eCTD/Non eCTD electronic Submission (NeeS):

Impact on the Centralised Procedure

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eCTD Implementation Strategy at EMEA: Key Milestones

- From *1 July 2008:*
  - The EMEA accepts electronic-only submissions, either in eCTD format or non-eCTD format (eCTD is the recommended electronic format), with no additional requirement for paper copies
  - This applies to all applications (new and existing) and all types of submissions to the EMEA in the context of the centralised procedure (e.g. new applications, supplementary information, variations, renewals).
  - Rapporteurs and CHMP members may, however, still have paper-copy requirements at this point.

eCTD Implementation Strategy at EMEA: Key Milestones

- From *1 January 2009:*
- The EMEA strongly recommends electronic-only submissions, either in eCTD or non-eCTD format (eCTD is the recommended electronic format)
- Paper will be an exception to the general e-format recommended for any application. This will apply to all applications (new and existing) and all submission types.
- Rapporteurs and CHMP members will not receive paper copies from this date.

eCTD Implementation Strategy at EMEA: Key Milestones

- From *1 July 2009:*
- The EMEA will strongly recommend eCTD-format electronic-only submissions.
- Paper and other electronic formats will be an exception to the general e-CTD format recommended for any application.
- This will apply to all applications (new and existing) and all submission types.
- Rapporteurs and CHMP members will not receive paper copies or other electronic formats from this date.

Mandatory eCTD for the Centralised Procedure

- The introduction of mandatory eCTD is an extension to the existing EMEA strategy for implementation of electronic-only submission and eCTD

- Based on further legal advice from EMEA, instruction was given that, although electronic-only submission for the Centralised Procedure cannot be mandated due to lack of legislative basis, it *is* possible to mandate the format of the electronic-only submission if received:
  - Hence new milestone in EMEA eCTD Implementation Strategy
  - Published December 2008

Mandatory eCTD: New Milestone

- From *1 January 2010:*
  - The EMEA will mandate the use of the eCTD format for all electronic-only submissions for all applications (new and existing) and all submission types.
  - Rapporteurs and CHMP members will not receive paper copies or other electronic formats.

- In addition, until 1 January 2010, any non-eCTD electronic submission provided in the context of the Centralised Procedure must also comply with the EMEA's new specific guidelines for non-eCTD electronic submissions. All other current guidance remains in force.

Mandatory eCTD: Implications

- Non-eCTD format electronic submissions will be rejected
- Paper-only submissions would be accepted as an alternative, but:
  - Will lead to significant handling and review issues, as all EMEA processes will be engineered towards electronic submissions

Current Status EMEA

- Number of eCTDs are increasing exponentially at EMEA
- European Review System for eCTDs (EURS) is used by the entire agency as the sole tool for the handling and review of all eCTD submissions as well as non-eCTD submissions still received by the Agency
- Although still the majority of eCTDs are new applications, the last 6 months have seen an increase in the number of converted eCTD baselines received for authorised products with ongoing regulatory activity

eCTD Statistics EMEA

- October 2008:
  - 573 electronic submissions received by EMEA
  - 112 of those eCTD
- November 2008:
  - 561 electronic submissions received by EMEA
  - 63 of those eCTD
- December 2008:
  - 787 electronic submissions received by EMEA
  - 204 of those eCTD (highest no. received in a month so far)
- January 2009:
  - 485 electronic submissions received by EMEA
  - 162 of those eCTD
- 988 eCTD submissions received since 1st July 2008
- 228 products currently managed in eCTD format (approximately half of all CP active products)

Non-eCTD Electronic Submissions for the Centralised Procedure: Background

- EMEA still receives, and will continue to receive until 1st January 2010, non-eCTD format electronic submissions (referred to as 'NeeS')
- These 'NeeS' vary considerably in format and quality, leading to practical handling and review difficulties for EMEA and member States
- Non eCTD electronic submissions that are not structured correctly have to be re-structured into the NeeS format by CIG in order to be loaded into the EURS review environment – a lengthy process
- European Guidance for industry has been produced on formatting the NeeS by the Telematics Implementation group for eSubmission (TIGes) – not always followed for CP and needs highlighting

Non-eCTD Electronic Submissions for the Centralised Procedure: Background

- EMEA considered that the European document could be complemented by a condensed, focussed guidance highlighting the aspects of non-eCTD electronic submission crucial to EMEA

- Guidance intended as a transitory measure to improve the standardisation and quality of all non-eCTD electronic submissions provided in the context of the Centralised Procedure , until eCTD is mandatory

- Adherence to the guidelines is further intended to facilitate the transition to the eCTD format for all submissions.

Non-eCTD Electronic Submissions for the Centralised Procedure: Implications

- NeeS Guidance was published December 2008 and must be followed for all Centralised Procedure submissions where eCTD is not used, from 1st February 2009
- Validation procedures will be applied to all NeeS submissions by EMEA to ensure compliance
- Other formats (volume based etc.) no longer accepted
- Guidance will apply for a finite period of time, 01/02/2009- 31/12/2009

Non-eCTD Electronic Submissions for the Centralised Procedure: Practical Guidance

- NeeS is:
  - eCTD submission without the index.xml and eu-regional.xml files, and the util folder containing other eCTD technical components
- Key points:
  - Adhere to CTD/eCTD file and directory structure
  - Include dynamic table of contents to facilitate navigation
  - Use recommended file formats (PDF v1.4, MS Word)
  - Use recommended file-naming convention (fixed and variable part, separated by hyphens)
  - OCR scanned legacy documents if possible
- NeeS is intended to facilitate the move to full eCTD

Electronic Submission: Available Guidance

- eCTD and electronic submission: Statement of Intent
- Mandatory eCTD: Statement of Intent
- NeeS Implementation: Statement of Intent
- Q&A on eCTD/electronic-only Strategy
- Practical/technical guidance on submitting eCTD to EMEA
- Practical guidance on submitting NeeS to EMEA

All available at:

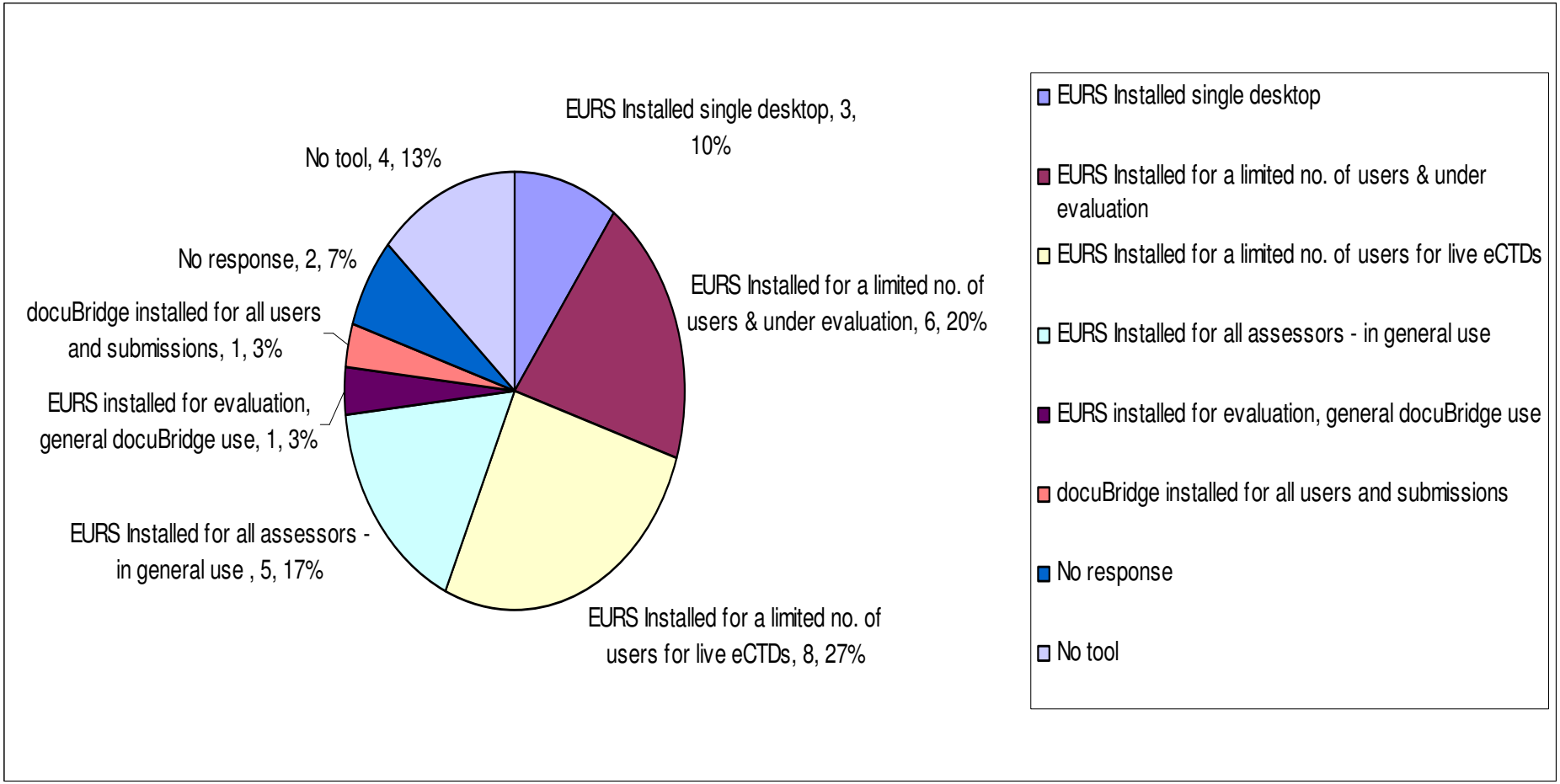
- http://www.emea.europa.eu/htms/human/genguidance/genreg.htm
  - Or contact EMEA: eCTD@emea.europa.eu

- Specific practical guidance on using eCTD for PMF and ASMF submission currently being drafted

Current Status EU

- 22 agencies have the EURS installed for eCTD review and processing, but with varied implementation:
  - Used for processing all eCTDs
  - Used for processing all eCTDs and other NeeS
  - In pilot for centralised e-submissions only
  - Single desktop installation for evaluation
- 3 agencies using a different eCTD review tool
- Several agencies integrating EURS with existing workflow systems/case management systems
- All agencies moving (at varying rates) towards the end 2009 deadline of acceptance of electronic-only submissions and eCTD
- eCTD submissions are still less common for MRP/DCP and national procedures – most eCTDs sent via CP
- Many agencies using a review tool for the processing of centralised applications only – support for implementation of Central Repository

EURS Overview: MS



Further Work

- Increased experience with eCTD has led EMEA to understand that there is still much work to be done on the development of lifecycle management requirements, particularly for such scenarios as parallel variations (including development of technical support and guidance for the above)
  - This work should also be, and is being, coordinated at a pan-European level (TIGes etc).

Key Messages for Industry (1)

- Concern at EMEA that the majority of electronic/eCTD applications are STILL accompanied by a paper copy – this is disposed of on receipt by EMEA
- Many companies receiving requests for paper from NCAs – please do not provide paper but instead contact EMEA for guidance and resolution
- Limit submissions to one per CD/DVD, clearly labelled
- Send DVD in place of multiple CDs (multiple CDs lead to handling difficulties)

Key Messages for Industry (2)

- Companies should refer to the EMEA's practical guidance for detailed information on presentation and structure of the eCTD
- Envelope meta-data still not used as effectively/consistently as desired by EMEA – particularly the submission description
- Not always sufficiently clear which regulatory activity a submission belongs to (correct use of application number in PA submissions, related sequence, submission description)
- Information relating to multiple regulatory activities should not be combined within a single eCTD submission (applies particularly to FUMs/SOs/PSUR – we have seen several submissions that combine all these into one sequence)
- EU M1 v1.3 must be used for all applications
- List not exhaustive...if in doubt about any aspect of eCTD use, ask EMEA

Central Repository

- Testing and implementation of the Central Repository for CP continues at EMEA and within the EURS Implementation Group
- Test Phase I, involving UK, NL, BE and HU, is complete:
  - Test National Cache Manager & Central Repository
  - Propose any enhancements
  - Stress Testing
  - Produce Evaluation report
- Test Phase II:
  - Involve 10 Agencies to test NCM enhancements and CR – Initial meeting held on 20/2 to inform participants of status and preparation for Next phase testing
  - Series of structured and ad-hoc tests
  - Involved MS have all necessary NCM installation and technical documentation
  - Vendor to commence NCM enhancements shortly
  - Vendor and 3 agencies met on the 19th of Jan 2009 to discuss API solution. Vendor reviewing solution

Electronic-Only Submission for Paediatrics, Orphan Drugs and Scientific Advice

- An electronic repository for Paediatric applications, orphan drug applications and scientific advice is currently being set up – should be in place March 2009
- The repository will be appropriately scaled to accommodate the requirements for these application types in years to come (similar to eCTD repository for MAAs)
- Applications to come in electronic-only format once repository is in place
- Applications to be further processed internally in electronic-only format
- Standardised/structured electronic formats will not yet be introduced for these applications
- The EURS will not be used for the review of these applications
- Possibility that this repository will one day be opened up to MS

Electronic Application Form (eAF)

- Project Stakeholder Groups:

- EU Core Group – involving industry and NCAs, with regulatory and technical input. Involvement in workshops for supplying/gathering business requirements and adoption of technical solutions.
- EMEA Core Group – Administration and operational facilitation group with signoff authority for the two Business Owners and the Sponsor
- EMEA Business Group – EMEA business impact assessment & project updates
- IT Project Team – Delivering IT solution for eAF project

eAF - Deliverables

Stakeholders	Data Exchange Standard	Authoring Tool	Validation Tool	EMEA Receiving Tool	NCA Receiving Tool
Owner	NtA	TIGes	NtA	EMEA	NCA
Sponsor	EMEA	EMEA	EMEA	EMEA	NCA
User	Applicants EMEA NCAs	Applicants	Applicants EMEA NCAs	EMEA	NCA
Location	Applicants EMEA NCAs	Applicants EMEA	Applicants EMEA NCAs	EMEA	NCA

Community (In Scope)	Corporate EMEA (In Scope)	Corporate NCA (Out of scope)

eAF – Implementation Phases

- Iteration 1:
  - *1A:*
    - Maintain Data Exchange Standards for current New MAA / Variations / Renewals, incorporating Granularity, where possible & available controlled Terms
  - *1B:*
    - Establish Data Exchange Standards for New MAA / Variations / Renewals incorporating changes for electronic management reasons, such as alignment with RDM, Controlled Terms, Substances, other interfaces, etc.
    - Proof of Concept
- Iteration 2:
  - Create the Authoring Tool (Online / Offline) for Applicants
  - Create the Validation Tool (used at the Applicants, EMEA / NCAs)
  - Allow XML data to be available for NCAs internal systems (using their own Receiving tool)
- Iteration 3:
  - Create a Receiving Tool (edit, view, review, export, print, etc for EMEA)
- Iteration 4:
  - Create DES for other EMEA forms and Integrate into the 3 tools

eAF - Draft Timelines (to be confirmed)

Iterations		2009											
		Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
1	DES (1A) DES (1B)												
2	Authoring / Validation Tool												
3	Receiving (extracting data) Tool												
4	DES Other Forms + Integration with other tools												

eAF – Current Status

- Project Brief distributed to all stakeholders
- Preparing for kick-off meeting with various groups
- Analysis started on the Iteration 1A DES for New applications, Variations, Renewals
- Analysis to commence shortly on Iteration 1B DES for New applications, Variations, Renewals
- Project team established.
  - Business Analyst work commenced
  - Software Architect work commenced
  - One Developer commenced
- EU Core Group proposed via Interlinking group: representation from 4 NCAs, NtA, EMEA, EFPIA and EGA
- Business Group set up for EMEA

Conclusions

- Implementation of eCTD at an Agency level has been successful so far
- Still work to do internally regarding deep understanding of the eCTD on an operational level
- Work really only just beginning on lifecycle management requirements, integration with existing systems and further eCTD development
- EMEA will comply with HMA statement by end 2009
- Many electronic submission initiatives to come together throughout 2009 and into 2010
- Learning process for all – applicants are encouraged to contact EMEA to discuss business and technical issues with eCTD – will lead to better understanding and guidance

Thank you for Your Attention