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U.S. FOOD & DRUG ADMINISTRATION

Safety Considerations for Container Labels and Carton Labeling to Minimize Medication Errors

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Disclaimer

- The views and opinions expressed in this presentation represent those of the presenter, and do not necessarily represent an official FDA position.
- The labeling examples in this presentation are provided only to demonstrate current labeling development challenges and should not be considered FDA recommended templates.
- Reference to any marketed products is for illustrative purposes only and does not constitute endorsement by the FDA.

Learning Objectives

- Describe general principles and special considerations in the design of container labels and carton labeling to minimize medication errors
- Describe safety considerations for other special container labels and dosing devices for oral liquid products

Background

- Medication errors are a significant public health concern
  - An estimated 7,000 deaths annually in the United States[1]
- Institute of Medicine's *Preventing Medication Errors* report[2]
  - Labeling and packaging issues as the cause of 33% of all medication errors and 30% of fatalities from medication errors.
  - Product naming, labeling, and packaging should be designed for the end user – the provider in the clinical environment and/or the consumer.

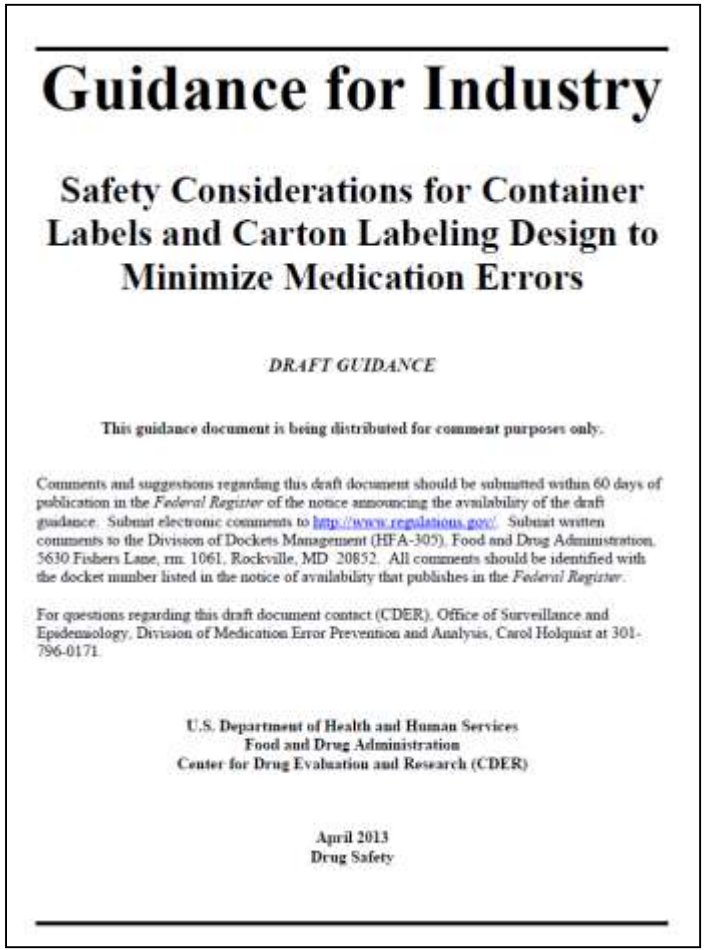
1. Phillips DP, Christenfeld N, and Glynn LM. Increase in US Medication-Error Deaths between 1983 and 1993. The Lancet. 351:643-644, 1998.
2. IOM, Preventing Medication Errors. Chapter 6, Recommendation 4, p. 280.

Typical Pharmacy Shelf


CYCLOGEL
MYDRIACYL
Tropicamide Ophthalmic Solution USP, 1%
Tropicamide Ophthalmic Solution USP, 1%


Aricept
10 mg
30 Tablets
Eisai Inc.
Aciphex 20
(rabeprazole sodium)
30
Eisai Inc.
JANSSEN


Nimbex
Nimbex
Nimbex
NovoLog



Guidance for Industry

Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov/. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact (CDER), Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis, Carol Holquist at 301-796-0171.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2013
Drug Safety

- This guidance applies to:
  - Rx drugs marketed under an approved NDA or ANDA,
  - Rx drugs marketed without an approved NDA or ANDA,
  - Biological products marketed under an approved BLA

- Product container labels and carton labeling should communicate information that is critical to the safe use of a medication.

General Considerations

Designing Drug Label, Labeling, & Packaging

- Consider a drug product's end users and its environment of use during development
- Assess and minimize risk of medication errors due to design of product labels and labeling
- See FDA draft Guidance for Industry: *Safety Considerations for Product Design to Minimize Medication Errors* for more information on analytical methods for risk assessments

Container Label Size

- Ideally, create container labels or packaging large enough to accommodate all critical information on the immediate product container label.
- FDA regulations provide an exemption from some drug labeling requirements when the container is too small.
  - Provided that all required information is present on the carton labeling or in the prescribing information.

Container Label Requirements

- Drug Products: minimum requirements under 21 CFR 201.10(i)
  - Proprietary name (if any) and established name
  - Product strength
  - Lot number
  - Name of manufacturer, packer, or distributor
- USP requires labels of official drug product to bear an expiration date

- Biologic Products: Minimum requirements under 21 CFR 610.60(c)
  - Name of product
  - Lot number
  - Manufacturer name
  - Recommended individual dose for multiple dose containers

Container Label Recommendation

- We recommend the principal display panel (PDP) include:
  - Proprietary name
  - Established name or proper name
  - Product strength
  - Route(s) of administration
  - Warnings (if any) or cautionary statements (if any)

Text Size and Style

- Choose easy to read font, not lightweight or condensed
  - Improved readability with larger font size such as 12-point sans serif (e.g. Arial)
- 12-point font preferred when label size permits

Contrast of Text and Background

- Choose text and background color to afford adequate legibility of text
- Avoid color combinations that do not afford maximum legibility of text

Proprietary Name
(Established name)

Proprietary Name
(Established name)

Information Crowding/Visual Clutter

- Crowded labels may make important information difficult to read or easily overlooked
- Separate lines or blocks of text with sufficient white space
- Move less important information to back panels, side panels, or prescribing information
- Remove information about business partnerships (apart from required manufacturer, distributor, or packer information)

Information Crowding/Visual Clutter

- Discourage use of:
  - Logos, bars, stripes, watermark graphics, lines, and symbols

- When such items are included, the graphic design should not compete with, interrupt, or distort important information.

Dangerous Abbreviations, Acronyms, and Symbols

Mistaken “µg” as mg (milligram) Use “mcg”	Mistaken “IU” for IV (intravenous) Use “units”

- Certain abbreviations, acronyms, and symbols are dangerous and should not be used.
- Non-standardized abbreviations, symbols, and dose designations can also lead to mistakes.
- Refer to The Joint Commission’s “Do Not Use” list
- Refer to the Institute for Safe Medication Practices’s (ISMP) “List of Error Prone Abbreviations, Symbols, and Dose Designations”

Color Differentiation

- Color differentiation is an effective tool that can:
  - Differentiate products within a manufacturer's product line
  - Differentiate strengths within a manufacturer's product line
  - Highlight certain aspects of the label, such as important warning statements
- Most effective when the color used has no association with a particular feature and there is no pattern in application of the color scheme

Color Coding

- Use color to designate a specific meaning
- FDA generally recommends avoiding color coding in most instances
  - Reserved for special circumstances after human factors testing and feedback on the prototype from all end users is received and evaluated by FDA prior to use

Color Coding

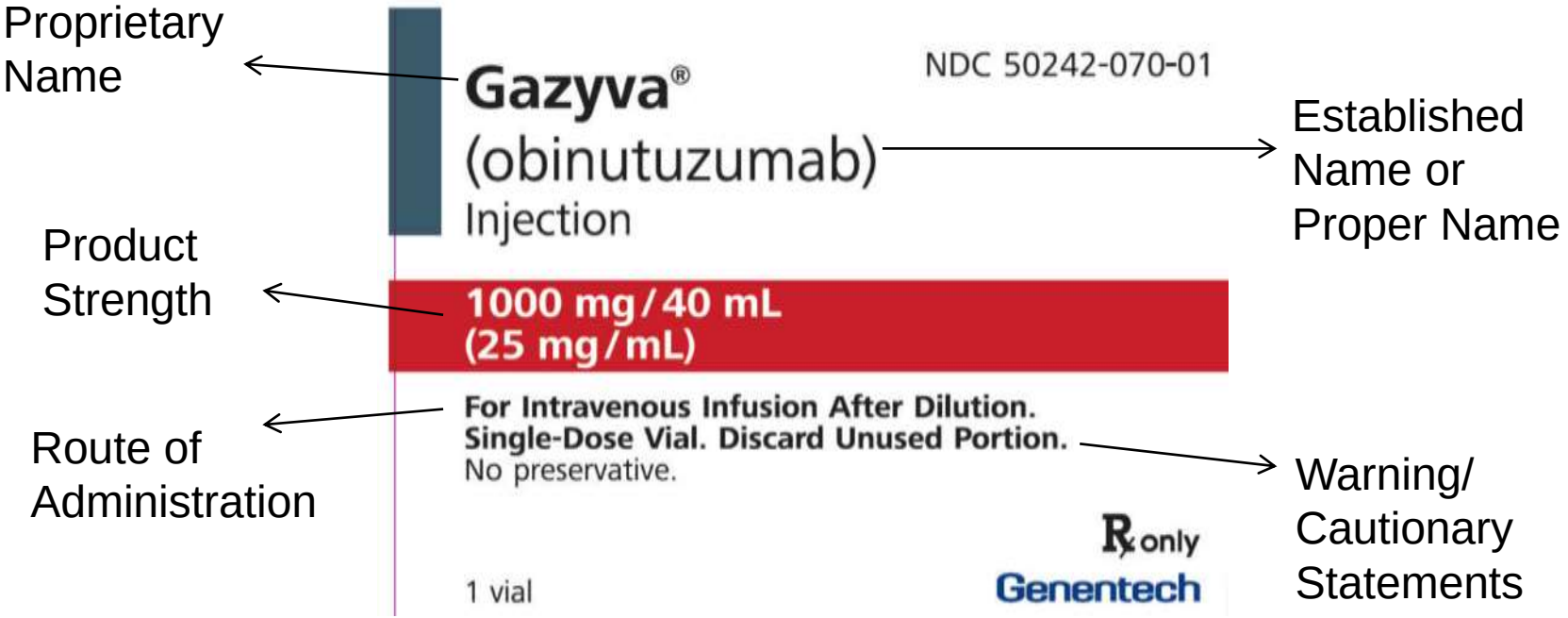
- Color coding can sometimes lead to confusion

Color Coding

- Certain applications of color coding are appropriate (e.g. warfarin)

Special Considerations

Principal Display Panel (PDP)



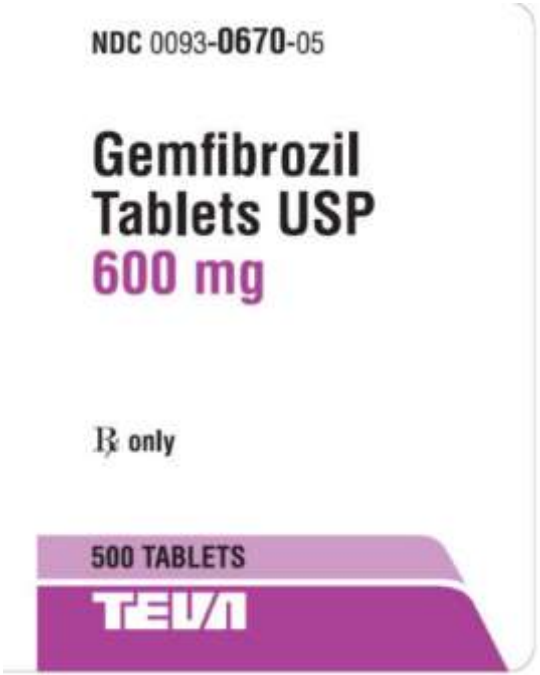
PDP is the panel of a container label or carton labeling that is most likely to be displayed, presented, shown, or examined under by the end user.

Product Strength

- Ensure that the product strength is prominent on the container label and carton labeling.
- Apply appropriate techniques to differentiate strengths of the same product, or similar strengths of different products stored in close proximity.
- Techniques include:
  - Boxing
  - Prominent typeface or type weight
  - Color differentiation


ADDERALL XR
(Mixed Salts of A Single-Entity Amphetamine Product)
Extended-Release Capsules
15 mg
100 Capsules
Rx only
Shire
ADDERALL XR
(Mixed Salts of A Single-Entity Amphetamine Product)
Extended-Release Capsules
20 mg
100 Capsules
Rx only
Shire
ADDERALL XR
(Mixed Salts of A Single-Entity Amphetamine Product)
Extended-Release Capsules
25 mg
100 Capsules
Rx only
Shire
ADDERALL XR
(Mixed Salts of A Single-Entity Amphetamine Product)
Extended-Release Capsules
30 mg
100 Capsules
Rx only
Shire


GABAPENTIN
Tablets
600 mg
GEMFIBROZIL
Tablets, USP
600 mg
TEVA
TEVA


NDC 0093-0670-05
Gemfibrozil
Tablets USP
600 mg
℞ only
500 TABLETS
TEVA

Product Strength

- The product strength units should match the units of measure described in the DOSAGE AND ADMINISTRATION section of the prescribing information to avoid error

Dosing for Perioperative Hypotension

Intravenous bolus administration:
50 mcg to 250 mcg

Product Strength

- Express the strength for small volume parenteral products in **total quantity per total volume** followed by quantity per milliliter (mL)
  - per USP General Chapter <1> *Injection.*

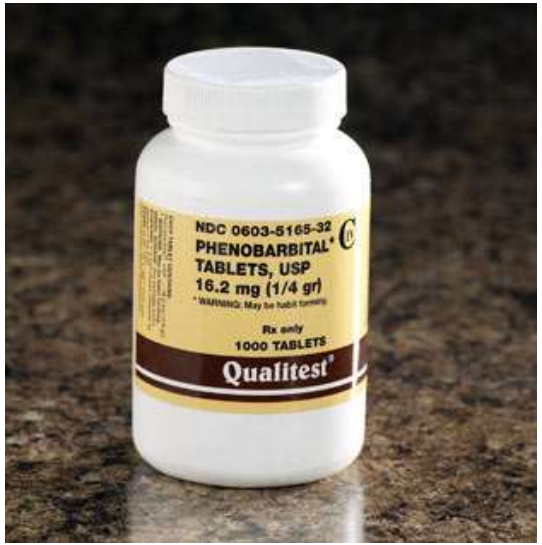
How many USP units are in this vial?

30,000 units

30,000 USP units/30 mL
(1,000 USP units/mL)

Product Strength

- Metric Measurements
  - Dose or strength expression should appear in metric units of measure such as mL, mg, and mcg
  - Avoid apothecary or household measurements such as tsp, TBSP, drams, grains, or ratios



Route of Administration

- Which is a better statement?
  - A. Not for intrathecal use
  - B. For IV Use only
  - C. For Intravenous Use only

Route of Administration

- Avoid use of abbreviations
- Use positive statements instead of negative statements
  - Easy to overlook the word “not”. Not for intrathecal use
  - Affirmative statements help to ensure readers understand the intended route of administration, even if they do not read every word

For Intravenous Use only

Expiration Dates

- Current practice
  - Expression of expiration dates varies
  - Abbreviations often used (e.g. MA19)
- Safety Considerations Draft Guidance (April 2013)
- DSCSA Draft Guidance[1] (Sept 2018) recommends

YYYY-MM-DD if only numerical

YYYY-MMM-DD if alphabetical month

[1]Draft Guidance for Industry: Product identifiers under the Drug Supply Chain Security Act Questions and Answers

Linear Barcode

- The linear barcode, required under 21 CFR 201.25, should be surrounded by enough white space to allow scanners to read the bar code properly

National Drug Code (NDC)

- Avoid assigning product codes that are numerically similar or identical.
- Assignment of sequential numbers for the product code is not an effective differentiating feature (e.g., 6666, 6667, and 6668) for injectable products containing the same concentration (quantity/mL) of drug but different total volumes

Drug Supply Chain Security Act (DSCSA)

- Product identifiers under DSCSA
- Please see Draft Guidance for Industry: Product identifiers under the Drug Supply Chain Security Act Questions and Answers
  - Available online at https://www.fda.gov/media/116304/download

Other Special Container Label and Carton Labeling

Unit-Dose Blister Pack

- Ideally, the proprietary and established names, strength, lot number, expiration date, bar code, and manufacturer should appear over each blister cell.
- The product strength should be described in milligram amount of drug per single unit

Dosing Devices for Liquids

- Dosing devices should be consistent with the recommended doses

- Volume preferably expressed in milliliters (mL)

Question 1

- Which of the following statement is false?
  - A. Container labels and carton labeling should be designed with the end users in mind.
  - B. The strength for a 5 mL injectable drug should be expressed in total quantity per total volume followed by quantity per milliliter (mL).
  - C. The abbreviation µg is commonly used to abbreviate microgram in today's drug labeling.

Question 2

- What is the best strategy to differentiate between the 3 different strengths (5 mg, 10 mg, and 15 mg) of a solid oral dosage form drug candidate your company is currently developing?
  - A. Color coding
  - B. Color Differentiation
  - C. List the strengths in both mg and grains.

Summary

- Container labels and carton labeling should promote the safe use of drug products.
- The principal display panel should display critical product information towards easy identification of the drug product.
- Consider size, color, layout, and other printing features when designing container labels and carton labeling.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