Electronic Regulatory Submission (ERS) in the EU – Overview

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Introduction

"At the Reykjavik meeting on 24 February 2005 HMA adopted the **end of 2009 as a target date for ICH's eCTD implementation**. This means that by the end of 2009 all members of the European Regulatory Network will require to have the infrastructure and the processes in place to handle electronic submissions of eCTD for marketing authorisation applications **without paper** and be able to make the best use of them. (…) This target will have an impact on national legislation in many cases."

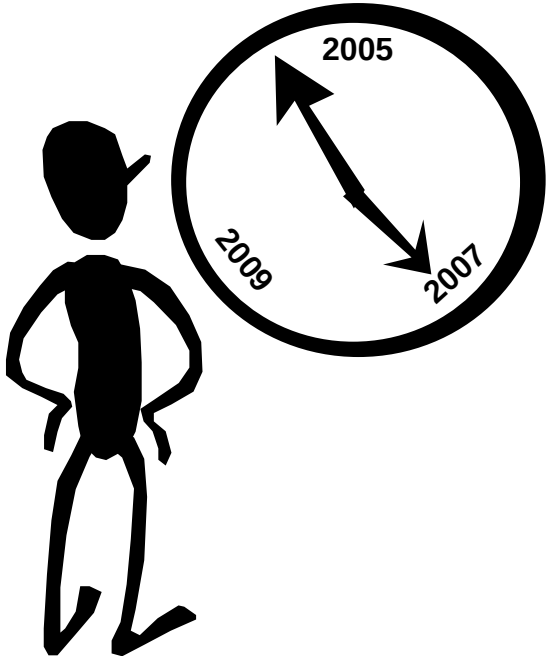
Source: http://www.hma.eu/uploads/media/Section_8_IT_Information_Systems.pdf

Half-time for eCTD Implementation in the EU – 2½ Years left

- 2005
  - Portugal
  - Belgium
  - UK
- 2006
  - Netherlands
- 2007
  - ???
- 2008
  - Norway
- 2009

Several European NCAs already accept (“early adopters”) or plan to accept e-only eCTDs before end of 2009

But currently the majority of NCAs still require paper as archival format (due to national archival law)



23 countries still to implement e-only eCTD by end of 2009

CP, MRP, DCP and national

- **Centralized Procedure**
  - EMEA accepts eCTD with accompanying paper for M1 and M2 and acceptance of e-only submissions is scheduled for February 2008
  - “early adopters” co- /rapporteur even save more paper today
  - Paper can be produced using an eCTD as the source submission
  - No announcement yet to mandate the eCTD for CP
  - Central repository and European Union Review System (EURS)
- **Mutual Recognition, Decentralized Procedure**
  - MRP / DCP Lifecycle’s best practice under discussion
- **National Procedure**
  - Various regional requirements for paper / electronic (eCTD and non-eCTD)

European Union Review System (EURS)

- The commercial software “EURS is Yours” (IABG) is recommended by EMEA to review and validate eCTDs for Centralized Procedures at associated NCAs, but member states are free to choose vendor
- Central EMEA repository for Centralized Procedures
- Review & validate against ICH and EU eCTD specifications

Non-eCTD Electronic Submission (NEES)

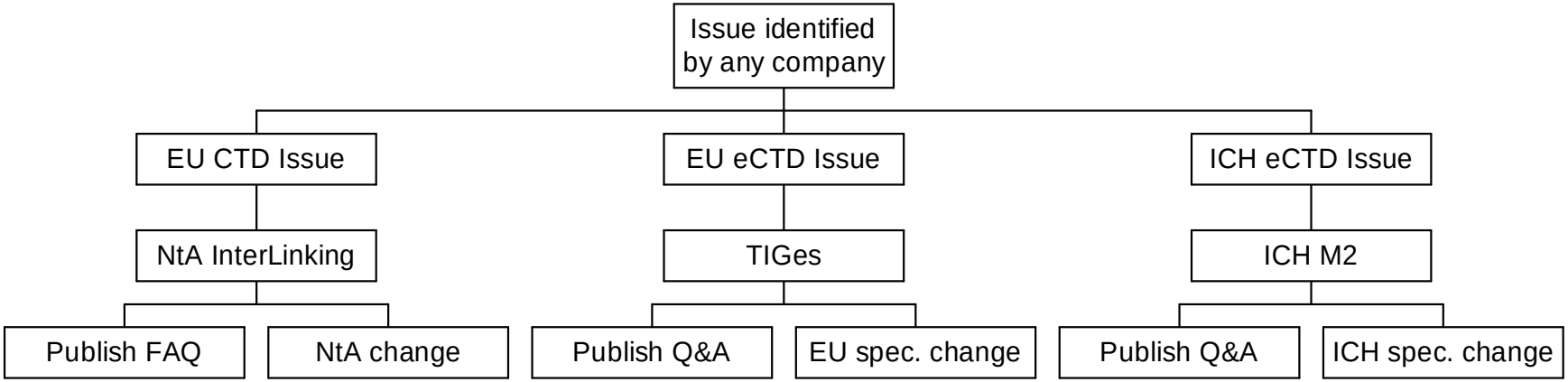
- A detour to eCTD?
- Various national requirements – no standard
- TIGes subgroup to harmonise NEES guidance
  - Expected to be eCTD without the index.xml backbone (i.e. granular PDFs, eCTD folder structure and naming conventions, electronic navigation (hyperlinks, bookmarks))
- No parallel (new) standard, but a stepping stone to eCTD
- Electronically without full risk of…
  - eCTD Lifecycle
  - Dossier rejections due to deficiencies (e.g. attributes)
  - High investments in wrong systems

Updated EU Guidance

- **eCTD EU Module 1 v1.2.1**
  - Released in Oct 2006
  - Corrected inconsistency in section 1.5 between EU M1 CTD and eCTD specification

- **Electronic Application Form (eAF)**
  - Electronic Application Form-New (version 2.1, March 2007)
  - Electronic Application Form-Variation (version 1.1, March 2007)
  - Electronic Application Form-Renewal (version 1.0, March 2007)
  - eAF XML Tool (AFSSAPS) available on Belgium DGMP website

Change processes: EFPIA eCTD Topic Group, TIGes, NtA Interlinking Group, ICH



- **Telematic Implementation Group for Electronic Submission and ICH Implementation (TIGes)**
  - Change request form http://esubmission.emea.europa.eu/tiges
- **NtA Interlinking** - Change request form http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev2.htm
- **ICH M2** – Change request form http://estri.org/eCTD/

Portugal & Belgium

- **Portugal**
  - Infarmed requests e-only submissions since Feb 2005 (several formats accepted)
- **Belgium**
  - DGMP started in October 2005 to request all dossiers to be submitted in electronic format
  - Since Jan 2007 eCTD is the recommended format for new registrations, also accepted ‘BeSt1’ (eAF, no xml backbone, CTD structure, eCTD file names) and ‘BeSt2’ (no xml, CTD structure, eCTD file names),
  - Zero Tolerance (structure and naming check)
  - Plans to mandate eCTD for all submitted dossiers (full & variations)

UK & Netherlands

- **UK**
  - MHRA announced in Apr 2005 “Sentinel” and went live in Oct 2005. In April 2006 the Electronic Portal was launched.
  - Accepting eCTDs or NEES complying with eCTD folder structure and naming conventions, but without XML backbone (hyperlinks are not currently supported within the Sentinel system)
  - Planned eCTD compliance of all initial submissions (and subsequent changes) for new active substances by April 2008 and for all new applications by the end of 2008.
  - No acceptance of EU M1 v1.2.1 yet – meanwhile submit v1.1
- **Netherlands**
  - MEB stated in March 2006 that paper copies are no longer a requirement
  - eCTD structured dossier without XML but with hyperlinked PDF TOCs per module and an overall PDF TOC (accepted until Jan. 2008)

Norway & Germany & Sweden & Denmark

- **Norway**
  - NoMA's ambition to go fully electronic by start of 2008
- **Germany**
  - Since 20th April 2007 variations for MRPs and DCPs can be submitted electronically ("Elektronische Änderungsanzeige") using online forms at www.pharmnet.bund.de after initial registration
- **Sweden**
  - MPA still requires all applications submitted in paper format, but appreciates an electronic copy beside. The eCTD format is strongly encouraged for the electronic copy. Intends to accept e-only applications by 2008.
- **Denmark**
  - eSubmission highly recommended and appreciated. Received few eCTDs and many NEES.

Ireland & Austria & France

- **Ireland**
  - Regulatory Information Online (RIO) Project
  - First phase of operation started 30th March 2007
  - Submit online applications for Type 1A, 1B and Type 2 variations for human medicines.
  - The system provides
    - Online forms, Documentation upload facilities
    - On-line tracking services for all applications submitted.
- **Austria**
  - Announced 2003 to accept eCTDs if application form, table of contents and labelling are still in paper and a full paper copy can be delivered within 3 days
- **France**
  - eCTD Pilot phase in 2006. Legal context of eSubmissions seem to be the same value than paper.

When to switch to eCTD? To be considered…

- "Once electronic, always electronic!"
- 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 eCTD pilot
  - Chance to avoid technically differences
  - Test your favorite software systems (e.g. build pilot eCTD)
- European member states committed to accept e-only eCTD submissions by end of 2009, but eCTD might be mandated on a national basis before!

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 European Health Authorities still require paper, but a few…
  - "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 a backup beyond 2009?
  - Submissions to non-ICH countries still require paper dossiers for the majority of the countries

Product Information Management (PIM)- Current Status

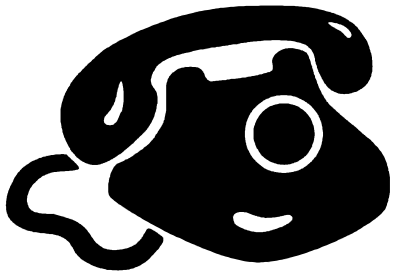
- Electronic management and exchange of product information
- **PIM Review System (PRS)**
  - Regulators' system for reviewing and commenting hosted at EMEA
- **Light Authoring Tool (LAT)**
  - Free-of-charge, basic tool to create and manage PIM submissions
- **Centralised Procedure**
  - Two pilot applications are being progressed (new products)
  - Pilot of 3-4 post authorisation procedures from Q2/2007
- Pre-specification work for PIM in MRP&DCP is anticipated for completion early 2008

Last but not least –
Communication is key

Whatever you plan to submit,

first contact your agency!

Guidance usually reflects a snapshot of the requirements, which might have changed in the meantime.



Questions

Thank you for your attention!

Any questions?

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