Best Practices for Standard Response Documents

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Background

Standard Response Documents (SRDs) are developed by pharmaceutical companies to respond to unsolicited requests from Healthcare Providers (HCPs). However, no standardization currently exists in industry practice. This lack of consistency across pharmaceutical companies can yield SRDs of varying format, content, and representation of data. Although the literature supports the need to establish some level of consistency, currently no Best Practices have been identified for SRDs.

Objective

To identify Best Practices and develop an evidence-based rubric to guide the standardization of SRDs within the pharmaceutical industry.

Methodology

Part 1: Evaluate Evidence-Based Resources for Best Practices

1. Food and Drug Administration (FDA) Draft Guidance on Responding to Unsolicited Requests 2011
2. Drug Information Association (DIA) Core Curriculum 2014
3. DIA Published Literature (Therapeutic Innovation & Regulatory Science Journal)
4. Drug Information (DI): A Guide for Pharmacists 5th edition

Part 2: Evaluate Current Landscape for Best Practices

1. Two different product SRDs were obtained from each of the top 20 companies (based on 2015 global sales) using the following criteria:
   Inclusion
   - Both within top 10 selling drugs per company (2014)
   - Drug inquiry involved adverse events, drug interaction, or pharmacokinetics information

   Exclusion
   - Customized responses
   - Generic product available
   - Pipeline drug
2. Best Practices were defined as being observed in >50% of SRDs

The results of Part 1 and Part 2 were combined to create the SRD CORE-4 Rubric.

Results – SRD CORE-4 Rubric

Part 1

Completeness

- ✓ FDA approved indications (FDA)
- ✓ Package Insert (PI) included (FDA)
- ✓ All important safety information (FDA)
- ✓ FDA disclaimer on off-label use (FDA)
- ✓ All necessary components of a response letter (FDA, DIA, DI):
  - Executive summary
  - Background section
  - Supporting data/studies
  - Reference section

Organization

- ✓ Studies organized by hierarchy of data (DIA)
  - Meta-analyses using high quality randomized trials
  - Randomized, double-blind, controlled clinical trials
  - Single blind clinical trials
  - Open-label clinical trials
  - Retrospective / post hoc analysis
  - Case reports / letters to the editor
  - Animal or in vitro studies (if no human data exist)
  - Review articles (limit use to Background section)
- ✓ Use of bulleted format in executive summary (DIA)
- ✓ Use of graphs and/or tables when possible (DI)

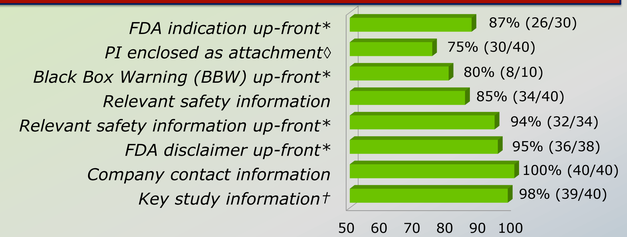
Referencing

- ✓ Complete list of references (FDA)
- ✓ American Medical Association (AMA) reference format (DIA)
- ✓ Include complete copies of original literature, not just summary documents or abstracts (FDA)

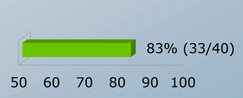
Equal representation of information

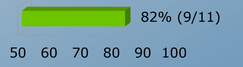
- ✓ Balanced presentation of benefit/risk (FDA)
  - All efficacy data should be accompanied by safety data (DIA)
- ✓ May include data on file if responsive to the specific request, but should rely on published peer-reviewed articles when possible (FDA)
- ✓ Stick to methods and results sections, and avoid investigator's opinion (DIA)
- ✓ Do not use language that exaggerates/minimizes data (DIA)

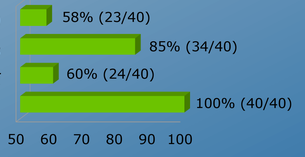
Part 2



* Included in the cover letter or beginning of the SRD ◊ As compared with hyperlink to PI
† Study design, total N, treatment regimen, and results or data including safety information







Results

Alternative practices observed but not seen in >50% of SRDs included:

- Literature search strategy
- Risk Evaluation and Mitigation Strategy (REMS) up-front
- Auto-update HCP if new information becomes available
- Quick Response (QR) code to drug information website

Discussion

This study helped identify several best practices for SRDs. In addition, the results provided some additional findings of interest. Of the 40 SRDs reviewed, 10 (25%) failed to include the FDA approved indication and 2 (5%) completely omitted any disclaimer on off-label use. Moreover, statistical significance was not provided in 16 SRDs (40%). Of the 40 drugs reviewed, 14 had an associated BBW and 5 had a REMS restriction. However, 4 (29%) and 3 (60%) of SRDs did not mention the BBW and REMS, respectively.

There were 3 general approaches used by pharmaceutical companies to provide the PI – enclosed as attachment (75%, 30/40), direct hyperlink (15%, 6/40), or indirect hyperlink to company homepage (10%, 4/40). For HCPs who prefer the response mailed or faxed, the hyperlinks offer minimal value. Thus, providing the PI as an attachment may be a more appropriate approach.

Now that the SRD CORE-4 Rubric has been developed, next steps will be to assess company SRDs for consistency with these best practices using a control question.

Limitations

The small sample size used in Part 2 (n=40 SRDs) may affect the generalizability of our findings. Furthermore, the threshold of Best Practices as >50% may be subjective, as ideas and practices not observed in >50% of SRDs were excluded by definition.

Conclusions

We propose a new approach to develop more consistent, organized, and fair balanced SRDs by following the CORE-4 Rubric.

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