Defining DITA for Pharmaceutical Documentation

an OASIS webinar
Agenda

• Welcome & Introductions
  OASIS

• Content Challenges in the Pharma Industry
  James Averback

• Is DITA the Answer?
  Steffen Frederiksen

• The OASIS DITA Pharma Subcommittee
  James Averback

• What is in it For Me?
  Steffen Frederiksen

• Q&A, Closing Remarks
  OASIS
DITA provides a content supply chain for Internal and Regulatory documents throughout the Product Lifecycle.
The Many Sources of Pharmaceutical Change Control Content

  “a drug made with a manufacturing change (whether a major manufacturing change or otherwise) may be distributed only if, before distribution of the drug as so made, the holder involved validates the effects of the change on the identity, strength, quality, purity, and potency of the drug”

 Sources of Change Requiring Change Control Documentation

<table>
<thead>
<tr>
<th>Source of Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>The synthetic pathway used to manufacture the drug substance</td>
</tr>
<tr>
<td>-- material change in one of the bond forming steps</td>
</tr>
<tr>
<td>-- change in a solvent used for the last reaction and/or crystallization step</td>
</tr>
<tr>
<td>-- change resulting in a different impurity profile</td>
</tr>
<tr>
<td>The manufacturing process that can affect the quality of a drug substance produced by fermentation or derived from a natural source (plant, animal, or human)</td>
</tr>
<tr>
<td>The manufacturing process that can directly or indirectly affect viral or impurity clearance for a drug substance produced by fermentation or derived from a natural source</td>
</tr>
<tr>
<td>The manufacturing method from one manufacturing method (chemical synthesis, fermentation, or derivation from a natural source) to another</td>
</tr>
<tr>
<td>Source material (e.g., plant to animal, species, part used) or country of origin for a drug substance derived from a natural source</td>
</tr>
<tr>
<td>The method of sterilization of the drug substance or drug product</td>
</tr>
<tr>
<td>Species and/or strain of microorganism for a drug substance produced by fermentation</td>
</tr>
<tr>
<td>The route of administration</td>
</tr>
<tr>
<td>The composition and/or dosage form of the drug product</td>
</tr>
<tr>
<td>The drug product manufacturing process that can affect product quality</td>
</tr>
<tr>
<td>The drug product container closure system that can affect product quality (e.g., metering capability, dose delivery)</td>
</tr>
</tbody>
</table>
DITA Opportunity – Pharmaceutical Change Control Content

Background

*In the course of developing and marketing a drug, thousands of changes may be required to manufacturing processes.*

Goal

*Streamline the change control documentation process enabling internal and external service providers in creating content for regulatory submissions and internal documents.*

<table>
<thead>
<tr>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Changes in a manufacturing process are documented as “topic-based” change control packages with input from multiple sites and sources which can be automatically assembled and published on demand.</td>
</tr>
</tbody>
</table>

Benefits

- Reuse of change control documentation to generate regulatory reports saves resource time and improves quality as content is written once and used both for internal change control processes and for regulatory submissions.
- Using standard text components to describe changes reduces time to create change control documentation.
- Content from prior change control packages can be re-purposed as a prototype components for new documents.
- Enables efficient documentation practices across sites and with external service providers as content components are well defined and writing tasks are assigned to the most appropriate source.

Opportunity Cost

- Manufacturing Development reports created as standalone documents are difficult to find and reuse.
- Assembly of change control information to meet regulatory requirements for reports is a manual process requiring copy & paste and significant overhead for document review.
Change Control in the Product Lifecycle

10 – 15 Years

First in Human | Phase 1 | Phase 2 | Phase 3 | Tier 1 Markets | Rest of World

Major Changes

Other Changes

Market Authorization Submission

Supplemental Submission

Annual Submission

DITA Topics

DITA Maps

DITA Pharma SC
Intelligent Content Design (ICD) integrates document and topic-based authoring in a content supply chain approach to prospectively plan, design and create the complete collection of documents required to bring a pharmaceutical product to the market.

- ICD is based on industry standards and addresses key issues including:
  - When to use documents? When to use Topics?
  - What terminology standards to use for metadata population?
    (e.g., HL7, ICH, FDA, Pharmacopeia, ...)

- Shows how content can be designed and created to meet multiple business needs?
  - How text can be “reused” in multiple documents
  - How information can be “re-purposed” about products, processes and standards

- Shows how content can be created as a single source
  - And used in multiple forms to reduce the need for transcription
  - And be consumed efficiently by both people and systems

- ICD enables Regulatory Submissions, Content Supply Chain Management, Collaboration with external business partners and Knowledge Management
Designing the Protocol

Medical Writer selects clinical protocol template based on study design, experience and standards.

Writing the Protocol

Medical Writers & Clinical Scientists write study specific text using MS Word.

Text is collaboratively reviewed and updated.

Using the Protocol

Reusable text is mapped to future clinical documents.

Protocol document is published and delivered to clinical sites.

Consumer

Study configuration information is delivered to clinical systems.

Clinical Trial Management Systems

Clinical Data Management Systems

Source

Study Hypothesis

Input

Templates apply previously created reusable text to reduce re-writing.

Process

Design, Develop and Use a Clinical Protocol
Topic-based Content in Clinical Documents

- **Content Reused**
  
  "Use of a text fragment in multiple documents"

  For example:
  
  Clinical Protocol: ICH E6(R1)
  
  6.2 Background and Rationale
  
  Reuse in:
  
  Clinical Study Report: ICH E3
  
  7. Introduction
  
  8. Study Objectives

- **Content Re-purposed**
  
  "Provision of text to users in multiple roles to provide context and supporting information for multiple business uses"

  For example:
  
  Clinical Protocol: ICH E6(R1)
  
  6.9 Statistical Methods-Efficacy Analysis
  
  6.9 Statistical Methods-Safety Analysis
  
  6.13 Data Management and Monitoring

  Re-purpose information for:
  
  Clinical Study Report: ICH E3
  
  9.5.1 Efficacy Evaluation
  
  9.5.2 Safety Evaluation
  
  9.6 Data Quality Assurance
Is DITA the Answer?
Our Vision: A Common Base Format

Publishing/presentation tier:

MANY formats and apps.

Working/Collaboration tier:

ONE format, many tools

Repository/database tier:

ONE format…

Common Base Format
Common Base Metadata Architecture
Our Vision: A Common Base Format

**Publishing/presentation tier:**
MANY formats and apps.

**Working/Collaboration tier:**
ONE format, many tools

**Repository/database tier:**
ONE format…

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DITA?
What is DITA?

• DITA = “Darwin Information Typing Architecture”

• OASIS managed open standard:
  – Content and metadata architecture
  – XML standard
  – Basic, growing set of free tools
  – Forrester: “Fastest growing XML standard”
  – Tools, services, competencies, and content MARKET
  – Exceptionally strong business case
DITA: The Content Architecture

The basic building blocks:

- topic
- task
- concept
- reference
DITA: The Content Architecture

The DITA map:
Compose topic references to create a publication or a document
The map is a separate XML file
DITA: The Content Architecture

The DITA map:
Compose topic references to create a publication or a document
The map is a separate XML file

Reusable topics *.xml

Composing publications *.ditamap

Reusable documents *.???

The Result
Single Source Publishing

- Manual
- SOP
- CSR
- Proposal
- Study Protocol
- Clinical Report

website
PDF
CD-ROM
Extranet
PDF
PDA
XML
PDF
Intranet
XML
PDF
Extranet
PDF
DOC
...

Ditamap.xml
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice.

In controlled clinical studies as both monotherapy and combination therapy with metformin or pioglitazone,

Two placebo-controlled monotherapy studies, one of 18- and one of 24-week duration, included patient
Who is using DITA?

- symantec
- AVAYA
- vmware
- Taleo
- Kodak
- HONDA
- BOMBARDIER
- HUAWEI
- KONE
- numonyx
- IBM
- Qimonda
- Schlumberger
- NOKIA
- intel
- MasterCard
- Sun
- BlackBerry
- Freescale
- Sanofi-Aventis
- Siemens
- Oracle
- ITT
- americ
- SIEMENS
- ORACLE
- BOEING
- FedEx
- SYSPRO
- CISCO
- STM Microelectronics
- Algorithmics
- Adobe
- Applied Materials
- National Semiconductor
- Novellus
- Ericsson
- Johnson & Johnson
- GE Healthcare
- Microsoft
- Novartis
- Emerson
- Wyeth
- OASIS
- DITA Pharma SC
DITA: The Business Case

• Share and collaborate:
  – Team
  – Enterprise
  – B2B
  – B2C

• Cut content-related costs (by 50%-80%):
  – Single-source publishing
  – Content reuse
  – Translation
  – Reduce “time-to-market”
  – Fewer revision cycles

• Improve:
  – Brand consistency
  – Quality
  – Compliance
Requirements for a **Common Base Format**

- Solid business case, verifiable ROI
- Non-proprietary, open standard
- Cross-media/-platforms/-products/-vendors/-companies/-time
- Tools support and tools availability
- Handle *existing* special pharma standards
- Adapt to *future* special pharma standards
- Handle special company requirements
- Modular to support re-use
- Advanced metadata capabilities
- Field proven
- Industry acceptance
DITA: Handling Special Requirements

- “D” as in “Darwin”: Evolution and inheritance:
  - Specialize and Generalize
- Built-in flexibility:
  - `<data>`, `<foreign>`, and `<unknown>` elements
- Extensible: Specializations:
  - Domain vocabularies
  - Domain metadata architectures
  - Domain topic types:
<section>
<title>Clinical Trials Experience</title>
<p>Because clinical trials on <active-ingredient>sitagliptin phosphate</active-ingredient> are conducted un</p>
<p>In controlled clinical studies as both monotherapy and combination therapy with metformin or pioglitaz</p>
<p>Two placebo-controlled monotherapy studies, one of 18- and one of 24-week duration, included patient</p>
</section>
Why DITA as the Common Base Format?

- Solid business case, verifiable ROI
- Open standard
- Cross-media/platforms/products/vendors/companies/time
- Tools support and availability
- Handle existing and future special pharma standards as well as special company requirements
- Topic-oriented to support re-use
- Advanced metadata capabilities
- Field proven
- Industry acceptance
- YOU can influence this!
OASIS DITA Pharmaceutical Content Subcommittee

The OASIS DITA Pharmaceutical Content Subcommittee (DITA-PSC) will define DITA topics, maps, associated metadata properties and terminology to streamline design and creation of the complete body of pharmaceutical documentation required to represent a product for scientific and regulatory purposes throughout its lifecycle.

Initial objectives are to define topics and maps as required to implement:
- ICH CTD (Common Technical Document) content specification
- US IND (Investigational New Drug) content specification
- EU CTA (Clinical Trial Authorization) content specification
- FDA Structured Product Labeling content specification
- EU Product Information Management content specifications.

To optimize the value of DITA it is an objective to consider additional topics and maps for facilitating the internal business processes of content design, authoring, document review, submission assembly and regulatory portfolio management.
This is in it For You...

• Direct Influence:
  – Participate directly in defining how DITA is implemented as a standard for the pharmaceutical industry

• Early Warning:
  – Get early information on what is coming

• Knowledge Sharing among Peers:
  – Probably THE most important thing to bring back from participating...
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