ICH and European Update

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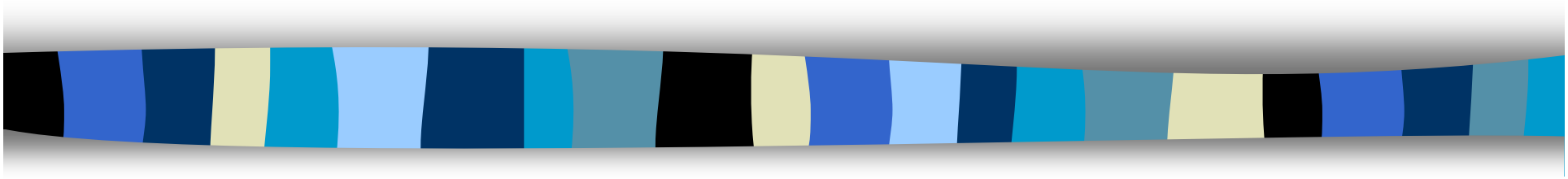
CAPRA Meeting
1-2 June 2004

Outline of Presentation

- ICH status
  - ICH processes
  - change control process
  - current areas of issue
  - study tagging file
- European implementation
  - support for European regulatory processes
  - Module 1 specification
    - status and content
  - making the business case

ICH Update



The ICH Process

- Step 1 - working draft
- Step 2 - agreement from all parties in the Expert Working Group that it can be issued for widespread review
- Step 3 - the review/consultation process
- Step 4 - agreement from the US, EU and Japanese regulatory agencies that it can progress to implementation
- Step 5 - incorporation into regional guidance/regulations
  - with effective dates

Change Control

- Little changes - change control process
  - tidying up the eCTD specification
  - handled by eCTD Implementation Working Group (IWG)
- Big changes - ICH Step process
  - changing the scope of the eCTD
  - significant changes to the backbone
  - handled by ICH M2 Expert Working Group (EWG)

IWG or EWG?

- We’re the same people!

IWG

EWG

EWG

eCTD group does not work in isolation

- We meet with other ICH groups

Typical Interactions

- November 2003
  - Meeting with E2E and CTD-E to discuss location of Pharmacovigilance Plan
  - Meeting with CTD groups to discuss Q&As and Granularity
  - Agreement on on-going interactions with CTD groups
    - CTD Implementation Co-ordination Group (ICG) will continue
    - CTD IWGs will still exist virtually - with rapporteur
    - CTD IWGs should always have someone present at ICG

Media Type Recommendations

- November 2003
  - Updated Floppy Disk
  - Updated CD-R
  - Approved new DVD-RAM
- June 2004
  - Reviewing secure gateway recommendations

Q&A Process/Change Control

- November 2003
  - 1 Q&As
    - granularity, study tagging file and legacy reports
  - 4 new change requests
    - positions agreed
  - 19 change requests closed
    - mostly by inclusion in new version of specification document/DTD driven by
      - mandatory id
      - revised nomenclature for reference to modified file
  - Broken Link issue deferred until more experience is gained. Also referred to Adobe

Q&A Process/Change Control

- June 2004
  - very limited number of Q&As and Change Requests posted
    - will review these
  - will review all pending change requests
  - do not expect a new version of the DTD or specification
    - need some stability

Study Report Tagging File

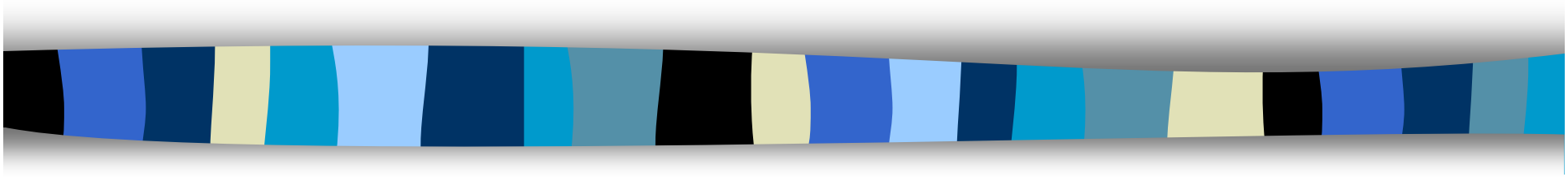
- Long term user requirements agreed
  - deficiencies have been recognised in current STF
    - duplicative
    - complex
    - not comprehensive
- No major difference in pros and cons between inclusion in the backbone or as a separate file
- Options to be developed for Washington (June 2004)
  - Target is still Step 2 in June 2004, Step 4 November 2004

EWG

Granularity Document

- November 2003 - significant review
  - Updated to be graphical representation
  - Minor amendments at ICH meeting
  - Approved by Steering Committee
  - Posted on ICH website
  - Minor error found in one table - corrected and re-posted
- Suggest that you read this document
  - applicable to CTD and eCTD

European Update



European Union

Existing Member States

- Austria
- Belgium
- Denmark
- Finland
- France
- Germany
- Greece
- Ireland
- Italy
- Luxembourg
- Netherlands
- Portugal
- Spain
- Sweden
- United Kingdom

New from May 1st 2004

- Cyprus
- Czech Republic
- Estonia
- Hungary
- Latvia
- Lithuania
- Malta
- Poland
- Slovakia
- Slovenia

Statistics

	Current EU	Enlarged EU
Member States	**15**	**25**
Population	**370 m**	**470 m**
Competent Authorities (ie Agencies)	**26**	**49**

Plus Iceland, Norway and Liechtenstein

EU Approval Procedures

- Centralised Procedure
  - Co-ordinated by EMEA
  - Reviewed by 2 agencies (rapporteur & co-rapporteur)
  - Assessment commented on by all agencies via CPMP
  - Single central licence issued
- Mutual Recognition Procedure
  - Submitted, reviewed and approved nationally by one agency
  - ‘Sponsored’ through MRP by this Reference Member State
  - Assessment commented by all Concerned Member States via MRFG
  - National Licences issued
- National Procedures
  - relevant only to old products
  - maintenance of individual national licences
  - no reference between any individual states

CTD Implementation Status

- Mandatory format for submission in Europe
- 20+ NCEs, numerous line extensions and new indication submissions
- Too many to count because of the different procedures and agencies
- Rush of non-CTD documents to beat the deadline for mandatory CTD
- No particular issues
  - still some areas of uncertainty

Variations in CTD - Europe

- Variations required in CTD format
- Has been a lack of clear guidance from agencies
- Experiences building up
  - eg. GSK
    - approx 20+ submissions to date - with no refusal to file
  - Agencies
    - beginning to receive significant
- Recently issued clearer guidance (but probably not detailed enough)
  - company ‘standards’ being adopted in interim

European Guidances

- Formal guidances for CTD are issued as ‘Notice to Applicants’ by NTA Group
- This will apply to Regional eCTD specifications and guidances
  - none formally issued at present

Parties Involved

- Telematics Implementation Group e-submission (TIGes)
  - agency group charged with responsibility for eCTD and related implementations
- EFPIA eCTD Topic Group
  - Research-based industry implementation support group
- Joint Implementation Group (JIG)
  - TIGes + EFPIA + EGA (generics) + AESGP (self-medication)
  - Implementation & Change Control
- InterLinking Group
  - subgroup of TIGes + NTA Group
- NTA Group
  - official guidance issuing group

Current State of Guidances

- CPMP adopted
  - v3.0 & v3.2 eCTD specifications - refer to www.ich.org
  - Q&As
  - Study Tagging File not yet adopted
- Draft Module 1 specification 0.9
  - http://esubmission.eudra.org/regional.html
  - currently being updated for finalisation
    - at v0.95.1

EU Acceptance of the eCTD

- The eCTD is not mandatory in the EU
- There are no dates set for making the eCTD mandatory in the EU
- General rule
  - eCTD submissions will be accepted in parallel with paper submissions; the latter remain the official submissions
    - some paper reduction in some markets

Important Implementation Needs

- Support for MRP in Module 1 specification
- Ability to reduce amount of paper provided and streamline process for production of paper
- Review system availability and training
- Ability to file ‘experimental submissions’

EU Implementation Status

- Interim implementation phase through 2004
- Agencies are implementing eCTD review tools
  - 13 by end March
  - all by end July (including accession)
- Limited number of ‘live’ submissions received
  - ranging from 20+ (Netherlands) to 0

Paper Production from the eCTD

- Need to ensure an efficient process for the production of paper and eCTD whilst both are required
  - provide an easier path to produce a paper submission from an eCTD
  - Seen as critical during period where paper has to be submitted in parallel to electronic
- Areas to address
  - **Who prints?**
  - **Number of copies?**
  - **Sequence of printed submission? - according to index.xml or file/folder structure**
  - **Tabs - beginning of each file - extra internal tabs can be used (eg legacy report)**
  - **Printed table of contents - one at the beginning of the submission covering 1-5 and repeated at the beginning of 2,3,4&5**
  - **What's in the TOC - list of documents (titles as in backbone?) with volume number where they will be found**
  - **Cross-reference strings - as agreed in latest ICH Q&A**

Paper from eCTD (Cont.)

- Application form if XML-based - need to determine if latest version of the stylesheet is printable
- What to do with documents ‘available on request’
- No use of Operation attribute in paper submission - only an eCTD issue
- Reference to previous submission sequence - only an eCTD issue

Experimental Submissions

- Principle of eCTD - once electronic, always electronic
  - needed to facilitate the lifecycle management
- Problem for industry to adopt
  - what if it's not that easy and that problems are encountered along the way?
- Needed ability to file eCTD without long-term commitment
  - accepted by agencies

Lessons Learnt

- Finalise the regional guidance early
- Facilitate experimental filings
- Have mechanism to test exchange of eCTDs & validation prior to live filings
  - too much tool variability
- Build the business case for industry
  - paper reduction is critical
- Expose the reviewers to review tools early
  - ensure training available
- Ensure submissions are available
  - work with industry
  - provide the incentive

Q&As

- Contact details
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