CDER Prescription Drug Labeling Conference
December 4th and 5th 2019

U.S. FOOD & DRUG ADMINISTRATION

Labeling Finalization: Recommendations for Final Check of Prescribing Information Format and Appearance

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Labeling Policy Team | Office of New Drugs Policy
Office of New Drugs |CDER | US FDA

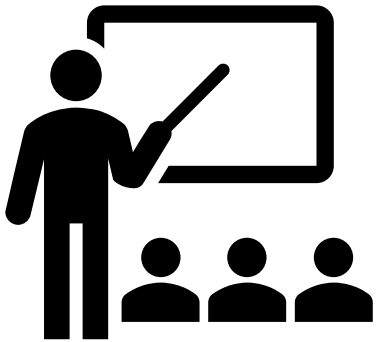
Disclaimer

- The views expressed in this presentation are those of the speaker, 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

Learning Objectives

- Understand labeling quality and important format/appearance issues that can arise
  - Learn to identify and correct the 5 common format[1] issues in the Prescribing Information



1. This presentation will not focus on content issues

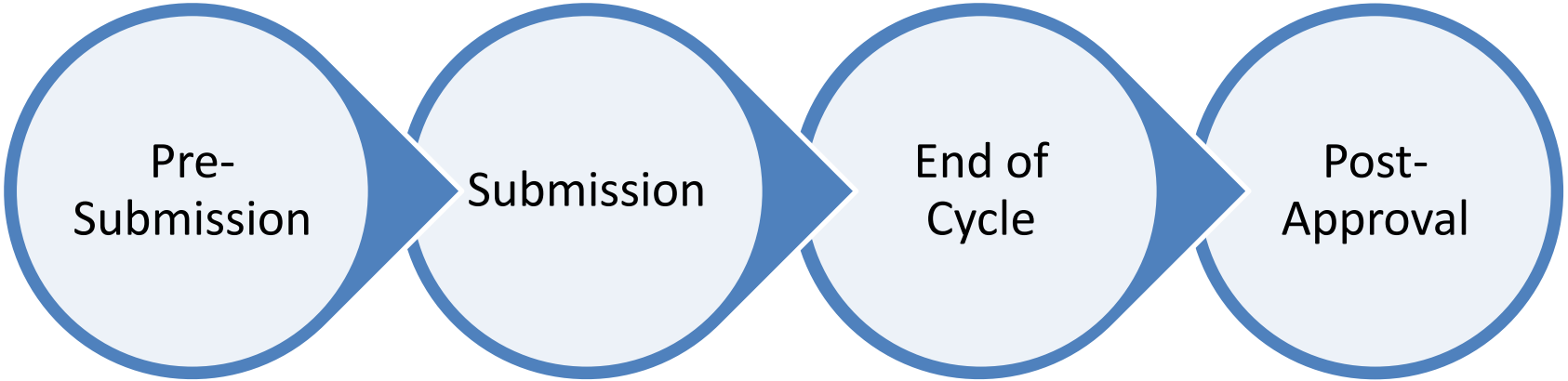
Importance of Quality

VS

CDER Cares About Quality Too!

- Prescription Drug Labeling is CDER's primary tool for communicating drug information
- CDER has developed an internal process to identify and correct Prescribing Information format/appearance issues
  - Labeling review specialists
  - Multiple types of internal labeling training
  - Collaborative review of the Prescribing Information
  - Access to various labeling format/appearances resources (e.g. Selected Requirements of Prescribing Information)

CDER Looks for Every Opportunity to Increase Format Quality



Post Approval Labeling Quality Review Is Key

- Quality is based on labeling regulations and guidances, scientific content, and format/appearance
- We evaluate overall labeling format/appearance quality routinely
  - Publicly available approved labeling (Drugs@FDA)
  - Reviewed approximately 1400 PLR labeling in the past year[1]

1. Last approved labeling for all CDER regulated NDA and BLA products with PLR labeling. CBER products are not included on Drugs@FDA. Did not include ANDA products

Labeling Format/Appearance Analysis Summary of All Approved PLR Labeling

- Of the 1400 PLR labeling the majority do not have format/appearance issues
- Of the labeling that do contain significant format/appearance issues; a noticeable trend arose. These 5 issues will be the focus of my presentation today
  - Significant format/appearance issues are confusing and distract from information in the Prescribing Information

Suboptimal Labeling

- May decrease confidence in quality of all FDA-approved labeling.
- May distract from required and recommended information in labeling.
- May diverge from regulatory requirements and guidance recommendations.

Challenge Question: Can You Find the 5 Major Format Issues in the Following Labeling?

Highlights of Prescribing Information (Highlights)

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: XXXX

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)
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ADVERSE REACTIONS
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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: 4/2017

Full Prescribing Information: Contents (Table of Contents)

FULL PRESCRIBING INFORMATION: CONTENTS*

1. Annotations

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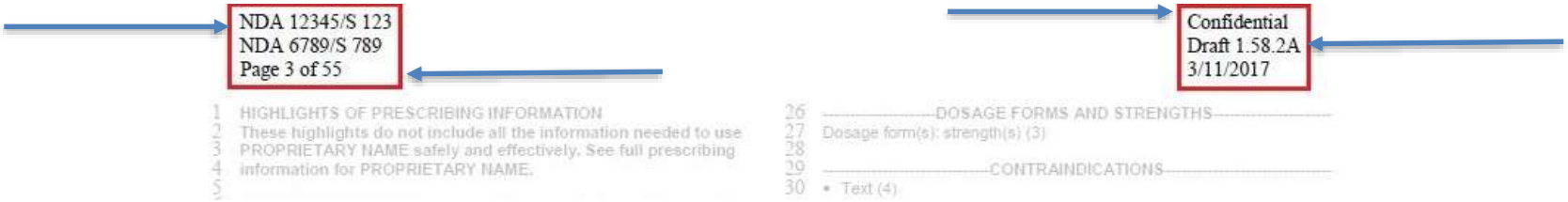

Confusing → Unhelpful → Incorrect → Poor Quality

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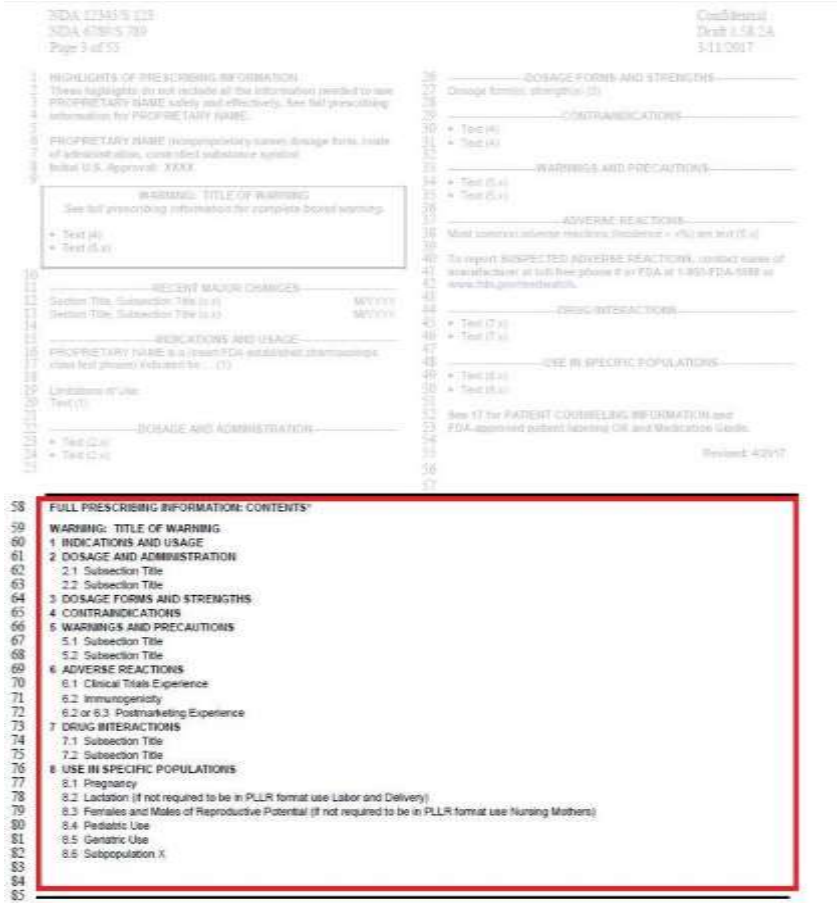
FULL PRESCRIBING INFORMATION: CONTENTS*

3. Number of Columns



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  2.2 Subsection Title
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4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
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6 ADVERSE REACTIONS
  6.1 Clinical Trials Experience
  6.2 Immunogenicity
  6.2 or 6.3 Postmarketing Experience
7 DRUG INTERACTIONS
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  8.2 Lactation (if not required to be in PLLR format use Labor and Delivery)
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  8.4 Pediatric Use
  8.5 Geriatric Use
  8.6 Subpopulation X

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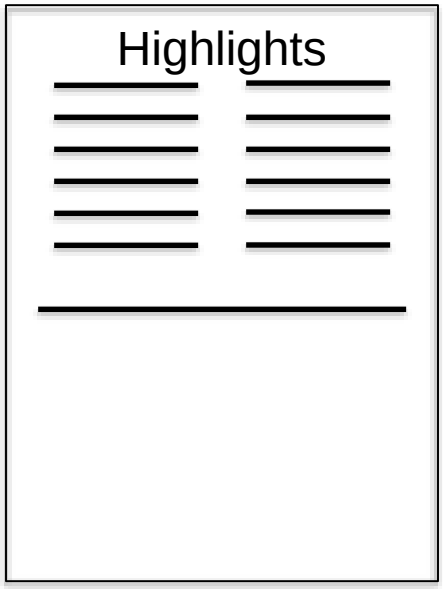

Highlights

- Should be in <u>two</u> column format*

* 21 CFR 201.57(d)(8) and guidance for industry: Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements (February 2013)

3. Number of Columns

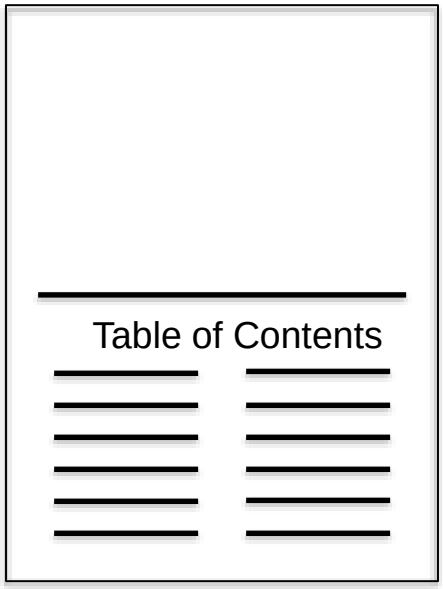

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Table of Contents

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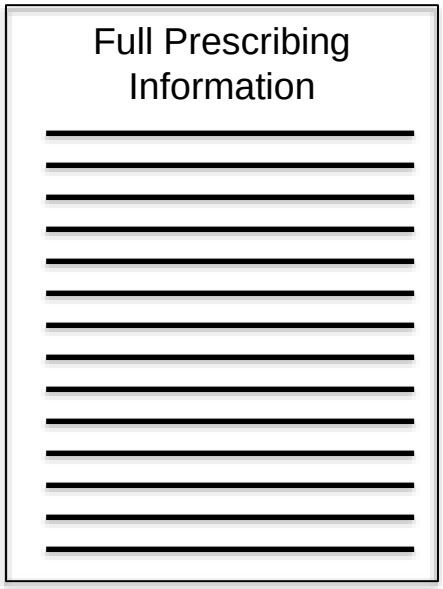

Highlights

- Should be in <u>two</u> column format

Table of Contents

- Should be in <u>two</u> column format

Full Prescribing Information

- Consider putting into <u>one</u> column format

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Revised: 4/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

4. Correct Dates

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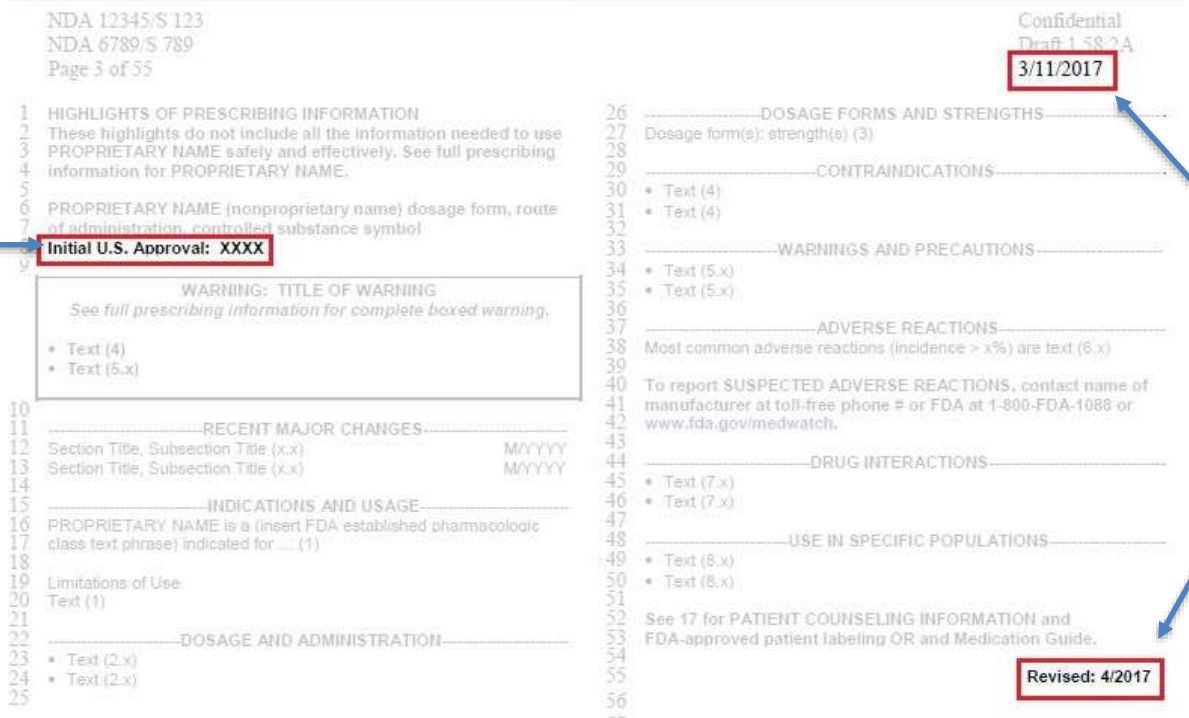

NDA 12345/S 123
NDA 6789/S 789
Page 3 of 55

Confidential
Draft 1.58.2A

3/11/2017

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Revised: 4/2017

Never updated

Conflicting

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Revised: 4/2017

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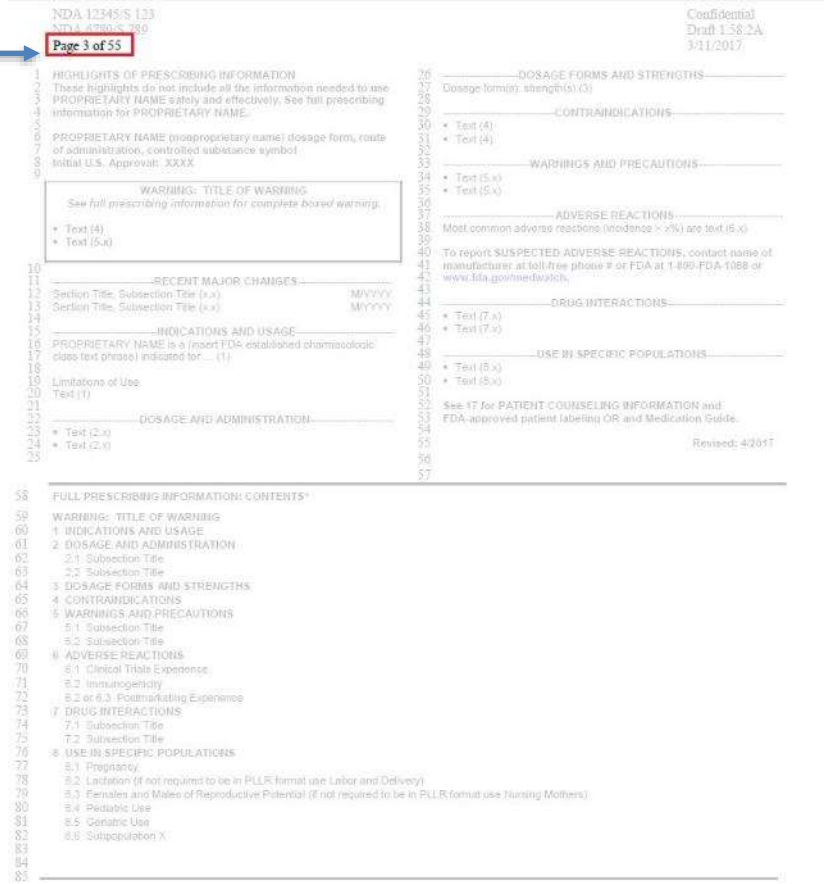
5. Appropriate Page Numbering

This is not page 3, it is page 1.


NDA 12345/S-123
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Confidential
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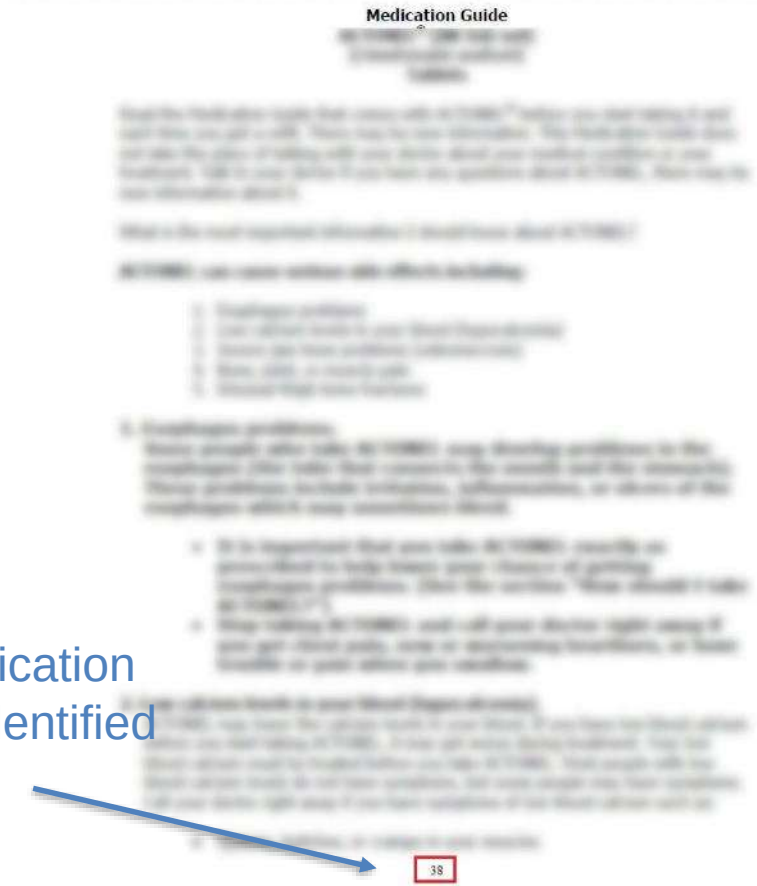


First page of the Medication Guide is incorrectly identified as page 38

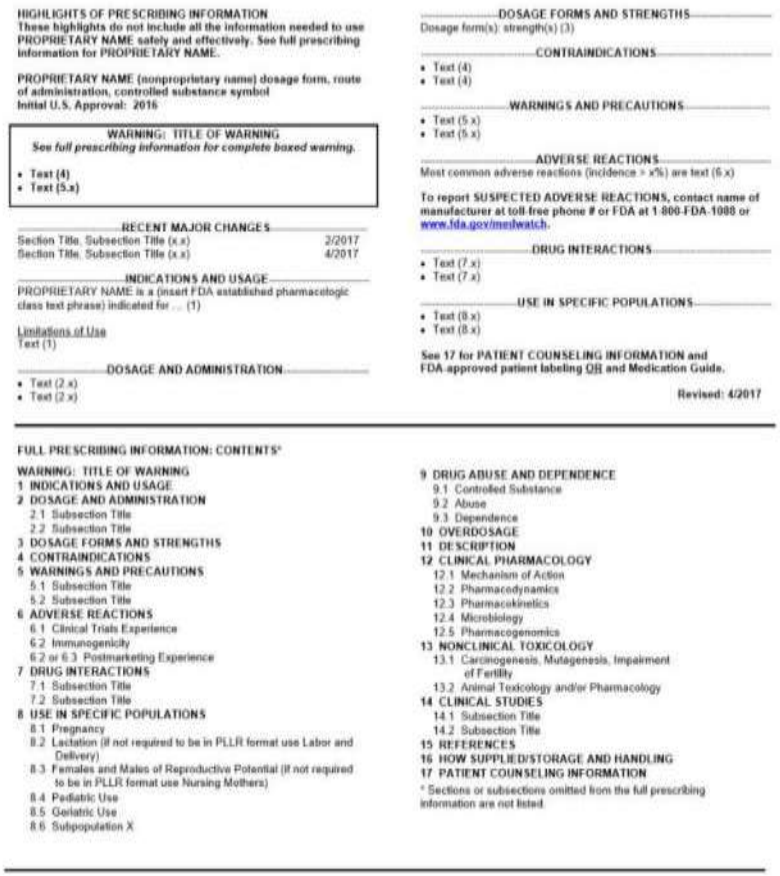
5. Appropriate Page Numbering

For example, a labeling document with attachments is 40 pages long (30, 5, and 5 pages for PI, MG, and IFU, respectively). Ensure that:

- PI is numbered Pages 1 to 30
- MG is numbered Pages 1 to 5
- IFU is numbered Pages 1 to 5

PI = Prescribing Information, MG = Medication Guide, IFU = Instructions for Use

Updated Optimal Labeling



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Section Title, Subsection Title (x.x)	4/2017

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8.5 Geriatric Use
8.6 Subpopulation X
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology
12.5 Pharmacogenomics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
14.1 Subsection Title
14.2 Subsection Title
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
* Sections or subsections omitted from the full prescribing information are not listed.

Resources for Format and Appearance of the Prescribing Information

FDA's Prescription Drug Labeling Resources website provides format resources for the development of Prescribing Information:

https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources

- Selected Requirements of Prescribing Information (SRPI) – A 41-item, drop-down checklist of important format elements of the PI based on regulations (21 CFR 201.56 and 201.57) and guidances.

- Sample PLR Template.

Summary

- Lets collaborate together, so we can maintain quality labeling and identify and correct any format issues
  - We are working hard to improve format and appearance issues within CDER.
  - Perform a quality check of labeling prior to approval that includes the following items:
    - Annotations, Line Numbers, Correct Number of Columns, Correct Dates, Appropriate Page Numbering

Thanks!


FDA
U.S. FOOD & DRUG
ADMINISTRATION