DRUG INFORMATION ASSOCIATION

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eCTD Submission

Overcoming Initial Hurdles

Joerg Schnitzler[1,2], Prof. Dr. Harald G. Schweim[1]
[1] University of Bonn, Department of „Drug Regulatory Affairs“, Germany
[2] Merck Serono, Regulatory Operations, Germany

MERCK SERONO

universitätbonn
RHEINISCHE FRIEDRICH-WILHELMS-UNIVERSITÄT

Content

- Driving force
- Identify Business Case
- Software evaluation
- System Setup & Scenarios
- Paper – only backup?

External Driving Force

- All European Union member states are committed to accept eCTDs from end 2009
- Currently most agencies still require paper as archival format
- Several European agencies already accept or plan to accept eCTDs before end of 2009
- Some European agencies intend to make eCTD a national mandatory requirement
- Withdrawal of FDA eNDA Guidance (effective 1st January 2008)

eCTD Know-how

- ICH eCTD Specification v3.2
- eCTD IWG Q&A
- Regional Guidance (e.g. STF, EU M1)
- eCTD related XML basics – e.g. Document Type Definition (DTD), XML backbone, Style sheet (XSL), attributes

Identify Business Case

- Which product to switch to eCTD?
  - New MAA
    - Document creation according to eCTD specification
    - Lifecycle in one system
  - Existing authorization (e.g. variation)
    - Legacy documents (e.g. rework, parallel systems)
  - Centralized Procedure
    - EMEA: eCTD and paper copies of Modules 1 and 2
    - Co-/Rapp.: Negotiate number of paper copies
    - Central repository and EURS
  - Mutual Recognition, Decentralized or National Procedure
    - Various regional requirements for paper / electronic
    - MRP / DCP Lifecycle's best practice under discussion

Identify Business Case (cont'd)

- Submissions to United Kingdom, Belgium, Netherlands, Portugal or Norway (Jan '08)?
  - e-only submissions accepted
    - Less paper copies (production-, shipment costs)
    - Effort to comply with regional requirements (e.g. OCR, naming convention, …)
    - or Non-eCTD eSubmission formats
  - But paper dossier still required by majority of EU members states and non-ICH countries
- Savings of first eCTD might be reduced by technical rework of documents and changing existing processes

Non-eCTD eSubmissions (NEES)

- UK: PDF files conforming to eCTD leaf standards prefixed with the relevant CTD section number in the filename; eCTD folder structure may be used; no XML backbone file; hyperlinks are not currently supported within the Sentinel system
- BE: eCTD structured dossier without XML but with hyperlinked PDF TOCs (BEST2); volume based PDF files no longer accepted
- NL: eCTD structured dossier without XML but with hyperlinked PDF TOCs per module and an overall PDF TOC (accepted until Jan.2008)

eCTD Pilot Submissions

- Most agencies offer technically validation of an eCTD pilot submission prior to live submission
- This offer might expire, therefore take now the chance to submit your pilot eCTD
- Chance to avoid technically differences
- Test your favorite software systems (e.g. build pilot eCTD)

To be considered…

- “Once electronic, always electronic!”
- Do not resubmit already approved paper submissions in electronic format

- eCTD software?
  - eCTD can be done manually, but software definitely supports your work

Evaluation of eCTD Software

- **Analyze current process of document creation**
  - Submission ready documents
  - or technical rework required?
- **Documents including…**
  - hyperlinks and bookmarks
  - scanned signature pages
  - and finally QCed
- **Legacy documents according to eCTD specification?**
  - e.g. PDF v1.4 or higher, maximum of 100 MB per file, granularity according to ICH M4 (‘one document equals one PDF’ and not volumized PDF files), …
- **Adapted regional requirements?**
  - e.g. OCR, if submitting to MHRA, …
- Software for different document creation approaches available

Legacy Documents - Hyperlinks

- Add internal and external hyperlinks
  - Technical and content know how required
  - At the worst – rework every page
  - Quality check doubles the time!
  - Tools available to automate checks (e.g. broken links)

Legacy Documents - Bookmarks

- If not automatically added during publishing using headings, add bookmarks for every item listed in the table of contents
- No more than 4 levels in the hierarchy
- Tools available to OCR TOC entries and copy them as bookmarks

Software to build eCTDs

- Compile structure
- “Drag & drop” leaf elements
- Assist in reworking documents
  - hyperlinks, bookmarks
  - File splitting
- Create XML backbone
- Maintain attributes (e.g. envelope, lifecycle)
- Validation

Software to validate eCTDs

- Check against
  - eCTD specification (DTD)
  - IWG eCTD Q&A No.36
  - Regional requirements
- Validation report

Software to re-/view eCTDs

- Visualize lifecycle (current active, cumulative or sequence view)
  - Present lifecycle file relationships
  - Style sheet only offers sequence view
- Comment / annotate / collaborate
- Same tool as the agency? Which?

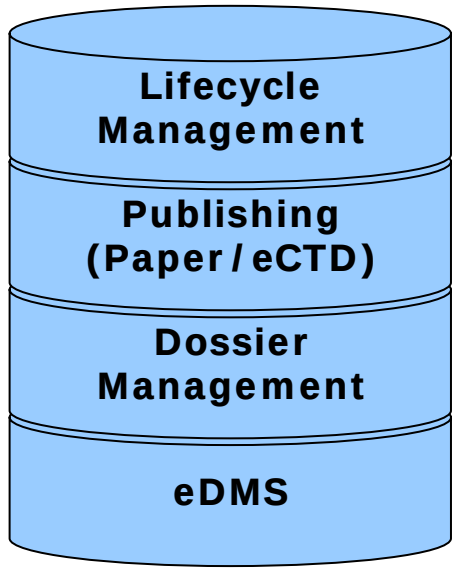
System Setup

- Global or local access
  - exchange of final publish (several GB)
  - software support (24h)
  - Web based or client installation
- Interface to other systems (e.g. eDMS)
- Supporting different output formats (paper, eCTD, report publishing, …)

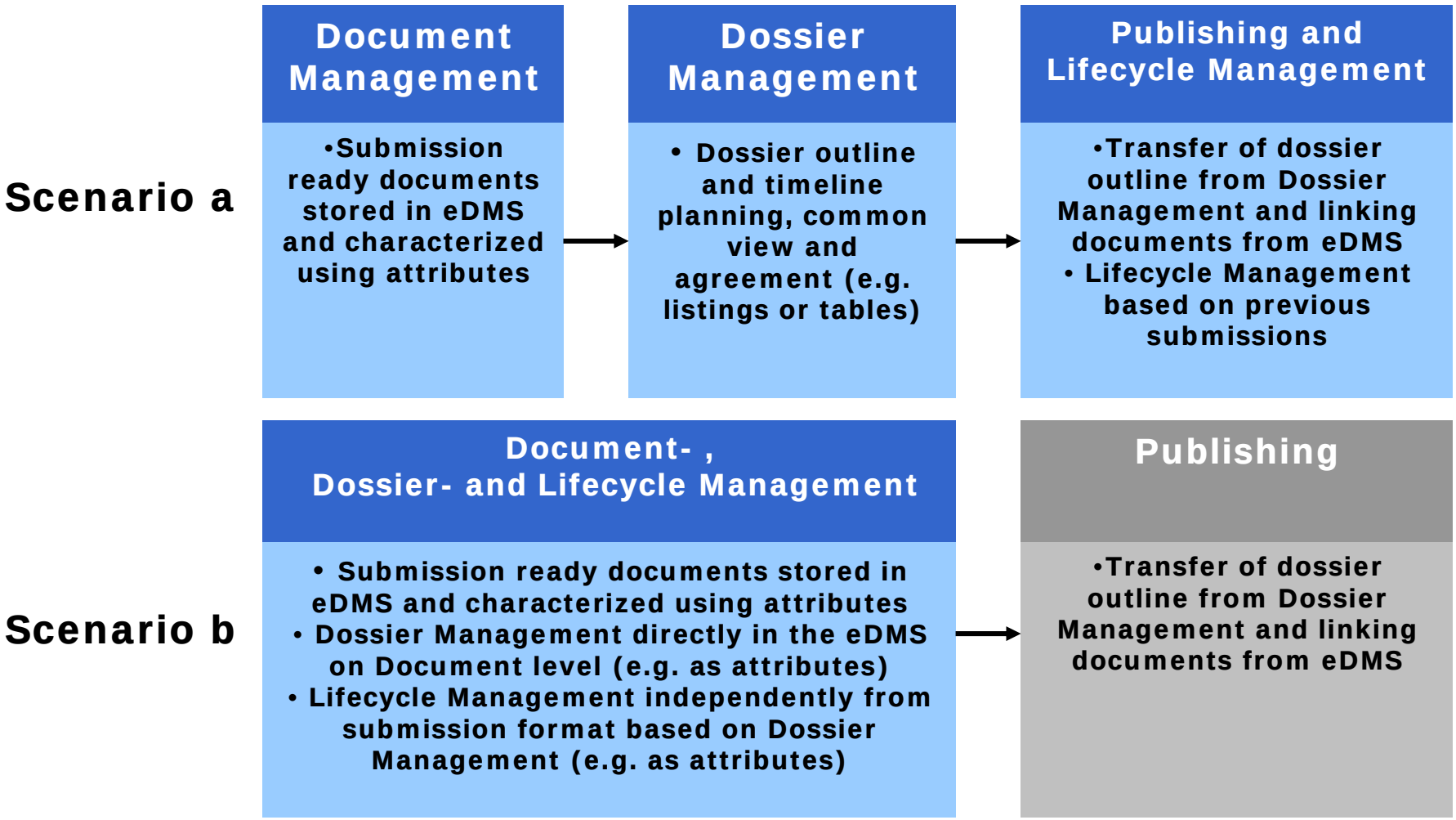
- Several small changes – or one big one

System Setup (cont'd)

- Product lifecycle should be accessible in one tool and not be distributed in several tools
- Steadiness of the format 'paper' in the past might not apply for the e-formats in the future
- Different submission formats might be required
- Combine the different system components to facilitate exchangeable submission formats



System Scenarios



Transition period – Paper from eCTD

- **“Practical guidance for the paper submission of regulatory information in support of a marketing authorisation application when using the Electronic Common Technical Document (“eCTD”) as the source submission.”,**
  v1.0, Notice to Applicants, Vol. 2B, February 2006

- All eCTDs and associated paper submissions that are submitted to the EMEA and/or National Competent Authorities through…

  - centralized procedure
  - national
  - mutual recognition
  - or decentralized procedure

Paper Submissions

- Most of the Health Authorities still accept paper, but…
  - "Companies are strongly encouraged not to submit applications on paper. Submissions sent electronically are likely to be processed to a quicker timescale than paper submissions." MHRA, Special Mail 5
- Paper – only backup beyond 2009?
  - Submissions to non-ICH countries still require paper dossiers for the majority of the countries

Last but not least - Communication is key

Whatever you plan to submit,

first contact your agency!

Guidance usually reflects a snapshot of the requirements.

Contact

Thank you for your attention!

Joerg.Schnitzler@merck.de

Links

- http://estri.org/eCTD/
- http://esubmission.emea.europa.eu/
- http://www.fda.gov/cder/regulatory/ersr/ectd.htm
- http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm