U.S. FOOD & DRUG ADMINISTRATION

Process for Reviewing Nonproprietary Name Suffix for Biological Products

Safety Considerations for Product Design, Container Labels, and Carton Labeling

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Learning Objectives

- Understand how FDA evaluates nonproprietary name suffix for biological products
- Understand the safety considerations for product design that minimizes the risk of medication errors
- Understand how FDA recommends sponsors design their container labels and carton labeling to minimize medication errors

Objectives Of The Naming Convention:

Transparency:

- Facilitates identification of products for safe use and pharmacovigilance
- Facilitates prescribing and dispensing of the intended product
- Patients and providers want to know what the patient received

Trust:

- Provides FDA and others with another critical tool to perform product-specific pharmacovigilance in all settings of care

Uptake:

- Enhanced prescriber and public confidence may facilitate market uptake

Reason for the Naming Convention

Pharmacovigilance systems, both active and passive, vary in their use of identifiers to differentiate among biological products.

Many active pharmacovigilance systems, have limited ability to track to its manufacturer a biological product that shares the same proper name with other biological products.

Other product identifiers, such as NDC numbers, are not routinely recorded in billing and patient records in many clinical settings in which biological products are dispensed and administered.

Nonproprietary names that include distinguishing suffixes can serve as a key element to identify specific products in billing and claims records used for active pharmacovigilance.

Other product-specific identifiers, such as proprietary names or NDCs, may not be available or could change over time.

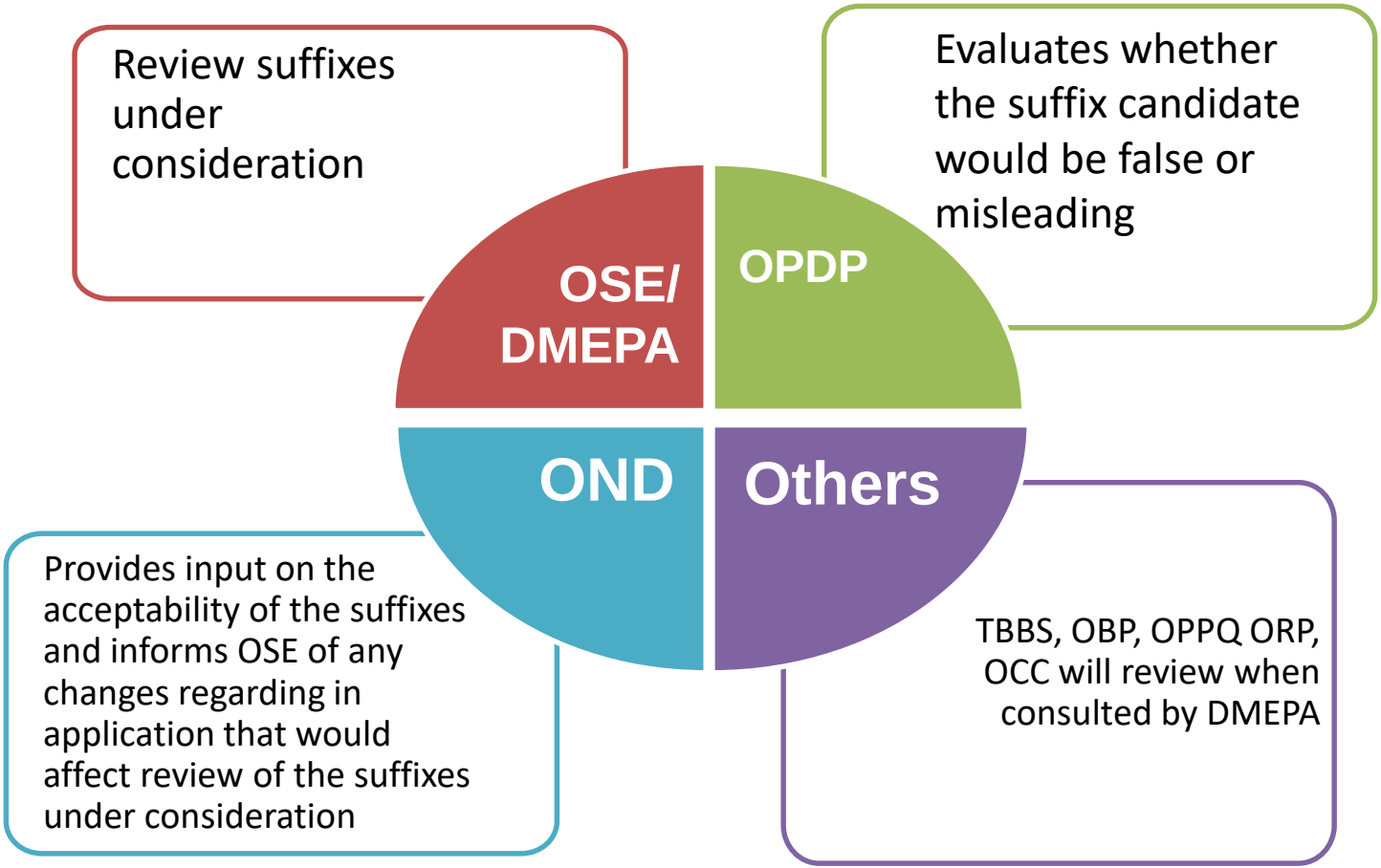
Process for Suffix Review

- Suffix evaluation by FDA occurs as part of the BLA review
  - In CDER, coordinated by Division of Medication Error Prevention and Analysis (DMEPA)
  - In CBER, coordinated by the Advertising and Promotional Labeling Branch

- FDA may generate a suffix for designation in the proper name, if an applicant
  - Requests an FDA-generated suffix be assigned to their product
  - Does not request FDA review of proposed suffix(es)
  - Does not request review of a suffix FDA finds acceptable or within an appropriate time frame to allow FDA sufficient time to review

- FDA encourages applicants requesting FDA review of suffixes to conduct due diligence on their proposed suffixes
  - Any supporting information that is provided will be considered by FDA in its evaluation of proposed suffixes

Suffix Review: Roles



How FDA evaluates suffixes

FDA's review begins by assessing format looking to see whether the suffix is:

- Composed of four lower-case letters of which at least three are distinct
- Does not Contain numerals and other symbols
- Devoid of meaning
- Unique to each product
- Nonproprietary
- Attached to the core name with a hyphen

How FDA evaluates suffixes

If the suffix format does not raise any concerns, FDA proceeds to review each suffix to determine that it will not

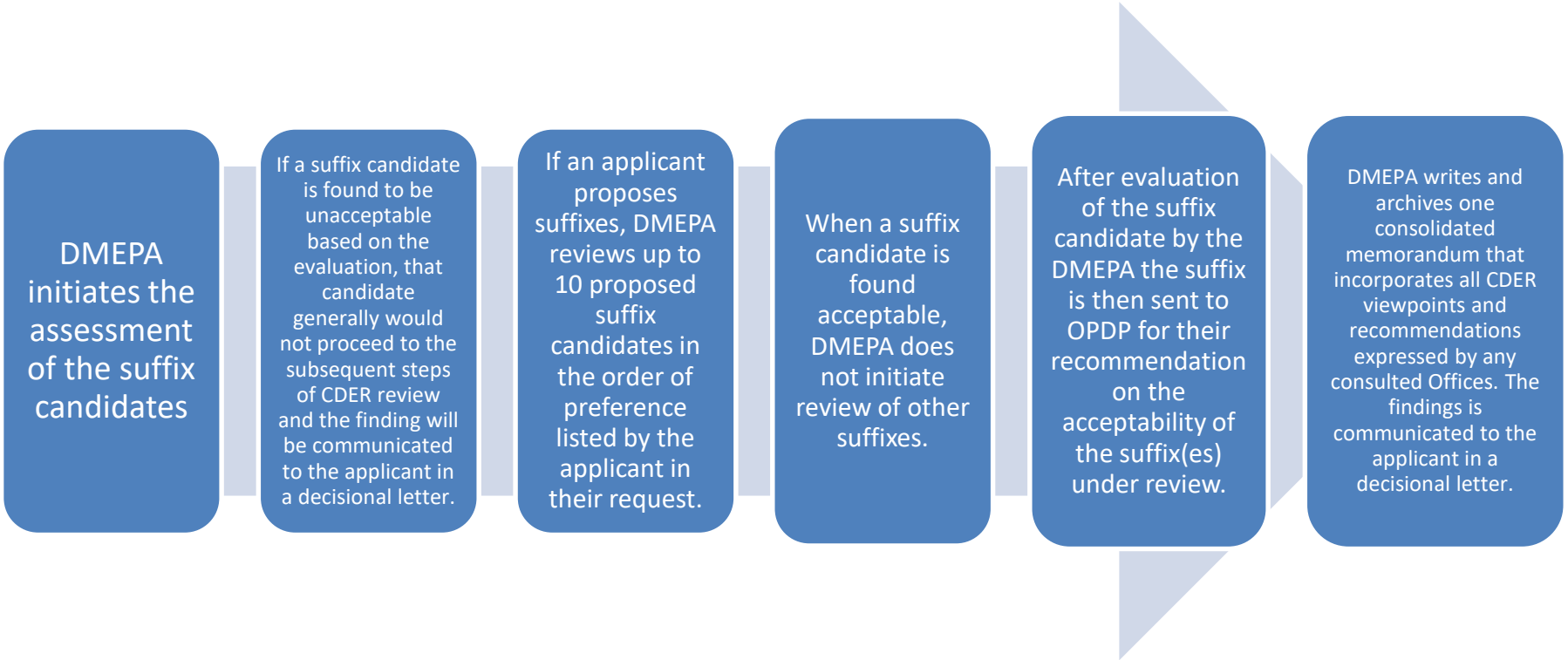
- Include abbreviations commonly used in clinical practice in a manner that may lead the suffix to be misinterpreted as another element on the prescription or order
- Contain or suggest any drug substance name or core name
- Look similar to or be capable of being mistaken for the name of a currently marketed product (e.g. should not increase the risk of confusion or medical errors with the product and/or other products in the clinical setting)
- Be too similar to any other FDA-designated nonproprietary name suffix
- Look similar to or otherwise connote the name of the license holder
- Be false or misleading, such as making representation with respect to safety or efficacy

Process for identifying similar names and similar suffixes

To identify similar drug names	FDA uses the Phonetic and Orthographic Computerized Analysis (POCA) tool and sets the program to search those names listed on drugs@fda and pending proposed proprietary names.
To identify similar suffixes	FDA uses the POCA tool and sets the program to search for suffixes that are similar in spelling, writing or pronunciation to those suffixes that have been conditionally accepted or approved by FDA*

*FDA maintains two separate repositories of suffixes using the POCA tool: one will be publicly accessible and allow users to search their suffix candidate against only those suffixes that are associated with approved biological products, the other non-public repository will consist of those suffixes associated with INDs and pending BLAs and will only be accessible to FDA staff to use in their review of suffix candidates.

Process for Suffix Review



U.S. FOOD & DRUG ADMINISTRATION

Safety Considerations for Product Design, Container Labels, and Carton Labeling

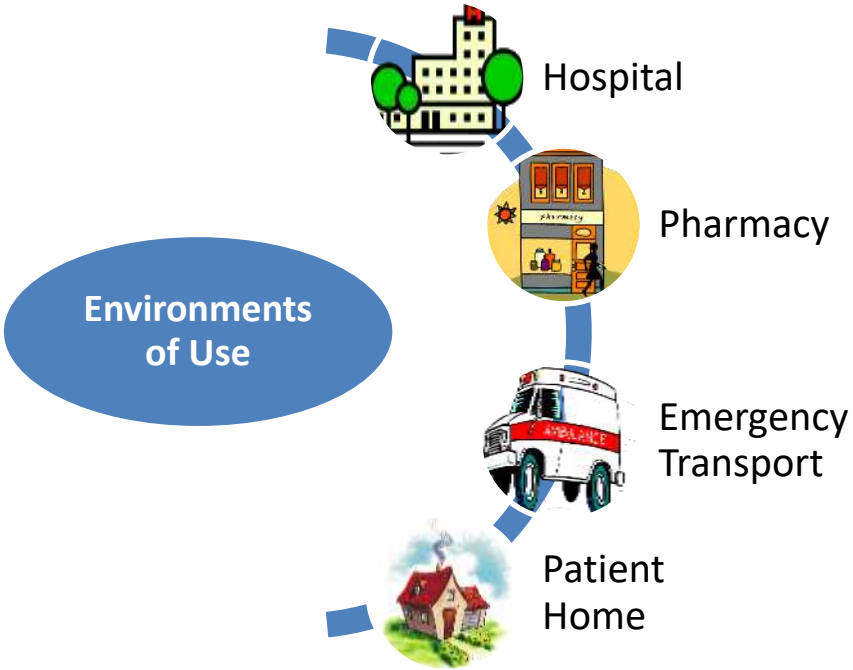
Safety Considerations for Product Design to Minimize Medication Errors

Guidance for Industry

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

April 2016
Drug Safety

Early Stage Considerations



- Who are the end users?
- What critical tasks must the end user perform?
- Is extensive manipulation or cognitive process required to use the product?
- Are there physical or mental limitations?
- In what environment will product be used?
- How are drugs stored and obtained in the environment?
- Are there similar products used in the environment?

Drug Product User Interface

- Evaluate how and why problems have occurred with similar products
  - Identify error prone features and eliminate them from design
  - Prevent same errors from occurring
- Sponsors should consider lessons learned to minimize risks associated with their designs

Examples of Known Problems Due to Product Design

Product Line Extensions

- Creating extended-release product strength(s) that overlap in strength(s) with immediate release products
- Creating extended-release product strengths that are achievable from the marketed immediate-release product strength(s)

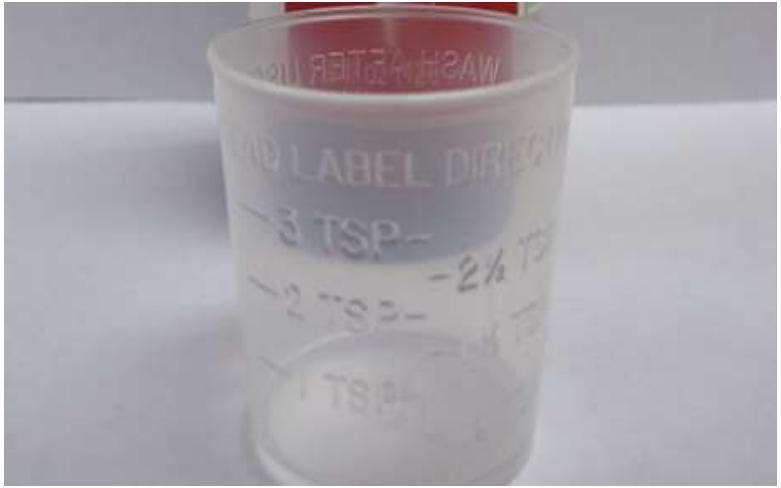
Special Considerations for Transdermal Products

- Include an identifying label on the backing membrane that includes the Drug Name and Strength. For a transdermal system strength should be presented as a transdermal delivery rate (e.g. XX mg/day).
- Ensure the ink has adequate contrast (i.e., ink is visible)
- Marking should be visible for the duration of patch wear
- Clear patch difficult to see on skin

FDA

Inconsistency between drug product strength and dosing

- Multiple units (e.g. tablets, capsules, vials, syringes) required to achieve a usual single dose
  - Dosing errors due to miscalculations
  - Dosing errors due to forgetting how much has already been administered



- Dosing Devices not appropriate for dosages to be measured
- Difficult to see dose markings on dosing device

Intravenous Products

- 2 step dilution for a product already in solution
  - Overdoses due to failure to dilute product
  - Improper doses due to incorrect dilution
- Co-packaging of special diluent
  - Diluent separated from dry powder
  - Confusing diluent as drug

- Container closures that look similar within a product line
- Container closures serving as labels that have illegible information

Capsules for inhalation swallowed whole

Topical products packaged in container/ closures that look similar to eye, ear, nasal, or oral products

Proactive Risk Assessments

Develop drug products using analytical methods to investigate, understand, and correct identified risks

These methods should be applied early in drug development to build safety into the product design and throughout a drug product's life cycle

Failure Mode and Effects Analysis

- Systematic evaluation of proposed product within the medication use system
- Provides understanding of relative impact of different types of system failures
- Considers everyone in the medication use process

Proactive Risk Assessments

CDER recommends human factors studies be conducted to characterize risks as well as develop mitigation strategies.

Simulated Use Testing

- Systematic collection of data from representative participants in realistic situations
- Help determine whether users can safely and correctly perform critical tasks
- Seeks to assess actual use
- Results can be used to update the FMEA

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.

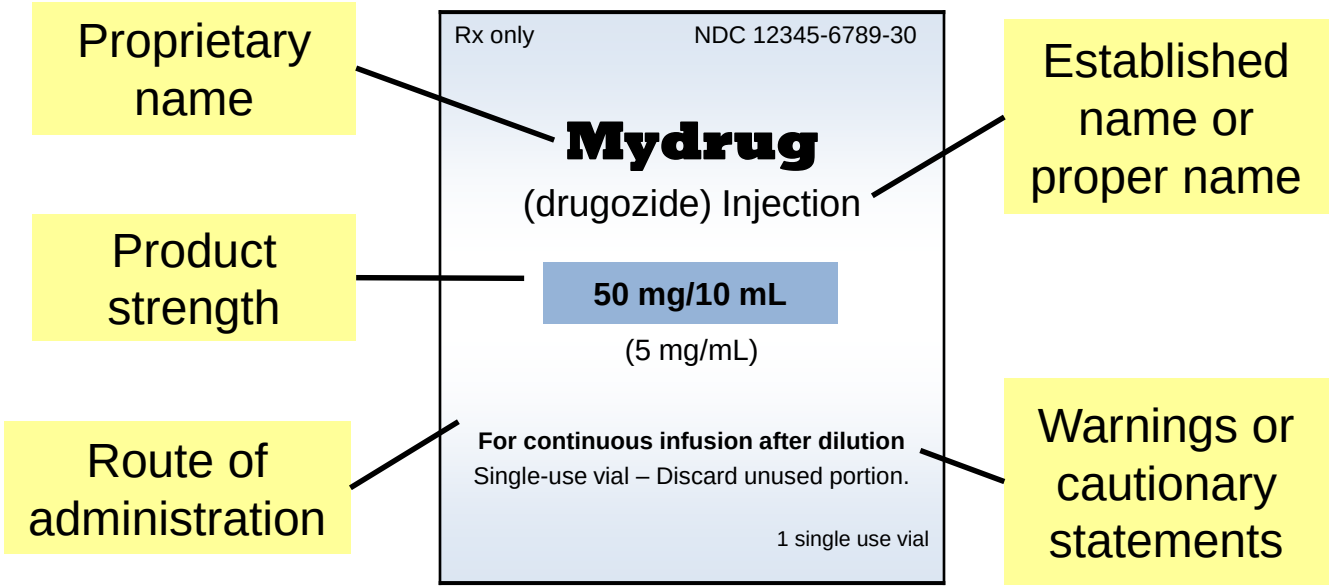
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2013
Drug Safety

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

- Initial prescription
- Procurement
- Preparation
- Dispensing
- Administration to the patient

Principal Display Panel (PDP)



General Considerations For Labels and Labeling

Container Label Size

Create larger container labels or unique packaging to accommodate all critical information on the immediate product container label.

21 CFR 201.10(i) exempted small containers provide that the following required information are present:

- Proprietary name and established name (if any)
- Product strength
- Lot number
- Name of manufacturer, packer, or distributor

USP requires labels of official drug product to bear an expiration date

Text Size and Style

- Select a font that is easy to read, not lightweight or condensed.
- Recommend the use of at least a 12-point font whenever label size permits
  - 12-point sans serif (e.g. Arial)
  - Improves readability

Contrast of Text and Background

Proprietary Name
(Established name)

Proprietary Name
(Established name)

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

Information Crowding and Visual Clutter

- Crowded labels may make important information difficult to read and/or easily overlooked
- Safety Considerations:
  - 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 and Visual Clutter

- Logo immediately before or after the proprietary name can be misinterpreted as an additional letter in the proprietary name

- <u>Safety Consideration:</u>

  – Don’t superimpose text over images or logos

Images of Tablets/Capsules

- Can help healthcare professionals confirm they are dispensing the correct medication
- Images should appear at bottom of labels and labeling
- Should not compete in size or prominence with proprietary name, established name, or strength
- Images should represent the actual tablet or capsule, reflecting true size, color, shape, and imprint.
- DO NOT use schematic or computer-generated images

Dangerous Abbreviations, Acronyms, and Symbols

- Certain abbreviations, acronyms, and symbols are dangerous and should not be used
  - µg (microgram) mistaken as mg (milligram)
  - IU (international unit) confused as intravenous route of administration
- Non-standardized or unfamiliar abbreviations, symbols, and dose designations can also lead to mistakes
- Refer to:
  - Institute for Safe Medication Practices (ISMP) “List of Error Prone Abbreviations, Symbols, and Dose Designations”
  - The Joint Commission’s “Do Not Use” list

Typical Pharmacy Shelf

Look-alike Container Labels and Carton Labeling

- Create labels and labeling sufficiently distinct from that of their other products and the products of other manufacturers

- Consider when products are customarily stored side-by-side or near one another

Look-alike Container Labels and Carton Labeling

Look-alike Container Labels and Carton Labeling

- Avoid/minimize use of corporate trade dress
- Use color prudently to bring attention to important information (e.g. product name, strength, important warnings)
  - Consider variation in color perception
  - DO NOT want to encourage identification by color only since it may discourage reading of labels

Examples of Look-Alike Trade Dress

Adderall XR (Shire)

Citalopram

Clonazepam (Teva)

Teva

Pfizer

Color Differentiation vs. Color Coding

- 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: Uses 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

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

In other cases, color coding can lead to confusion

How Proprietary, Established, and Proper Names should be Displayed

- Maximize the readability of proprietary name and established name
- Display the names in a manner that is consistent with 21 CFR 201.10(g)(2) to ensure that the proprietary and established names have commensurate prominence
- Established name for drug products should include finished dosage form

Mydrug (drugozide injection)	**OR**	Mydrug (drugozide) injection	**OR**	Mydrug (drugozide) Injection

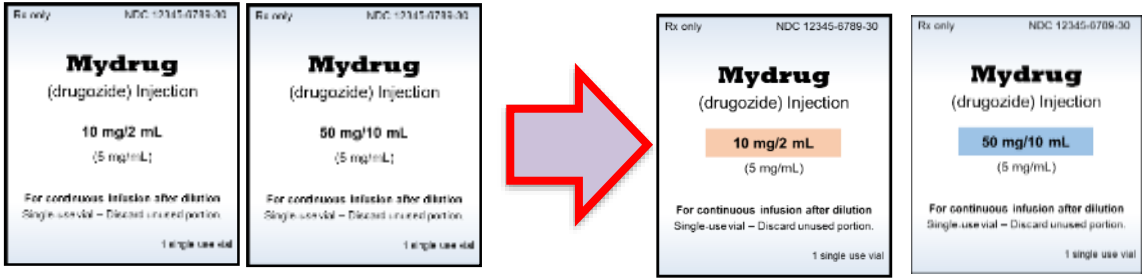
Product Strength should be well differentiated

Strength Differentiation:

- Ensure the product strength stands out on the container label and carton labeling

Techniques include:

- Boxing
- Prominent typeface or type weight
- Color differentiation



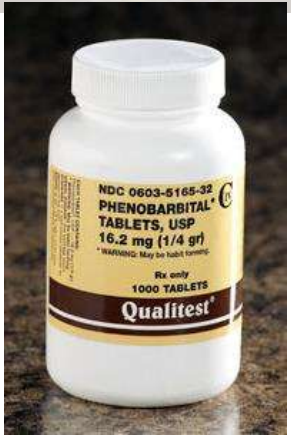
Use Consistent Unit of Measure

Strength Designations should use a consistent unit of measure across all elements of labels and labeling

Dosing for Perioperative Hypotension

Intravenous bolus administration:
50 mcg to 250 mcg

Product Strength



Small Volume Parenteral Products

Follow USP General Chapter <7> *Labeling*

- Total quantity per total volume followed by concentration per milliliter (mL)

Metric Measurements

Dose or strength expression should appear in metric units of measure (mL, mg, and mcg)

Warnings for Critical Information

- Use affirmative statements
  - For intravenous infusion
  - Fatal if given by any other route
  - Must dilute before use

Consider whether the statement is helpful to ensure safe use

Doctor's Prescription:
Take 6 mg orally once daily.

Patient: Took 1 mg orally once daily.

Patient stated she was following directions on the bottle

Institute for Safe Medication Practices. Safety Briefs: Positive change, negative consequence. ISMP Med Saf Alert Acute Care. July 2014;19(15):1.

Question 1

Certain abbreviations, acronyms, and symbols should not be used on labels because;

A. They could be misinterpreted (e.g. µg (microgram) mistaken as mg (milligram))

B. They could be confused as route of administration

C. Non-standardized or unfamiliar abbreviations, could lead to mistakes

D. All of the above

Question 2

Suffix evaluation in CDER is coordinated by:

A. Division of Medication Error Prevention and Analysis
B. Office of Biotechnology Products
C. Therapeutic Biologics and Biosimilar Staff

FDA U.S. FOOD & DRUG ADMINISTRATION