DIA 2019
GLOBAL ANNUAL MEETING
SAN DIEGO | JUNE 23-27

Updates from FDA/CDER: Drugs@FDA vs. DailyMed, Labeling Resources, and Future Labeling Guidances

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The labeling examples in this presentation are provided only to demonstrate current labeling development challenges and should not be considered FDA recommended templates.

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Overview of Presentation

- Prescribing Information
- Drugs@FDA and DailyMed: Labeling Differences
- Labeling Resources
- Future Labeling Guidances

Prescribing Information (PI)

- Written for healthcare practitioners and must:[1]
  - Contain a summary of essential scientific information needed for safe and effective use of **human prescription drug and biological products**
  - Be informative and accurate and neither promotional in tone nor false or misleading
  - Be updated when new information becomes available that causes labeling to become inaccurate, false, or misleading
- There are only two PI formats:
  - "Physician Labeling Rule" (PLR) labeling[2] (based on 2006 rule)
  - "Old" (non-PLR) format labeling[3] (based on 1979 rule)

[1] 21 CFR 201.56(a)(1) and (2); [2] 71 FR 3922 (January 24, 2006); [3] 44 FR 37434 (June 26, 1979)

CDER Prescription Drug and Biological Product Labeling in PLR Format – Over the Last Five Years[1]

Month/Year	Proportion of CDER Prescription Drug and Biological Product Labeling in PLR Format (NDAs/BLAs only)
January 2014	~ 45%
January 2016	~ 56%
January 2017	~ 61%
January 2018	~ 63%
March 2019	**~ 66%** → **NDAs = ~64%** **BLAs = ~94%**

CDER = Center for Drug Evaluation and Research at FDA; NDAs = New Drug Applications; BLAs = Biologics License Applications

[1] Analysis based on Structured Product Labeling (SPL) files - generally only includes marketed products and excludes repacker and authorized generic labeling

Principles of Updating Prescribing Information[1]

- Ensure labeling meets statutory/regulatory requirements and is consistent with guidance recommendations[2,3]
- Ensure consistent message
- Improve organization/formatting
- Update terminology and remove/revise outdated, misleading, or clearly inapplicable information[4]
- Update safety information
- Consider adding/modifying indications, usages, and/or dosages[3]

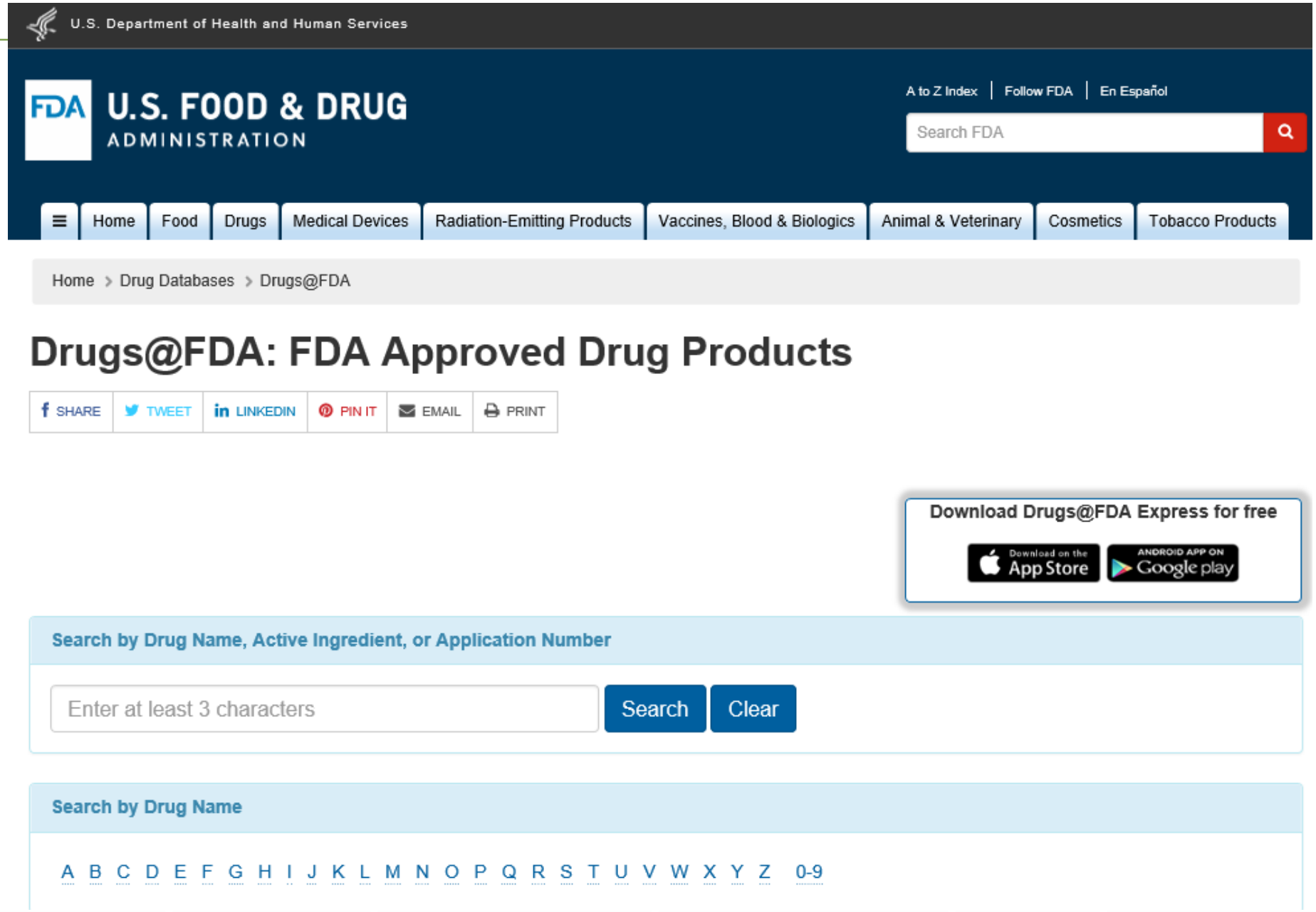
[1] Implementing PLR Content and Format Requirements Guidance;
[2] Final guidances represents the Agency's current thinking (alternative approaches are acceptable if they satisfy statutes/regulations)
[3] If applicable; [4] 21 CFR 201.56(a)(2) and 21 CFR 201.56(d)(4)

Opportunities for Application Holders to Update Labeling

Before submitting any supplement to an NDA/BLA, review entire labeling and assess if information is outdated

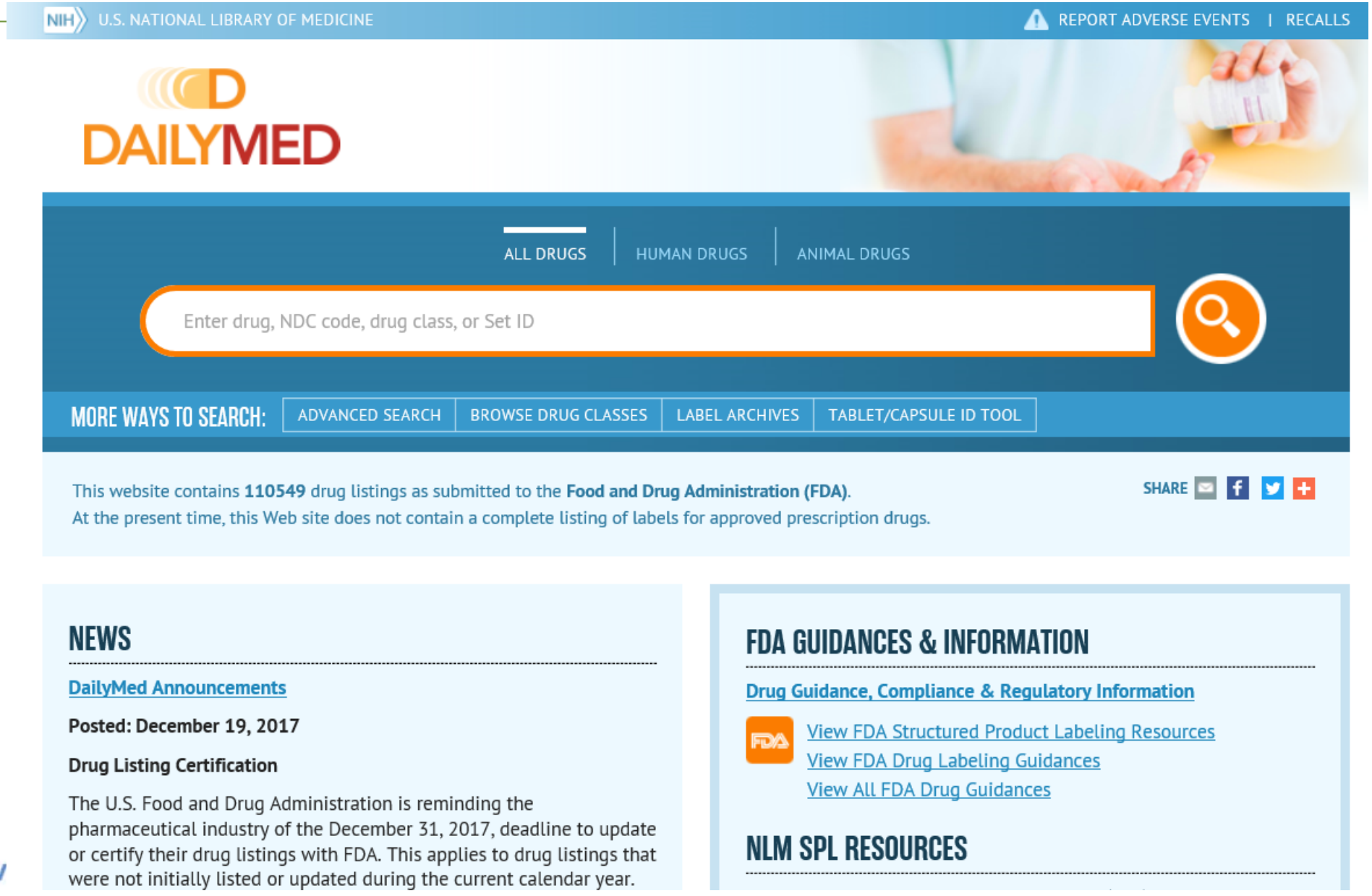
- PLLR conversion labeling supplements provide an opportunity to assess and update entire labeling
- Voluntary PLR conversion of "old" format labeling
  - Converting Labeling for Older Drugs from Old Format to PLR Format (https://www.fda.gov/media/109318/download)

Drugs@FDA (www.fda.gov/drugsatfda)



www.fda.gov

DAILYMED (https://dailymed.nlm.nih.gov/dailymed/)



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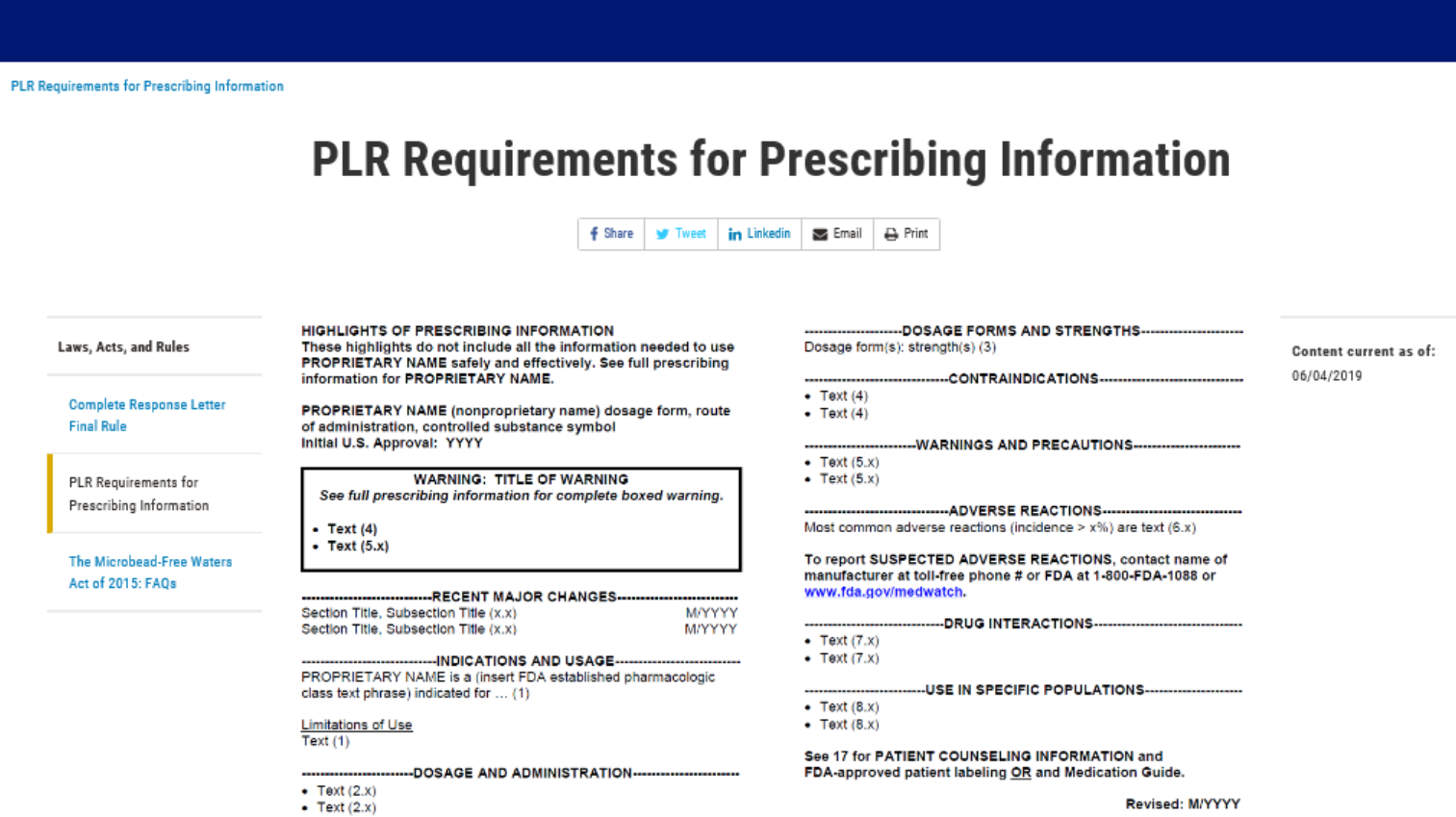
Drugs@FDA vs. DailyMed: Labeling Differences

	Drugs@FDA	DailyMed
Labeling Type	Last FDA-approved PI[1]	Most recent labeling submitted to FDA (may not be FDA-approved)
Format	PDF	SPL (hyperlinks, allows indexing)
Includes recent PI updates: • Annual reportable changes • Pending CBE-0 supplements	No	Yes
Includes carton/container labeling	Sometimes	Always
Includes previously approved labeling, regulatory history, and FDA reviews	Yes	No
FDA reviews labeling prior to posting	Always	Generally, no

PI = Prescribing Information; PDF = Portable Document Format; SPL = Structured Product Labeling; CBE = changes being effected; [1] Drugs@FDA does not always include the last FDA-approved PI

PLR Requirements for Prescribing Information Website

(https://www.fda.gov/drugs/laws-acts-and-rules/plr-requirements-prescribing-information)



PLR Requirements for Prescribing Information

PLR Requirements for Prescribing Information

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Laws, Acts, and Rules

Complete Response Letter Final Rule

PLR Requirements for Prescribing Information

The Microbead-Free Waters Act of 2015: FAQs

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.

- **Text (4)**
- **Text (5.x)**

----------RECENT MAJOR CHANGES----------
Section Title, Subsection Title (x.x) M/YYYY
Section Title, Subsection Title (x.x) M/YYYY

----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for … (1)

Limitations of Use
Text (1)

----------DOSAGE AND ADMINISTRATION----------
- Text (2.x)
- Text (2.x)

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------
- Text (8.x)
- Text (8.x)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling OR and Medication Guide.

Revised: M/YYYY

Content current as of:
06/04/2019

Overview of Website

FDA's *PLR Requirements for Prescribing Information* website provides resources for the development of human prescription drug and biological product labeling regulated under New Drug Applications, Biologics License Applications, and Abbreviated New Drug Applications.

- Labeling for such products includes but is not limited to:
  - Prescribing Information (PI)
  - FDA-approved patient labeling [Medication Guides, Instructions for Use, and Patient Information (also called Patient Package Inserts)], and
  - Carton and container labeling.
- The PI has two formats: "Physician Labeling Rule" (PLR) format and "old" (non-PLR) format). Given that all new human prescription drug and biological products approved since June 2001 and certain new human prescription drug and biological products approved before June 2001 (e.g., those approved for new uses after June 2001) must have PI in PLR format, this website focuses on providing resources for the development of PI with PLR format labeling.

PLR Requirements for Prescribing Information Website (https://www.fda.gov/drugs/laws-acts-and-rules/plr-requirements-prescribing-information)

- Labeling Requirements and Rules
- Prescribing Information Guidances
- Presentations – Labeling Sections
- Presentations – Broad Labeling Content
- Sample Templates and Format Labeling Tools
- Product Quality-Related Labeling Resources
- Established Pharmacologic Class Resources
- ANDA Labeling Resources
- Biological Product Labeling Resources
- Patient Labeling Resources
- Labeling Databases
- Additional Labeling Resources

Future Labeling Guidances[1]

- PK in Patients with Impaired Renal Function – Study Design, Data Analysis and Impact on Dosing and Labeling (revised draft)
- Drug Abuse and Dependence Section of Labeling (draft)
- Instructions for Use for Human Prescription Drug and Biological Products (draft)
- Pregnancy, Lactation and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products (revised draft)
- Quantification of Sodium, Potassium, and Phosphate in Human OTC and Prescription Drug Labeling (draft)

[1] See March 2019 Guidance Agenda https://www.fda.gov/media/124386/download; PK = pharmacokinetics

Want to Learn More About Labeling?

2019 CDER Prescription Drug Labeling Conference[1]

Topics:

Updates: Prescribing Information, carton/container labeling, and FDA-approved patient labeling

Logistics:

- December 4th and 5th, 2019
- "The HOTEL" at the University of Maryland in College Park, Maryland
- Check website for online or in person registration: https://www.fda.gov/drugs/development-approval-process-drugs/cder-small-business-industry-assistance-sbia

[1] CDER Small Business & Industry Assistance (SBIA): Regulatory Education for Industry (REdI)

Thank You!

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- For general questions about the Prescribing Information: See the Labeling Development Team webpage: https://www.fda.gov/about-fda/center-drug-evaluation-and-research/labeling-development-team
- For specific questions about labeling under an NDA, BLA, or ANDA: Please contact the regulatory project manager assigned to the application

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