Regulatory Writing for the Digital Era
A Paradigm Change

AMWA 2018

Becky Nuttall
Lead Medical Writer, EMD Serono
November 2018
Agenda

- Intro and Role of the Medical Writer
- Background – perspective on the digital age
- The Paradigm Shift and Evolution of Medical Writing
- Research into Reading Behavior, Library Sciences, Eye-tracking and Website Design
- Introduce a New Approach to Developing Documents in the Digital Age (an Example)
- What Does the Future Hold?
Introduction

- We live in a digital age
- As medical writers, we must evolve to meet the needs of evolving practices

- This presentation focuses on strategic documents (ie, eCTD submission documents, briefing books, etc) that will be submitted to Health Authorities electronically
- However, the concepts in this presentation are applicable to all documents and can be used in print
Role of the Medical Writer

3 core competencies

Strategic
(eg, succinctly distill data, layout information and knowledge logically)

Technical
(eg, grammar, punctuation)

Leadership/Project Management
(eg, lead teams through document development and review)

The “art” of medical writing
Knowledge management with use of meta information

We bring new knowledge to our project teams to improve development of documents
History of Marketing Application Submissions in the Computer Age

1988 – FDA “believes the increased use of computers may improve … efficiency of drug review process.”

1991 – 65 CANDAs submitted

1992 – Prescription Drug User Fee Act (PDUFA)

1995 – EMA formed – harmonized (prior to this, 15 different submissions)

~2000 – ICH eCTD guidelines

1981: IBM first PC

1983: Apple Macintosh

1985: Modern Internet established

90’s: Advanced Microprocessors Gaming

1995: wireless “wifi”

~2000/2001: Mac OSX Windows XP First USB flashdrives
History of New Marketing Application Submissions

2006 – FDA electronic submissions gateway established

2010- EMA: eCTD mandatory for centralized procedure
2011 – FDA Update – include USB submissions
2015,2017 – EMA – mandatory electronic for all non-centralized procedures
5 May 2017 – FDA mandatory electronic
2018/2019 – EMA: mandatory electronic for all

Parallel development of eCTD documents and CSR to shorten time to market

2005: Youtube
2007: iphone
2009: Windows 7
2010: Google Chromebook
2011: Facebook 1 billion users
2012: Facebook 1 billion users
2017: Defense Advanced Research Projects Agency (DARPA) developing molecules as computers
### Time to Approvals is Speeding Up

<table>
<thead>
<tr>
<th>Then</th>
<th>Now</th>
</tr>
</thead>
</table>
| 1992 - PDUFA (prescription drug user fee act) – approval times were more than 2 years  
  - Prior to this, FDA was underfunded and understaffed. | • Median time to approval for Health Authorities continues to improve.  
  • **However**, the percentage of applications approved on first cycle has changed very little |
| 1993 and 2003: the median approval time for priority NDAs and BLAs decreased by over ½ *(from 13.2 to 6.4 months)* and median approval time for standard NDAs and BLAs decreased by over 1/3rd *(from 22.1 to 13.8)*. | 2015/2016* Median Approval Time:  
  FDA = 333 days (~11 months)  
  EMA = 422 days (~14 months)  
  PMDA (Japan) = 311 days (~10 months) |

* Regulatory Reviewers are busy

* RAPS website: Posted 11 August 2017, Zachary Brennan
Regulatory Reviewers Have Limited Time

Write to your audience – basic writing axiom for medical writing
Our audience is Regulatory Reviewers who

- have limited time to review documents
- are part of the digital age

We need to strategically design our documents to
- meet their needs
- make knowledge easily accessible
- provide knowledge in a succinct and readable form
- work in the digital environment

Incorporate this into the Paradigm Shift
**Paradigm Shift**

Reviewers:
- Review on screens
- Limited time – need navigational help to easily find information
- Use documents as “tools” to find answers*
  - No longer read “the story” from beginning to end)
- Use keywords, TOCs, subheadings, and table and figure titles to navigate

*McCulley-Cuppan; Greg Cuppan
Strategic Writing for Regulatory Documents is Evolving

“old” : Tell the story: Reviewers read from the first page to the end on paper

Writing Key Messages

“new”: Implement knowledge of Reviewer Behaviors on Screens
Print vs Screen

- Background
  - All the way back in the 1980’s
    - Personal computers were new
    - Users still mostly reading from print (no ipads, phones, Kindles)
    - Screens were small, resolution was low, fonts were limited
    - “Above the fold” (ATF) meant newspapers (most important info to be placed ATF)
  - Users were not used to scrolling, clicking, browsing
- Today: Personal computers and personal devices are a way of life
- Ongoing debate; do people still read faster in print?
## Print vs Screen

No published data on how Regulatory Reviewers read

<table>
<thead>
<tr>
<th>Library Science Research</th>
<th>Website Design Research</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Review/reading paper vs screen</td>
<td>• Eye-tracking data</td>
</tr>
<tr>
<td>• Reading behavior</td>
<td>• Layout and design architecture</td>
</tr>
<tr>
<td></td>
<td>• Natural Mapping/Stimulus Response</td>
</tr>
</tbody>
</table>
A screen-based reading behavior is emerging *

- “Skimming (to read quickly to get the main idea) has become the new reading…”

The layout of a text can have a significant effect on the reading experience.**

“While skimming your goal is to grasp the most amount of information about a certain topic in a very quick amount of time and without reading every single word. Hence, you have to look for key words that tell you the main idea of each line you are reading.” ***

*Liu 2005, ** Dyson M 2004, ***Fastreaders data
Web Design Research

- Eye tracking data
  - Eye tracking involves measuring either where the eye is focused or the motion of the eye as an individual views a web page
  - F pattern, scrolling and browsing

- Information/layout architecture
  - High findability and discoverability are the results of a well-defined information architecture and well-designed navigation system.

*Cardello J, 2014*
Eye-tracking Data: “F” Pattern

F-pattern
- On screen, people read in an “F-pattern”
- Horizontal attention leans left
- 80% of viewing time on Left Half of Screen
- 20% on Right Half

Nielsen 2010, Fessenden 2017
Eye-tracking Data: Scrolling

What appears at the top of the screen matters
- People don’t scroll “for fun” – they scroll for a purpose
  - Scrolling is extra work
  - Real estate “above the fold” is more valuable
  - Users selectively scroll “below the fold”
  - Users exhibit scrolling “fatigue” – the farther down they scroll, the less time they spend on information

“We don’t go to a page, see useless and irrelevant content, and scroll out of the blind hope that something useful may be hidden 5 screens down”**


“Web users spend 80% of their time looking at information above the page fold [on the main screen].“
Eye-tracking Data: Browsing

- Digital screen readers are engaged in greater use of shortcuts such as browsing for key words and selectivity *

FDA screen using browsers and key words.**

### Implications for MW – Library Science and Eye-tracking Data

<table>
<thead>
<tr>
<th>On Screen</th>
<th>Strategy for MW</th>
</tr>
</thead>
</table>
| Screen-based reading pattern (skimming) | • Avoid use of long paragraphs.  
• Split up into paragraphs that allow for skimming |
| People read in an “F” pattern  
80% of viewing time on Left Half of Screen | • Put the most important things first and to the left  
• Put key words on left (help navigate)  
• Start subheaders, paragraphs, and bullet points with information-carrying words that users will notice when scanning down the left side |
| The real estate “above the fold” is more valuable than stuff below the fold for attracting and keeping users' attention | Put the most important information first  
Hyperlink to more exhaustive analyses elsewhere |
| Scrolling fatigue – users will continue “below the fold” only if something is of value/interest  
Readers use shortcuts such as browsing for key words and selectivity | • Put main message up front and follow with supportive information  
• Identify keywords and place them strategically |
Information/Layout Architecture: Inverted Pyramid (Deductive Reasoning)

- Start with the conclusionary statement first (key, take-away message)
  - Supporting information next
  - Details, other, last
- Electronic pages are a linking medium
  - Writing for interlinked information spaces is different
  - Split writing into smaller, coherent pieces and link to other information

Information Architecture

- Deductive sentence organization is the most direct approach for presenting information
  - Each paragraph has one idea (topic sentence) followed by supporting information

- The Key Message is the main take-away point.
  - The Key Message is a conclusionary statement
  - The Key Message is the topic sentence

- Too much information is damaging
  - Key messages may be “buried” in the middle of long, unbroken text, or strung out across too many wordy sentences
  - **When someone says “go ahead and put it in, it can’t hurt” – red flag**
Dead white space – can be used to tell the reader the main takeaway or ready to reader for what you want them to read

Split up long paragraphs with **key messages** first. These are hard to find and lost in the document

Redundancies: Reader fatigue can lessen the impact of the message.

Template Headings are usually uninformative, but subheadings can usually be adjusted

- **Title**
- **Subtitle**
- Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. **Part of key message**. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. **Part of key message**. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. **Part of key message**. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. **Rest of key message**. Lots and lots of text. **Redundant** text. Lots and lots of text. Lots and lots of text. Lots and lots of text. **Redundant** Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Lots and lots of text. Conclusion **Redundant** text (hopefully succinct key message).
Layout Architecture

- Break up long blocks of unbroken paragraphs (skimming)
- Topic sentence first, followed by supporting information within the paragraph
- One idea per paragraph
- Reviewer can skim down the left side to find what they need
- Electronically link to other sections or to background information in an appendix
- Too much information is damaging
## Implications for MW – Design Architecture

<table>
<thead>
<tr>
<th>On Screen</th>
<th>Strategy for MW</th>
</tr>
</thead>
</table>
| Use of inverted pyramid  
Deductive sentence organization is the most direct approach for presenting information | • Key message first – topic sentence  
• Supporting data next  
• Details in another section/appendix  
• One topic per paragraph |
| Writing for interlinked information spaces is different than writing linear flows of text | • Split text into smaller paragraphs  
• Use short, active voice sentences  
• Use Tables and Figures to summarize complicated data (break up text) |
| Key messages                                              | • Main take-away  
• Topic sentence  
• Conclusionary statement  
• Always come first |
Developing Documents in the Digital Age

A New Approach
A Look at the “Old” Paradigm

MW complaints about document development:

- People/teams develop the documents as we go
- Time is tight - not enough time to think things through
- We have many draft reviews and get bogged down
- We re-write what we’ve already wordsmithed

How can we write to the message without all of this distraction?
Start with Key Messages

Key Messages are:
- The takeaway, master narrative; essence of what you want to communicate
- What’s needed to engage people
- Summations that articulate the important points/concepts you want the Regulatory Reviewer to understand.

Why are they important?
- Prioritize and crystallize information
- Ensure consistency, continuity and accuracy within and across documents
How Do We Identify the Key Messages?

- What was the key take-away from the 2 busy slides earlier in the presentation?
- What are you trying to say?
A New Way to Develop Strategic Regulatory Documents: Develop the Key Messages First

Start with the Key Messages

Before DBL:
- We usually know what we hope will be the outcome
- Write the expected results
- Write the conclusions = these are a form of the key messages
- Time to strategize

After DBL:
- The top-line results usually have the key messages or it is easily derived from them
- Not much time
Step One: Develop the Key Messages Outside of the Document

Use Powerpoint – a powerful tool
- Bullet key messages and sub-bullet supporting statements
- People think “differently” when writing bullets vs full text
  - Focuses on key points
  - Minimizes distractions
- Better able to strategize data needed to support each message

The end goal is a summary - not a beautiful PPT presentation
- Craft the key message to its fullest extent
Develop the Key Messages First – Engage Your Team

- Train/introduce team to this paradigm and process
- Hold a Kickoff to explain the process (educate your team)
  - Provide a shell PPT to team members
  - Provide an example set of slides with instructions
- Hold a meeting (or series of meetings per function) to align and agree on key messages and data
  - Record all of this on the slides
Example of Powerpoint “Example Slide”

**Key Message Statement:** Wonderdrug x mg given orally twice daily in subjects with Bad Disease who are on standard of care, significantly reduced X symptoms, with no increased safety risk, compared with placebo/active.

<table>
<thead>
<tr>
<th>Supporting Information in Bullet points</th>
<th>Tables/Figures In Text</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Primary Endpoint Key Message: Wonderdrug X mg po, BID, in subjects with Bad Disease on SoC statistically significantly decreased [disease symptom] (p&lt;0.001; CI xx) compared with placebo.</td>
<td>Table: Stats analysis, including Hazard Ratio (HR), p values, etc.</td>
</tr>
<tr>
<td>• Secondary Endpoint Key Message: Text</td>
<td>Figure: Line plot : (SAP figure #)</td>
</tr>
<tr>
<td>• Secondary Endpoint Key Message: Text</td>
<td>Text only – include stats (p value, CI )</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

Add slides as needed
Step Two: Transfer Bullet Points As-is

- Put agreed messages into the shell as-is
- Determine strategic placement of key message
  - What order should they be in? More than one place?
  - Where to showcase?
  - Add them to other appropriate sections (e.g., Conclusions)
- Key statements are the topic sentences to begin each paragraph
- Skim: focus on left side: logic? Flow?
- Check for density: *Rule of thumb: at least 3-4 paragraphs per page*
Step Three: Determine Logic Architecture

- Determine where to put the supporting data
  - Do all of the results/details need to be up front?
  - Can you keep the key supporting statements in early sections, then link to the more detailed data in a later section or another document? (use of hyperlinks)
  - Will the information be better presented in a table instead of a paragraph?
  - Busy/long tables in an appendix/at the end?
Step 4: Review for Searchable Words

- Identify “search” words
  - Efficacy key words = do your key statements begin the key word (left side)?
  - Safety key words = begin the topic paragraph with those words, on the far left.

- Example:
  Cardiac Toxicity (including x, y, and z preferred terms) was balanced across treatment arms. Incidence of cardiac toxicity was x (x%)…….

Notice, key message sentence first, then supporting data.
Step 5: Ensure Navigational Help

- Check the TOC
  - Numbered subheaders
  - Unnumbered subheadings within sections
  - Titles of the Tables and Figures

Step 6: Final Key Message Search

- Go through the document and cut/paste the key messages you find
  - Should be the first sentence of each paragraph
  - Are all important messages in your list?
  - Are they in the conclusions?
- Compare the key messages with your original PPT messages
What Does the Future Hold?
New Research on Current Use of Digital Media

- Landscape Orientation
  - Readers have an overwhelming instinct to swipe horizontally
  - Horizontal swiping is the new vertical scrolling
  - The user experience (e.g., textural feedback)

* A Perrin 2016: Pew Research Center
Social Networks

- Will we be writing in shorter and more succinct snippets?
- Will we be referencing Facebook pages?

External Links

- Qr reader code
  - Link to online background/educational webpages designed to help the reader during Reg review

Huffington post: https://www.huffingtonpost.com/suren-ramasubbu/paper-books-vs-ebooks-the_b_9890584.html
Electronic Voice Assistants

- Despite problems with user interactions, popularity is rising
- Single most common use of Personal Voice Assistants is information retrieval (trivia, word meanings, facts)
- Replace the keyboard, mouse, tablet and smartphone (hands free)
Effect of Transparency Policies on Writing

- With advent of transparency, keeping in mind the needs of the Lay General Public and Regulatory Reviewers will we need to be writing even simpler?
  - Short to-the-point text so that the public can read and understand better?
  - How much is too much? Too little?
Final Thoughts

- Things are changing and we need to be able to change with the times - Leaders
- Pressure to reduce time from development to approvals continues to increase
- There is now no country on earth that has not been introduced to the digital age

We are the leaders for Medical Writing in the Digital Age
It is our responsibility to be agents of change
Questions?