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

Eric Brodsky, M.D.
Associate Director
Labeling Development Team, Office of New Drugs
Center for Drug Evaluation and Research (CDER), FDA

U.S. FOOD & DRUG ADMINISTRATION
Disclaimer

The views and opinions expressed in the following PowerPoint slides are those of the individual presenter; should not be attributed to DIA, its directors, officers, employees, volunteers, members, chapters, councils, Communities or affiliates; 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.

For work prepared by US government employees representing their agencies, there is no copyright and these work products can be reproduced freely. Drug Information Association, Drug Information Association Inc., DIA and DIA logo are registered trademarks.
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

<table>
<thead>
<tr>
<th>Month/Year</th>
<th>Proportion of CDER Prescription Drug and Biological Product Labeling in PLR Format (NDAs/BLAs only)</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 2014</td>
<td>≈ 45%</td>
</tr>
<tr>
<td>January 2016</td>
<td>≈ 56%</td>
</tr>
<tr>
<td>January 2017</td>
<td>≈ 61%</td>
</tr>
<tr>
<td>January 2018</td>
<td>≈ 63%</td>
</tr>
<tr>
<td>March 2019</td>
<td>≈ 66%</td>
</tr>
</tbody>
</table>

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

www.fda.gov
Principles of Updating Prescribing Information

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- Update terminology and remove/revise outdated, misleading, or clearly inapplicable information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

---

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)

www.fda.gov
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](https://www.fda.gov/media/109318/download))
This website contains 110549 drug listings as submitted to the Food and Drug Administration (FDA).
At the present time, this Web site does not contain a complete listing of labels for approved prescription drugs.

**NEWS**

**DailyMed Announcements**

**Posted: December 19, 2017**

**Drug Listing Certification**

The U.S. Food and Drug Administration is reminding the pharmaceutical industry of the December 31, 2017, deadline to update or certify their drug listings with FDA. This applies to drug listings that were not initially listed or updated during the current calendar year.

**FDA GUIDANCES & INFORMATION**

**Drug Guidance, Compliance & Regulatory Information**

- [View FDA Structured Product Labeling Resources](https://www.fda.gov/drugs/ResourcesForYou/Labels/ucm189085.htm)
- [View FDA Drug Labeling Guidelines](https://www.fda.gov/drugs/ResourcesForYou/Labeling/ucm189085.htm)
- [View All FDA Drug Guidances](https://www.fda.gov/drugs/ResourcesForYou/Labeling/ucm189085.htm)

**NLM SPL RESOURCES**
<table>
<thead>
<tr>
<th><strong>Labeling Type</strong></th>
<th><strong>Drugs@FDA</strong></th>
<th><strong>DailyMed</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Last FDA-approved PI</td>
<td>Most recent labeling submitted to FDA (may not be FDA-approved)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Format</strong></th>
<th><strong>Drugs@FDA</strong></th>
<th><strong>DailyMed</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PDF</td>
<td>SPL (hyperlinks, allows indexing)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Includes recent PI updates:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual reportable changes</td>
</tr>
<tr>
<td>Pending CBE-0 supplements</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Includes carton/container labeling</strong></th>
<th><strong>Drugs@FDA</strong></th>
<th><strong>DailyMed</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sometimes</td>
<td>Always</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Includes previously approved labeling, regulatory history, and FDA reviews</strong></th>
<th><strong>Drugs@FDA</strong></th>
<th><strong>DailyMed</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>FDA reviews labeling prior to posting</strong></th>
<th><strong>Drugs@FDA</strong></th>
<th><strong>DailyMed</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Always</td>
<td>Generally, no</td>
</tr>
</tbody>
</table>

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
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, Biologies License Applications, and Abbreviated New Drug Applications.

- Labelling 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

- 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](https://www.fda.gov/media/124386/download); PK = pharmacokinetics
Want to Learn More About Labeling?

2019 CDER Prescription Drug Labeling Conference¹

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) www.fda.gov
Thank You!
Eric Brodsky, M.D.
Associate Director
Labeling Development Team, Office of New Drugs
Center for Drug Evaluation and Research, FDA

- 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

Join the conversation #DIA2019