Using a Focused Authoring Strategy to Create a Message-Driven Deliverable

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Dr. Seuss is quoted saying...

“It has often been said there’s so much to be read, you never can cram all those words in your head.

So the writer who breeds more words than he needs is making a chore for the reader who reads.

That's why my belief is the briefer the brief is, the greater the sigh of the reader's relief is.
Our job as MWs...

Take the work out of reading.

Can the reader **easily** interpret the **key** message(s)?

- Is the text needed?
- Is the text clear?
- Is the text accurate?
Benefits of Focused Authoring

- Allows key messages to be easily identified
- Reduces writing, review, & QC time
- Increases quality by reducing redundancy
Understand Your Audience

Why are you reading my document?

<table>
<thead>
<tr>
<th>Regulatory Audience</th>
<th>Healthcare Providers and Patients</th>
<th>Academic Audience (eg, manuscripts, posters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>To make decisions about the safety &amp; efficacy of a compound</td>
<td>To make a decisions on best patient or self-care</td>
<td>To learn or inform their research rather than to decide</td>
</tr>
</tbody>
</table>

Varying backgrounds, needs, priorities, and interests:
- Therapeutic area experts? No medical background? Somewhere in between?
- Well-organized and reader-friendly.
- Intended messages and conclusions clearly articulated.
- Easy to process/understand SPONSOR’s point of view
- Very busy people!!
Before we start…

DANGER

EXPECTATIONS
Setting Team Expectations

- Focused authoring may be...
  - different
  - unexpected
  - anxiety-provoking

- Help your teams understand **UP FRONT** why it is...
  - different
  - better
  - the new industry-wide standard

- Discuss at kick-off/authoring meetings

- Proactively communicate to reviewers
  - Example: introduce changes in a “Reviewer Email”
Setting Team Expectations

**Sample "Reviewer Email"**

Please note that a focused authoring style was used throughout this document. Below is a list of aspects of other styles that you may be used to seeing in past CSRs/manuscripts/etc but are now handled differently. This new approach really helps the reader stay focused on key messages.

<table>
<thead>
<tr>
<th>INSTEAD of…</th>
<th>EXPECT to SEE…</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repetition of methodology in the results sections…</td>
<td>…very brief “reminders” with cross-references to the relevant sections, and only when absolutely necessary.</td>
</tr>
<tr>
<td>Lots of numbers from in-text tables repeated in the text…</td>
<td>…text that describes the results and keeps the focus on the key points, without “cluttering” the text with lots of numbers.</td>
</tr>
<tr>
<td>“Roadmaps” describing what will be discussed in the current and subsequent sections…</td>
<td>…no roadmaps, as the navigation pane and table of contents provide information about what is coming up.</td>
</tr>
<tr>
<td>Descriptions of in-text tables (eg, Demographic information for all enrolled subjects is summarized in [Table 10-1])…</td>
<td>…launching right into describing the results, with the table cross-referenced at the end (eg, “Of the subjects enrolled in the trial, approximately half were female, and the majority were white and ≥65 years of age [Table 10-1]).</td>
</tr>
</tbody>
</table>

**RULE of THUMB:** Every word in a sentence should either serve a grammatical purpose or should help to drive our “story” forward!
In Today’s Presentation

Is the text needed?

• Tailor introductions
• Avoid methods in results
• Avoid repeating data in text

Is the text clear?

• Maintain consistency
• Consider presentation format
• Remain concise

Is the text accurate?

• Use effective comparisons
• Reduce bias
Is the Text Needed?

- Tailor introductions
- Avoid methods in results
- Avoid repeating data in text
Tailor the Introduction

What does your audience need?

**Patients**
- No medical background
- Keep at higher level

**Academic audience**
- Advanced technical/scientific knowledge
- Orient to indication and product

**Regulatory**
- Therapeutic area experts
- Focus on the rationale for the program/study

**Healthcare providers**
- General medical background
- Orient to indication and product
1.1.1 Joy Deficiency Disorder

Joy Deficiency Disorder (JDD) is a growing cause of unhappiness worldwide; estimates by the World Happiness Organization indicate that it will be the second leading cause of unhappiness by 2020 (Smith et al 2019). JDD in high prevalence areas (eg, Eastern US, some EU regions, Latin America, and Asian countries) accounts for 22% to 45% of reported unhappiness, and up to 70% of clinical depression cases diagnosed in these patients {Blu et al 2017}. The European Medicines Agency (EMA) and European Centre for Disease Prevention and Control (ECDC) estimate that 25,000 new cases of depression per year are a direct consequence of JDD and these new diagnoses result in approximately €1.5 billion in healthcare expenses and productivity loss {McDown et al 2017}.
Joy Deficiency Disorder (JDD) is a growing cause of unhappiness worldwide; estimates by the World Happiness Organization indicate that it will be the second leading cause of unhappiness by 2020 (Smith et al 2019). JDD in high prevalence areas (eg, Eastern US, some EU regions, Latin America, and Asian countries) accounts for 22% to 45% of reported unhappiness, and up to 70% of clinical depression cases diagnosed in these patients (Blu et al 2017). The European Medicines Agency (EMA) and European Centre for Disease Prevention and Control (ECDC) estimate that 25,000 new cases of depression per year are a direct consequence of JDD and these new diagnoses result in approximately €1.5 billion in healthcare expenses and productivity loss (McDown et al 2017).
Activity
Tailoring Introductions
### 1.1.1 Joy Deficiency Disorder

Joy Deficiency Disorder (JDD) is a growing cause of unhappiness worldwide (Smith et al 2019). **Reminder that JDD is an important health concern.**

JDD is typically treated with antidepressants; however, only approximately one-third of patients experience full remission after 6 months of antidepressant treatment (Buddy et al 2018). Nearly two-thirds of patients did not achieve remission due to 1 or more of the following reasons: (1) low efficacy, (2) side effects that lead to discontinuation, or (3) general compliance issues due to inconvenient treatment regimens. **Current treatment options & why they’re not good enough.**

Alternative treatment options need to be developed for individuals with JDD that offer simple, highly effective regimens with minimal side effects. **State unmet medical need.**
Avoid Methods in Results

- Methods belong in the methods section
- Use a cross-reference if needed, but don’t repeat

Primary Efficacy Results

The primary efficacy endpoint was the change in joy rating scale (JRS) score from baseline to Day 24. The JRS is a 12-item, self-report rating scale that measures levels of joy. Participants completed the JRS daily in their participant diary by assigning a value of 1 to 10, where 1 was the least joy and 10 was the most joy, to each of the 12 items. Participants then added up their total scores at the bottom of each diary page. At each study visit, the total scores for each day since the prior study visit were entered into the clinical database.

The change in JRS score from baseline to Day 24 is summarized by treatment group in Table 11-5. The mean (SD) changes from baseline to Day 24 were \(-2.5 (1.2)\) and \(-2.3 (1.0)\) in the PP-123 and placebo treatment groups, respectively (\(P = 0.871\)). There were no statistically significant differences between treatment groups in the primary efficacy endpoint.
Avoid Repeating Data in Text

Data and Results are NOT the same

Data are facts/numbers, while results interpret what the data demonstrate

Throughout the review of safety, tables should be included to provide important reference information, or to support an essential point. Generally, tables should be associated with text that provides an interpretation of key points, but the text should not recapitulate the data in the table. For example:

“The demographics of subjects included in the development program are similar to the target population in the United States; exceptions include subjects of African ancestry and subjects over the age of 75, which were both underrepresented. Underrepresentation of subjects of African ancestry is related, in part, to the significant fraction of subjects enrolled in Europe. Underrepresentation of elderly subjects is a key issue, and is discussed in section X.”

Copying the applicant’s tables into the review without providing interpretation should be avoided.

http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ManualofPoliciesProcedures/
Demographic Results
Participant demographics and baseline characteristics are summarized in Table 10 1. Of the subjects in the mITT population, 13/21 (61.9%) in Treatment Group 1 (PP-123) and 7/10 (70.0%) in Treatment Group 2 (comparator - Happimab) were male, and 8/21 (38.1%) in Treatment Group 1 and 4/10 (40.0%) in Treatment Group 2 were female. Eighteen out of 21 (85.7%) subjects in Treatment Group 1 and 9/10 (90.0%) in Treatment Group 2 were white. The mean age was 58.6 years in Treatment Group 1 and 61.3 years in Treatment Group 2.

Demographic Results
In the mITT population, approximately two-thirds of subjects were male, the majority were white, and the mean age was 59.9 years. Both treatment groups were similarly well-balanced for all baseline characteristics; no clinically meaningful differences between the groups were observed (Table 10-1).
Activity

Writing Focused Results
The primary efficacy endpoint was the change in Joy Rating Scale (JRS) score from baseline to Day 24. The JRS is a 12-item, self-report rating scale that measures levels of joy. Participants completed the JRS daily in their participant diary by assigning a value of 1 to 10, where 1 was the least joy and 10 was the most joy, to each of the 12 items. Participants then added up their total scores at the bottom of each diary page. At each study visit, the total scores since the last study visit were entered into the clinical database.

The change in JRS score from baseline to Day 24 is summarized by treatment group in Table 11-1. In Treatment Group 1 (PP-123), across all 21 subjects the mean score at baseline was 3.3 (95% CI, 2.3-4.5) (Table 11-1) and the mean score at Day 24 was 6.8 (95% CI, 6.0-8.6). The mean (SD) change in JRS score from baseline to Day 24 for Treatment Group 1 (PP-123) was 3.5 (1.2). In Treatment Group 2 (comparator - Happimab), across all 10 subjects the mean score at baseline was 3.1 (95% CI, 2.1-4.4) (Table 11-1) and the mean score at Day 24 was 6.4 (95% CI, 5.8-8.2). The mean (SD) change in JRS score from baseline to Day 24 for Treatment Group 2 (PP-123) was 3.3 (1.0). In comparing the mean (SD) changes from baseline to Day 24 for PP-123 (3.5 [1.2]) and Happimab (3.3 [1.0]), the p value was 0.871. Thus, there were no statistically significant differences between treatment groups in the primary efficacy endpoint.
The JRS scores for both treatment groups increased by Day 24. The changes from baseline were comparable between the two groups ($P = 0.871$) (Table 11-1).

<table>
<thead>
<tr>
<th>Mean Score</th>
<th>Treatment Group 1 (PP-123) (n=21)</th>
<th>Treatment Group 2 (Happimab) (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3.3 (95% CI, 2.3-4.5)</td>
<td>3.1 (95% CI, 2.1-4.4)</td>
</tr>
<tr>
<td>Day 24</td>
<td>6.8 (95% CI, 6.0-8.6)</td>
<td>6.4 (95% CI, 5.8-8.2)</td>
</tr>
<tr>
<td>Mean (SD) Change From Baseline to Day 24</td>
<td>3.5 (1.2)</td>
<td>3.3 (1.0)</td>
</tr>
</tbody>
</table>
When can I put numbers in text?

When the table being discussed isn’t close (eg, CSR Sec 14 or CTD module appendix)

- Consider placing key numbers in parentheses
  “Participants with moderate renal insufficiency had a higher clinical response rate (83%) than those with normal renal function (53%) or with mild renal insufficiency (47%).”
  OR

- Consider placing the table in-text or making a smaller table to highlight the key results (if the point is really important)

When summarizing key efficacy and safety results (eg, End of Sections 11 & 12)

- State messages clearly and include supportive numbers in parentheses
- Never use numbers in the conclusions section (eg, Section 13)
Impact of Electronic Era

Agencies review **electronic** submissions. What are the **implications** of this?

- Cross-reference is 1-click away
  - Methods in the protocol
  - Result details from the CSR
  - Tables in Sec 14 or appendices

- Reviewers don’t read cover-to-cover
  - Abbreviations often not first use
  - Introductions go unread

- Readers can find what they are looking for
  - Navigation bar instead of roadmaps
  - Standard, single location for the information
In Today’s Presentation

Is the text needed?
- Tailor introductions
- Avoid methods in results
- Avoid repeating data in text

Is the text clear?
- Maintain consistency
- Consider presentation format
- Be concise

Is the text accurate?
- Use effective comparisons
- Reduce bias
Is the Text Clear?

- Maintain consistency
- Consider best presentation format
- Be concise
Maintain Consistency

- Use Parallel Structure: present information in a consistent order throughout document

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4 Efficacy Endpoints

4.1 Primary Endpoint: Change From Baseline to Day 24 in Joy Rating Scale Scores

4.2 Key Secondary Endpoint: Change From Baseline to Day 48 in Joy Rating Scale Scores

4.3 Other Secondary Endpoints

4.3.1 Smiliness Severity Scale

4.3.2 Elation Impact Scale

4.3.3 Happiness Quality Index

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5 Statistical Analysis of Efficacy Results

5.1 Primary Efficacy Analysis: Change From Baseline to Day 24 in Joy Rating Scale Scores

5.1.1 Full Analysis Set

5.1.2 Per Protocol Set

5.1.3 Subgroup Analyses

5.2 Secondary Efficacy Analysis

5.2.1 Key Secondary Efficacy Analysis: Change From Baseline to Day 48 in Joy Rating Scale Scores

5.2.2 Other Secondary Efficacy Analyses

5.2.2.1 Smiliness Severity Scale

5.2.2.2 Elation Impact Scale

5.2.2.3 Happiness Quality Index
Maintain Consistency

- Use terms consistently throughout – “One Voice”

- Develop a “convention sheet” early in the project

<table>
<thead>
<tr>
<th>Do Use</th>
<th>Don’t Use</th>
<th>Notes &amp; Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participant</td>
<td>Subject, patient</td>
<td>Okay to use “patient” when discussing epidemiology data or actual patient cases from the literature</td>
</tr>
<tr>
<td>GW-1 subtype</td>
<td>GW-1 cohort</td>
<td>&quot;Participants with the GW-1 subtype...&quot; instead of Participants in the GW-1 cohort...&quot;</td>
</tr>
<tr>
<td>Study treatment</td>
<td>Study drug, study medication, investigational product</td>
<td>&quot;Participants who discontinued from study treatment...&quot;</td>
</tr>
</tbody>
</table>
Consider Presentation Format

- Consider bullet points or other visual cues
  - Instead of lengthy sentences or paragraphs
  - Easier to read and identify key messages

**Strategic Use of Bullets**

- Have a lot of commas? 
  Switch to bullets.
- More than 5 items? 
  Separate into sections.
- >1 sentence per bullet? 
  Break apart. Reduce text.

The safety endpoints include the incidence of AEs, change in blood chemistry analytes from screening to end of study, and change in vital sign measurements from randomization to each study visit.

The safety endpoints include:
- incidence of AEs,
- change in blood chemistry analytes from screening to end of study, and
- change in vital signs from randomization to each study visit.
Consider Presentation Format

- Consider using figure or table instead of text
  - Visual organization of information is easier to read and interpret

Approximately 670 subjects with chronic laughter (guffawing or snickering subtype) will be enrolled into 1 of 2 treatment arms. Approximately 500 subjects (target of 370 subjects with guffawing subtype and 130 subjects with snickering subtype) will be enrolled in treatment arm 1 and will take 40 mg of JDJ-101 once daily for 6 weeks. Approximately 170 subjects (target of 130 subjects with guffawing subtype and 40 subjects with snickering subtype) will be enrolled in treatment arm 2 and will take 80 mg tablet of PLJ-101 twice daily for 10 weeks.

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>GT Enrollment</th>
<th>Drug Regimen Treatment/Dose</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>n ~ 500</td>
<td>JDJ-101/40 mg QD</td>
<td>6 weeks</td>
</tr>
<tr>
<td></td>
<td>• Guffawing (n ~ 370)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Snickering (n ~ 130)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>n ~ 170</td>
<td>PLJ-101/80 mg BID</td>
<td>10 weeks</td>
</tr>
<tr>
<td></td>
<td>• Guffawing (n ~ 130)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Snickering (n ~ 40)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Be Concise

Rule to Remember
Every word should be needed!
(adding information or for correct grammar)
Be Concise

Ask yourself:

- Can you read this sentence out-loud in 1 breath?
- Is this semicolon the best choice?
- Is this sentence ~2 lines or less?
- Is this word or phrase adding value to the sentence?

If the answer is “No,” your sentence may be too long!
# Be Concise

<table>
<thead>
<tr>
<th>Tip</th>
<th>Original Text</th>
<th>Being Concise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keep table references</td>
<td>Table 10-3 presents subject medical history conditions with an incidence rate of &gt;5% in 1 or more group.</td>
<td>Medical history conditions were balanced across all groups [Table 10-3].</td>
</tr>
<tr>
<td></td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td></td>
<td>As shown in Table 10-3, medical history conditions…</td>
<td></td>
</tr>
<tr>
<td>Avoid repetition</td>
<td>Group 1 had a mean systolic blood pressure of 15.8 mm Hg at Week 1 and Group 2 had a mean systolic blood pressure of 13.2 mm Hg at Week 1.</td>
<td>The mean systolic blood pressure at Week 1 was 15.8 mm Hg in Group 1 and 13.2 mm Hg in Group 2.</td>
</tr>
<tr>
<td>Remove roadmaps</td>
<td>Sec. 11.1.1 discusses the primary efficacy analysis of the change in JRS score for each treatment group. Sec. 11.1.2 discusses the secondary and Sec. 11.1.3 discusses the exploratory efficacy analyses.</td>
<td>No text needed: Rely on the navigation bar</td>
</tr>
</tbody>
</table>
### Be Concise

**Fewer Words  ➡️  Simpler Language**

<table>
<thead>
<tr>
<th>Wordy</th>
<th>Simple</th>
</tr>
</thead>
<tbody>
<tr>
<td>at the present time</td>
<td>now</td>
</tr>
<tr>
<td>in the event that</td>
<td>if</td>
</tr>
<tr>
<td>chemotherapeutic agent</td>
<td>drug</td>
</tr>
<tr>
<td>despite the fact that</td>
<td>although</td>
</tr>
<tr>
<td>perform an assessment of</td>
<td>assess</td>
</tr>
<tr>
<td>over the course of</td>
<td>during</td>
</tr>
<tr>
<td>with regard to</td>
<td>regarding</td>
</tr>
<tr>
<td>a higher proportion of</td>
<td>more</td>
</tr>
<tr>
<td>in order to</td>
<td>to</td>
</tr>
<tr>
<td>with the exception of</td>
<td>except</td>
</tr>
</tbody>
</table>
1. Demographic information collected for the subjects enrolled in the trial indicated that all subjects with the exception of one, were of white race (31 of 32 subjects [96.9%]) as shown in Table 10-4.

Nearly all enrolled subjects were white (Table 10-4).

2. The safety population included all subjects who were dispensed study medication in the study and were documented to have taken at least one dose of investigational treatment.

All subjects who received at least one dose of study treatment were included in the safety population.
In Today’s Presentation

Is the text needed?
- Tailor introductions
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Is the text clear?
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- Consider presentation format
- Be concise

Is the text accurate?
- Use effective comparisons
- Reduce bias
Is the Text Accurate?

- Use effective comparisons
- Reduce bias
  - Stick to facts; avoid editorial text
Effective Comparisons

Rule #1: Establish an order & stick with it

• Parallel structure helps the reader move quicker thru the messages
  *Example: Active treatment group followed by placebo*

Rule #2: Use consistent comparison language

• Consistent terminology helps the reader interpret the messages
  *Example: Number of subjects who survived OR who died; not both*
Effective Comparisons

Rule #3: Start with the most important information

“The headaches were reported by a comparable number of subjects in both groups during the 13-week treatment period.” vs. “During the 13-week treatment period, a comparable number of subjects reported headache in both groups.”

Rule #4: Precise statements = accurate interpretation

“The occurrence rate of severe AEs was comparable between treatment groups.” vs. “The treatment groups were comparable with respect to severe AEs.”

Rule #5: Be careful when there are many comparisons

Limit the discussion of subgroups analyses that do not differ from the study population as a whole or that are difficult to interpret due to small numbers.
Effective Comparisons

Which Would You Choose?

A) In men, 50% of subjects receiving PP-123 and 25% of subjects receiving placebo achieved the primary endpoint. In women, 48% of subjects receiving PP-123 achieved the primary endpoint and 28% of subjects receiving placebo achieved the primary endpoint.

Too detailed? No meaningful differences between men & women.

B) The proportions of subjects in each treatment group who achieved the primary endpoint were similar for men and women.

Missing a key message? More subjects in the PP-123 group achieved primary endpoint in both subgroups.

C) More subjects achieved the primary endpoint in the PP-123 treatment group than in the placebo group. Results were comparable in men and women.

Just right? Effective and succinct summary of a subgroup analysis.
Reduce Bias
# Reduce Bias - Spotting It

<table>
<thead>
<tr>
<th>Clue for Spotting Bias</th>
<th>Example of What Not to Do</th>
<th>Example of What To Do Instead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opinion presented as statement of fact</td>
<td>“We can conclude from these data…”</td>
<td>“These data demonstrate…”</td>
</tr>
<tr>
<td>Absolutes of any kind</td>
<td>“Always,” “never,” “certainly,” “totally”</td>
<td>“The majority,” “in rare cases,” “no instances were reported in this trial”</td>
</tr>
<tr>
<td>Inconsistent application of approximate terms</td>
<td>“Most” means something different for active vs comparator</td>
<td>Set consistent standards for when to use “most” (eg, ≥80%)</td>
</tr>
<tr>
<td>Dismissal of negative data</td>
<td>“Although the primary endpoint was not achieved, the study drug was still more efficacious than the comparator.”</td>
<td>“The primary endpoint was not achieved.”</td>
</tr>
<tr>
<td>Sensationalized terms</td>
<td>“…dramatic differences between study drug and comparator”</td>
<td>“…statistically significant differences between study drug and comparator”</td>
</tr>
</tbody>
</table>
Spot the Bias!

There were **staggering** differences in the incidence of increased liver function tests between the PJ-888 group and the active comparator group. Treatment with PJ-888 **never** resulted in increased liver function tests, whereas treatment with the active comparator **frequently** resulted in increased liver function tests. These data prove that PJ-888 is **safer** than the active comparator.
In Today’s Presentation

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Focused Authoring Reminders

- Refer when possible; don’t repeat
  - Reference to appendices, tables, other sections
- **Interpret** the results
  - Don’t just repeat numbers
  - The stronger the data, the less text you need
- Consistency throughout
  - Content and structure
- Say more with less
  - Every word should be necessary
- Be precise and unbiased
Questions?