General Chapters

General Tests and Assays

Apparatus for Tests and Assays

⟨17⟩ PRESCRIPTION CONTAINER LABELING

Change to read:

INTRODUCTION

■This chapter applies to labeling instructions and information on prescription containers that are directly dispensed to the patient to promote better patient understanding. 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.■1S (*USP39*) 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 ■■1S (*USP39*) may be available, the prescription container label must fulfill the professional obligations of the prescriber and pharmacist. These obligations include giving patients the ■■1S (*USP39*) essential information ■they will need ■1S (*USP39*) to understand how to safely and appropriately use the medication and ■how■1S (*USP39*) to adhere to the prescribed medication regimen.

Inadequate understanding of prescription directions for use and auxiliary information ■provided■1S (*USP39*) 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 ■common and■1S (*USP39*) troublesome in patients with low or marginal literacy and in patients receiving multiple medications that are scheduled for administration using ■■1S (*USP39*) complex, nonstandardized time periods. In one study, patients with low literacy were 34 times more likely to misinterpret prescription medication warning labels ■than patients with adequate literacy.■1S (*USP39*) 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 that have been 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 ■■1S (*USP39*) need for ■■1S (*USP39*) auxiliary label information ■requires further study in comparison to ■1S (*USP39*) explicit, simplified language alone. ■■1S (*USP39*)

Lack of universal standards for labeling on dispensed prescription containers is a root cause ■of■1S (*USP39*) patient misunderstanding, nonadherence, and medication errors. ■■1S (*USP39*)

■USP developed■1S (*USP39*) 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. ■■1S (*USP39*)

Change to read:

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 the patient's safe and effective use of the medicine. At the top of the label, specify the patient's name, the drug name (spell out full generic and brand name) and ■drug■1S (*USP39*) strength, and explicit clear directions for use in simple language.

The prescription directions should follow a standard format so ■that■1S (*USP39*) the patient can expect that each element will be ■presented■1S (*USP39*) in a ■specific, predictable■1S (*USP39*) order each time a prescription is received. ■Use of a methodology that simplifies the administration instructions for the patient's medication should improve the individual's ability to understand prescription instructions, to take the correct dose, and to organize multi-drug regimens. Employing best practices of patient-centered instructions—which utilize the principles of health literacy, medication therapy management, and education, to explicitly describe how to take daily-use, solid dose-form medications—has resulted in improved patient understanding. One such patient-centered method is the universal medication schedule (UMS). The UMS shifts medication-taking into four standardized time periods (morning, noon, evening, bedtime) and uses simplified language and formatting to promote understanding (e.g., "take 1 pill in the morning and 1 pill at bedtime" rather than "take one tablet twice daily"). Such methods may be particularly useful for simplifying daily medication regimens that include multiple oral therapies. [NOTE—The word "pill" is used in the UMS to enhance health literacy and may not reflect a USP definition for an oral dosage form (see *Compendial Nomenclature, USP Nomenclature Guidelines* on the USP website at www.usp.org/usp-nf/development-process).]

When oral liquid dosage forms are prescribed, the appropriate dosing component (e.g., oral syringe, dosing cup) shall be provided to the patient or caregiver to accurately measure and administer the oral medication. The graduations on the component shall be legible and indelible, and the associated volume markings shall be in metric units and limited to a single measurement scale that corresponds with the dose instructions on the prescription container label (see *Packaging and Storage Requirements* ⟨659⟩).■1S (*USP39*)

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 ■can distract■1S (*USP39*) patients, which can impair their recognition and understanding.

Simplify Language

The 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 ■for simplifying■1S (*USP39*) short excerpts of text ■such as ■1S (*USP39*) those on prescription labels. Instead, use simplified, standardized sentences that ■were■1S (*USP39*) developed ■■1S (*USP39*) by seeking feedback from samples of diverse consumers. ■Such language will promote correct understanding of the instructions.■1S (*USP39*)

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 ■differ■1S (*USP39*) 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 ■at■1S (*USP39*) precise hours of the day is less readily understood and may present greater adherence issues ■(due to individual lifestyle patterns such as shift work)■1S (*USP39*) 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. ■A set of standardized, explicit instructions (the universal medication schedule, UMS) were developed and tested in English and other languages to improve patient understanding.[1]■1S (*USP39*)

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.

[1] Explicit and Standardized Prescription Medicine Instructions. December 2014. Agency for Healthcare Research and Quality, Rockville, MD. http://www.ahrq.gov/professionals/quality-patient-safety/pharmhealthlit/prescriptionmed-instr.html.

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. ■Practitioners should■1S (USP39) always ask patients their preference when ■writing the prescription.■1S (USP39) Confidentiality and FDA approval for intended use (e.g., labeled ■versus■1S (USP39) 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 ■and presented■1S (USP39) in simple explicit language that is minimized to avoid distracting patients with nonessential information. Most patients, particularly those with ■limited■1S (USP39) 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 ■depict visually■1S (USP39) 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(s)■1S (USP39) shall be in English so that emergency personnel and other intermediaries can have quick access to the information. ■Standardized translations of universal medication schedule instructions are available.[2] ■1S (USP39)

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, ■with the use of■1S (USP39) trained interpreter services ■■1S (USP39) 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 ■translated inconsistently or incorrectly, which is■1S (USP39) potentially hazardous. Standardized translated instructions and technology advances are needed to ensure the accuracy and safety of prescription container labeling for patients with ■limited■1S (USP39) English proficiency.

Improve Readability

Labels should be designed and formatted so they are easy to read. Currently, no strong evidence supports the superiority, in ■terms of■1S (USP39) legibility, of serif ■versus■1S (USP39) sans serif typefaces, ■therefore■1S (USP39) 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 ■New■1S (USP39) Roman or Arial)
- Sentence case (i.e., punctuated like a sentence in English: Initial capital ■letter■1S (USP39) followed by lower-case words except proper nouns)
- Large font size (e.g., minimum 12-point Times ■New■1S (USP39) Roman or 11-point Arial) for critical information. Note that point size is not the actual size of the letter, so two fonts with the same nominal point size can have different actual letter sizes ■The height of the typeface, x-height,■1S (USP39) 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 ■New■1S (USP39) Roman. Do not use type smaller than 10-point Times ■New■1S (USP39) Roman or the equivalent size ■in■1S (USP39) another font. Older adults, in particular, have difficulty reading small print.

[2] Available at http://www.ahrq.gov/professionals/quality-patient-safety/pharmhealthlit/prescriptionmed-instr.html.

- Adequate white space between lines of text (25%–30% of the point size)
- White space ■to separate■ 1S (USP39) sections on the label such as directions for use ■versus■ 1S (USP39) pharmacy information
- Horizontal text only

Other measures that can also improve readability:

- ■■ 1S (USP39) Minimize the need to turn the container in order to read lines of text
- Never truncate or abbreviate critical information
- ■Use■ 1S (USP39) highlighting, bolding, and other ■cues to■ 1S (USP39) preserve readability (e.g., high-contrast print and light color for highlighting) and ■■ 1S (USP39) emphasize ■patient-centered■ 1S (USP39) information or information that facilitates adherence (e.g., refill ordering)
- Limit the number of colors used for highlighting (■i.e.,■ 1S (USP39) no more than ■■ 1S (USP39) two)
- Use of separate lines to distinguish when each dose should be taken

■Alternative-Access Methods to Address Visual Impairment

Patients with visual impairment who are unable to read printed prescription container labels often report inadvertently taking the wrong medication or amount, or taking it at the wrong time or under the wrong instructions, compromising their own safety. Similarly, if a caregiver is visually impaired, the patient they care for is at risk for medication errors. The magnitude of this problem increases with aging, as the risk of visual impairment and the number of prescribed medications both increase with age.

- Follow standards for patient-centered prescription labels■ 1S (USP39)
- Provide alternative access for visually impaired patients (■alternative-access methods include■ 1S (USP39) tactile, auditory, or enhanced visual systems that may employ advanced mechanics of assistive technology)■[3]
- Enhance communication between the pharmacist and visually impaired patients (and their designated representatives) such that the pharmacist can explain alternative-access options and together they can identify those best suited to the patient's needs
- Once an alternative-access method is identified for the individual patient, the pharmacist shall provide the service or direct the patient to a pharmacy that offers that type of alternative access
- Ensure that duplicate accessible labels preserve the integrity of the print prescription drug container label and provide the same sequence of information as the printed label
- Follow specific best practices for each respective alternative-access format employed■ 1S (USP39)

Microbiological Tests

⟨55⟩ BIOLOGICAL INDICATORS—RESISTANCE PERFORMANCE TESTS

Change to read:

■INTRODUCTION

A biological indicator (BI) is a well-characterized preparation of a specific microorganism with a known resistance to a specific sterilization process. The correct use of BIs in the development, validation, and control of sterilization processes requires that their population and resistance be accurately known. The population and resistance can be selected to confirm the adequacy of individual sterilization process conditions for an article. The recommendations of *Sterilization of Compendial Articles* ⟨1229⟩ should be followed for effective BI usage. The methods described below can be used to establish population and resistance, such that the response of the BI to the subject sterilization process is appropriate. Although the BI manufacturers are required to maintain rigorous control of population and resistance using the number of replicates as specified below, the end users are not required to use the same number of replicates for verification of those determinations. Conduct all of the tests described in this chapter under appropriate microbiological laboratory conditions (see *Microbiological Best Laboratory Practices* ⟨1117⟩).

[3] See Working Group Recommendations from Access Board Working Group on Accessible Prescription Drug Container Labels: http://www.access-board.gov/guidelines-and-standards/health-care/about-prescription-drug-container-labels/working-group-recommendations.