. Format – “Refills: [number remaining]” or “No refills,” using whole numbers only and managing partial fills through the pharmacy recordkeeping system.
- h. Product description.
  - i. Written or graphic description of medication dosage form.
- i. Auxiliary information.
  - i. Auxiliary labels – information should be evidence based, standardized, and demonstrated to complement the prescription label.

Examples of compliant labels include the following:

Pharmacy Name:	Date Filled: MM/DD/YY	Cautions:
Phone:	Rx No.:	
<b>Purpose:</b>		Description:
<b>Patient Q. Name</b>		
Prescriber:		
<b>Take 1 tablet in the morning and 2 tablets at bedtime.</b>		
<b>Drug Name and Strength</b>		
<b>Generic for:</b>	Qty:	
<b>Use by: MM/DD/YY</b>	Refills:	

## Report of the Task Force on Uniform Prescription Labeling Requirements

Pharmacy Name: Phone: Patient Q. Name Rx No.: Date Filled: MM/DD/YY Prescriber: Drug Name and Strength Generic for: Qty:                      Refills: Use by: MM/DD/YY	Purpose:  Take 1 tablet in the morning and 2 tablets at bedtime.  Cautions:  Description:
--	---

### **Recommendation 3:**

The task force recommends that NABP work with federal and state agencies and pharmacy stakeholders to advocate for and ultimately achieve changes in state or federal laws and regulations and industry standards to support a patient-centered label.

#### **Background:**

The task force recognized that Recommendation 2 represents a significant change in the philosophy of what defines a prescription label and the purpose of the prescription label. In some situations, this recommendation will be contrary to existing federal and state laws and regulations and industry standards. The *Model Act* cannot and is not intended to contravene state and/or federal laws or regulations. The task force understands this and supports NABP working with relevant agencies and organizations to allow the use of a patient-centered label.

### **Recommendation 4:**

The task force recommends that the NABP Executive Committee approve amendments to the *Model Act* to note that the following additional data elements may appear on the prescription label:

- Bar codes
- Pharmacy address
- Pharmacy store number

#### **Background:**

The task force wanted to give states the option to allow pharmacies to include these elements on the label if they felt they were necessary.

### **Recommendation 5:**

The task force recommends that NABP work with relevant organizations, including the American Medical Association, the Federation of State Medical Boards, and the Centers for Medicare and Medicaid Services (CMS), to require that medication indications be included on all prescriptions including but not limited to written and electronic prescription drug orders.

**Report of the Task Force on Uniform Prescription Labeling Requirements**

**Background:**

Task force members agreed that this item of information is vital for appropriate medication counseling. It was felt that this was a good time to approach CMS about the possibility of requiring prescribers to include such information in order to be reimbursed for their services.

# Attachment 9

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Display Settings: Abstract

Arch Intern Med. 2011 Feb 28;171(4):300-5. doi: 10.1001/archinternmed.2011.39.

## Helping patients simplify and safely use complex prescription regimens.

Wolf MS, Curtis LM, Waite K, Bailey SC, Hedlund LA, Davis TC, Shrank WH, Parker RM, Wood AJ.

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### Abstract

**BACKGROUND:** There is considerable variability in the manner in which prescriptions are written by physicians and transcribed by pharmacists, resulting in patient misunderstanding of label instructions. A universal medication schedule was recently proposed for standardizing prescribing practices to 4 daily time intervals, thereby helping patients simplify and safely use complex prescription regimens. We investigated whether patients consolidate their medications or whether there is evidence of unnecessary regimen complexity that would support standardization.

**METHODS:** Structured interviews were conducted with 464 adults (age range, 55-74 years) who were receiving care either at an academic general medicine practice or at 1 of 3 federally qualified health centers in Chicago, Illinois. Participants were given a hypothetical, 7-drug medication regimen and asked to demonstrate how and when they would take all of the medications in a 24-hour period. The regimen could be consolidated into 4 dosing episodes per day. The primary outcome was the number of times per day that individuals would take medication. Root causes for patients complicating the regimen (>4 times a day) were examined.

**RESULTS:** Participants on average identified 6 times (SD, 1.8 times; range, 3-14 times) in 24 hours to take the 7 drugs. One-third of the participants (29.3%) dosed their medications 7 or more times per day, while only 14.9% organized the regimen into 4 or fewer times a day. In multivariable analysis, low literacy was an independent predictor of more times per day for dosing the regimen ( $\beta = 0.67$ ; 95% confidence interval, 0.12-1.22;  $P = .02$ ). Instructions for 2 of the drugs were identical, yet 31.0% of the participants did not take these medications at the same time. Another set of drugs had similar instructions, with the primary exception of 1 drug having the added instruction to take "with food and water." Half of the participants (49.5%) took these medications at different times. When the medications had variable expressions of the same dose frequency (eg, "every 12 hours" vs "twice daily"), 79.0% of the participants did not consolidate the medications.

**CONCLUSIONS:** Many patients, especially those with limited literacy, do not consolidate prescription regimens in the most efficient manner, which could impede adherence. Standardized instructions proposed with the universal medication schedule and other task-centered strategies could potentially help patients routinely organize and take medication regimens.



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Original Investigation | February 28, 2011

HEALTH CARE REFORM

## Helping Patients Simplify and Safely Use Complex Prescription Regimens FREE

Michael S. Wolf, PhD, MPH; Laura M. Curtis, MS; Katherine Waite, BA; Stacy Cooper Bailey, MPH; Laurie A. Hedlund, BA; Terry C. Davis, PhD; William H. Shrank, MD, MS; Ruth M. Parker, PhD; Alastair J. J. Wood, MD

*Arch Intern Med.* 2011;171(4):300-305. doi:10.1001/archinternmed.2011.39.

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### ABSTRACT

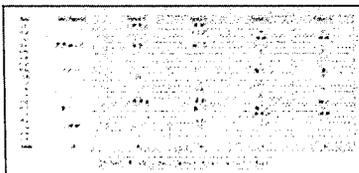
[ABSTRACT](#) | [METHODS](#) | [RESULTS](#) | [COMMENT](#) | [ARTICLE INFORMATION](#) | [REFERENCES](#)

**Background** There is considerable variability in the manner in which prescriptions are written by physicians and transcribed by pharmacists, resulting in patient misunderstanding of label instructions. A universal medication schedule was recently proposed for standardizing prescribing practices to 4 daily time intervals, thereby helping patients simplify and safely use complex prescription regimens. We investigated whether patients consolidate their medications or whether there is evidence of unnecessary regimen complexity that would support standardization.

**Methods** Structured interviews were conducted with 464 adults (age range, 55-74 years) who were receiving care either at an academic general medicine practice or at 1 of 3 federally qualified health centers in Chicago, Illinois. Participants were given a hypothetical, 7-drug medication regimen and asked to demonstrate how and when they would take all of the medications in a 24-hour period. The regimen could be consolidated into 4 dosing episodes per day. The primary outcome was the number of times per day that individuals would take medication. Root causes for patients complicating the regimen (>4 times a day) were examined.

**Results** Participants on average identified 6 times (SD, 1.8 times; range, 3-14 times) in 24 hours to take the 7 drugs. One-third of the participants (29.3%) dosed their medications 7 or more times per day, while only 14.9% organized the regimen into 4 or fewer times a day. In multivariable analysis, low literacy was an independent predictor of more times per day for dosing the regimen ( $\beta = 0.67$ ; 95% confidence interval, 0.12-1.22;  $P = .02$ ). Instructions for 2 of the drugs were identical, yet 31.0% of the participants did not take these medications at the same time. Another set of drugs had similar instructions, with the primary exception of 1 drug having the added instruction to take "with food and water." Half of the participants (49.5%) took these medications at different times. When the medications had variable expressions of the same dose frequency (eg, "every 12 hours" vs "twice daily"), 79.0% of the participants did not consolidate the medications.

**Conclusions** Many patients, especially those with limited literacy, do not consolidate prescription regimens in the most efficient manner, which could impede adherence. Standardized instructions proposed with the universal medication schedule and other task-centered strategies could potentially help patients routinely organize and take medication regimens.



### Figures in this Article

Patients frequently misunderstand common instructions and warnings that accompany prescription drugs, resulting in unintentional misuse and potentially adverse drug events.<sup>1-6</sup> This should not be surprising, as prescription labels may provide seemingly simple but often unclear directions that are confusing to most patients. In the United States, physician prescriptions and pharmacy labeling typically include vague information detailing recommended medication schedules described either in hourly intervals (eg, every 4-6 hours) or times per day (eg, twice daily). Davis et al<sup>1</sup> found that nearly half of patients misinterpreted common instructions when attempting to dose a single prescription medication.

Yet the problem may be more serious than these findings suggest, as patients are increasingly managing multiple prescriptions and over-the-counter medications. According to the Medical Expenditure Panel Survey, the average adult in the United States fills 9 prescriptions annually,<sup>7</sup> while adults older than 65 years fill on average 20 prescriptions a year. Greater regimen complexity, based on multiple medications and/or multiple daily doses per drug, may lead to poorer adherence, which in turn will lead to worse health outcomes.<sup>8-12</sup> From a health system perspective, the known variability and poor quality in the manner in which prescription instructions are written by physicians and translated by pharmacies impede an individual's ability to organize and properly dose multiple medications.<sup>13-14</sup>

The Institute of Medicine, in its 2008 report *Standardizing Medication Labels*, recognized the need for setting standards within prescribing and dispensing practices to promote safe and accurate medication use for patients.<sup>6</sup> Because approximately 90% of prescriptions are taken 4 or fewer times a day,<sup>12</sup> a universal medication schedule (UMS) was proposed in the Institute of Medicine report specifying 4 standard times (morning, noon, evening, and bedtime) for the prescribing and dispensing of medication.<sup>14</sup> The UMS would describe when to take a drug in the same manner on all prescription labels, removing the current variability often found in the manner in which prescriptions are written by physicians and transcribed by pharmacists.<sup>13-15</sup> All prescriptions would instruct patients to take their medications using these specified times, and label instructions would subsequently be described in a single standardized fashion. This standardization was viewed with both promise and controversy by the pharmacological and medical communities. While it might help patients organize and group increasingly complex medication regimens for daily use, it was concluded that further evidence would be needed to support the need for the UMS. In the present study, we sought to fill the gap of existing literature and to investigate whether patients complicate multiple prescription regimens by taking medications more than 4 times a day. Specifically, we evaluated the accuracy and variability in the way patients implemented a typical 7-drug regimen.

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## METHODS

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### PARTICIPANTS

Adults between the ages of 55 and 74 years who received care either at an academic general internal medicine ambulatory care clinic or at 1 of 3 federally qualified health centers in Chicago, Illinois, were recruited for a National Institute of Aging study, referred to as *LitCog*, that examined performance on everyday health tasks, including medication use. Patient enrollment took place between August 2008 and December 2009. Patients were ineligible if they had severe visual or hearing impairments, were too ill to participate, or were non-English speaking. The institutional review board of Northwestern University approved the study, and all patients gave informed consent before participation. A total of 2168 patients were identified through electronic health record systems at clinic sites as initially eligible to participate in *LitCog* by age. A random sample of 1012 eligible patients were selected to be contacted by research staff via telephone and invited to participate in the study. Of those contacted, 479 refused to participate, 12 were deceased, and 521 ultimately consented to participate. Initial screening deemed 57 participants as ineligible because of severe cognitive or hearing impairment ( $n = 22$ ), limited English-language proficiency ( $n = 11$ ), or not being connected to a clinic physician (defined as  $\geq 2$  visits in the past 2 years [ $n = 24$ ]). In all, 464

patients participated in the study, for a determined response rate of 52.1%, following American Association for Public Opinion Research guidelines.<sup>16</sup>

## DATA AND PROCEDURE

Participants completed a 2-hour, structured cognitive interview that included an assessment of their ability to perform everyday health tasks, including dosing a 7-drug medication regimen over the course of a 24-hour period. A research assistant gave patients a hypothetical drug regimen, which consisted of 7 actual prescription drug pill bottles with mock-up labels, each with a retired drug name and different dosing instruction (Table 1). The drug names that were chosen were specifically used to avoid the influence of participants' potential current or prior experience with an actual drug.

**Table 1. Drug Names and Instructions**

Drug Name	Instructions
1. [Illegible]	[Illegible]
2. [Illegible]	[Illegible]
3. [Illegible]	[Illegible]
4. [Illegible]	[Illegible]
5. [Illegible]	[Illegible]
6. [Illegible]	[Illegible]
7. [Illegible]	[Illegible]

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The task presented to participants was to demonstrate when they would take the entire regimen by dosing fake pills contained with each prescription bottle at the times of day that they would take the drug. The research assistant gave patients a medication box, which had 24 slots labeled with every hour of the day (12 AM-11 PM), and instructed them to place the correct number of pills in the slots that identified the times when they would take a medicine. Unlike a pill organizer, the medication box was not meant to assist participants. Instead, it allowed them to demonstrate precisely at what times during the course of a day they would take each drug. The scripted verbal instruction given to patients was, "Imagine that your doctor has prescribed you these medicines. I would like you to please show me when you would take these medicines over the course of 1 day." Detailed guidance was then provided to patients on how to demonstrate, with the fake pills, how to dose the regimen using the medication box.

In addition to completing this task, patients answered basic demographic questions and completed a literacy assessment known as the Newest Vital Sign.<sup>17</sup> This is a 6-item measure that includes reading comprehension and numeracy items based on a nutritional facts label. The Newest Vital Sign is strongly correlated with the Short Test of Functional Health Literacy in Adults.<sup>18</sup>

## OUTCOME AND ANALYSIS PLAN

The outcome of interest was the number of times per day that patients would propose to take the medicine, based on the manner in which they dosed the 7-drug regimen throughout a 24-hour period as demonstrated using the medication box. Descriptive statistics were calculated for each variable. The association between participant sociodemographic characteristics and the number of reported times per day that patients would take the 7-drug regimen were evaluated with *t* tests. Multivariable linear regression analyses were then conducted to examine patient characteristics that independently predicted taking medication at more times throughout a single day. Only variables that were found to be associated with the outcome with a set value of  $P < .20$  were included in the multivariable model. All statistical analyses were performed using Stata version 10 (Stata Corp, College Station, Texas).

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## RESULTS

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The mean (SD) age of the participants was 63.3 (5.3) years; most (71.1%) were female, white (60.8%), and highly educated (61.4% college graduates), with a household income greater than \$50 000 (61.9%). Nearly half of the participants, however, were identified as having either low (20.7%) or marginal (22.8%) health literacy skills. Eighty-four percent of the participants reported having 1 or more chronic health conditions (Table 2).

**Table 2.** Mean Number of Doses Identified in a 24-Hour Period, Stratified by Patient Characteristics

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When dosing the 7-drug regimen, participants on average identified 6 times (SD, 1.8 times) in 24 hours to take medicine. Regimen dosing ranged from as few as 3 to as many as 14 times a day. Approximately one-third of the participants (29.3%) dosed the regimen 7 or more times within 24 hours, while only 14.9% organized the medication 4 or fewer times a day, as would be suggested through the proposed universal medication schedule. Examples of how patients actually dosed the regimen is shown in the Figure.

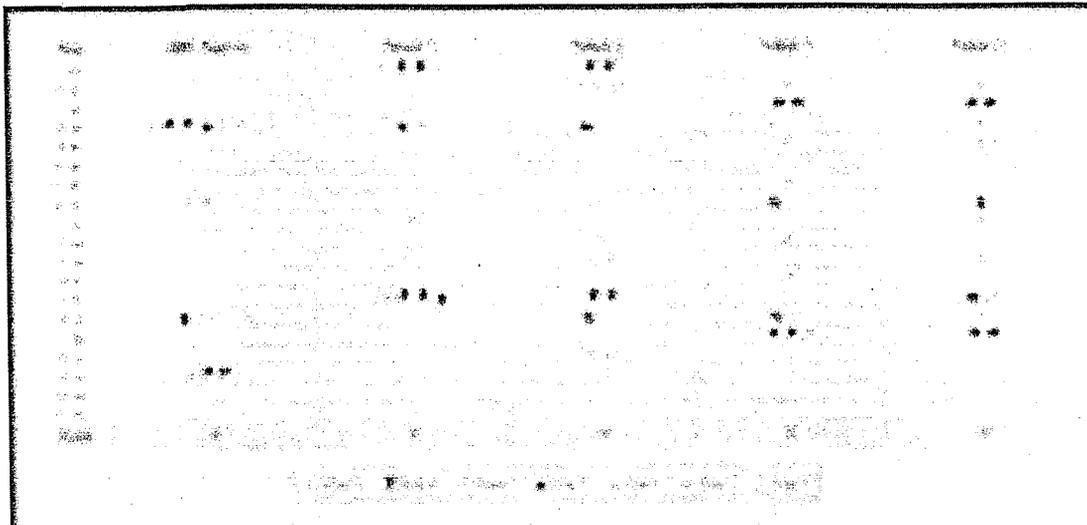
### Figure.

Case examples of older adults' dosing of a 7-drug regimen. UMS indicates universal medication schedule.

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In

multivariable analysis that included the covariates of education, health literacy, and number of self-reported chronic conditions, low health literacy was found to be the sole independent predictor of a greater number of times per day for dosing the 7-drug regimen ( $\beta = 0.67$ ; 95% confidence interval, 0.12-1.22;  $P = .02$ ). Interactions between all patient characteristics were examined. Patients with low health literacy and no



chronic conditions on average dosed the regimen the most times daily compared with others (8.4 times a day vs range of 5.6 to 6.3 times per day)

among other groups by literacy and chronic conditions,  $P = .005$ ). No other interactions by age, race, education, literacy, or chronic conditions were statistically significant.

To identify explanations for participants' failure to consolidate the medications into 4 or fewer times per day, we examined in detail how they handled 3 specific sets of drugs within the hypothetical regimen that could have been taken at the same time. Suspected root causes linked to each set were (1) overall difficulty taking multiple medications and coordinating doses (set 1); (2) distraction of secondary, or auxiliary, instructions (set 2); and (3) variability in language used to identify the interval between doses (set 3). In the first set, the dosage instructions were exactly the same (drugs E and F, Table 1). Nearly one-third of the participants (30.8%) did not take these drugs at the same hours of the day despite having identical label instructions.

In the second set, we investigated 2 drugs (F and G) that could also be taken at the same daily intervals (3 times daily), yet 1 drug included the additional instruction to be taken "with food and water." Half of the participants (49.5%) did not take these medications at the same time of day. In the final set, medications that were to be taken 2 times a day (drugs A and B) were compared; drug A expressed frequency as "twice daily," while drug B stated that it was to be taken "every 12 hours." Four of 5 patients (79.0%) did not consolidate these variable expressions of dose frequency and took the 2 drugs at different times. Notably, drug A instructions also included an auxiliary comment that the medication should be taken for 10 days, and in both the second and third sets investigated, the dose (1 or 2 tablets) also varied.

Beyond examination of the drug set scenarios described herein, Table 3 details how long the participants demonstrated that they would wait between doses for medications that were to be taken 2 (drugs A, B, and D) and 3 (drugs E, F, and G) times a day. Considerable variability was found among participants with regard to how many hours they would allot between doses for both 2- and 3-times-a-day regimens. For drugs to be taken twice daily, participants averaged 10.3 hours (SD, 3.0 hours) between doses, with as few as 1 and as many as 18 hourly intervals (interquartile range, 0-12 hourly intervals). For regimens of 3 times a day, the hourly intervals ranged from 1 to 13 hours, with the mean (SD) being 5.4 (1.8) hours between the first and second dose (interquartile range, 4-7 hours) and 6.5 (1.5) hours between the second and third doses (interquartile range, 6-8 hours).

**Table 3.** Older Adults' Dosing of Medications to Be Taken 2 or 3 Times a Day

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## COMMENT

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Our findings demonstrate that most patients may self-administer multidrug regimens more times a day than necessary and that those with limited literacy are at greater risk. This increased complexity, at the very least, translates to taking medication too often each day, leading to substantial interference with patients' lives. As a result, doses may be frequently missed or incorrectly administered. Given the heightened concerns of medication safety and adherence, particularly among the elderly, who take more medicine and are increasingly cognitively challenged,<sup>19</sup> we offer evidence that previously was unavailable. In particular, strategies are needed to help patients not only to understand how to take a particular medicine but also to consolidate and simplify how to take an entire drug regimen.

The inherent complexity of the task of organizing multiple medications into as few times per day may be an apparent reason that so many patients do not use more efficient consolidation strategies. This is evident in our finding that 1 in 3 older adults did not take 2 medications (drugs E and F) that had the exact same dosage instruction at the same time. Variability in how prescriptions are written, both in describing the timing of doses and the expression of auxiliary instructions, further distracts individuals from the goal of consolidating regimens. Yet many patients may not explicitly perceive finding the most efficient medication-taking strategy to be the objective. It is also possible that patients might not understand that they can take different medications at the same time, especially when the instructions are not identical.

Our study has certain limitations. First, we investigated older adults' dosing of a hypothetical medication regimen and not their actual medication. Therefore, the context and task of demonstrating use via the medication box might not directly reflect the way that participants would self-administer prescribed drugs

in their daily life. Further research is needed to investigate in-depth patient dosing strategies and beliefs about their own regimens. Second, our study was limited to the outcome of demonstration of medication use for a multidrug regimen, and not adherence. While prior studies support the premise that taking medication more times daily could negatively affect long-term regimen adherence, our findings do not directly offer evidence for that association. Third, our analysis of root causes of overcomplicating regimens was post hoc and exploratory, and other aspects of the instruction for sets 2 and 3, such as different doses (1 vs 2 tablets), could have contributed to patient confusion. Fourth, our sample was representative of older adults of higher socioeconomic strata, as indicated by education attainment and household income. However, our findings should be viewed as the best case scenario, as more socioeconomically disadvantaged patients are more likely to have limited health literacy and face even greater difficulty in organizing and dosing complex medication regimens.<sup>20-21</sup> Finally, we provided participants only with the task of demonstrating how and when they would take a 7-drug regimen; a large proportion of chronically ill and elderly patients take far more medications daily. Therefore, our findings may provide a conservative estimate of the potential confusion older adults face when attempting to consolidate and manage all of their prescribed medications.

The UMS was not directly evaluated, but our study highlights patient confusion surrounding medication use. Standardized instructions could be one of many remedies to aid patients and families. Of note, an efficacy trial of the UMS to improve patient comprehension was also conducted recently; findings show that patients are better able to dose medications safely with UMS vs current standard instructions.<sup>22</sup> With these findings and the Institute of Medicine report, legislation has already been approved and passed by the State Board of Pharmacy in California requiring pharmacies to use these UMS instructions when applicable.<sup>23</sup> Further study of the possible benefits, as well as risks, of the UMS strategy is warranted, and evidence will soon be available from ongoing National Institutes of Health and Agency for Healthcare Research and Quality (AHRQ) studies that are currently testing the UMS in actual use (AHRQ grants R01 HSO17687 and R01 HSO19435).<sup>24</sup>

If standardizing prescription instructions does aid patients in consolidating and taking their medication regimens, the UMS could further unite medical and pharmacological practice. Beyond pharmacy labeling, physicians could write the instructions with the more explicit UMS times to help patients have an adequate understanding of when to take not only their newly prescribed medications but also their entire regimen at the point of prescribing. Opportunities now exist with medical practices increasingly adopting electronic health record systems to leverage these tools and to standardize prescribing practices following the UMS concept (National Institutes of Health grant R21 CA132771 and AHRQ grant R18 HSO17220). By working across the medication prescribing and dispensing continuum, the previously noted variability within and between physician prescription writing and pharmacist transcribing can be reduced, and patient understanding and adherence to medication regimens can be improved.<sup>14-16</sup>

We offer compelling, preliminary evidence of the need to help all patients more clearly understand, organize, and simplify their medication regimens. While providing standard, explicit instructions is one possible response, other interventions will likely be necessary. For instance, drug labeling is meant to support, not replace, prescriber and pharmacist spoken communication with patients. Educational and health system strategies are needed to target provider communication skills and screening methods for identifying those at risk for complicating regimens and poor adherence. Similarly, prescribing 1-a-day regimens and bundling medications by times per day at the pharmacy might also be possible solutions.

Ultimately, public health initiatives should help patients acquire a fundamental understanding of prescription medication use and when it would be safe and appropriate to take medications together.

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## ARTICLE INFORMATION

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**Author Contributions:** *Study concept and design:* Wolf, Davis, Parker, and Wood. *Acquisition of data:* Wolf and Waite. *Analysis and interpretation of data:* Wolf, Curtis, Bailey, Hedlund, Davis, Shrank, Parker, and Wood. *Drafting of the manuscript:* Wolf, Davis, and Wood. *Critical revision of the manuscript for important intellectual content:* Wolf, Curtis, Waite, Bailey, Hedlund, Davis, Shrank, Parker, and Wood. *Statistical analysis:* Wolf, Curtis, and Shrank. *Obtained funding:* Wolf and Davis. *Administrative, technical, and material support:* Wolf, Waite, Bailey, and Hedlund. *Study supervision:* Shrank.

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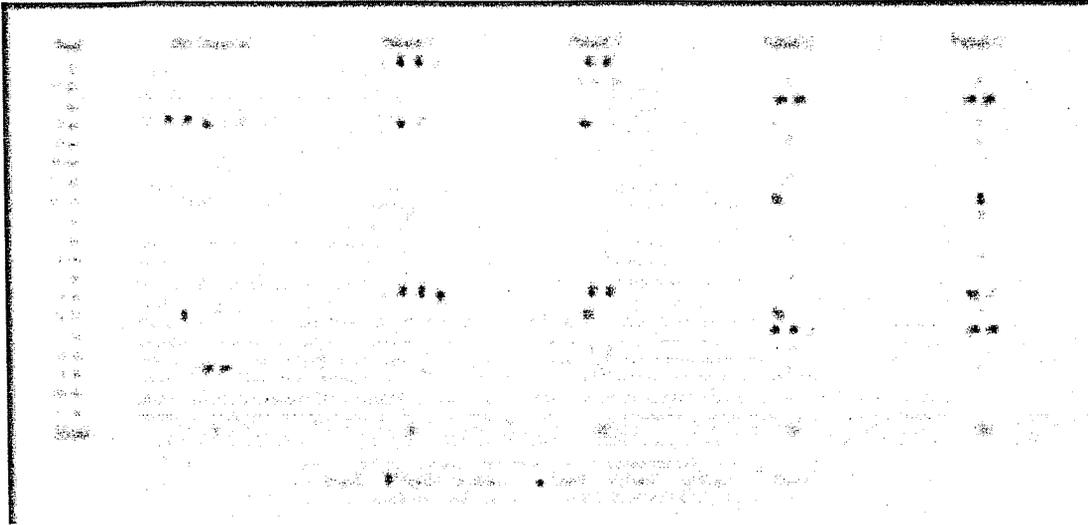
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## Figures

Figure.

Case examples of older adults' dosing of a 7-drug regimen. UMS indicates universal medication schedule.



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## Tables

**Table 1. Drug Names and Instructions**

Drug Name	Instruction
Drug 1	Instruction 1
Drug 2	Instruction 2
Drug 3	Instruction 3
Drug 4	Instruction 4
Drug 5	Instruction 5
Drug 6	Instruction 6
Drug 7	Instruction 7

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**Table 2. Mean Number of Doses Identified in a 24-Hour Period, Stratified by Patient Characteristics**

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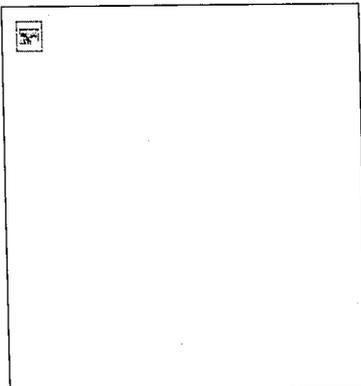


Table 1. Country-specific mortality and growth failure data and their association with maternal education and material stature. Data are presented as percentages (95% CI).

Country	Infant mortality (%)	Early childhood mortality (%)	Growth failure (%)
USA	10.5 (9.8-11.2)	12.1 (11.4-12.8)	15.2 (14.5-15.9)
UK	11.2 (10.5-11.9)	13.8 (13.1-14.5)	16.7 (16.0-17.4)
France	12.1 (11.4-12.8)	14.5 (13.8-15.2)	17.4 (16.7-18.1)
Germany	13.8 (13.1-14.5)	15.2 (14.5-15.9)	18.1 (17.4-18.8)
Italy	14.5 (13.8-15.2)	16.7 (16.0-17.4)	19.8 (19.1-20.5)
Spain	15.2 (14.5-15.9)	17.4 (16.7-18.1)	20.5 (19.8-21.2)
Japan	16.7 (16.0-17.4)	18.1 (17.4-18.8)	21.2 (20.5-21.9)
China	18.1 (17.4-18.8)	19.8 (19.1-20.5)	22.9 (22.2-23.6)
India	19.8 (19.1-20.5)	21.2 (20.5-21.9)	24.6 (23.9-25.3)
South Africa	21.2 (20.5-21.9)	22.9 (22.2-23.6)	26.3 (25.6-27.0)
South America	22.9 (22.2-23.6)	24.6 (23.9-25.3)	28.0 (27.3-28.7)
Sub-Saharan Africa	24.6 (23.9-25.3)	26.3 (25.6-27.0)	29.7 (29.0-30.4)
World	26.3 (25.6-27.0)	28.0 (27.3-28.7)	31.4 (30.7-32.1)

## Interactive

### Video



### Country-Specific Mortality and Growth Failure in Infancy and Young Children and Association With Material Stature

Use interactive graphics and maps to view and sort country-specific infant and early childhood mortality and growth failure data and their association with maternal

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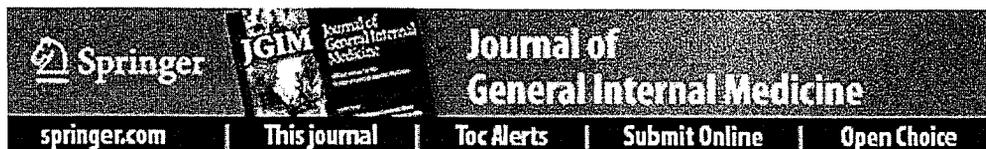
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## Improving Patient Understanding of Prescription Drug Label Instructions

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### Abstract

#### Background

Patient misunderstanding of instructions on prescription drug labels is common and a likely cause of medication error and less effective treatment.

#### Objective

To test whether the use of more explicit language to describe dose and frequency of use for prescriptions could improve comprehension, especially among patients with limited literacy.

#### Design

Cross-sectional study using in-person, structured interviews.

#### Patients

Three hundred and fifty-nine adults waiting for an appointment in two hospital-based primary care settings: one federally qualified health center in Shreveport, Louisiana; Chicago, Illinois; and New York, New York, respectively.

#### Measurement

Correct understanding of each of ten label instructions as determined by a blinded panel review of patient verbatim responses.

#### Results

Patient understanding of prescription label instructions ranged from 53% for the least understood to 100% for the most commonly understood label. Patients were significantly more likely to understand instructions with explicit times periods (i.e., morning) or precise times of day compared to instructions stating times :

(i.e., twice) or hourly intervals (89%, 77%, 61%, and 53%, respectively,  $< 0.001$ ). In multivariate analysis, dosage instructions with specific times or time periods were significantly more likely to be understood compared to instructions stating times per day (time periods — adjusted relative risk ratio (ARR) 0.34, 95% Confidence Interval (CI) 0.34–0.52; specific times — ARR 0.60, 95% CI 0.49–0.74). Low and marginal literacy remained statistically significant independent predictors of misinterpreting instructions (low - ARR 1.81–4.03; marginal - ARR 1.66, 95% CI 1.18–2.32).

## Conclusions

Use of precise wording on prescription drug label instructions can improve patient comprehension. Patients with limited literacy were more likely to misinterpret instructions despite use of more explicit language.

**Key Words:** literacy, health literacy, drugs, prescription medications, labels, patient safety, medication regimens

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Patient misunderstanding of instructions on prescription drug labels is a medication safety and health concern<sup>1–3</sup>. The 2006 Institute of Medicine Report, *Preventing Medication Errors*, cited poor patient comprehension and subsequent unintentional misuse of prescription drugs as a root cause of medication errors, poor adherence, and worse health outcomes<sup>3</sup>. A recent study by our research team found nearly half of low literacy care patients misunderstood common dosage instructions on prescription container labels<sup>4</sup>. Patient limited literacy and those taking more medications were at greatest risk. As patients, particularly those taking an increasing number of prescription drugs, the ability to accurately interpret medication instructions becomes even more critical for ensuring proper and safe use<sup>5,6</sup>.

While limited literacy may impede patient comprehension of medication dosage instructions, the instructions also may not be written in the most clear and precise manner<sup>7–10</sup>. There is little evidence supporting best practices for writing prescription medication dosage instructions to promote patients' understanding. Data from our previous study and earlier cognitive factors research suggest that less complex and more explicit dosage instructions might improve patient understanding<sup>4,7,11–15</sup>. The purpose of this study was to evaluate whether the use of more explicit language to describe the dose and frequency of prescribed drugs could improve comprehension, especially among patients with limited literacy. We hypothesized that more explicit instructions would improve patient interpretation, and the association between literacy and understanding how to take prescribed drugs would be reduced.

## METHODS

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### Subjects

Study participants were adult patients who attended one of three outpatient primary care clinics in Louisiana, Chicago, Illinois and New York, New York. All of these study clinics provide care for a large number of indigent patients. Subject recruitment took place from May to December 2006. The Shreveport and New York clinics were within a public university hospital while the Chicago study clinic was a Federally C

Health Center. Institutional Review Boards at the affiliated institutions (Louisiana State University Sciences Center at Shreveport, Northwestern University, Mount Sinai School of Medicine) approved

Patients at the three clinics were eligible if they were 18 years of age or older. Research assistants (RA) approached consecutive patients in each clinic while they were waiting to see physicians. Patients were excluded from participation if they reported they had severely impaired vision, hearing problems, were ill, or did not speak English. A total of 401 patients were approached and 373 consented to the study. Individuals were excluded based on language barriers, and three were ineligible due to visual impairment. All, 359 consented to the study (90% response rate).

### Selection of Prescription Instructions

We studied instruction labels for three commonly prescribed medications: glyburide, metformin, and atenolol. Three physicians and one pharmacist identified a typical dose for each medication, along with various frequencies of use for the drug's daily administration. Atenolol was written to be taken once a day, while glyburide and metformin were written for twice a day. A minimum of three variations of the dosage instructions were used per drug, ranging from vague to most explicit. Specifically, frequency of use for a prescribed drug was presented either as 1) number of times per day ("twice daily"), 2) hourly intervals ("every 12 hours"), 3) time periods ("morning", "evening"), or 4) specific times ("8 A.M.", "5 P.M."; Table 2). Ten mock pill bottles were developed based on these different presentations of dose (number of pills and frequency of use (number of times to be taken per day) for the three drugs.

Instruction Type	Low Literacy		Medium Literacy		High Literacy	
	Correct	Incorrect	Correct	Incorrect	Correct	Incorrect
Number of times per day	100	10	80	20	95	5
Hourly intervals	80	20	70	30	90	10
Time periods	70	30	60	40	85	15
Specific times	60	40	50	50	80	20
Total	310	100	260	140	350	50

**Table 2**

Correct Interpretation of Prescription Medication Instructions, By Literacy Level

### Structured Interview and Literacy Assessment

After obtaining informed consent, a trained RA administered a structured interview that lasted approximately 20 minutes and included a self-report of sociodemographic information (age, gender, race/ethnicity, education, number of prescription medicines taken daily) and a brief literacy assessment. The RA then presented each patient the ten prescription bottles one at a time and asked "How would you take this medicine?" The RA documented patients' verbatim responses. All patients viewed the pill bottles in the same order, which was determined by random assignment. This procedure has been widely used by this research team to assess patients' functional understanding of prescription drug instructions and warnings<sup>4,7,11</sup>.

Patient responses were independently rated as either correct or incorrect by three general internal medicine attending physicians from two academic medical centers. Physicians were blinded to patient information and were trained to follow stringent coding guidelines previously agreed upon by the research team<sup>7</sup>. Coders were given only if patients' responses included both the proper dose (number of pills to be taken at a time) and frequency of use (number of times drug is to be taken daily) as stated on the label. For label instructions that detailed a drug's frequency using hourly intervals or time periods, raters followed a predetermined set of acceptable responses for coding purposes to allow for some variability in interpretation. Instructions that included specific times for taking the medicine had to be precise or give a very close approximation.

correct. If frequency was stated using the number of times per day, responses were correct if either 1 number was reported back, or if appropriate specific times or time periods (i.e., 8 A.M., noon, 5 P.M. lunch, dinner) were described. If patients' responses were inaccurate or incomplete in their interpretation, they were scored as incorrect.

Inter-rater reliability between the three physicians coding the patient responses was very high (Kaplan's  $\kappa = 0.91$ ). Responses that received discordant ratings between the three reviewers ( $n = 252$ ) were scored by a panel consisting of a primary care physician and two behavioral scientists with expertise in health literacy. Each panel member was blinded to patient information, independently coded the responses as correct or incorrect. A consensus was achieved for 91% of responses. A majority rule was used for the remaining 24 responses.

**Literacy Assessment** Patient literacy was assessed using the Rapid Estimate of Adult Literacy in Medicine (REALM), a reading recognition test comprised of 66 health related words<sup>16,17</sup>. The REALM is the most commonly used test of patient literacy in medical settings<sup>18</sup>. Raw scores can be converted into one of three reading levels: sixth grade or less (0–46), seventh to eighth (45–60), ninth grade and above (61–66). REALM is highly correlated with other standardized reading tests and the Test of Functional Health Literacy in Adults (TOFHLA)<sup>18,19</sup>.

### Analysis Plan

All statistical analyses were performed using SAS software version 9.1 (Cary, NC). Descriptive statistics (percentage, mean and standard deviation) were calculated for each variable. Chi-square tests were used to evaluate the association between sociodemographic characteristics and patient understanding of each of the ten prescription label instructions. In multivariate analysis, the ten binary repeated responses of correct or incorrect understanding per subject were modeled using a generalized linear model with a complementary log–log link function. A generalized estimating equation (GEE) approach was used to adjust model coefficients and standard errors for within-patient correlation using PROC GENMOD (SAS Institute, Cary, NC). 95% confidence intervals were calculated for adjusted relative risk ratios using the robust estimate of the error as detailed by Liang and Zeger<sup>20,21</sup>. The final multivariate model included the variables age, gender, race (white vs. African American), education, site, and number of medications currently taken daily. The language used to state frequency of use (times per day, hourly intervals, time periods, specific times) entered in the model as the primary independent variable of interest. The complexity of the instruction (one tablet a day vs. two tablets twice daily) was considered to be a potential risk factor to patient understanding and also entered in the analysis as a covariate. Patient literacy was classified either as low (6th grade or below), marginal (7th–8th grade) or adequate (9th grade and higher). In order to examine whether explicit instructions could overcome the barrier of limited literacy on patient understanding, an interaction term for literacy and type of language used in the instruction was included in the final model.

## RESULTS

The mean age of patients was 48.4 years (SD = 13.7; range 20 to 80 years); 72% were female and 61% were African-American. Approximately half of patients were recruited in Shreveport (56%), 25% in New Orleans and 19% in Chicago. Twenty percent of respondents had less than a high school education; 15% were reading at or below a 6th grade level (low literacy), and 30% were reading at the 7th–8th grade level.

(marginal literacy). Patients were currently taking an average of 2.8 prescription medications (SD = 1.5). Marginal literacy was associated with older age ( $< 0.001$ ), African American race ( $< 0.001$ ), and less education ( $< 0.001$ ; Table 1).

**Table 1**  
Sample Characteristics Stratified by Literacy Level

Each patient provided interpretations for ten different instructions for a total of 3,590 responses for drugs. Of these 839 (23%) were coded as incorrect. Seventy-eight percent of patients misunderstood more instructions, with 37% misunderstanding a minimum of three labels. The prevalence of incorrect interpreting one or more label instructions among patients with adequate, marginal and low literacy was 84%, and 93%, respectively ( $< 0.001$ ). Rates of correct interpretation were lowest for instructions that depicted frequency in hourly intervals or the number of times of day (“Take 1 pill by mouth every 12 hours”, “Take two tablets by mouth twice daily”; 53% and 61%, respectively) and highest for those that depicted time periods (“Take 2 pills in the morning and 2 pills in the evening”, “Take 1 pill by mouth every day”; 89% for both labels).

Patients with low literacy were more likely to misinterpret seven of the ten instructions compared to adequate literacy (Table 2). Two of three label instructions where literacy was not significantly associated with correct interpretations were for atenolol, which had the most basic frequency schedule (1 tablet a day). Statistically significant differences in rates of understanding the medication labels were noted by either the number of prescription medications currently taken by patients.

In multivariate analyses, prescription instructions that gave time periods (morning, evening) or specific times (8 A.M. and 5 P.M.) were significantly less likely to be misinterpreted compared to those using the number of times per day [twice daily] (time period — adjusted relative risk ratio (ARR) 0.42, 95% confidence interval (CI) 0.34–0.52; specific times — ARR 0.60, 95% CI 0.49–0.74; Table 3). Frequency of use stated in hourly intervals (i.e., every 12 hours) was significantly more likely to be misinterpreted compared to writing frequency as a number of times per day (ARR 2.87, 95% CI 2.29–3.60). The reference group was then altered from previous times per day to time periods in order to determine if this latter format significantly improved comprehension compared to the use of specific times. Misinterpretation of instructions was higher for specific times compared to time periods (ARR 1.43, 95% CI 1.19–2.71).

**Table 3**  
Generalized Estimating Equation (GEE) Model\* for Misunderstanding Prescription Medication Label Instructions

Low and marginal literacy were also statistically significant independent predictors of misinterpreting label instructions (low — ARR 2.70, 95% CI 1.81–4.03; marginal — ARR 1.66, 95% CI 1.18–2.32). Fewer years of education ( $< high school$ , ARR 1.36, 95% CI 1.03–1.77) and greater dose complexity (four tablets taken daily [glyburide]); ARR 1.47, 95% CI 1.20–1.83) were also found to be significantly and independently associated with misinterpretation.

with misinterpretation. The interaction term for literacy and type of language used to depict drug frequency was included in the final multivariate model; it approached but did not reach statistical significance (OR 0.91, 95% CI 0.85–1.01;  $p = 0.079$ ).

## DISCUSSION

Physicians may assume patients can interpret prescription drug label instructions, yet four out of five (79%) in this study misinterpreted one or more of the ten common prescription label instructions they encountered. Although the instructions were brief and of minimal reading difficulty, rates of patient understanding varied widely across all literacy levels. More explicit language instructing patients with the medicine using time periods were better understood compared to instructions that more vaguely stated number of times per day or hourly intervals. This finding is supported by prior research demonstrating that older adults have greater difficulty interpreting medication instructions that do not explicitly detail when to take a prescribed medicine<sup>13–15</sup>.

Labels that instruct patients to take medications “twice daily” or “every 12 hours” require patients to take additional mental steps to infer when to take a medicine. For patients with limited literacy, this adds an unnecessary cognitive burden, resulting in poorer comprehension<sup>12</sup>. Despite the use of more precise instructions, however, comprehension among those with low literacy skills was still significantly lower than among patients with marginal or adequate literacy skills. This is also not surprising, as earlier health literacy research found that materials with low reading grade levels were likely to improve comprehension among patients with adequate literacy, but had only variable success in improving comprehension among patients with low literacy<sup>22</sup>.

Interestingly, identifying specific times each day (8 A.M., 5 P.M.) for administration was a more easily understood instruction format than stating times per day or hourly intervals. However, patients were significantly more likely to misinterpret these instructions compared to those stating time periods in general (morning, evening). It is possible that patients do not need such precision when following medication instructions. Stating frequency using time periods of day rather than precise times may better reflect patient preference to tailor the implementation of their drug regimens to their daily schedule. Also of note, more complex dose regimens requiring patients to take more pills a day was a significant independent predictor of misinterpretation of instructions. A prescription requiring a patient to take four pills a day was 47% more likely to be misinterpreted than instructions for a ‘one-a-day’ regimen. Patients with low literacy did not differ significantly from those with adequate literacy in interpreting instructions to take one pill a day, or in understanding “Take 2 pills by mouth every day” and “Take 1 with breakfast and 1 with supper.” Although the latter instruction involved taking pills two times daily, the label broke down the instructions for dose and frequency and provided a context for the time of day.

The limitations to our study should be noted. First, we investigated patient understanding of different writing instructions included on the primary label for prescription medications only. The association between misunderstanding of these instructions and medication error was not examined. We also did not study patients’ actual prescription drug-taking behaviors. Patients’ motivation, concentration and comprehension might have been greater if they were reporting on their own medicine given by their physician for conditions they or their children actually had<sup>14,23,24</sup>. Second, since the study design did not include a chart review

not have information on patients' health information; in particular whether they had actual experience with the study medications. Third, we primarily manipulated the language for frequency of use; however, more subtle differences in word choice and numeric presentation of dose on the various drug instructions may also have altered patients' understanding. Fourth, patients in our study were mostly socioeconomically disadvantaged individuals from three primary care clinics in diverse areas of the country. Our sample addresses those individuals disproportionately affected by poor health outcomes, and whose health was targeted for improvement by Healthy People 2010<sup>25</sup>. Finally, the generalizability of our findings are limited by the fact that patients were predominantly female (an accurate depiction of the clinic patient populations), and that participation was limited to patients who spoke English. This was due in part to using the Rapid Estimate of Adult Literacy in Medicine (REALM) as our literacy assessment.

While further improvements might be made in the design of prescription drug labels, it is likely that patient counseling will also be needed to address health literacy deficits. Previous research has found that physicians commonly review the instructions when prescribing medications, nor do pharmacists routinely verbally counsel patients when filling a prescription<sup>26-29</sup>. Both the American Medical Association and American Pharmacists Association recommend provider training in health literacy communication 'best practices' a highly efficacious approach described in recent cognitive factors research, known as "implementation intention" might also aid provider training activities<sup>31</sup>. This could be a promising health literacy strategy at the provider level, as it refers to a process of helping patients visualize exactly how a prescribed medication should be self-administered within the context of their own daily routine. As minimal standards exist to guide physician and pharmacist best practices for writing and transcribing the dose and frequency of use on label instructions for patients, both professionals should make it their goal to be simple, clear and explicit in directing patients on how to self-administer their medication.

### Acknowledgement

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**Conflict Of Interest** None disclosed.

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