Electronic Regulatory Submission in the EU:

Afssaps perspective – France

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Agence française
de sécurité sanitaire
des produits de santé

afssaps

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Electronic Regulatory Submission
Afssaps perspective

Agenda

- eCTD priority
- Benefits and Requirements
- Status of implementation
- e-Submission
- Next Steps
- Conclusion

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Electronic Regulatory Submission Afssaps perspective

eCTD priority

European perspective:

- CTD is mandatory but eCTD is optional for industry;
- Heads of Agencies committed to implement eCTD by end of 2009, meaning that all agencies would be prepared to accept eCTD without paper by that target date;
- Some agencies are implementing eCTD earlier (PT, UK, BE, NL) and making electronic submission mandatory;
- EU eCTD review system ready for deployment in all MSs by EMEA;
- A Roadmap on eCTD implementation has been requested by HMA;

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eCTD priority

National Perspective :

- Committed executive management;
- Part of the Information Systems Development Plan 2006-2008;
- Part of Afssaps's vision (One of the 3 key projects for MAA);
- Communication with partners (NCA, Industry, Leem/EFPIA);
- Designation of a Core team/ Project Manager (Project team in place)
- Pilot phase – pragmatic approach
- Sharing understanding among teams

Electronic Regulatory Submission
Afssaps perspective

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- **Benefits and Requirements**
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Electronic Regulatory Submission
Afssaps perspective

Benefits

- Improved handling and archiving of submissions
- Simplified business process
- Better information management and support of **Life Cycle Management**
- Immediate Access to complete and up-to-date information
- Search functionality for assessors and increased tracking ability
- Facilitated evaluation and better visibility of the process
- Reduced workload and reuse of information for assessment reports
- Controlled communication with external experts
- Better use of resources

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Afssaps perspective

Requirements

- Improvement of IT infrastructure (Hardware, Network, Security)
- Building of a storage platform for long-term archiving
- Development of new processes
- Integration with workflow system and in-house databases
- Implementation of review tools
- Staff training
- **Change Management**

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Status of implementation : Pilot Phase

Objectives:

- Make sure that we understand the challenge
- To come up against the various potential problems linked with eSubmission in the « real life ».
- To find the appropriate solutions and adapt our business processes accordingly.
- To anticipate issues and solve them before accepting eCTDs and e-Submissions on a routine basis.
- To plan tasks and Resources allocation

Electronic Regulatory Submission Afssaps perspective

Status of implementation : The Deal

- Accompanied dossier : assistance of a consultant that linked with applicants to enter and follow up the pilot,
- Unique contact within agency,
- NO PAPER requested from Afssaps,
- Flow of eCTDs, various procedures and submission types,
- Technical assistance (readability),
- Controlled assessment timeframe,
- Change management strategy

Electronic Regulatory Submission
Afssaps perspective

Status of implementation : The Strategy

- Change is inevitable
- New ways of working (receipt, validation, processing and storage of CDs)
- Reluctance (Preparation stage, acceptance phase)
- Positive perception but Moderate implication of some users
- Convince External Experts

Electronic Regulatory Submission Afssaps perspective

Status of implementation : The Submission

- Submission meeting in Afssaps
- Afssaps project team leader, IT representant and records manager
- IT representant from the company assists
- CDROM directly /personnaly handed
- CDROM tested immediately for readibility

Electronic Regulatory Submission Afssaps perspective

Status of implementation : Issue 1

- Technical requirements
- Communication with external experts
- Business process

Solution

- More powerful computers
- Double screens (19 inch)
- Adobe Acrobat 7.0
- Training of concerned assessors just before arrival of dossier
- Remote access to a server / web-based application
- Development of workflow system

Electronic Regulatory Submission Afssaps perspective

Status of implementation : Issue 2

- Non eCTD compliance

Solution

- The TIGes subgroup “eSubmissions Harmonisation Topic Group” works for harmonised guidance also for so called **NEES** (**Non eCTD Electronic Submissions)**
- Afssaps strongly recommend eCTD format but also accept NEES if conform to the CTD format.
- Check of structure and file name convention
- Generation of an index.xml file for archiving by an internal application.

Electronic Regulatory Submission
Current eCTD issues

- **Status of implementation : Issue 3**

Current eCTD Issues

- Impact of changes to specifications and MA application form and tools and agency systems
- Interoperability of eCTDs from different tools
- No strict adherence to the ICH specifications (Files not referenced in the backbone)
- Printing issues

Solution

- Production experience is the only way to resolve these issues
- Need for pre-process validation tool for applicants ?
- Access for external Experts
- Better Management of change process
- Printers

Electronic Regulatory Submission
Afssaps perspective

Status of implementation : The outcome

- 25 dossiers – 62 submissions (25 Go)
- All types of procedures (FR = Rap or RMS)
- All types of dossiers (NCE, Ext. Indic., Line ext, Var, FUM, RMP)
- 15 dossiers - more than 1 sequence
- Staff involved (n=20) - All skills
- 40 people trained

Electronic Regulatory Submission Afssaps perspective

Status of implementation : The Conclusion

- Benefits of eCTD recognized at the agency,
- Afssaps willing to move from paper to electronic asap,
- Facts:
  - Limited number of companies ready to embrace eCTD
  - Limited understanding of implications
  - Transition might be long if eCTD remains optional ,
- EU agencies that made the move expect ROI in the short term,
- Handling electronic **AND** paper processes is cumbersome ,
- NEES begin to be accepted by some (EU Guidance to streamline implementation towards eCTD in preparation)

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e-Submission : Legal Context

Archiving paper or electronic : 2 imperatives

- Access to the dossier for the users
- Master the LCM of document in conformity with the legislation (environment for storage, legal delay (France 30 years))

Electronic Regulatory Submission Afssaps perspective

1. **Submission 0000**

   

   NEW Document: **Each Document newly added to the submission**

2. **Submission 0001 and the following**

   

   DELETE Document: The document was added in submission 0000 and deleted in submission 0001

   

   REPLACE Document: The document was added in submission 0000 and replaced in submission 0001

   

   APPEND Document: The document was added in submission 0000 and appended in submission 0001

   

   NEW Document: The document is added to the current submission for the first time

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e-Submission : Legal Context

- Afssaps = PUBLIC INSTITUTION
  → under National Archives supervision by law (3 January 1979)
- Law of 13 March 2000: e-Submission same value as far as
  - Identification
  - Authentication
  - Integrity of data within the concerned legal timeframe
- Does not include implementation guideline

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Afssaps perspective

Legal aspects

- **eCTD = Original should be shown in case of lawsuit**
- **The company should ensure :**
  - Authenticity
  - Integrity
  - Everlastingness
  - Accessibility
  - Confidentiality

  → To maintain quality of physical archive
- **Logistics & Economic**

1  → 30 

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Afssaps perspective

1 - e-Submission type
- eCTD or NEES

2 - Completeness of the dossier
- Size (Mo)
- Number of folders/sequence
- Number of files/sequence
- Number of PDF pages (if available)

3 - Quantitative and Qualitative description per module
- Size
- Number of folders by module
- Number of files by module
- Qualitative description

4 - Durability
- CD-R (size < 650 Mo) otherwise DVD-R or DVD+R

5 – Software used for the generation of the eCTD
- Name of the software, Version, Company

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Conclusion

- eCTD is triggering and driving a fundamental change in publishing and assessment practices,
- The challenge of eCTD implementation is moving from an autonomous standalone model to a structured model of work,
- Current LCM is document based : submission of complete new documents taking into account new data,
- Future LCM is data based : submission of pieces of new information updating existing data,
- Replacement of current processes is the major change for both, agencies and industry,
- Once this is done, publishing and assessing e-CTD is relatively easy

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Next Steps

- Finalize reception/circulation/distribution processes for electronic dossiers,
- Complete e-Submission protocol for electronic dossiers and develop recommendations for applicants,
- Open tender for the outsourcing of archiving,
- Share experience with other EU agencies and contribute to guidance development

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Conclusion

- Afssaps is willing to accept NEES within a limit,
- Electronic dossiers' folder structure **MUST** follow CTD,
- Full benefits of e-Submission will not be available before industry is capable of structuring the dossier appropriately, and ultimately submit eCTD
- Afssaps is willing to accompany industry in the process,
- Pharmaceutical industry, French (LEEM) and European (EFPIA) syndicates will be kept informed,
- Pre-submission meetings could be arranged during the development of recommendations.
- At the end of the day Afssaps might strongly discourage paper submissions

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Thank you for your attention