OASIS
Electronic Trial Master File Standard Technical Committee

Electronic and Digital Signatures Discussion

March 3, 2014

9:00 – 10:00 AM PST

OASIS eTMF

Introducing Electronic and Digital Signatures

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Agenda

Topic	Presenter
9:00-9:05 Call to Order & Roll Call	Zack Schmidt
9:05-9:10 Approval of Minutes https://www.oasis-open.org/committees/documents.php?wg_abbrev=etmf	All
9:10-9:15 Tech Pres – Electronic / Digital Sigs - Overview	Zack Schmidt
9:15-9:25 Tech pres – Esig/Dsig differences, FDA/EMA legal	Peter Alterman
9:25-9:50 Tech Discussion – Esig/Dsig's – eTMF Std Direction	All
9:50-9:55 Outreach Committee / New Business	Jennifer Alpert All
9:55-10:00 Next meeting agenda / Date (Mar 17 2014) Charter: Data Model / eTMF Record Export Format	Z. Schmidt

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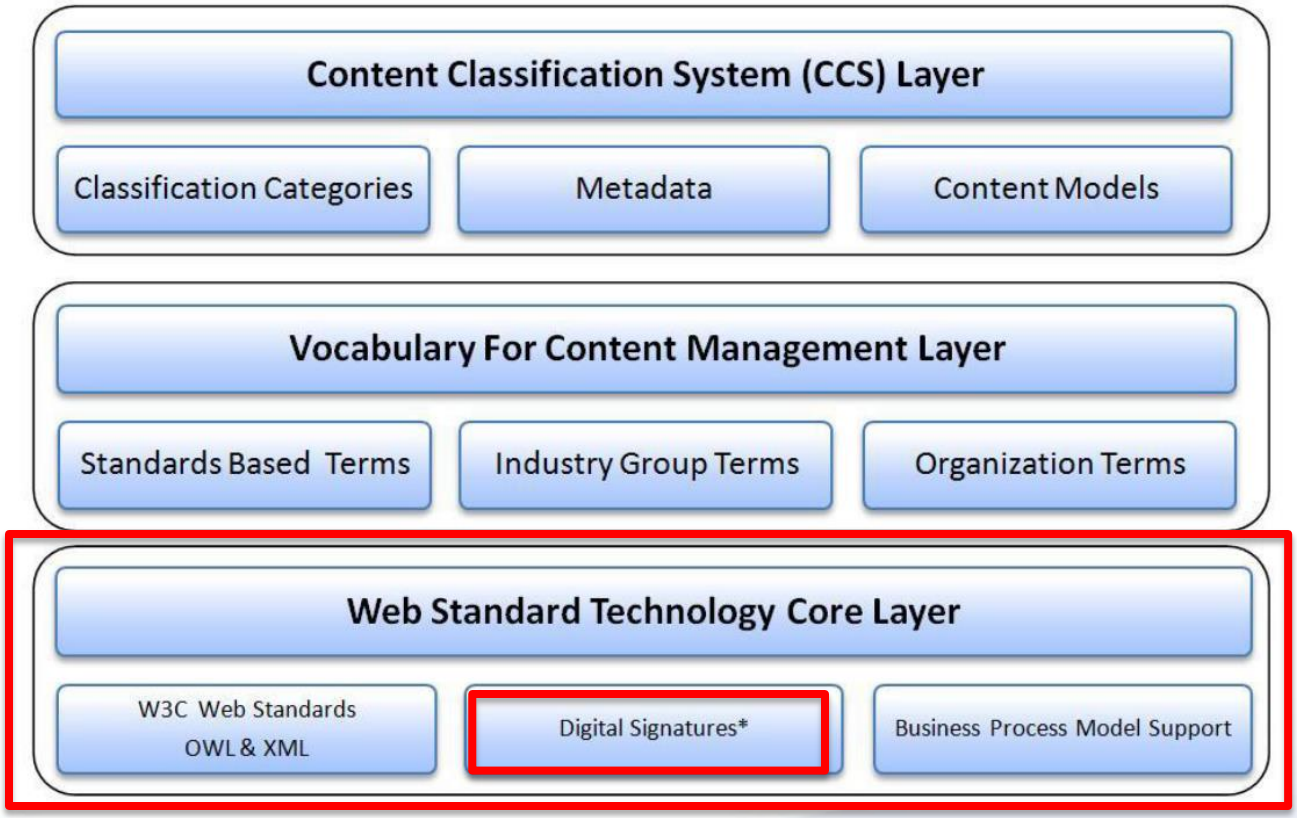
Web Standard Tech Layer

- **Digital Signatures**
  - Policies, standards for electronic signing
  - What should be E-signed
  - How



Introducing Electronic and Digital Signatures

Objectives

- Enable removal of wet signatures on paper
  - Productivity, quality, signature validation
- Move toward all electronic source content in eTMF
- Support for agency compliant electronic and digital signatures – support for both FDA, EMA
- Enable validation of signing party through digital certificate technologies using a third party Certificate Authority validation website

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Considerations for eTMF Standard TC:

- **What is the format** of documents that would be e-Signed?
  - FDA Part 11: Export of records shall be in common formats such as: PDF, XML, or SGML*
  - Associated Processes: eCTD – Esubmission requires PDF format (EMA, FDA).
    - PDF format seems ideal as common format for both eTMF and eCTD documents (ISO-32000 PDF standard)
- **How** should docs be e-Signed?
  - Differences between electronic signature, digital signatures
  - EMA, FDA e-Signature policy differences, commonalities
- **What are the requirements** for e-Signed documents in an eTMF?

*Source: FDA guidance http://www.fda.gov/regulatoryinformation/guidances/ucm125067.htm (as of Mar 2 2014)

21 CFR Part 11 Regs: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11

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Definitions

- Two main types of Electronic Signatures:
  - Electronic Signature – Ex: Digital mark
    - Pro: Accepted today by agencies (depends – requires audit trail, etc)
    - Con: Signing party not easily verifiable (typical)
  - Digital Signature – Ex: X.509 Certificate
    - Pro: Accepted today by agencies
      Signing party easily verifiable
    - Con: Signing party initial verification

Electronic Signature:
Stylus/Pen, Keyboard, etc.

Digital Signature:
Verifiable Digital Certificate

Certificate Authority
Signed Certificate

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Comparison of Electronic and Digital Signature Features

Feature	Electronic Signatures	Digital Signatures
Tight binding to the individual through face to face or other strong identity verification	No	Yes
Legally enforceable	Maybe	Yes
Supports strong non-repudiation	No	Yes
Maintains persistence, can be verified after certificate expires	N/A	Yes
Legal equivalent of hand written signature	Yes	Yes
Scalable	Yes	Yes
Tight binding to document signed (prevent “forgery”)	No	Yes
Detect document tampering	No	Yes

EU Legal Framework: E-signing

- Directive 1999/93/EC*
  - Two kinds of signature defined
    - the **electronic signature**
      - data in electronic form which are attached to or logically associated with other electronic data and which serve as a method of authentication
    - the **advanced electronic signature**
      - uniquely linked to the signatory;
      - capable of identifying the signatory;
      - created using means that the signatory can maintain under their sole control;
      - linked to the data to which it relates in such a manner that any subsequent change in the data is detectable
  - For **eSigned filings (eSubmissions)**, EMA requires advanced electronic signature (digital signature)

*Source: Tim Buxton, EMEA: "EMEA Perspective on the Advance to Fully Electronic Submissions", DIA Annual Conference, June 23, 2009

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US FDA Legal Framework: E-signing

Two major regulations:

- **US Federal ESIGN law, passed by US Congress, June 30, 2000**, 15 U.S.C. ch. 96
  - Allows use of electronic signature as legal replacement for wet-ink signatures
  - States that any contract signed electronically has same validity as wet-ink paper doc
  - Applies to all US Interstate and global foreign commerce

- **Title 21 CFR Part 11** – Originally passed in 1997
  - FDA broadly defines 'Electronic Signatures' to include both Electronic Sigs, Digital Sigs
  - **Electronic signatures, Digital Signature Requirements (Partial List)**
    - Uniquely linked to the signatory; used only by signatory
    - Verified identity
    - Timestamped audit trail for all signatures; password controls
    - Linked to the data to which it relates in such a manner that any subsequent change in the data is detectable

- For **eSubmissions**, FDA requires submission to be digital signature with certificate
  - Per FDA, Self-signed digital certificates acceptable under current regulations.

*Source: US Code http://www.law.cornell.edu/uscode/text/15/chapter-96
US FDA Regs: US CFR 21 Part 11, Electronic signatures

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Discussion – Esig / Dig Sig

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Outreach Subcommittee - Recap

Outreach occurred in multiple phases

- Charter Development
  - Refined Charter, developed as two phases
  - Charter Comment Log – Requirements/issues from Members, Public
- TC Formation Process
  - Solicitation by Oasis staff and some initial TC members 50+
  - CDISC, HL7, DIA, leading pharma, CROs and tech vendors
  - FAQ developed; Member and Public Comment period
- Outreach Subcommittee - December 2013 – February 2014
  - Total 47 contacts, 41 unique orgs
  - Memberships still in process: Shire, SAS (Kaiser is member)
  - EMA & FDA will review specification when developed
  - Jira Comment Log – Requirements/Issues from Members, Public

Addendum: European Medicines Agency Moving to Require Digital Signatures on Electronic Submissions*

eSignature Webinar Participant Questionnaire

Please find attached a short survey which seeks to gather further information on exchanging digitally signed electronic documents in PDF format with EMA. It also seeks to understand electronic signature solutions already implemented by companies in the Pharmaceutical Industry or National Competent Authorities (NCA) and the extent that industry uses qualified certificates with their digital signatures

eSignature Testing Facilities

The EMA Frequently Asked Questions (FAQ) Document is digitally signed for you to test your verification of EMA's digital signatures. You can view the document be following the link on this page: http://esubmission.ema.europa.eu/eSignatures.html

Please email your test PDF electronic documents to esignatureuat@ema.europa.eu if you require EMA to test the verification of your digital signatures.

Useful links

For more information and answers to FAQs please visit:
http://esubmission.ema.europa.eu/eSignatures.html

Sending digitally signed documents to the EMA:
http://esubmission.ema.europa.eu/sending_digitally_signed_documents.html

Which forms can I digitally sign?
http://esubmission.ema.europa.eu/esignature_certified_application_forms.html

Receiving digitally signed documents from the EMA:
http://esubmission.ema.europa.eu/receiving_digitally_signed_documents.html

For further information, including specific technical information, please contact:
ITServiceDesk@ema.europa.eu

*Source: EMA E-submissions website, 2014

Addendum:
US FDA CFR 21 Part 11 requirements & eTMF

- **Systems used to store eTMF content with essential documents must adhere to US FDA CFR 21 Part 11**
  - Limiting system access to authorized individuals
  - Use of operational system checks
  - Use of authority checks
  - Use of device checks
  - Determination that persons who develop, maintain, or use electronic systems have the education, training, and experience to perform their assigned tasks
  - Establishment of and adherence to written policies that hold individuals accountable for actions initiated under their electronic signatures
  - Appropriate controls over systems documentation
  - Controls for open systems corresponding to controls for closed systems bulleted above (§ 11.30)
  - Requirements related to **electronic signatures** (e.g., §§ 11.50, 11.70, 11.100, 11.200, and 11.300)
  - Record Audit trail (timestamping of records)
  - **Record export** to common formats such as **PDF, XML or SGML**
  - Validation of the system (11.10 (a))

Source: http://www.fda.gov/regulatoryinformation/guidances/ucm125067.htm