COLLEGE

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CBG

MEB

MEDICINES

EVALUATION

BOARD

CBG MEB

eCTD Review

-An example from the Netherlands-

CAPRA 'Getting Ready for the eCTD' Symposium
April 2-3, 2003
Toronto, Canada

Stan van Belkum
Process Manager MEB
EU ICH M2 Topic Leader

Agenda:

- How the Dutch Medicines Evaluation Board has been and is preparing for the implementation of the eCTD
- Conclusions from experience on review

See: http://www.cbg-meb.nl

eSubmission experience of MEB

- New applications fully electronic:
  - PDF only > 30 (always came with full paper copies)
  - **eCTD: 6** = two generic product lines of 5 strengths and one NCE (!!)
- Other types of submissions electronically available, e.g. major variations (e.g. new indications), PSURs, etc: >50
- Submissions with electronic components, mostly Product Information: many

Areas of Activities

- IT infrastructure & soft ware developments
- Organisational matters
- Reviewers
- Review Tools
- Other XML developments

IT infrastructure and soft ware development

- ‘State-of-the-art’ infrastructure based on Win2000 (→XP), Oracle, LAN (with VPN connections), SAN, etc.
- Projects for 2003:
  - improve maintenance & control
  - advanced information security
  - improve workflow system combined with an eCTD aware Document Management System
  - Public Key Infrastructure

Organisation (1): key-areas

- Confirmation MEB products *(what do we do?)*
- High level description of business process *(how do we do it?)*
- Low level description of business process (SOPs) *(how do we do it exactly?)*
- Establishment of official security policy *(what should not be done?)*
- **New version MEB eSubmission Guidance Document**
- Management Support for eCTD in terms of vision, funding and communication to industry

Organisation (2): MEB Guidance Document (*WiP*)

- All products, applications and procedures
- Acceptable dossier and file formats:
  - *CTD:* eCTD + PDF only
  - *MAA:* PDF only
- New applications: only Modules 1 and 2 in paper, rest electronic only (NEW REGULATIONS in ARCHIVING LAW)
- For other types of submissions e.g. answers to questions, variations, etc, number of electronic and paper copies defined
- Navigation:
  - eCTD: XML backbone + style sheet
  - PDF only: adequate PDF ToC files

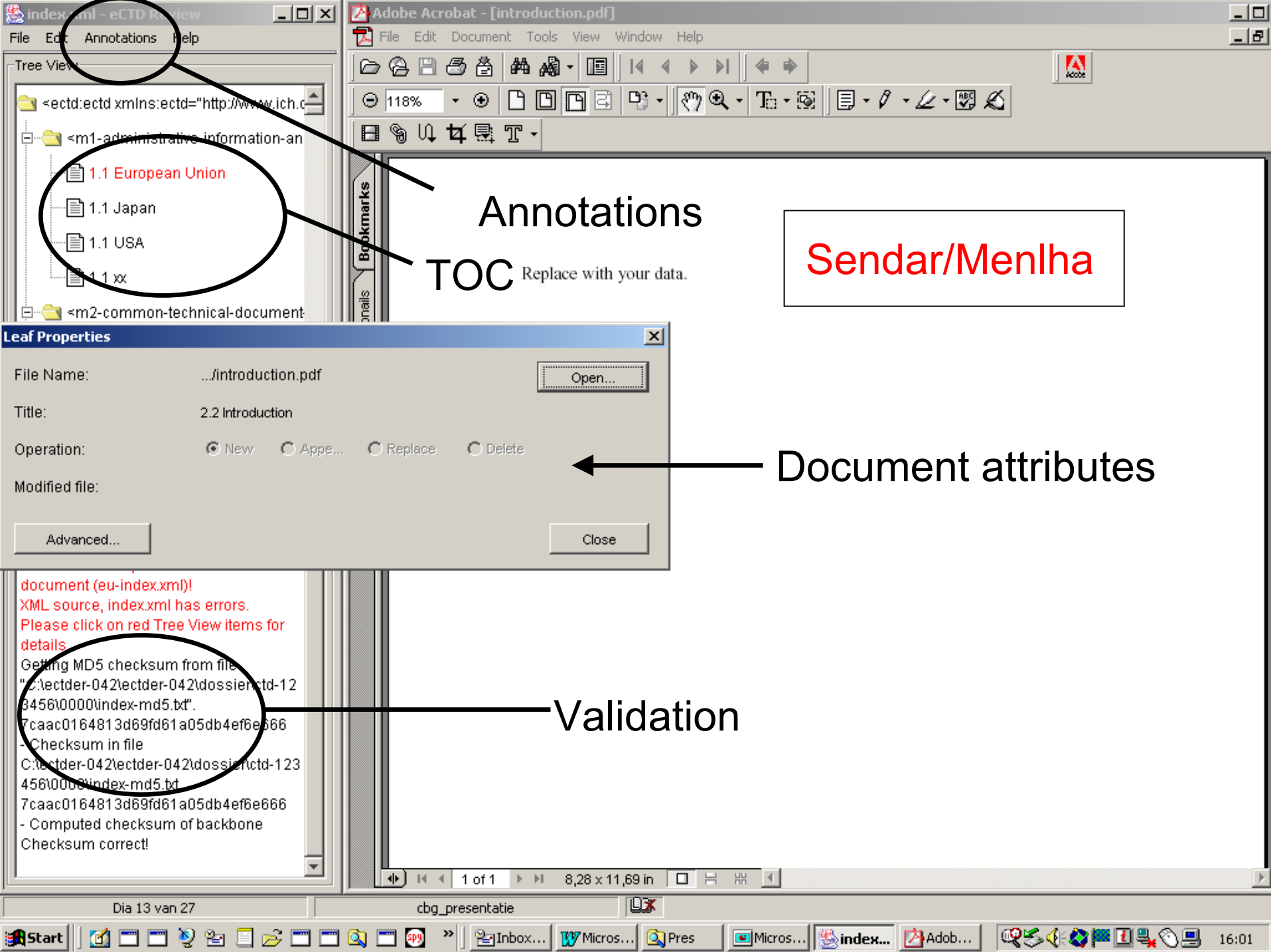
Organisation (3): MEB Guidance Document (*WiP*)

- PDF from electronic source highly preferred
- PDF only: sufficient navigation
- ‘Once electronic always electronic’
- Exchange medium: CDrom
- Refusal to accept is defined

New version foreseen in May 2003

Reviewers

- Technical environment (e.g. double (?) screens, etc.)
- *Active* communication on eCTD developments
- *Active* assistance during review of eCTDs
- Training, e.g. on use of PDF in Acrobat
- *Active* involvement in testing PDF plug-ins
- *Active* involvement in development of tools
- *Active* involvement in testing of tools:
  - tools provide by companies with submissions
  - Sendar/Menhla
  - Liquent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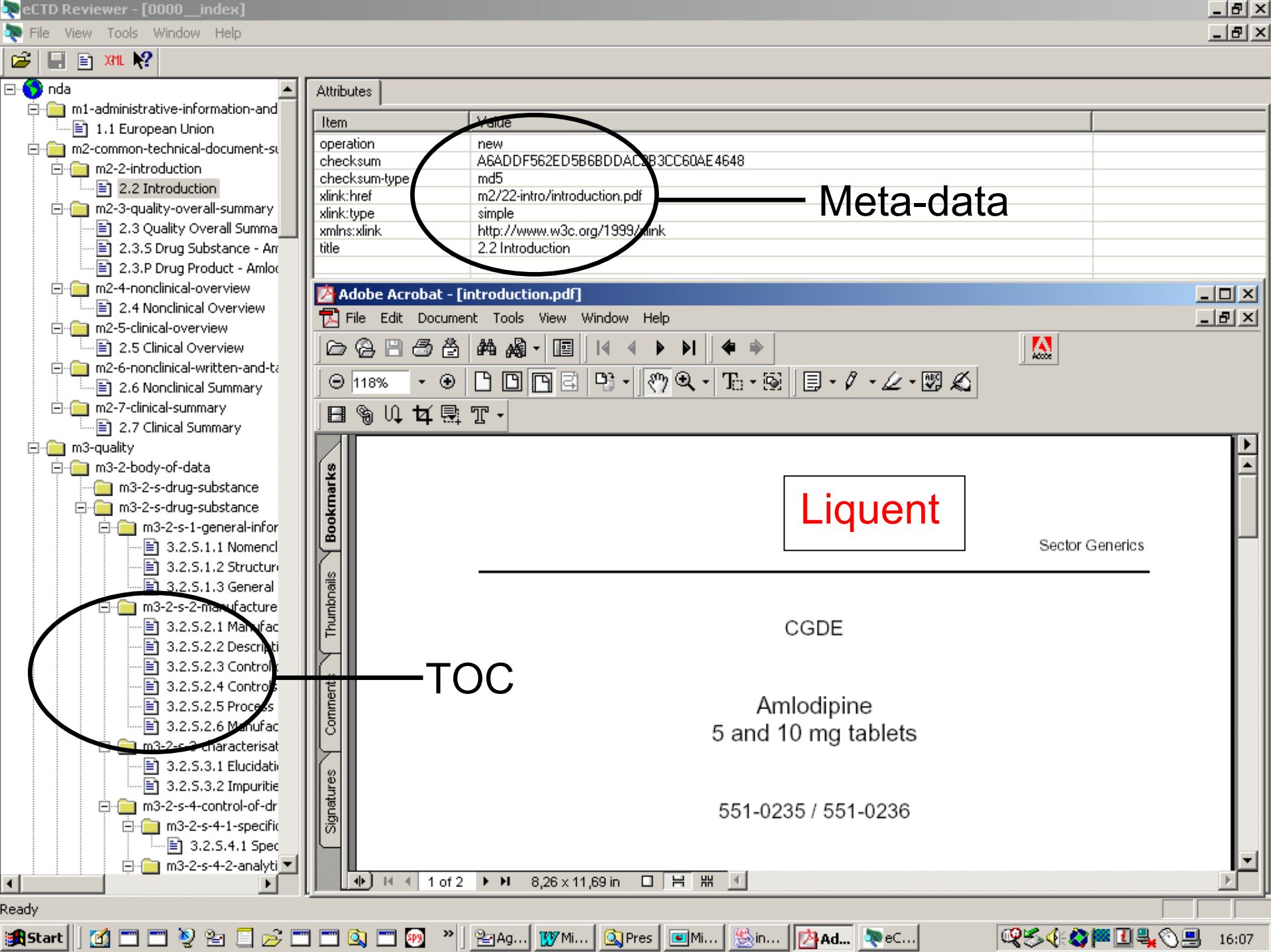
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m2-3-quality-overall-summary
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2.4 Nonclinical Overview
m2-5-clinical-overview
2.5 Clinical Overview
m2-6-nonclinical-written-and-t
2.6 Nonclinical Summary
m2-7-clinical-summary
2.7 Clinical Summary
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XML Developments

- EU PIM Project
- National implementation of PIM
- DIOS: application to generate XML assessment reports for data base storage
- Implementation of EU Application Form DTD

Conclusions from experience (1)

- **Case:** real electronic review of eCTD NCE: only Module 1 and 2 in paper, the rest electronic only + a good review tool provided by the Company
- *In general:* some reviewers find it easy and advantageous others have more difficulties; real benefits will come with LCM
- Good navigation and search is a MUST (intuitive!!!)
- Some fear of 'directed' hyperlinking
- Acrobat 5.0 is a MUST + good knowledge of the functionality (copy & paste)
- Opening multiple files/windows is a MUST

Conclusions from experience (2)

- Annotation functionality would be helpful
- Double or triple screens is a MUST: screen 1 = TOC to navigate, screen 2 = document display including bookmarks, screen 3 = assessment report
- Tendency to get lost in PDF navigation and hyperlinking
- Fast computer and connections to network in view of document size
- **CONCLUSION:** do-able but further improvements necessary + management of life-cycle and integration of agency business process is still unclear

Thank you for your attention!

Questions to:
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