Recommendations for Final Labeling Format Check Prior to End-of-Cycle Labeling Submission

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Quality Check for Format/Appearance of PI

Selected Requirements of Prescribing Information (SRPI)[1]

The Selected Requirements of Prescribing Information (SRPI) is a 41-item checklist of important format prescribing information (PI) items based on labeling regulations [21 CFR 201.56(d) and 201.57] and guidances. The word "must" denotes that the item is a regulatory requirement, while the word "should" denotes that the item is based on guidance. Each SRPI item is assigned with one of the following three responses:

- **NO**: The PI does not meet the requirement for this item (**deficiency**).
- **YES**: The PI meets the requirement for this item (**no deficiency**).
- **N/A**: This item does not apply to the specific PI under review (**not applicable**).

Highlights

See Appendix for a sample tool illustrating Highlights format.

HIGHLIGHTS GENERAL FORMAT

1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.

   Comment:

2. The length of HL must be one-half page or less unless (the HL Boxed Warning does not count against the one-half page requirement).

   Comment:

3. A horizontal line must separate:
   - HL from the Table of Contents (TOC), **and**
   - TOC from the Full Prescribing Information (FPI).

[1] SRPI on PLR Requirements for Prescribing Information website

Labeling Finalization During End of Review Cycle: NDA/sNDA/BLA/sBLA

Prior to sending in labeling documents to FDA at end of review cycle (after FDA and firm are close to an agreed-upon PI) recommend:

1) Remove annotations (e.g., in headers/footers)
2) If page numbers are included, ensure first page of each labeling document starts with Page #1
3) Remove line numbers
4) Ensure correct number of columns in three PI sections

[1] Labeling documents include prescribing information (PI) and FDA-approved patient labeling [Medication Guide (MG), Patient Package Insert (PPI), Instructions for Use IFU)]

What Can be Improved?

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 (non-proprietary 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/201Y
Section Title, Subsection Title (x.x) M/201Y

----------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: 10/2015

Remove Annotations

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Revised: 10/2015

Annotations Removed[1]

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Revised: M/201Y

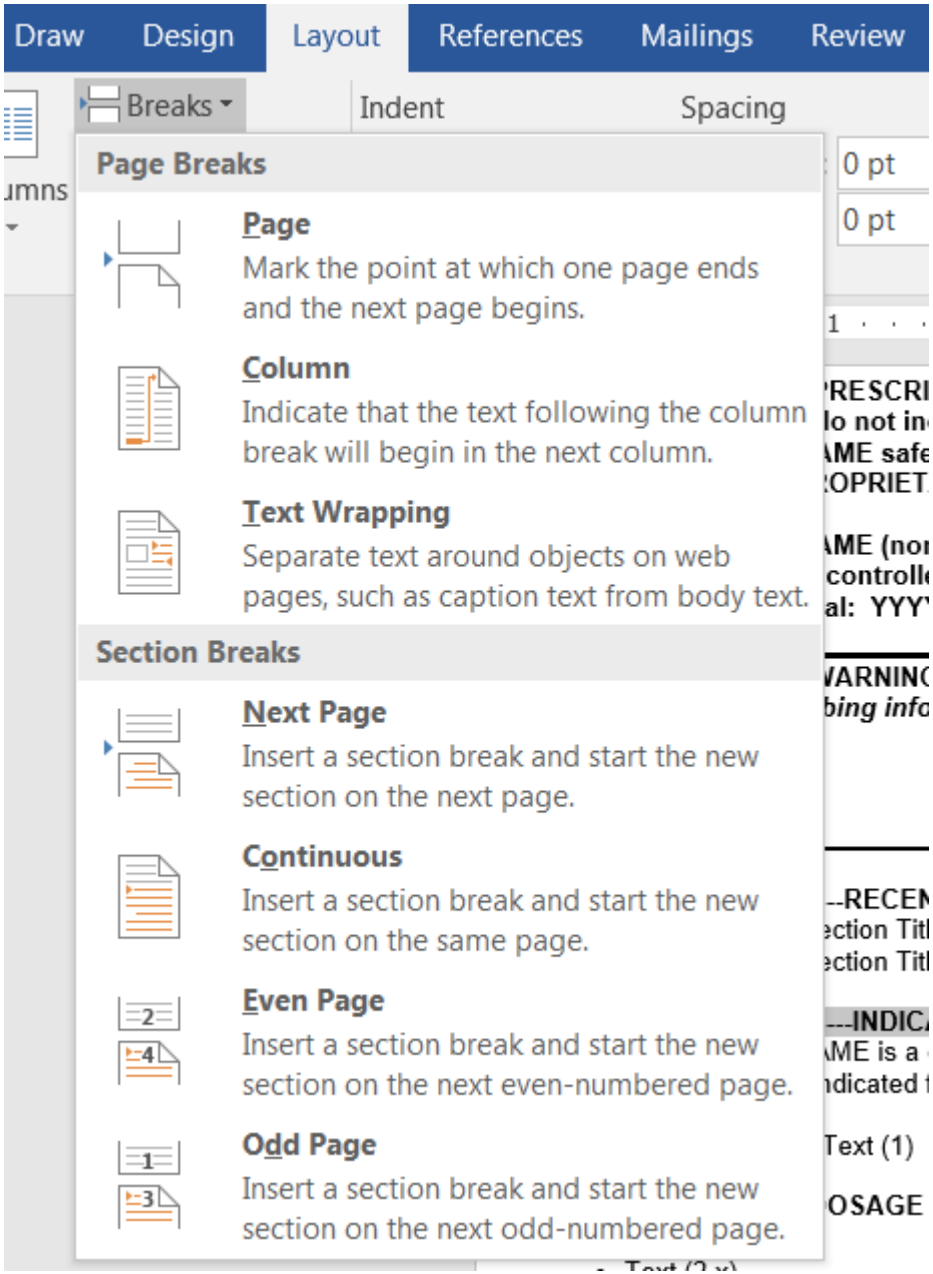
1 "Sample PLR Template – Highlights, Contents, and Full Prescribing Information" on PLR Requirements for Prescribing Information website

1) Recommend Removing Annotations

- Remove headers and footers (e.g., application numbers, product names, dosage forms, and firm names that appear in headers and footers)
  - How to remove headers/footers in labeling but retain headers/footers in cover letters to FDA - Slides #4 and #5

- May retain page numbers in labeling documents (see Slides #11-12)

How to Have Different Headers/Footers: Option #1



- Within Word document, include a section break between cover letter to FDA and labeling (under the "Layout" tab, click on "Breaks▾" and then select "Next Page")
- Now cover letter or different labeling documents can have different formatting within same document
- Retain headers/footers in cover letter and remove headers/footers in labeling documents (except for page numbers)

How to Have Different Headers/Footers: Option #2

Two or more labeling types are two Word documents:

- Retain headers/footers in labeling document #1 and remove headers/footers in labeling document #2 (except for page numbers)
- Open up Adobe Acrobat, click on "Create ▾" tab, and then click on "Combine Files into a Single PDF…"
- Add labeling document #1 (in Word or PDF)[1] and subsequently add labeling document #2 (in Word or PDF)[1]

[1] You do not need to convert labeling documents #1 and #2 to PDF (the "Combine Files into a Single PDF…" function converts Word documents into PDF and combines the files)

2) If Page Numbers are Included in Labeling Documents, Recommend First Page of Each Document Start with Page #1

- Recommend different numbering for each of labeling document (see Slides #4 or #5 to include different page numbers in footers/headers) to ensure first page of each document starts on Page #1

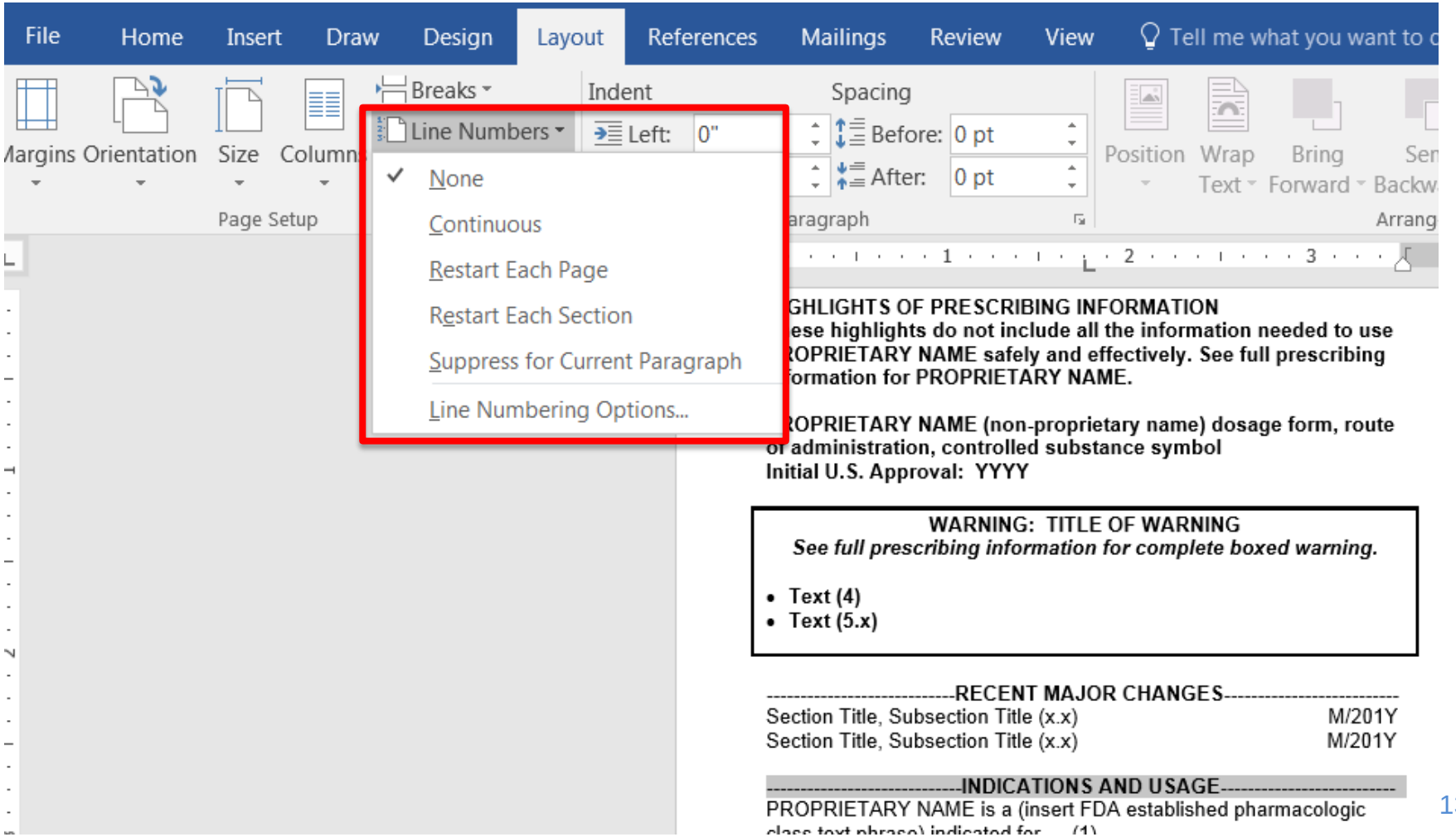
Different Page Numbers for Each Labeling Document

For example, one submitted document may be 35 pages long (25, 5, and 5 pages for PI, MG, and IFU, respectively). Ensure that:

- PI is numbered Pages 1 to 25
- MG is numbered Pages 1 to 5
- IFU is numbered Pages 1 to 5

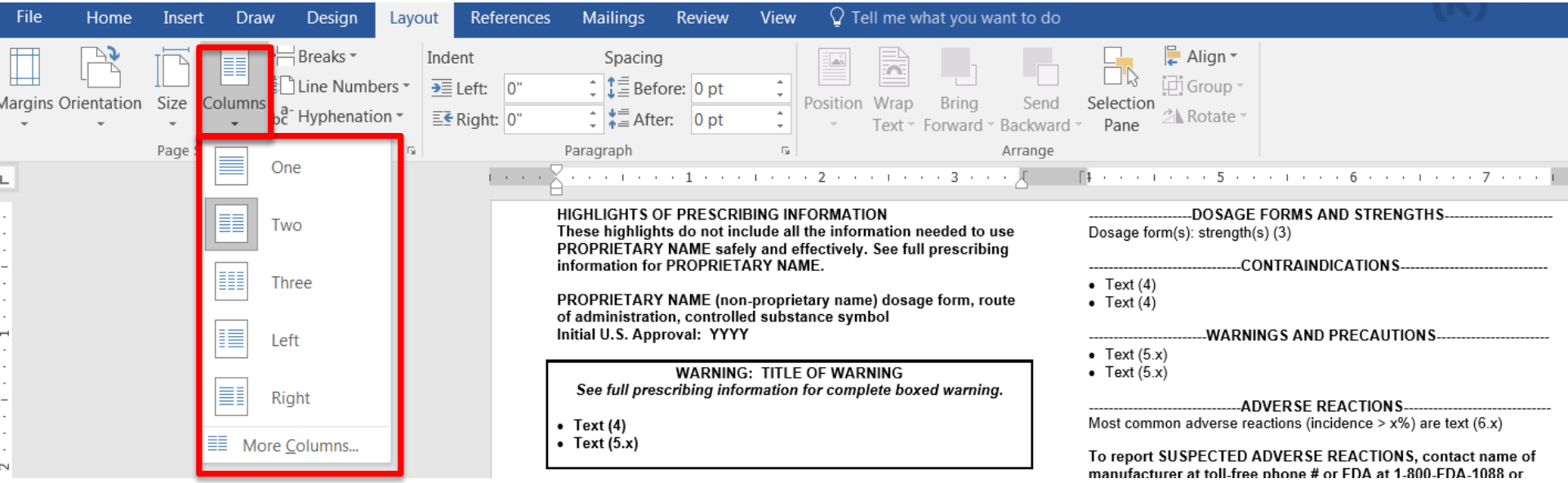
3) Remove Line Numbers Before Attaching Labeling to Approval Letter[1]

On “Layout” tab, choose “None” under the “Line Numbers” tab



4) Before Submitting PI: Ensure Correct Columns in PI

- Ensure <u>two</u>-column format for Highlights and Table of Contents[1]
- Recommend <u>one</u>-column format for Full Prescribing Information



- Ensure appropriate section breaks (e.g. On "Layout" tab, under "Breaks▾" choose "Continuous")
- On "Layout" tab, choose appropriate column under "Columns" tab

[1] 21 CFR 201.57(d) and Implementing the PLR Content and Format Requirements guidance

Thank you!