Generating Clinical Narratives
Using Structured Content Principles

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for
SANOFI
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Contents

- Background
- Key challenges to producing clinical narratives
- What is Structured Content Authoring/Management (SCA/SCM)?
- The Sanofi solution
- How does SCA/SCM help solve these challenges?
- The value statement
- What the future may hold
Background

- Sanofi embarked on Content Reuse program in 2011
- EnCORE platform for established in 2012
- Narrative service established in 2013
- Many new capabilities continue to be added as the service matures
- Narratives constitute a significant portion of clinical content produced
Challenges: Dependencies & Time Constraints

- Narratives cannot be finalized until after DBL ✔
- Limited time available between database lock (DBL) and clinical study report (CSR) ✔ finalization
- Narratives written pre-DBL will likely require additional changes and review after DBL ✔
- Authoring time is proportional to the number of narratives to be written ✔

✔ Challenges addressed by SCM/SCA
Challenges: Data Sources & Complexity

- Data come from multiple sources
  - SAS data sets
  - CIOMS / MedWatch safety reports
- Manual copy/paste of data points or tables required ✓
- Data availability may be delayed
- Changes to source data trigger re-review and potential edits to written narratives ✓

✓ Challenges addressed by SCM/SCA
Challenges: Writing & Study Design Needs

➢ Some data needed as writing aid, but not to be included in the final narratives ✓
  ❑ Need to keep them separate or remove before finalizing

➢ Some parts of narratives may be reused ✓
  ❑ Events from prior analysis periods or crossover studies

➢ Narratives may need to be regenerated/revised to include additional events ✓
  ❑ Interim CSRs or agency requests

➢ Concurrent authoring/review ✓

✓ Challenges addressed by SCM/SCA
Challenges: Regulatory & Submission Needs

- Subject data may need to be anonymized ✓
- Narratives need to be grouped and ordered in a specific way, which could vary with underlying data changes
- Generating list of subjects requiring narratives
- End-to-end tracking from planning to submission

✓ Challenges CAN be addressed by SCM/SCA
What is Structured Content?

➢ Unstructured content that has been analyzed and decomposed into smaller “chunks” or components
   ❑ Components can be: documents; sections; paragraphs; sentences; tables; graphics...

➢ Components are then classified according to their characteristics and behavior (metadata)

➢ Components can be created, managed, rearranged, and reused independently

➢ Document structures are constructed from components, often programmatically
When content is structured, you can:

- Define which components are used and in what order within a structure (e.g., for a document, or a submission)
- Enable automated or on-demand content reuse from elsewhere and/or allow de novo authoring
- Identify which components are optional and under what circumstances
- Enable editable and/or locked components
Narrative Guidelines Viewed with a Structured Content Lens

Specifically, narratives should include the following:

- patient identifier
- age and sex of patient; general clinical condition of patient, if appropriate
- disease being treated (if this is the same for all patients, this information is not required) with duration (of current episode) of illness
- relevant concomitant/previous illnesses with details of occurrence/duration
- relevant concomitant/previous medication with details of dosage
- test drug administered, including dose, if this varied among patients, and length of time administered
- the nature, intensity, and outcome of the event
- the clinical course leading to the event
- an indication of timing relevant to study drug administration
- relevant laboratory measures
- action taken with the study drug (and timing) in relation to the event
- treatment or intervention
- post-mortem findings (if applicable)
- Investigator’s and Sponsor’s (if appropriate) opinion on causality
What is SCA and SCM?

- Structured Content **Authoring** refers to the practice of and tools for writing content to predefined structure in order to promote consistency, reuse, and efficiency
  - Authoring tool can be ubiquitous MS Word or proprietary XML-based products.

- Structure Content **Management** refers to content management capabilities needed to provide an end-to-end feature set from content design, creation, management, and governance
  - Includes traditional content management capabilities such as versioning, audit trail, access control, etc.
SCA/SCM: Key Features

- Component content management
  - Create, manage, and govern components

- Component assembly and authoring
  - Create document structures from components
  - Component-level authoring, review, and approval

- Content reuse
  - Exact, derivative, substitution

- Publishing:
  - Conditional inclusion/exclusion
  - Publish to Word, PDF, etc.
  - Apply business rules (e.g., bookmarks)
  - Separation of content and presentation
Sanofi Solution

Implemented enterprise-wide SCA/SCM system:

- SharePoint as the Content Management platform
- DITA and DITA Exchange for structured content
  - XML standard for structured content
- SAS and SharePoint automation for creating and managing narrative components
  - Create, import, and assemble components according to business rules
  - Publish in Word format and merge into a single document
  - Provide pre- and post-DBL authoring support
Sanofi Solution (cont.)

High-level business process

➢ Create and import components into the system
➢ Assemble components into document structures (“maps”)
➢ Author and review at the component level
  ❑ Include/exclude components
  ❑ Lock some content for editing
➢ Reload components, as needed
➢ Publish as a single Word document for finalization
Challenges Addressed by SCA/SCM

Time Constraints & Data Complexity Challenges

➢ Allows for staggered import of components as data become available for QC and/or authoring needs
➢ Allows for reloading of corrected data/content due to QC findings with reduced impact
➢ Allows for reloading of revised data/content post-DBL
   □ Authoring could start pre-DBL
   □ Read-only sections are simply overwritten
   □ Authored content is reviewed and updated as needed
➢ Expedited review: read-only content no longer needs to be reviewed
Challenges Addressed by SCA/SCM (cont.)

Writing & Study Design Challenges

➢ Include tables and other data for authoring aid ONLY
  ☐ Remove from final publication via conditional publishing

➢ Reuse adverse event/-of special interest (AESI) content
  ☐ Include components from prior studies (eg, for crossover) or analysis periods

➢ Add new events with minimal rework
  ☐ Lego brick approach: additional events can be imported as components due to agency requests or revised narrative criteria
Challenges Addressed by SCA/SCM (cont.)

Regulatory & Submissions Challenges

➢ Apply predefined formatting per business rules
  ❑ Auto-populate header with metadata such as study, product, subject identifier, etc.
  ❑ Auto-apply styles for aiding in narrative compilation for submission

➢ Content tagging and conditional publishing (future)
  ❑ Automatic and user-defined tagging of content
  ❑ Redact/anonymize tagged content upon publishing
The Value Statement: Quantitative

- Estimated time per narrative decreased from 6-8 hours to 2-3 hours; **66% reduction**
- Savings exceed total cost (incl. operations)

<table>
<thead>
<tr>
<th>Year</th>
<th># Narratives</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>2,000</td>
<td>-</td>
</tr>
<tr>
<td>2013</td>
<td>854</td>
<td>-58%</td>
</tr>
<tr>
<td>2014</td>
<td>1,788</td>
<td>109%</td>
</tr>
<tr>
<td>2015</td>
<td>5,108</td>
<td>186%</td>
</tr>
<tr>
<td>2016</td>
<td>3,841</td>
<td>-25%</td>
</tr>
<tr>
<td>2017</td>
<td>7,258</td>
<td>89%</td>
</tr>
<tr>
<td>2018*</td>
<td>12,374</td>
<td>70%</td>
</tr>
</tbody>
</table>

- Year-over-year double digit growth
- Producing thousands of narratives; increasingly with more complex and/or study specific needs

* Year to date
The Value Statement: Qualitative

- Established standard narrative processes, templates, and libraries
- Improved quality
  - Eliminated ‘cut and paste’ & formatting errors
  - Consistent structure
  - Read-only content
- Quick turnaround to change requests
- Support multiple submissions a year
The Future/Other Possibilities

- Single document authoring experience in MS Word while retaining the power and benefits of SCA/SCM
- Automated workflows for QC, review and approval
- Shopping cart like approach to narrative template underway
  - Standardize narrative content to make available as libraries
  - Allow users to build their own templates
- End-to-end automation
  - Structured content-enabled narrative template for almost fully automated generation of narratives
  - Machine learning and Artificial Intelligence
Questions?
Thank You

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