



# Electronic Regulatory Environment - Developing Future Requirements and Processes

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# Agenda

- Transport of Regulatory Information
- Evolving Technology vs. Steady Standards
- Implementation of Electronic Standards
- Next Challenge – Linking Systems
- Product ID and Product Information
- The Ideal World

or

**Why eCTD is a success, why PIM is struggling and why RPS could be cure and poison at the same time?**



# Transporting Regulatory Information



Content

Structure

Transport  
/ Review

# Focus on Electronic Standards - within the remit of the ICH M2 Expert Working Group



## Electronic Standards

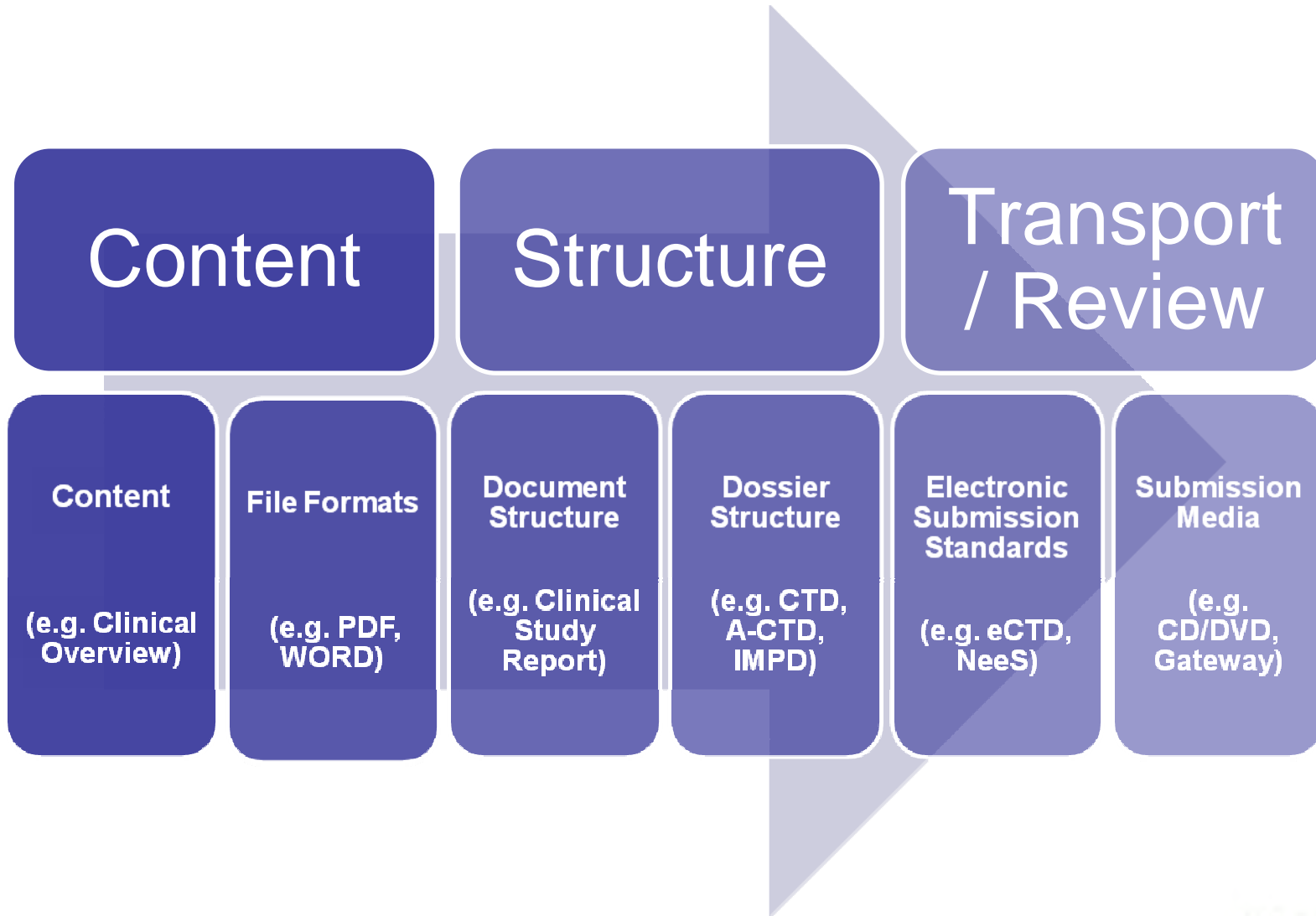
**Transport**

**Format**

**Security**

- Content definition is the responsibility of other ICH Expert Working Groups.
- Due to the rapidly changing nature of technology, it is anticipated that the standards will evolve.

# Standards for Regulatory Information

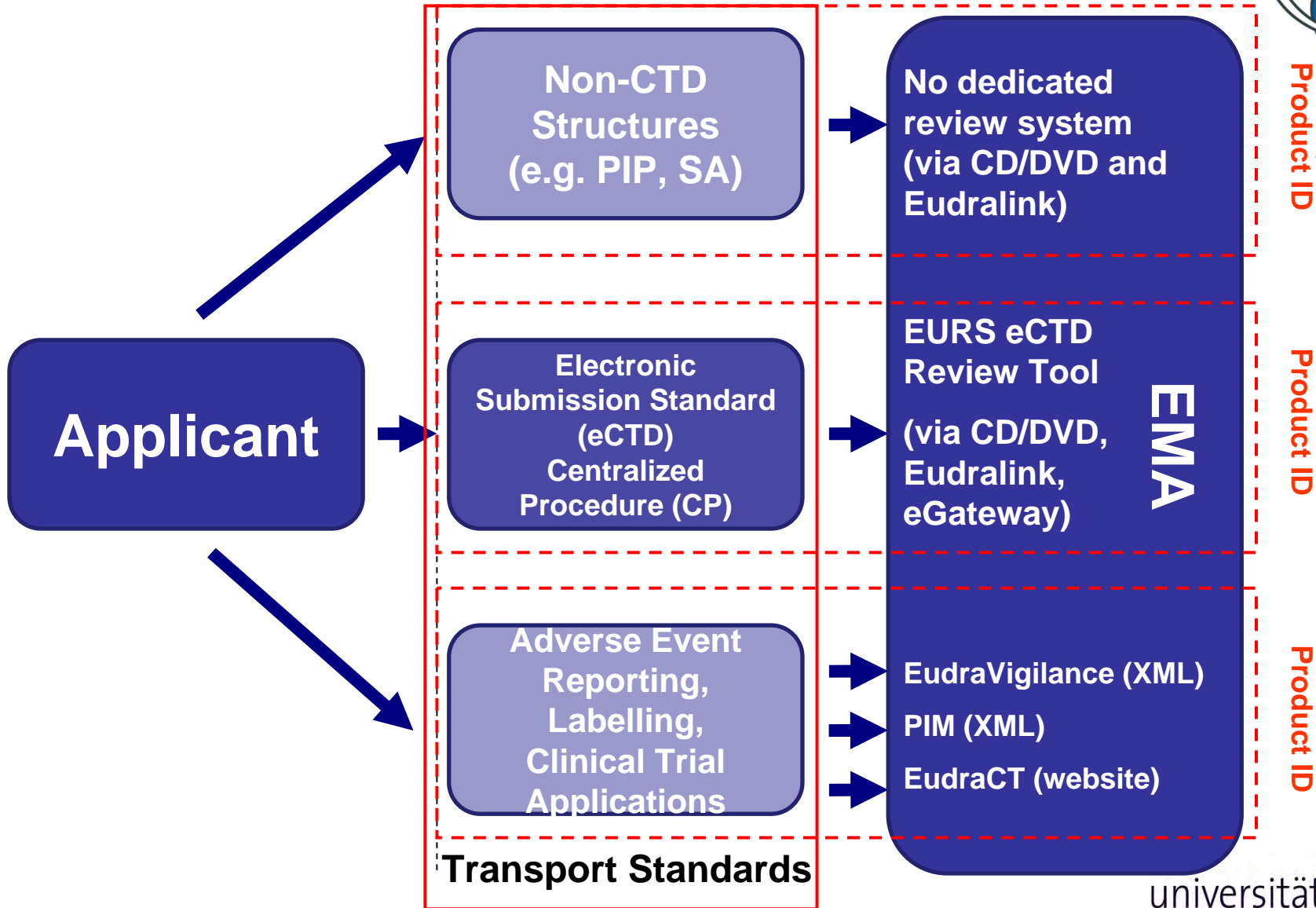


# More Electronic Standards in the Regulatory Environment



- **Submissions** (Regulatory)
  - ICH Standard: eCTD
  - Regional Standards: NeeS (EU), A-CTD (ASEAN)
  - National Standards: Basic eSubmissions or paper
- **Product Information** (Labelling, Regulatory)
  - Product Information Management (PIM, EU) (EudraPharm, EU)
  - Structured Product Labelling (SPL, US)
- **Clinical Trial Applications** (Clinical, Regulatory)
  - EudraCT Database, EMA
  - INDs as eCTDs, US
- **Pharmacovigilance** (Drug Safety, Regulatory)
  - Adverse Events Reporting (EudraVigilance, EU)
  - Adverse Events Reporting System (AERS, US)
  - ICH Standards for Individual Case Safety Reports (ICSRs) and Suspected Unexpected Serious Adverse Reactions (SUSARs)

# Transport between Applicant and EMA



# Product ID - Linked to Product Information



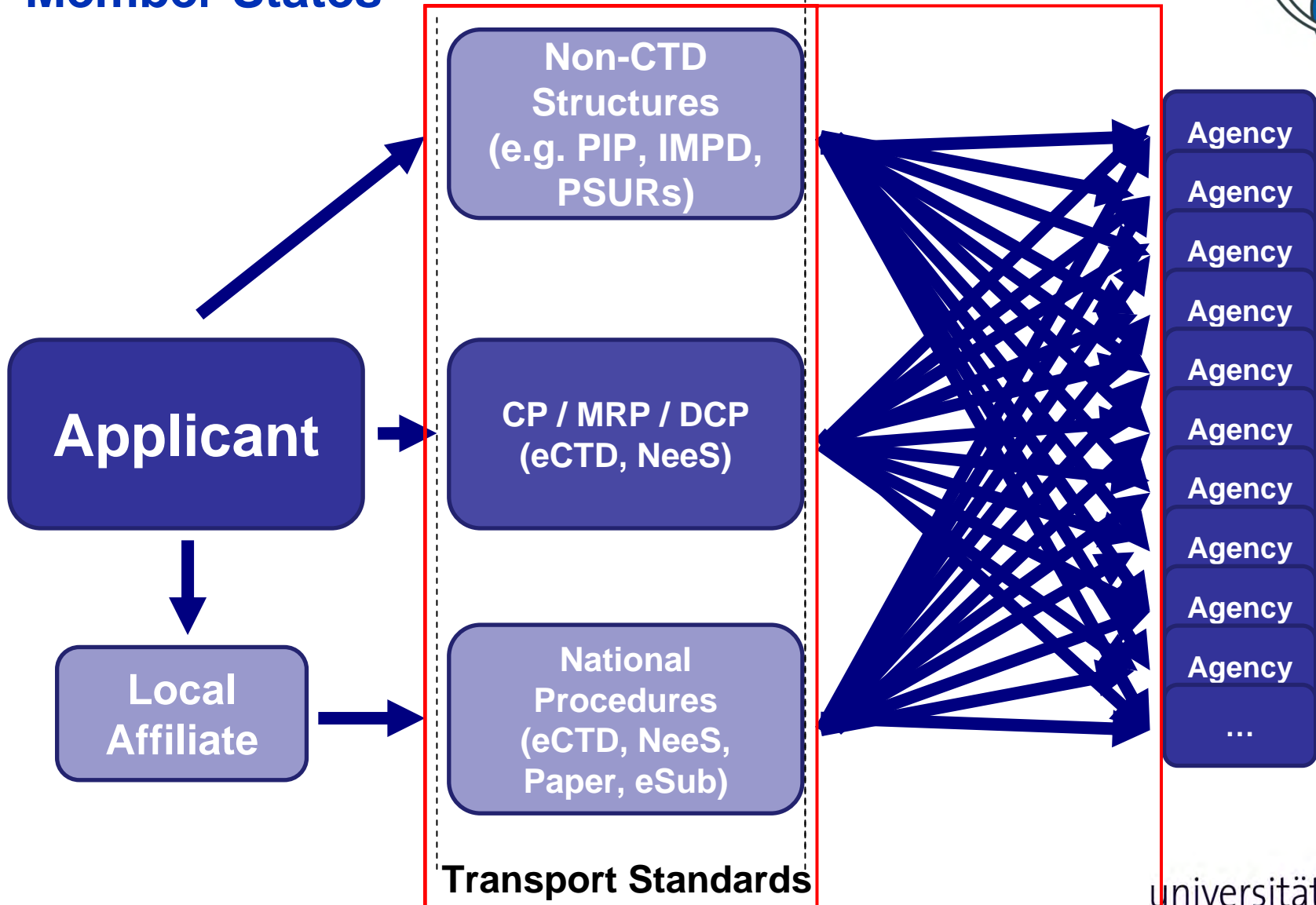
- All systems storing product related data require similar basic product information for identification purposes
  - **Unique ID**
  - **Product name**
  - **Registration number (national and / or central)**
  - **Active ingredient, strengths, dosage forms**
  - **Marketing Authorization Holder**
  - **Approval Status**
- Consistency checks or synchronization between the different databases would prevent from deviations (**database mapping**)
- **Centralized product identification** across agencies and / or countries would simplify the maintenance and ensure high quality data and integrity
- **Reference Data Model** – currently covering EudraPharm, EudraVigilance, EudraCT and M5 (Medicinal product identification) – EMA harmonises redundancies and inconsistencies between systems
- **Unique Product IDs** - this has been solved for other product groups like food & retail by developing global IDs (e.g. GS1) and linking these to corresponding product information

# Unique Product IDs

- Authorities and industry maintain product information tracking e.g. approval / marketing status in product databases combining all kind of local product IDs (i.e. **registration numbers**)
- **Unique product IDs** could
  - Harmonise the diversity of national registration numbers
  - Ease the identification and communication process between agencies and applicants
  - Be maintained centrally and information could be synchronized by agencies and applicants and used in their various systems
  - Ensure consistency across systems holding product related information
  - Avoid maintenance of redundant data at the agency and industry
  - Prevent oversights by automatic consistency checks



# Transport between Applicant and Individual EU Member States



**Harmonisation**

# Despite Standards - Still Lack of Harmonisation



- Lack of **electronic standards for non-CTD structures** like
  - Investigational Medicinal Product Dossier (IMPD)
  - Paediatric Investigational Plan (PIP)
  - Scientific Advice (SA)
- **Missing central infrastructure (except EU CP)** to share and review content using common electronic standards across countries
- **Central governance** for harmonized implementation and time commitments for telematic projects across Member States desired
  - HMA Telematics Steering Committee initiated Telematics Implementation Group (TIGes) – but national alignment, enforcement and implementation tracking required
  - Harmonisation group initiated by TIGes on voluntary basis for MSs
  - Official mandate committing each Member State to follow common decisions within defined timelines would be required
- Current transport standards e.g. eCTD/NeeS are bound to the dossier structure (i.e. CTD)
  - **Flexible transport standards irrespective of the content structure** would allow more broader and steady technology to be implemented

# Example 1 - A Global Standard and its Regional Implementation – eCTD in the ICH Regions US/EU/JP



- **ICH** eCTD Standard approved for implementation (Step 4) in 2002
- **US** – accepting eCTDs since 2003, eCTD mandated since 2008, initiated the development of the successor transport standard ‘Regulated Product Submission’ (RPS) for Regulatory Information extending the scope of eCTD
- **EU** – eCTD mandatory for Centralized Procedure (CP) since 2010, differing national requirements for MRP/DCP/National submissions (all accept optional eCTDs, a few consider mandating eCTD, some still require partially paper)
- **Japan** – Paper is still the official submission media, but eCTDs requested as ‘reference dossier’ (lifecycle concept different from US/EU concept, as always resubmitting full dossier and not only updated information)
- Additional countries adopted or will adopt the eCTD Standard directly or in slightly modified ways e.g. **Canada, Switzerland, South Africa, Australia.**
- CTD structure defines the transport format eCTD and prevents the reuse for other dossier structures (e.g. in Russia or China) or major changes to the current structure without affecting the transport standard as well
- Currently the **smallest entity** in the structure is **the document**

# Content Overlap - Reuse Instead of Duplication

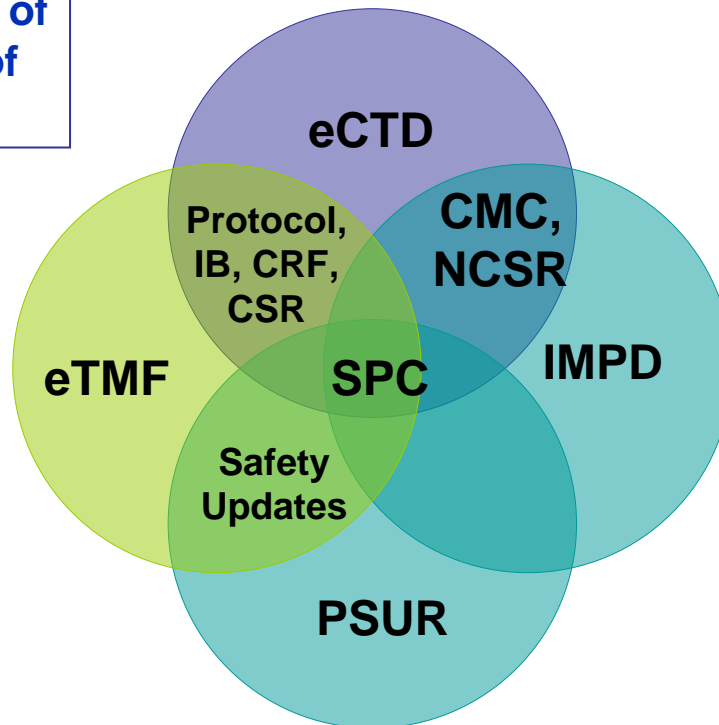


Content overlap  
between structures –  
Potential for reuse of  
content instead of  
duplication

Electronic Common  
Technical Document

Submitting content  
just once - without  
structure - and  
presenting it by  
assigning to structure

Electronic  
Trial Master File



Investigational Medicinal  
Product Dossier

Authoring sections  
instead of documents.

Periodic Safety  
Update Reports

# A Vision - Single Way of Transporting Regulatory Information



- **Regulated Product Submission (RPS)**
  - Health Level 7 developing as Standard Developing Organization (SDO) on behalf of ICH M2 EWG
  - Technical upgrades including e.g. **two-way communication** and approval status
  - **Extending the scope** to e.g. veterinary medicines, medical devices, food supplements, cosmetics
  - Scope is the **transport** of structured information, **not the presentation and review**
  - Presentation might be still according to CTD / eCTD standard for human pharmaceuticals – content should define the structure
  - But would be flexible enough to present any other structure if required
- Might be the future solution of submitting regulatory information **irrespective of the content or its structure**
- One **single technology** would ensure a quicker return of investment for involved stakeholders
- **Separating** the way of transporting Regulatory Information from the content and its structure (e.g. CTD/eCTD)
- Could also be used for non-ICH markets e.g. China, Russia to still use the same technology for transporting regulatory information with different structures

## Example 2 - A Regional Standard and its EU-wide Implementation – Electronic Product Information Management (PIM)



- Started 1999 as a joined project between EMA and EFPIA and first pilot was performed in 2000
- Today - 10 years later:
  - PIM still in pilot status
  - Complex technology and process for a very specific scope
  - Late and vague agency commitment
  - Limited to Centralized Procedure (at the moment)
  - High investments requiring a long-term stableness to guarantee the return on investment
  - When to implement an evolving standard which is still in development?
  - Still slow uptake by vendors and applicants
  - Only technical compliance with PIM does not offer great benefits for applicants
  - Long-term increase in efficiency from process simplification
  - PIM finally a success? – yet to decide in 2011 (planned migrations)

# Ideal World – Combine eCTD, PIM and RPS



- Harmonized format and presentation of the dossier structure easing the review (eCTD)
- Section authoring instead of document authoring (PIM)
  - maximising the reuse of content, avoiding overlap & duplication
  - streamlining the review of changes to sections instead of documents or complete structures
- Content could be assigned to multiple structures (RPS)
- Flexible transport standard irrespective of the structure (RPS)
- Two-way communication receiving feedback (e.g. approval status or comments) in the same environment – closed system (PIM, RPS)
- Broad scope would lead to wide implementation

# Impact of Updating Electronic Standards



- High investment costs versus limited time for return on investment due to short shelf-life of electronic standards
  - Costs of new systems, processes, trainings, skills



- Risk of excluding small / medium sized companies by new technologies
  - Investment hurdles triggers the need for outsourcing to service providers
  - Short-term goal to comply with new requirements (e.g. producing Product Information according to PIM Standard in XML format).
  - But real benefits to justify high initial investments are long-term by easing processes and increasing efficiency
  - Access to simple free-of-charge software necessary to comply with new requirements without high investments

# Implementations – Drivers and Hurdles



- Return-on-investment
  - Initial investments must be covered by long-term savings
  - If electronic standards change frequently the return on investment is not guaranteed and agencies / companies might hesitate to implement new innovations
  - The steadiness and long-term commitment to specific standards is essential for their wide/broad implementation
- Benefits derived from process changes (long-term)
  - Efficiency (streamlining, avoiding redundancy, handling large amounts of data, easy access of data)
  - Integrity & Compliance (preventing compliance risks)
  - Security (controlled systems and processes)

# Conclusions

- Electronic standards significantly improved the way of transporting and handling the increasing amount of Regulatory Information
- After initial efforts and investments for implementing new technologies the return on investment must be ensured by widely implemented and steady standards
- Central governance / committee desired - not only for development - but also for coordination of implementation of electronic standards
- Detach electronic transport standards from content structures in order to hold any kind of regulatory information irrespective of its structure
- Unify and centralise (or even globalise) the product ID and link to basic product information feeding into various systems holding product related information



# Questions



**Thank you for your attention!**  
**Questions?**

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# Backup Slide - Data Ownership



- Central data storage and maintenance
  - Who 'owns' the data and who the systems
  - Responsibility for integrity, maintenance and security
  - Data access for various stakeholders
  - Cost allocation - EMA's budget does only allow to focus on solutions for the Centralized Procedure
  - Governance of electronic initiatives for MRP/DCP/National procedures – e.g. HMA's Telematics Steering Committee or CMD(h)?
- Example - EMA is gathering and publishing product information on the EudraPharm website
  - Data providers are the National Competent Authorities and the EMA
  - No procedure currently in place for industry to verify or correct any of the published data on EudraPharm