Consistent with Labeling Final Guidance: Implications for Drug Products

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Practical Considerations

- Policy Development?
  - How to interpret SASS within company?
  - Formal summary document from each PRC review function?
  - Require formal “escalation review” or can it be handled by regular PRC team?
- Changes to PRC structure and process?
  - Who to engage as part of PRC?
  - How to train PRC members? Sales force? Research colleagues?
- Submission to OPDP for advisory comments?
- What other business considerations are raised?
- How does the CFL guidance impact corporate risk tolerance?
- Any increase in competitor complaints?

Substantive Challenges

- How to incorporate regulatory correspondence
  - How does it impact thinking about SASS?
  - How do you weigh negative FDA feedback in pre-2018 OPDP/DDMAC comments?
  - How do you consider data/claims removed by DA in label negotiations?
- Specific Data Types
  - Interim analysis data
  - Subset data
- Reprints currently disseminated under Good Reprint Practices Guidance
- Use of disclaimers
- Field direction and alternatives to direct promotion

Case Study

- Facts:
  - Company is considering inclusion of post hoc subgroup analysis in promotional materials
  - Is for approved indication and patient population
  - Data is from pivotal trial but subgroups were not pre-specified, not a stratification factor, and were not powered to show statistical significance

Case Study: Issues to Consider

- Are there any unique safety signals/concerns with this subgroup?
- Are there any different dosing or usage recommendations for this subgroup?
- What are the n-values for the subgroups?
- Is the subgroup data similar to effectiveness for overall patient population?

Structure of Promotional Asset

- Headline Claim
  - Be sure not to overstate what can be taken away from the data (i.e., direct or conclusive claims)
    - Example considerations:
      - ***DRUG X – demonstrated to improve progression free survival in male patients > 60 years of age***

      Vs.

      - ***DRUG X for pancreatic cancer – experience in males > 60 years old***
  - Depending on data limitations, probably have to avoid conclusive statements

Structure of Promotional Asset

- Presentation of data
  - Prominence considerations
    - Even if the headline doesn't make a claim, does the data visually imply something greater than what the data supports?
  - Fancy graphics vs. numbers only
  - What about inclusion of p-values? Confidence intervals?
  - Is this data promoted "stand-alone"? Or do you require inclusion of Primary Endpoint efficacy& safety data that supported the drug's approval?

Structure of Promotional Asset

- Disclaimers
  - Likely will have some level of disclosure of material limitations to the data
  - Ensure adequate prominence vs. treatment like standard “legalese”
  - Can’t disclaim an inadequately supported claim into something considered “consistent with label”
    - If the disclaimer essentially says the data/effect being communicated can’t be verified/relied upon – then the data probably isn’t considered SASS
  - Sometimes need to reinforce Commercial team not to be afraid of “full disclosure”. Transparency goes a long way for reputation with HCPs and public reputation (and FDA)

Reference Slides

CFL Guidance

If a firm communicates information that is not contained in its product's FDA-required labeling but that is determined to be consistent with the FDA-required labeling, FDA does not intend to rely on that communication to establish a new intended use.

2-Step Assessment

Step 1

- "Consistent with" the labeling?

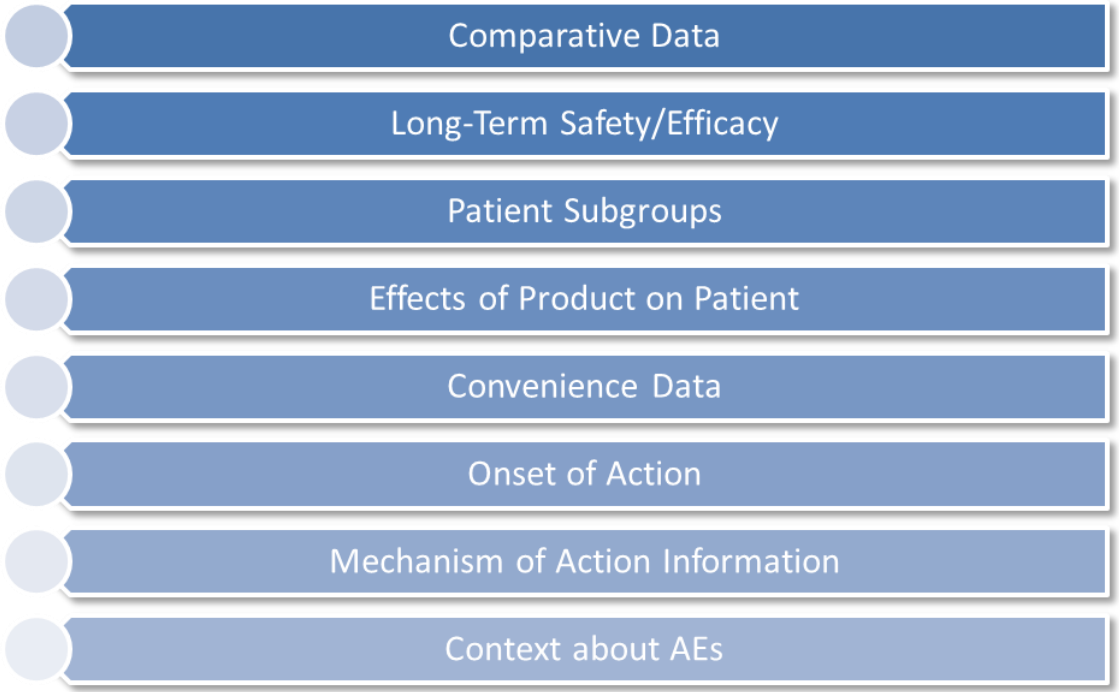
Step 2

- Is the presentation false/misleading?

Step 1: 3 Factors to Assess Consistent With…

- How the product communication **compares** to the information about the conditions of use in the FDA-required labeling?
- Whether the representations/suggestions about the use of the product in the product communication increase the **potential for harm to health** relative to the information in the FDA-required labeling?
- Whether the **directions for use** in the FDA-required labeling enable the product to be S and E used under the conditions represented/suggested in the product communication?

Examples of Types of Information that **MAY BE** consistent with…



Examples of Types of Information that are **NOT** consistent with…

- Different Disease/Health Condition
- Patient Subgroups Not in Approved Indication
- Different Stage, Severity, or Manifestation of Disease
- Monotherapy if Approved as Adjunct
- Different Route of Administration
- New Strength or Dosing Regimen
- Different Dosage Form

Step 2: Evidentiary Support

- **Is it false/misleading?**
  - Must be grounded in fact and science and presented with appropriate context
  - "Any data, studies, or analyses relied on should be **scientifically appropriate and statistically sound** to support the **representations or suggestions made** …"
    - Contemplates variety of data
  - FDA may still object based on inadequacy of supporting data or inaccurate characterization of data or limitations. **Mere disclosure of limitations of an inadequate study is not enough, can still be misleading**
  - Difficult to reconcile with final regulations that require substantial evidence for claims
  - Agency may be distinguishing between information and claims, which still require substantial evidence

Is it false or misleading?

- Presentation must accurately represent study results/data in the communications
  - Disclose material study design and methodology facts—type of study, study objectives, product dosage/use regimens, controls, patient populations studied, material limitations
  - Disclose unfavorable or inconsistent findings and accurately characterize and contextualize information presented
- If a communication presents data related to, but not specifically contained in, required labeling for the product, the presentation must include that related data from the required labeling in the communication