# MedImmune

# Document to Content Management: A Paradigm Change

**DIA DRM SIAC – Content Re-Use** 

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## **Continuous Improvement**



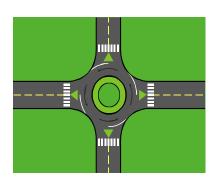
"Do you know that 87.166253% of all statistics claim a precision of results that is not justified by the method employed?"

- Unknown Statistician



## **Agenda**

- Why Move to Content Management?
- Re-Use & Content Management
- Tracking & Metrics
- Summary





### Why Move to Content Mgmt?

#### Labeling

Core Data Sheet mapped to Package Labeling

#### Global Dossier Re-Use

Global Dossier – similar content, different dossiers

#### Module 3 - CMC

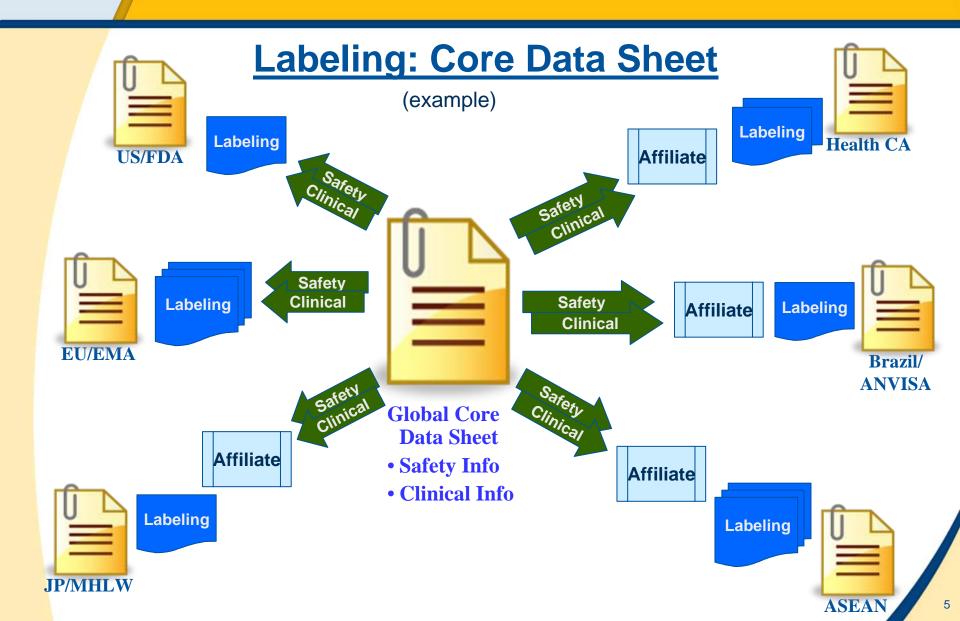
Granularity – same content, different sized documents

### Health Authority Q & A, Correspondence

- Track Qs & As by Content
- Track Qs & As by Health Authority

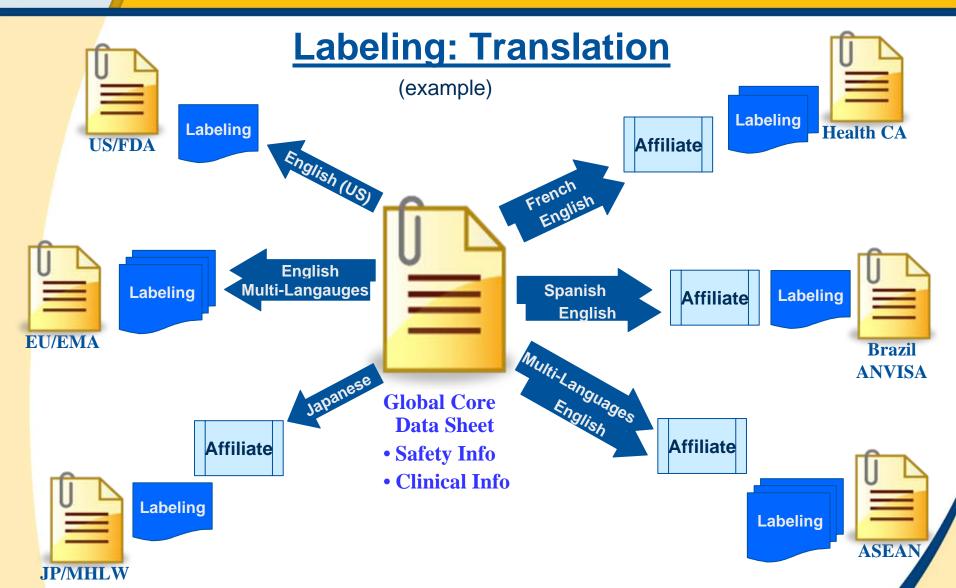


## **Consistency of Information**





### **Consistency of Translation**





### **Global Dossier** Marketing application in initial countries

(example Module 3)

### Europe

#### 🗐 EU 3.2.P Drug Product

- P.1 Description and Composition of the Drug Product
- P.2 Pharmaceutical Development
- P.3.1 Manufacturer(s) of Drug Product
- P.3.2 Batch Formula for Drug Product
- P.3.3 Description of Manufacturing Process and Process Controls
- P.3.4 Controls of Critical Steps and Intermediates for Drug Product
- P.3.5 Process Validation and or Evaluation for Drug Product
- P.4.1 Specifications for Excipients
- P.4.5 Excipients of Human or Animal Origin.
- P.5.1 Specification(s) for Drug Product
- P.5.2 Analytical Procedure for Description
- P.5.2 Analytical Procedure for Assay
- P.5.2 Analytical Procedure for Dissolution
- P.5.3 Validation of Analytical Procedures for Assay
- P.5.3 Validation of Analytical Procedures for Dissolution
- P.5.4 Batch Analyses for Drug Product
- P.5.6 Justification of Specifications for Drug Product
- P.7 Container Closure System for Drug Product
- P.7 Specification for Blister
- P.8.1 Stability Summary for Drug Product
- P.8.1 Stability Conclusion for Drug Product
- P.8.2 Post-approval Stability Protocol and Stability Commitment
- P.8.3 Stability Data for Drug Product

#### Upload to eCTD

Canada

#### Canada 3.2.P Drug Product

- P.1 Description and Composition of the Drug Product
- P.2 Pharmaceutical Development
- CA P.3.1 Manufacturer(s) of Drug Product
- P.3.2 Batch Formula for Drug Product
- P.3.3 Description of Manufacturing Process and Process
- P.3.4 Controls of Critical Steps and Intermediates for Drug
- P.3.5 Process Validation and-or Evaluation for Drug Produ
- P.4.1 Specifications for Excipients
- P.4.5 Excipients of Human or Animal Origin
- P.5.1 Specification(s) for Drug Product
- P.5.2 Analytical Procedure for Description
- P.5.2 Analytical Procedure for Assay
- P.5.2 Analytical Procedure for Dissolution
- P.5.3 Validation of Analytical Procedures for Assay
- P.5.3 Validation of Analytical Procedures for Dissolution
- P.5.4 Batch Analyses for Drug Product
- P.5.6 Justification of Specifications for Drug Product
- CA P.7 Container Closure Bystem for Drug Product
- P.7 Specification for Blister
- P.8.1 Stability Summary for Drug Product
- CA P.8.1 Stability Conclusion for Drug Product
- P.8.2 Post-approval Stability Protocol and Stability Commit
- P.8.3 Stability Data for Drug Product

**USA** 

🔚 US 3.2.P Drug Product

- US P.1 Description and Con position of the Drug Product
- P.2 Pharmaceutical Development
- W US P.3.1 Manufacturer(s) of Drug Product
- P.3.2 Batch Formula for Drug Product
- P.3.3 Description of Manufacturing Process and Process Controls
- P.3.4 Controls of Critical Steps and Intermediates for Drug Product
- W US P.3.5 Process Validation and or Evaluation for Drug Product
- P.4.1 Specifications for Excipients
- P.4.5 Excipients of Human or Animal Origin.
- US P.5.1 Specification(s) for Drug Product
- P.5.2 Analytical Procedure for Description.
- P.5.2 Analytical Procedure for Assay
- P.5.2 Analytical Procedure for Dissolution
- P.5.3 Validation of Analytical Procedures for Assay
- P.5.3 Validation of Analytical Procedures for Dissolution.
- US P.5.4 Batch Analyses for Drug Product
- US P.5.6 Justification of Specifications for Drug Product
- US P.7 Container Closure System for Drug Product
- 🚮 US P.7 Specification for Bottle
- 🚮 US P.7 Manufacturer for Bottle
- US P.8.1 Stability Summary for Drug Product
- US P.8.1 Stability Conclusion for Drug Product
- US P.8.2 Post-approval Stability Protocol and Stability Commitment
- US P.8.3 Stability Data for Drug Product

Upload to eCTD

Upload to eCTD

Thank you to Phyllis Thomas for this slide.



### **Global Dossier**

### Marketing application in subsequent countries

(example Module 3)

#### International

🗐 International 3.2.P Drug Product

IQD P.1 Description and Composition of the Drug Product
IQD P.2 Pharmaceutical Development
IQD P.3.1 Manufacturer(s) of Drug Product

P.3.2 Batch Formula for Drug Product

IQD P.3.3 Description of Manufacturing Process and Process Controls

M IOD P.4.1 Specifications for Excipients

P.5.1 Specification(s) for Drug Product

P.5.2 Analytical Procedure for Description

P.5.2 Analytical Procedure for Assay

P.5.2 Analytical Procedure for Dissolution

P.5.3 Validation of Analytical Procedures for Assay

P.5.3 Validation of Analytical Procedures for Dissolution

IQD P.7 Container Closure System for Drug Product

P.7 Specification for Blister

P.8.1 Stability Summary for Drug Product

IQD P.8.1 Stability Conclusion for Drug Product

🕮 IQD P.8.3 Stability Data for D ug Product

References only to Ph Eur

#### **ASEAN**

ASEAN 3.2.P Drug Product

P.1 Description and Composition of the Drug Product

ASEAN P.2 Pharmaceutical Development

ASEAN P.3.1 Batch Formula for Drug Product

ASEAN P.3.2 Description of Manufacturing Process and Process Controls

ASEAN P.3.3 Control of Critical Steps and Intermediates

ASEAN Process Validation Anenx 1

P.3.4 Controls of Critical Steps and Intermediates for Drug Product

P.4.1 Specifications for Excipients

ASEAN P.4.3 Excipients of Human or Animal Origin

P.5.1 Specification(s) for Drug Product

P.5.2 Analytical Procedure for Description

P.5.2 Analytical Procedure for Assay

P.5.2 Analytical Procedure for Dissolution

P.5.3 Validation of Analytical Procedures for Assay

P.5.3 Validation of Analytical Procedures for Dissolution

P.5.4 Batch Analyses for Drug Product

P.5.6 Justification of Specifications for Drug Product

P.7 Container Closure System for Drug Product

P.7 Specification for Blister

- M ASEAN Stability Annex 1

P.8.1 Stability Summary for Drug Product

P.8.1 Stability Conclusion for Drug Product

P.8.2 Post-approval Stability Protocol and Stability Commitment

P.8.3 Stability Data for Drug Product

Different numbering Additional documents China

China CTA Item 10.2 Drug Product

P.5.1 Specifications

P.5.2 Analytical Procedure Description

P.5.2 Analytical Procedure Assay

P.5.2 Analytical Procedure Dissolution

P.5..3 Validation of Analytical Procedure for Assay

P.5.3 Validation of Analytical Procedure for Dissolution

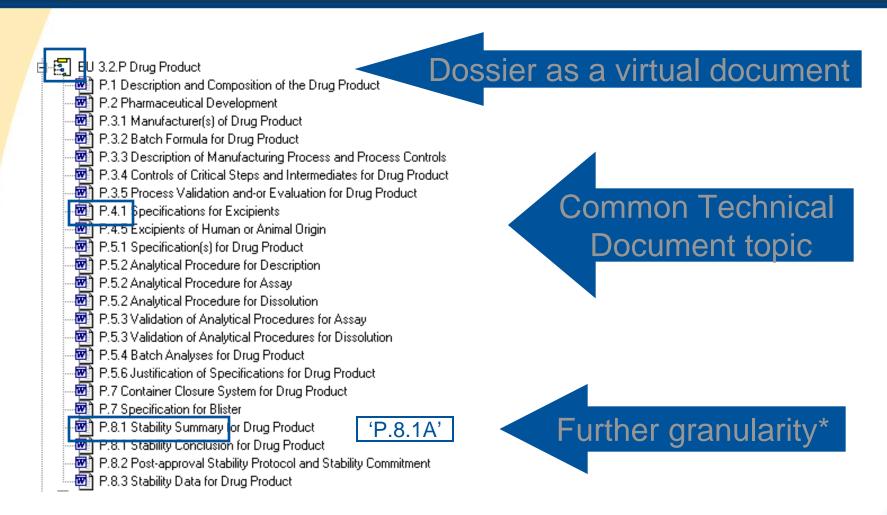
P.5.4 Batch Analyses

Different organisation (as 'Items')

Thank you to Phyllis Thomas for this slide.



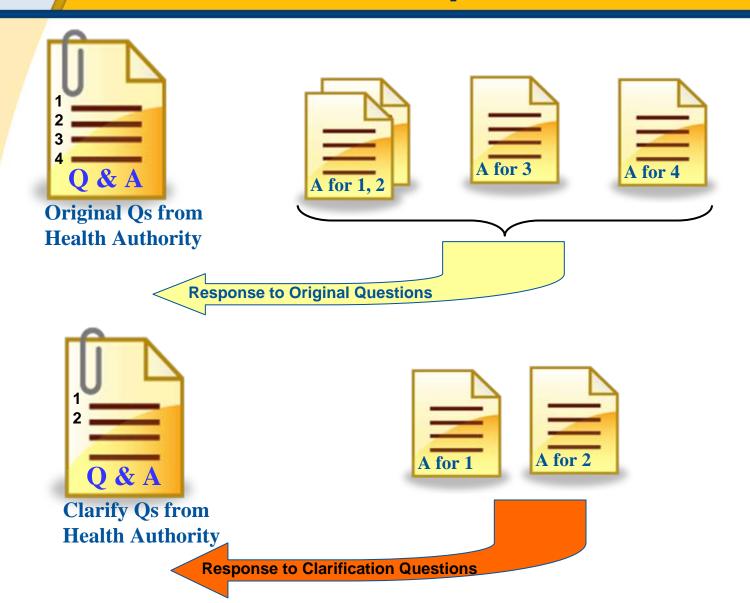
## **Granularity Module 3 – CMC**



\* Allowed by ICH M4 "granularity annex"



# Health Authority Q & A, Correspondence





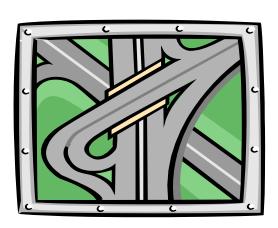
## **Continuous Improvement**





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## Re-Use & Content Management

#### Technical Manuals vs Submission Documents

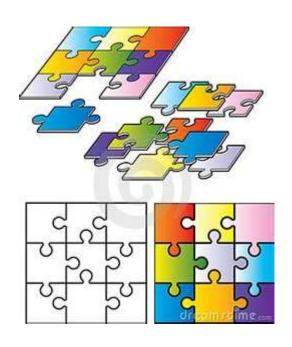
- Tech Manuals include highly re-useable content
- Submission Documents less re-useable content

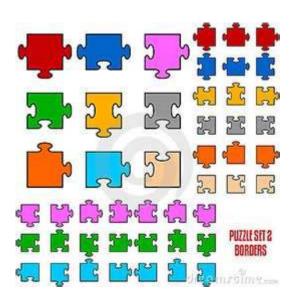
### Copy&Paste Re-Use vs Tracking Re-Use

- Re-Use via Copy&Paste looses tracking From
- Need Re-Use as traceable content



# Re-Use: Tech Manuals vs Submission Docs





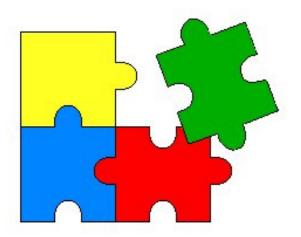
### Technical manuals have high re-use

- Many updates to same parts of same documents
- Hierarchic assemblies allow for scaled re-use (re-use sets of content)



## Re-Use: Tech Manuals vs Submission Docs





#### Submission documents have low re-use

- Few updates to same parts (Mod 3 main exception)
- Content re-use mostly re-use of same sections to different documents, not strictly hierarchic



# Global Dossier What could using Structured Authoring mean?

### Re-usability (quality and consistency):

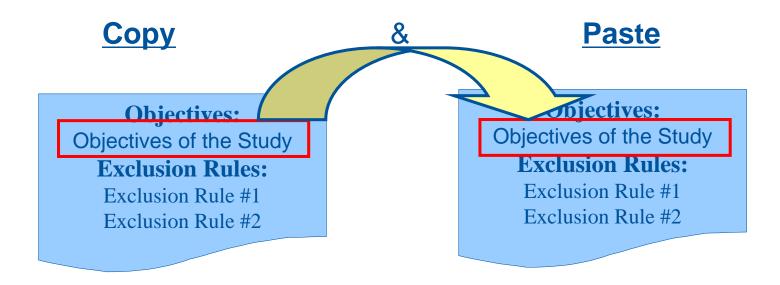
- Not caught out by changes that have implications on other documents' content
- More efficient generation of Module 2.3 Quality Overall Summary
- Establishment of databases for common information
- Eliminate transcription errors

### Potential M3 examples:

- ◆3.2.S and 3.2.P flow diagrams, specifications → Module 2.3
- ◆ Container closure specification → many eCTD applications
- ◆Manufacturing site addresses → many eCTD applications
- ◆ Facilities and Equipment → many eCTD applications
- ◆ Chemical structures → CTA (IB, IMPD), MAA (M2.3, M3)



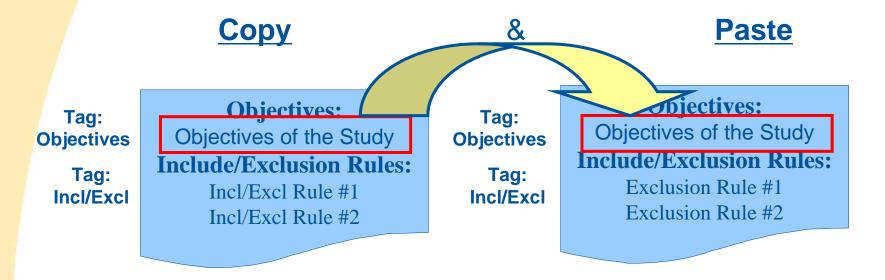
### Easy Copy & Paste: No Traceability



- No Traceability of Content (except in Author's head)
- If changes made to 'Paste' side, no ability to later check if correct except via manual review



# Tagged Copy & Paste: With Traceability



### Traceability of Content can be determined

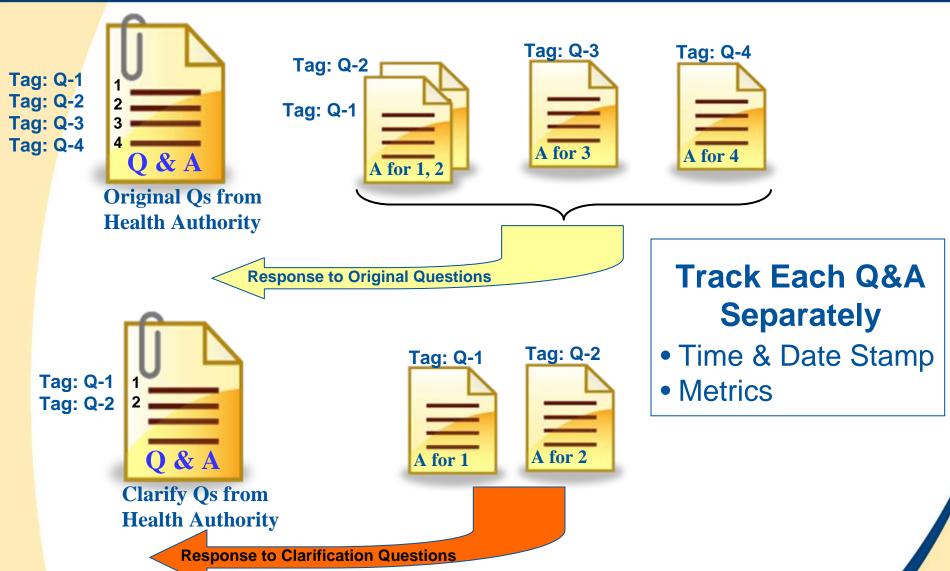
- Time and Date Stamp
- Hand-off Metrics

#### Content within tags can be:

- Used for regulatory & compliance purposes
- Used for quality check purposes



# Health Authority Q & A, Correspondence





## **Continuous Improvement**





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## **Tracking & Metrics**

- Registration (incl. Q&A & Correspondence)
- Labeling
- Global Dossier & Module Re-Use
- Quality Component
- Metrics Component (Improvement)



## **Ensuring compliance today Submission Lifecycle Information Management**

- Events track the outcome of submissions
- Outgoing package records which documents were sent to which country
- Monitor if submission has been
  - Dispatched, submitted, approved, withdrawn, divested
- Maintain supply links
- View data from different perspectives



Relies on manual input



## Global Dossier What might XML offer to applicants?

### Tracking:

- ◆ Reference links update M3 content and flag for M2.3
- Track at content level instead of document level
  - By approval in 40+ countries, can have territorial variation \*
- Track submissions by country
  - With XML tags can drag and drop a file on an Event to automatically recognize metadata for strength, product, dosage form, manufacturer



# Tracking Changes: Manual Processes

### **How is Change Tracked?**

- Author holds changes and change reasons in head
- Meeting Minutes of discussions?
- What about External / Contract Authors?

#### **How is Content Re-Use Tracked?**

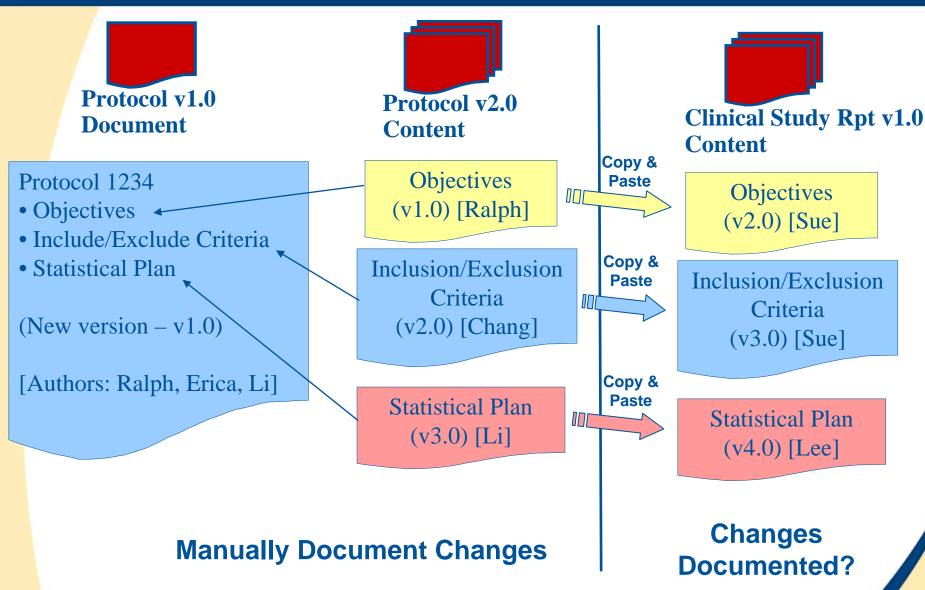
- Author knows where content 'copied' from
- How has content been changed when re-used?

### **How is Tracking Captured?**

- Manual Entry into Spreadsheets
- Manual Entry into Applications (DataBase)

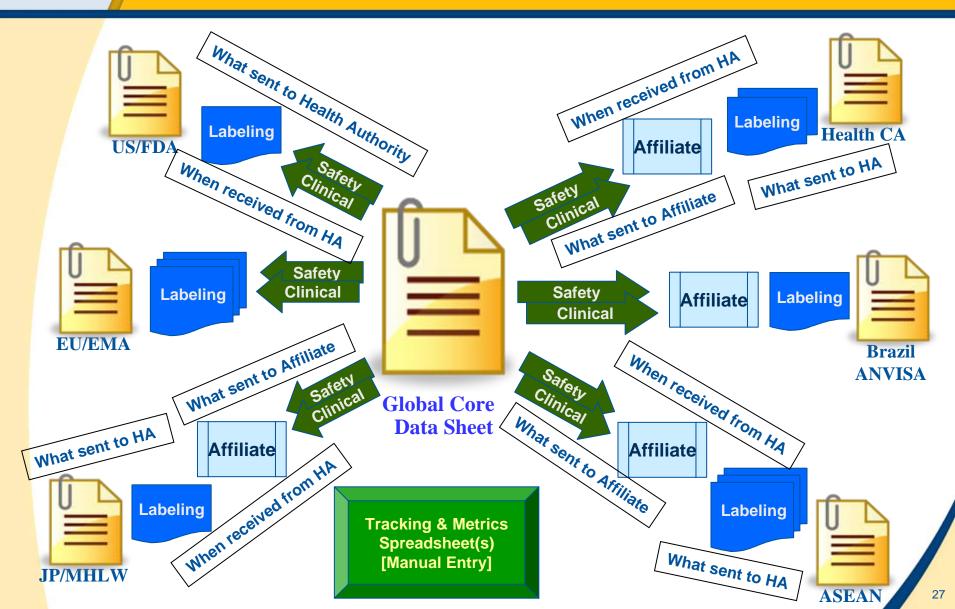


# Tracking: Protocol to Study Report Lifecycle



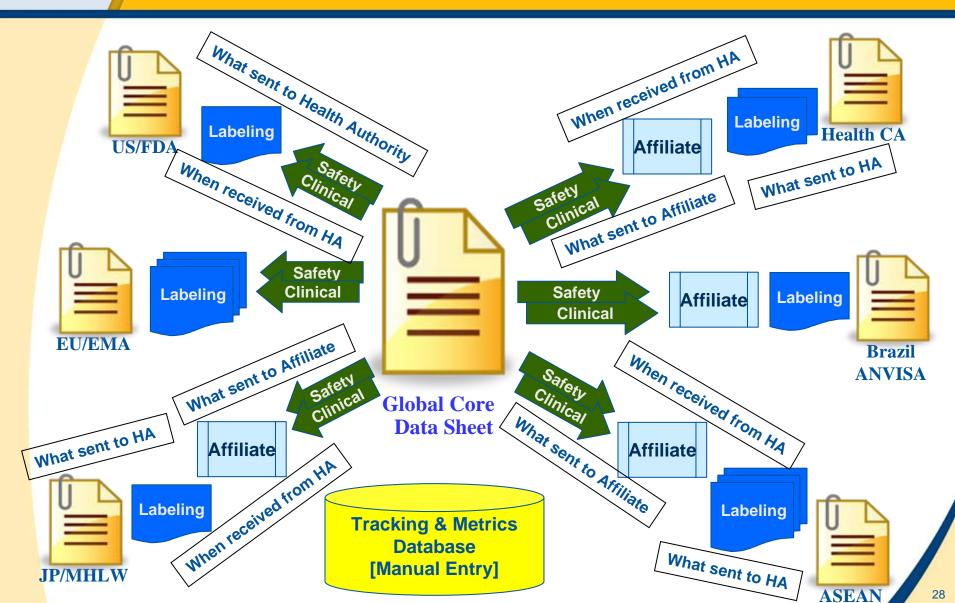


## Tracking & Metrics: Labeling - (Manual Entry)





## Tracking & Metrics: Labeling - (Manual Entry)





### Tracking Changes: Automated Processes

### **How is Change Tracked?**

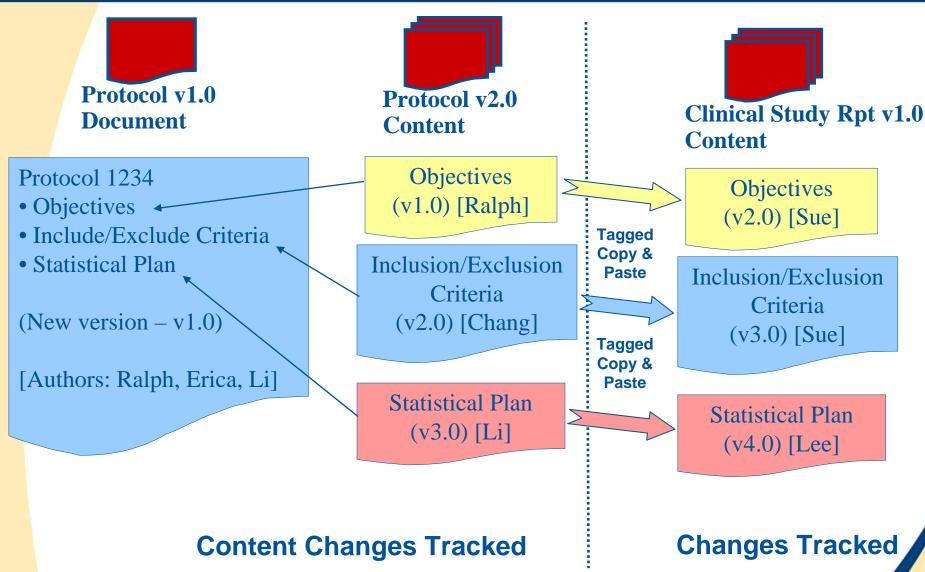
- Tagged content changes automatically tracked through authoring workflow (internal & external)
- Tagged content, comments & edits, automatically tracked through review workflow (internal & external)

#### **How is Content Re-Use Tracked?**

- Re-Use automatically tracked through tagged content and versions
- Changed, Re-Used content automatically tracked via tagging and versions – still needs manual review for changes

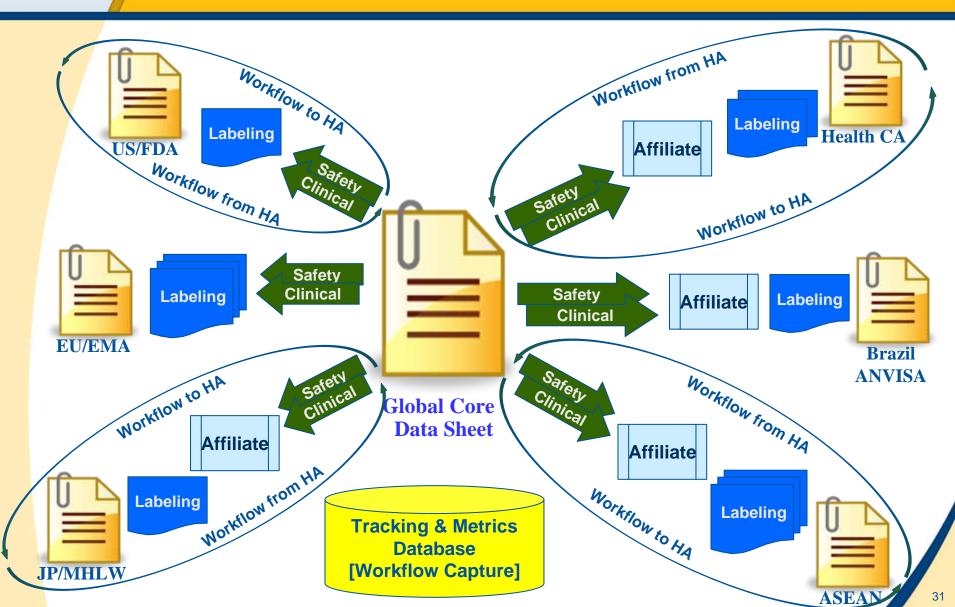


# Tracking: Protocol to Study Report Lifecycle





# Tracking & Metrics: Labeling - (Automated Entry)





### **Tracking and Metrics**

### Tracking for Management

Simple Tracking – Content Structured Templates

#### Metrics For Improvement

- Manual collection of metrics is time consuming and errorprone
- Ongoing Metrics gathering requires Automation

#### Workflow Automation

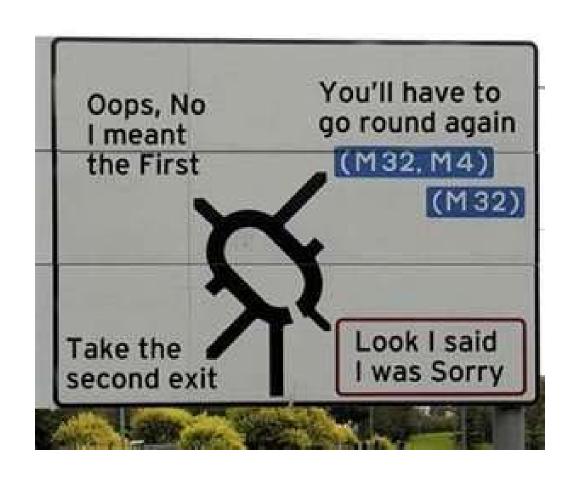
Ongoing Metrics gathering requires Automation

#### Quality Traceability

Traceability required to include Quality Component

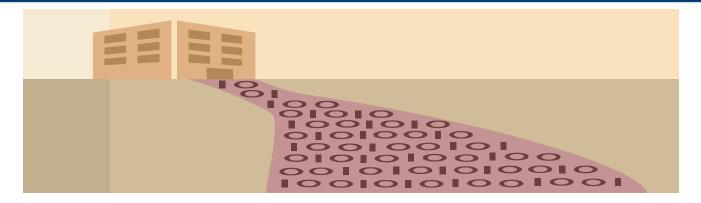


## **Continuous Improvement**





# Summary: Moving to Content Management



- Information needs to be managed at the Content level
- Re-Use is helpful requires Content level management
- Tracking Content & Re-Use is better
- Tracking Content needs to be Automated Workflows
- Auto-Tracking Content provides Metrics for Continuous Improvement



## **Continuous Improvement**



"There are three kinds of mathematicians; those who can count and those who can't."

Anonymous