

EU Regulatory Network
Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

E-submission:

From 2005 >2008, A great step forward

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13-14 November 2008, Rijeka - Croatia

Introduction - Program

- 1.MeSeA :e-system
- 2.Business Simplifications
- 3.E-submission
 - The Full Compliance checker
 - The CTD Tree Structure
 - The statistics

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

The project was realized up to now in 5 phases

Phase 0 (Feb. 2005)

- Project organisation and definition
- The project was realized up to now in 5 phases

Phases 1 and 2 (March - Oct. 2005)

- Analysis, Design, Build and Test
- All Medicines Registration processes (human drugs)

Phase 3 (Oct. 2005 - July 2006)

- Maintenance of first release
- Pharmacovigilance workflow (PSUR)
- Exchanging info on approved drugs
- Backlog cleaning : > 8.000 dossiers were closed
- Master Data entry team : 2.000 medicinal products entered

Phase 4 (Oct 2006 - June 2007)

- Management of concurrent drug variations ('multi-branching')
- Business process redesign
- Change Management

Phase 5 (June 2007-September 2008)

- Cleaning enterprises, Ingredients
- Update of the checker and zero tolerance
- Master Data
- Backlog cleaning

MeSeA: the approach

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Workflows

- Automate task flow between departments
- Monitor timetables through escalation on deadline expiration
- Present users with case screens

"Enforcing what needs to be enforced and allowing flexibility where acceptable"

has allowed to automate 160 business processes with 1 base workflow with generic steps

MeSeA: the approach

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13-14 November 2008, Rijeka - Croatia

The generic registration workflow supports multiple business processes through internal modelling of different scenarios and procedures

MeSeA: the approach

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13-14 November 2008, Rijeka - Croatia

Automatic reply's

- Dossier receipt confirmation,
- Start Assessment Mail
- Round up mail (start of the administrative closing)

Datamodel

Evolve from existing assets and experience towards a consolidated data model, incorporating European Reference Data Model aspects

Simplified Workflows

- Waiting Dossiers (only the first workflow is started)
- National Procedure type IA notifications and administrative changes (shortcut after validation directly to closing)
- NPIB variations (only the first workflow is started)

MeSeA: the approach

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13-14 November 2008, Rijeka - Croatia

Due to the new MeSeA approach, and the increasing number of submissions, business simplifications were necessary

- National approach – minor variations(2)
- National approach-major variations
- MRP CMS approach (Parking)

Business simplifications

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Scope: Administrative variations and variations type IA, IB

Automatic e-mail sent out

- after dossier upload for administrative variations and variations type IA
- after validation for variations type IB
- Applicant may implement the variation(s)
 - After 10 working days for administrative variations and variations type IA (legal time limit)
 - After 30 calendar days for type IB variations (legal time limit)

if no comment received from the authorities

Will be finalized with a variation type II clinical or a renewal (cluster but no master dossier!)

National Approach(1/2)

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Scope: Variation Type II Analytical

Automatic e-mail sent out after assessment,

- With the round up mail, applicants can implement the changes from the variation based on the positive advice given.
- Will be finalized with a variation type II clinical or a renewal (cluster but no master dossier!).

National Approach(2/2)

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Scope: Variations type IA, IB and II analytical

Automatic e-mail (Notification CMS approach) sent out after dossier upload in MeSeA

Applicant may implement the variation(s) after RMS's notification of approval (or validation)

Will be finalized with a variation type II clinical or a renewal (cluster with a master dossier)

Exceptions: type IB name change in BE, Pack size out of range

MRP CMS Approach

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Notification of dossier receipt
(National approach - administrative variations or variations type IA)

If your Dossier concerns an administrative variation or a National Procedure, variation type IA, please consider <Entry Date> + 10 working days as day of implementation, except when the DGMP sends you a mail that your dossier has been refused (invalid)

If your Dossier concerns a Mutual Recognition Procedure, variation type IA, for which Belgium acts as RMS, please consider <Entry Date> + 10 working days as day of implementation, except when the DGMP sends you a mail that your dossier has been refused (invalid)

Automatic mail(1/4)

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Start assessment
(National approach Variations type IB)

If your Dossier concerns a National Procedure, variation type IB, please consider Day 0 + 30 calendar days as day of implementation, except when the DGMP sends you comments on your dossier during procedure."

If your Dossier concerns a Mutual Recognition Procedure, variation type IB, for which Belgium acts as RMS, please consider Day 0 + 30 calendar days as day of implementation, except when the DGMP sends you comments on your dossier during procedure."

Automatic mail(2/4)

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Notification of round up
(National approach Type II Ana)

If your dossier concerns an analytical type II variation, following the national procedure, please consider the reception date of this 'Round Up' mail as the date of implementation for the concerned changes within this dossier. The chief executive has the intention to approve the concerned variation, based on the positive scientific advice given.

When the variation may be implemented, the marketing authorisation holder may attach a copy of this automatic mail to the marketing authorisation for the introduction of an application to the economic Affairs and INAMI/RIZIV. He must declare on his honour that no comments were received from FAMHP.

 Automatic mail(3/4)

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Notification of dossier receipt
(CMS approach - Parking)

"If your Dossier concerns a Mutual Recognition Procedure, variation type IA, for which Belgium acts as CMS, please consider the day of receiving a valid notification of the RMS as day of implementation."

"If your Dossier concerns a Mutual Recognition Procedure, variation type IB or variation type II analytical for which Belgium acts as CMS, please consider the day of receiving a notification of approval of the RMS as day of implementation."

 Automatic mail(4/4)

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

The Full Compliance checker



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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Experience since October 2005 until 2008:

Industry:

- Not enough feedback concerning the quality of the e-submission
- National guideline is a theoretical approach
- Training necessary

Agency:

- The e-dossiers were of poor quality,
- a lot of volume based pdf's without any structure
- difficult to find the information >>Paper dossier
- Protected files

A tool to check dossiers= the Best checker

 E-submission: background

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

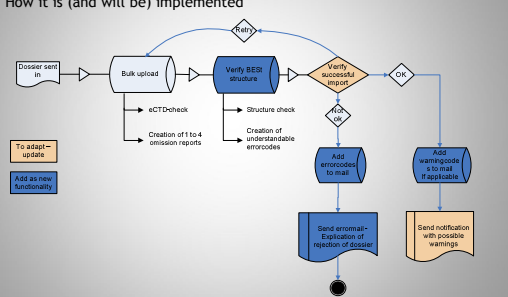
Goals of this module

- Make it easier to handle a dossier => make it easier to find all necessary information in a dossier
- Do a correct check on the structure of a dossier sent in by Enterprises
- Give accurate, up to date and clear feedback to the Enterprises
- Stimulate to grow to a situation where all dossiers are real eCTD's (with backbone and checksum)
- Make the check of a dossier up to date, conform all latest
- Guideline make it possible to check complex dossiers as well



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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

How it is (and will be) implemented



```

graph TD
    Start([Dossier sent in]) --> Bulk[Bulk upload]
    Bulk --> Verify[Verify BeSt structure]
    Verify --> Check{ }
    Check --> AddErrors[Add errorcodes to mail]
    AddErrors --> SendError[Send errormail - Evaluation of rejection of dossier]
    SendError --> End([End])
    Check --> AddWarnings[Add warnings to mail if applicable]
    AddWarnings --> SendWarning[Send notification with possible warnings]
    SendWarning --> End
    
```

 BeSt Verification – check implementation

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Report of the files sent in

BeSt Verification - Example

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5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

With clear color coding:

- Folder or file completely OK
- Folder contains files and should not (perhaps files not in lowest level)
- Folder or file name contains illegal characters
- The name of the file or folder is not conform the eCTD-guidelines
- This document has an extension that is not allowed in an eCTD-folder
- This file can not be checked accurately, because it is in an incorrect folder (so there is no rule to check it)

And a clear summary to the user and the enterprise

Number of files: 114
Number of subfolders: 73
Number of subfolders that are not eCTD folders: 3 (= 4,11%)
Number of subfolders that contain files and should't: 4 (= 5,22%)
=> Folder score: 64/73 (= 87,67%)

Number of files with wrong names: 114 (= 100%)
Number of files with wrong extensions: 0 (= 0,00%)
Number of files that could not be checked correctly because they are in a non eCTD folder: 19 (= 16,66%)
=> File score: 9/99 (4,59%)
(only taking into account the files that could be checked)

BeSt Verification - report summary

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

- New releases of the module when the guidelines are updated
(last update in december, next one 15 may together with new release of the e-guideline an reference to NEEs guideline)=> keep the module up to date
- keep also the offline checker up to date
(new version since december2007,version 2)=>
<http://www.fagg.be/>

BeSt Verification up to date

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

<http://www.fagg.be/>

BeSt Verification – Website

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

Introduction - Program

The CTD Tree Structure

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

- Empty e-CTD structure available on the FAMHP website (Wonderpil)
- Use tree-structure “as is”
 - Tree-structure should always be respected
 - Folder names should not be modified
 - Delete empty folders

The CTD Tree-structure

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

File naming conventions:

EU module 1 specification
->See Notice to Applicants
(www.ec.europa.eu/enterprise/pharmaceuticals/eudralex)

ICH E-CTD specifications for modules 2 - 5
• See ICH guidelines on CTD (www.ich.org)

File names

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Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

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The Full Compliance statistics

EU Regulatory Network
Challenges and Opportunities for Croatia
5th ALMP Anniversary
13-14 November 2008, Rijeka - Croatia

27/03/07:
Checker and wonderpil tree structure >website.
Special training with industry

27/03/07 – end june 07:
Self testing period –

Half september 07:
Start zero tolerance dossier rejection.
85% for folder score
No limit for file score

Half may 2008:
folder compliance 95%, file score 95%
>Up to full compliance
95% for folder score
85% for file score

June 2008:
Start a Pilot group for real e-CTD with industry to gain experience

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5th ALMP Anniversary
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E-submission, A Belgian Success story,
thanks to great involvement of concerned parties
(Industry, FAHMPS collaborators, ICT people)

Thank you for your attention!
Questions?