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Data -> DITA -> Documents

A Story of Efficiency

The Background

- Sanofi
  - Sanofi is a global healthcare company focused on patient needs. Their business includes pharmaceuticals (notably prescription drugs for diabetes, rare diseases, multiple sclerosis and oncology, consumer healthcare products and generics), vaccines and animal health.

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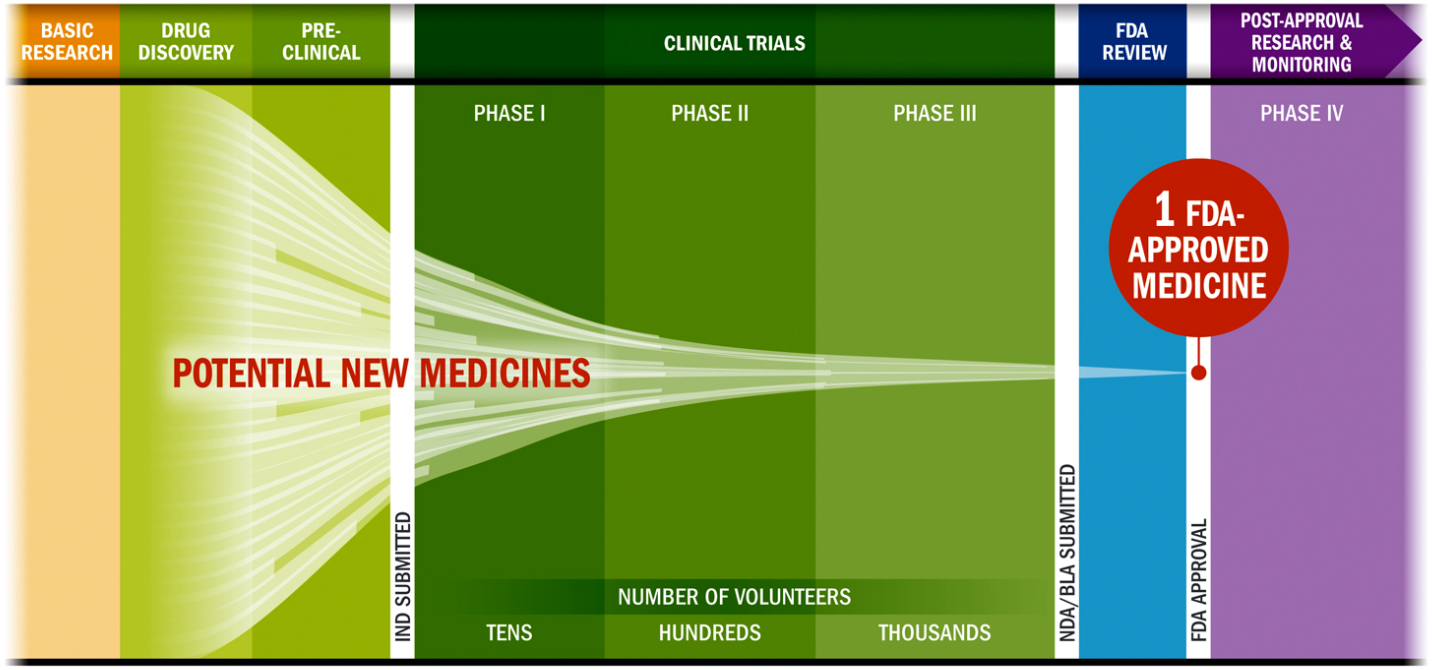
A Typical Timeline



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

* The average R&D cost required to bring a new, FDA-approved medicine to patients is estimated to be $2.6 billion over the past decade (in 2013 dollars), including the cost of the many potential medicines that do not make it through to FDA approval.

Source: PhRMA adaptation based on Tufts Center for the Study of Drug Development (CSDD) Briefing: "Cost of Developing a New Drug," Nov. 2014. Tufts CSDD & School of Medicine., and US FDA Infographic, "Drug Approval Process," http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/UCM284393.pdf (accessed Jan. 20, 2015).

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Sanofi's CRUISE Program

- Delivery of a highly adaptable and accountable service based platform enabled by innovative knowledge management tools and efficient, reusable processes.
- Structured authoring and re-use of both content and processes as well as separating content from presentation while proactively ensuring compliance
- Reduction of the effort required to prepare, compile and analyze content and documents through a synergy of optimized processes and enabling technology proactively scoped for value by a defined service catalog

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Clinical Documentation

- Integral department of Clinical Science and Operations platform
- Highly flexible global team of document specialists
- Service focus - state of the art expertise and resources for
  - management of clinical content
  - strategic production of submission-ready clinical documents
  - disclosure of clinical study protocols and results
- Goals
  - Innovative and strategic solutions for global life-cycle documentation
  - Accelerate and improve document preparation
  - Anticipate strategic documentation roadmap
  - Meet documentation needs across product life cycle
  - Build a structured library of product-specific content for intelligent reuse

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Business Drivers

ENSURE CONSISTENCY WITHIN THE ORGANIZATION AND BETWEEN PUBLIC DISCLOSURE AND REGULATED REPORTS (NDA, IND, CTA, PSUR...) AGAINST DATABASES

QUICKLY ASSESS VALUE AND NON-VALUE ADD ACTIVITIES AND MANAGE THE SOURCING OF THOSE ACTIVITIES WITHIN THE CAPABILITIES PORTFOLIOS BALANCING FIXED AND VARIABLE COSTS

REDUCE CYCLE TIMES, ENABLE EARLIER AND MORE EFFECTIVE DECISION-MAKING AROUND CLINICAL DEVELOPMENT PROGRAMS, AND REDUCE TIME TO MARKET

SHARE KNOWLEDGE BY MOVING TOWARD REUSABLE COMPONENTS OF INFORMATION THAT CAN BE MANAGED AND REUSED ACROSS PUBLICATIONS, DEPARTMENTS AND AUDIENCES.

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Reduce the effort required to prepare, compile and analyze content and documents

Lead, change and innovate within the transforming enterprise

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The Situation

- Unnecessary workload and time delays
  - Study reports & appendixes finalized late / not e-compliant
  - CTD lack of scientific consistency
  - No standard methodology nor tools for data collection & aggregation
- Lack of structure in CTA/CTD document review process leading to long review cycles
  - Multiple iterations
  - Recurrent remarks at different stages of review

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The Idea

- Refine submission documents preparation and review processes
  - Structure scientific information delivered throughout development to all stakeholders
  - Define process for preparation of source documents and summaries across product development including identification of process ownership of various documents
  - Refine CTA/IND review process
- Develop content re-use and structured authoring information system tool
  - Manage content and ongoing updates of CTA/CTD documents
  - Automate publishing of documents into different formats

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The Vision

- Increased Quality
- Faster Delivery
- Reduced Costs

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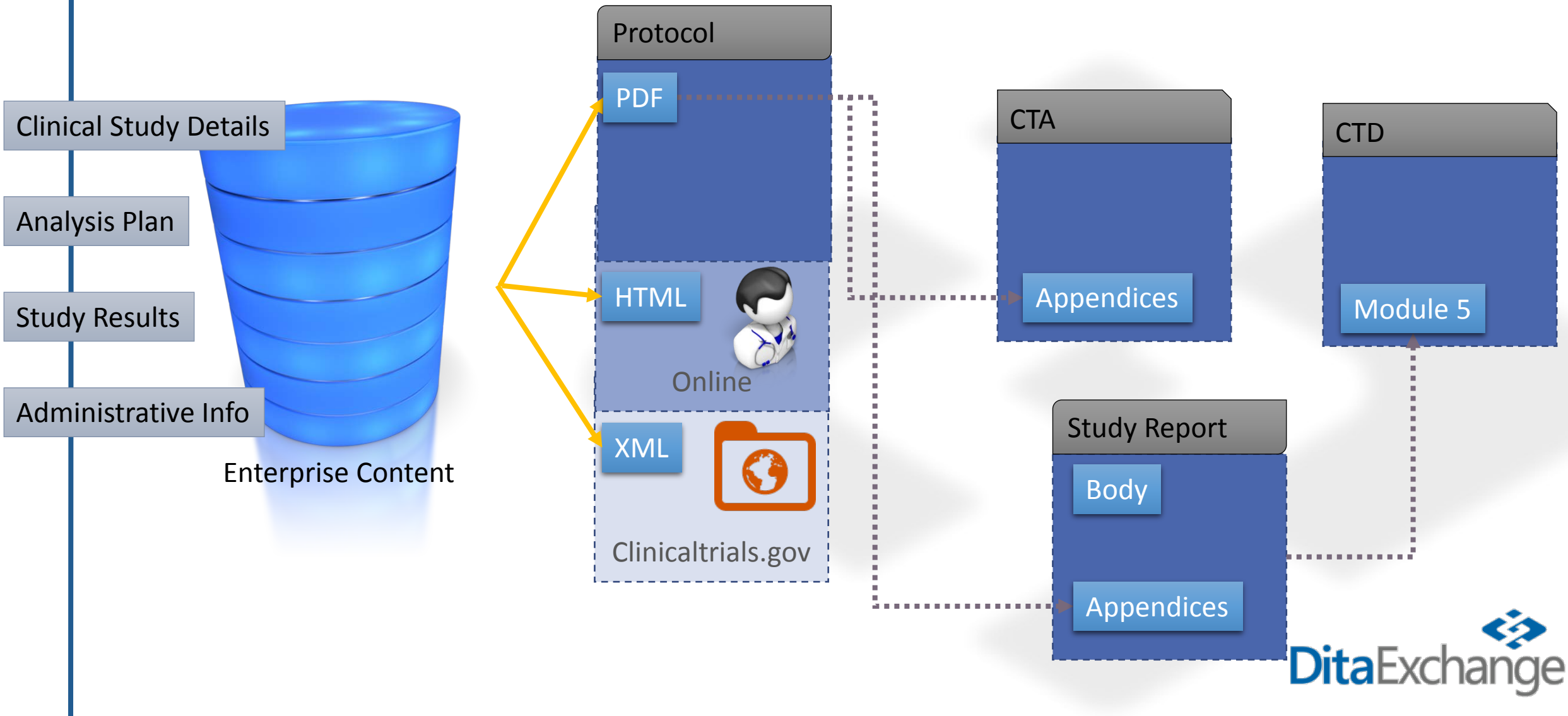
Content Re-use in Pharma



The Business Challenges

- REUSE: Value and benefits increase as content is repurposed across the product and clinical development lifecycle. How to author for reuse?
- DELIVERY: Program implementation iterative based on business priorities, capacity of business to absorb the changes
- PROCESS: Process simplification needs to be incremental and aligned with the SCM roadmap
- STANDARDS: Alignment with enterprise and industry standards namely the HL7, SDTM for narratives

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The Technical Challenges

- ENVIRONMENT: Desire to leverage Microsoft platform (Word and SharePoint)
- DELIVERY: Fast-paced Agile approach to delivery - Quarterly releases stretch the testing resources and capabilities
- PERFORMANCE: Complex data in content poses performance and optimization needs especially in the Publishing engine
- INTEGRATION: real-time Data integration needs in embedded content to other sanofi systems like biostatistics tables, document management systems

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The Core Principles

- Improve efficiencies
  - Separating content from context and presentation
- Improve quality, consistency and accuracy
  - Reuse of content across deliverables in the product or study lifecycle
- Ability to incorporate data, un-structured and structured content into output
- Component Content Management
  - Content managed and stewarded at a more granular level - Lifecycle policy applied to content across the product or study lifecycle
  - Governance/ stewardship of components
- Improve traceability
  - – Improve managing changes
  - – Visibility to impacts of change

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An Example

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What Are ‘Patient Narratives’?

- As Per ICH E3 guidelines, a patient safety narrative should describe the following:
  - the nature, intensity, and outcome of the event
  - the clinical course leading to the event
  - an indication of timing relevant to study drug administration
  - relevant laboratory measures
  - action taken with the study drug (and timing) in relation to the event
  - treatment or intervention
  - post-mortem findings (if applicable)
  - Investigator’s and Sponsor’s (if appropriate) opinion on causality

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Content in Patient Narratives

- Specifically, narratives should include the following:
  - patient identifier
  - age and sex of patient; general clinical condition of patient, if appropriate
  - disease being treated (if this is the same for all patients, this information is not required) with duration (of current episode) of illness
  - relevant concomitant/previous illnesses with details of occurrence/duration
  - relevant concomitant/previous medication with details of dosage
  - test drug administered, including dose, if this varied among patients, and length of time administered

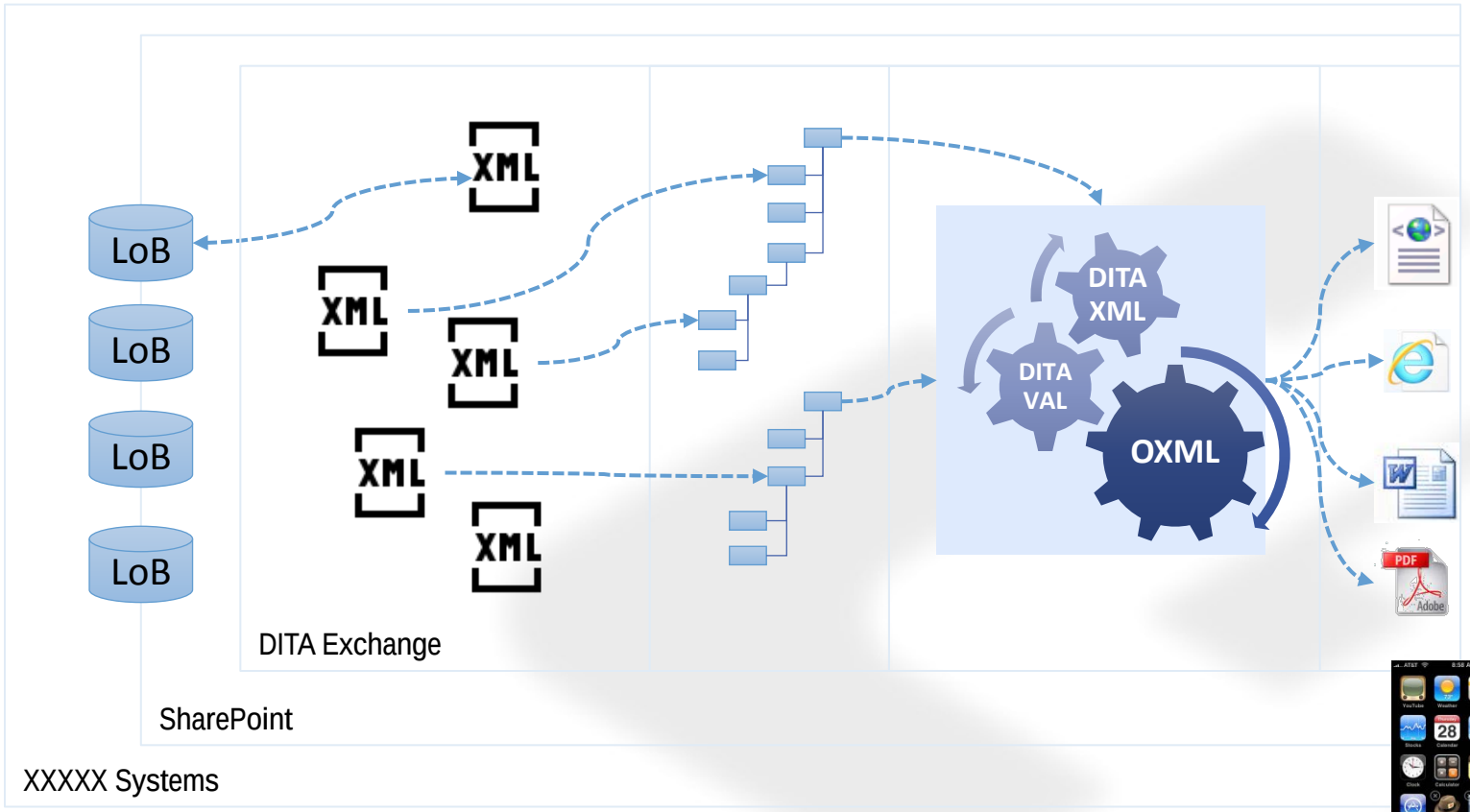
Typical Process

- Preparation of first draft narrative from patient/subject data by the Medical Writer
- Scientific and editorial peer review by the CRO project lead to check the document is accurate, complete, and consistent with requirements and across documents
- Clinical review of draft narrative: It is recommended that this be performed by the Sponsor or designate, although the CRO can provide this service as necessary
- Medical Writer revision based on clinical review: If the writer does not agree with clinical review comments, for example, when requested amendments conflict with the evidence or when changes would introduce inconsistencies between narratives, or when review comments are unclear, these should be discussed with the Sponsor or designate, as appropriate, and responses retained on file
- Quality control (QC) review based on final patient/subject data. Given the often large number of narratives required for individual studies and small size of each document relative to the CSR, it is recommended that a single QC review be performed toward the end of the process, rather than QC review of the first draft and final deliverable
- Medical Writer revision based on QC review findings. Note: when significant findings are identified during QC review, these should be discussed with the Sponsor and clinical reviewer, as appropriate, and further updates should be checked for consistency and accuracy
- Approval by the Sponsor after a final review

The Sources for Narratives

- A Medical Writer will use various sources of information when preparing patient safety narratives. These include
  - Council for International Organizations of Medical Sciences (CIOMS) forms
  - Case Report Forms (CRFs)
  - MedWatch forms
  - Data Clarification Forms (DCFs)
  - Clinical database listings

“The nuts and bolts…”



Clinicaltrials.gov
FDA: 1572
FDA: Patient Narrative

Product www
Country www
Language www

Submissions
Review

Submissions
Archive

Apps:
Review
Approve

IOS
Android
W8
…

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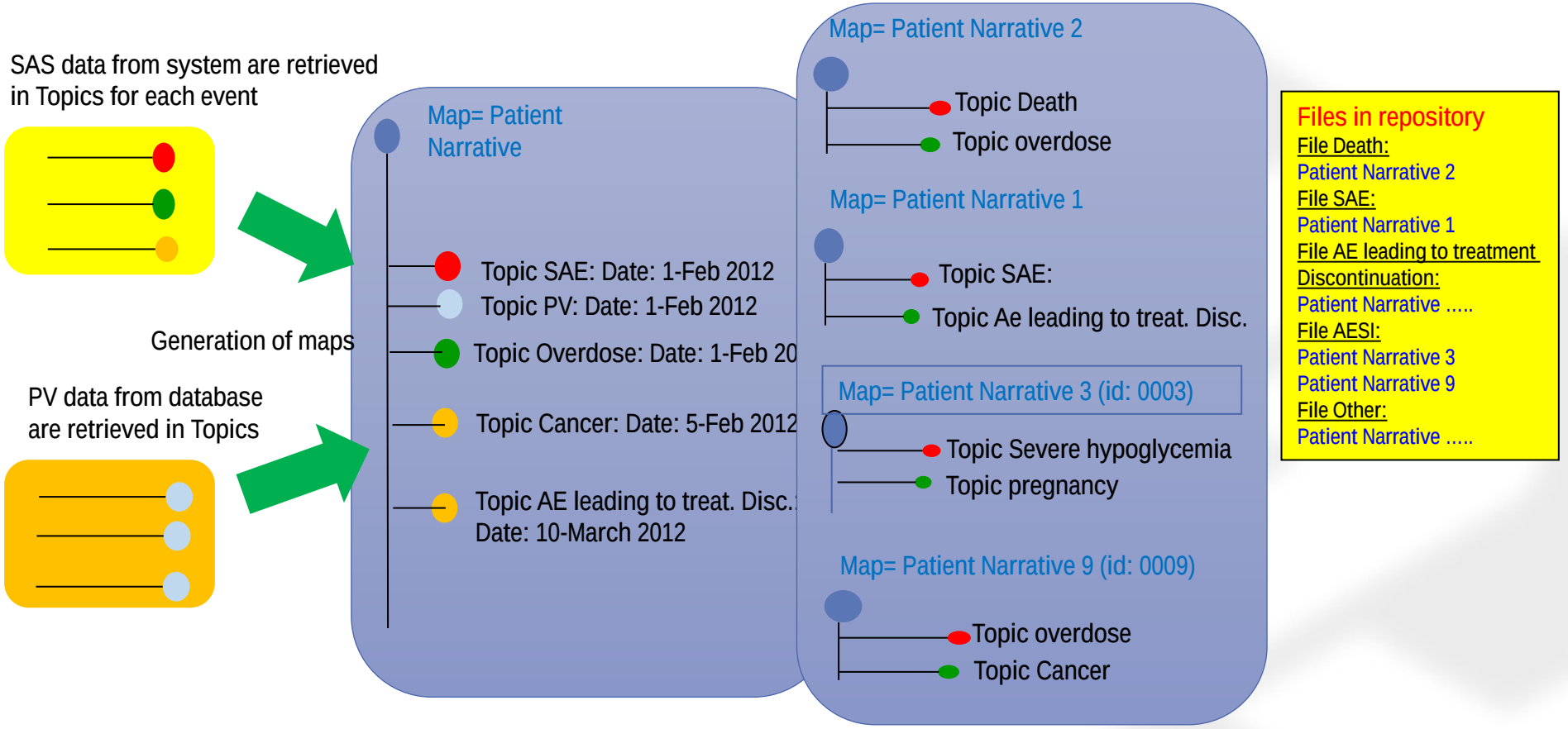
Case Study - Patient Narrative Creation

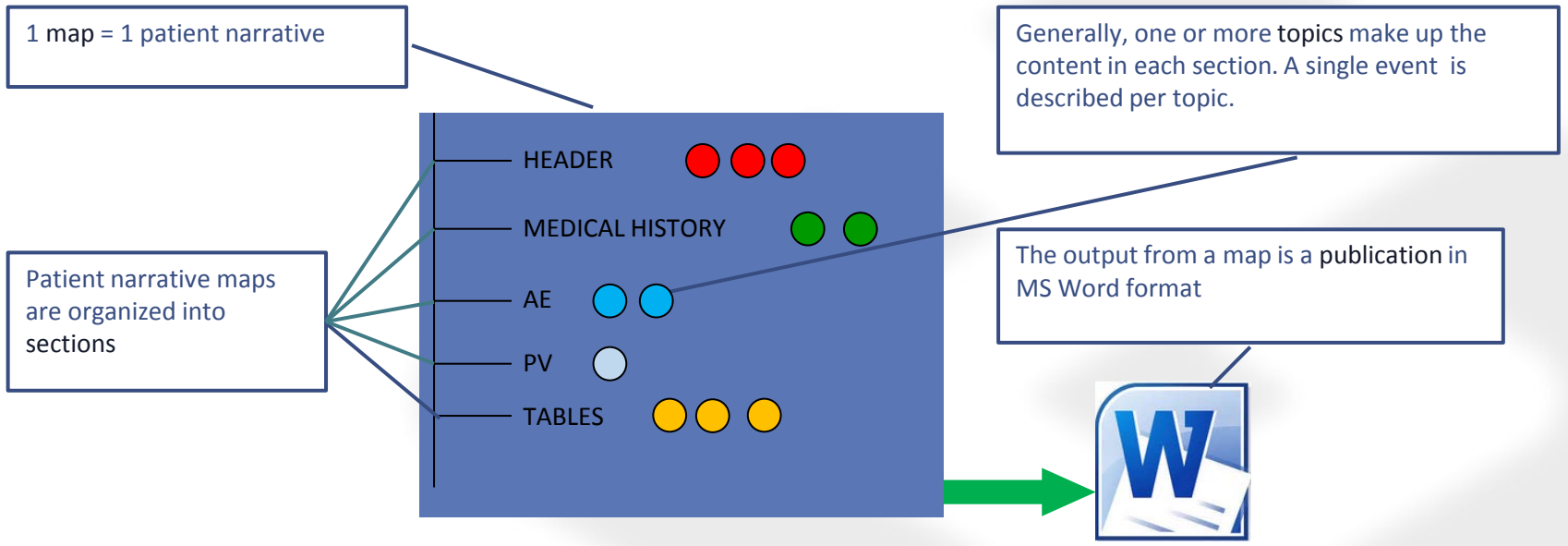
A single narrative will be provided for a given patient:

The system associates all events(SAS and PV summary) related to same Patient (following business rules) in order to create the complete Patient Narrative. Patient Narratives will be grouped by the system following a configured priority: Deaths>SAEs>AE leading to treat. Disc.>AESIs>Other – files used in CSR



- ✓ *Improved Quality: Data, unstructured and structured information aggregated automatically for reuse*
- ✓ *Improved productivity: automated generation of maps, style sheets to apply formats quickly*

Structure of patient narratives (1/2)



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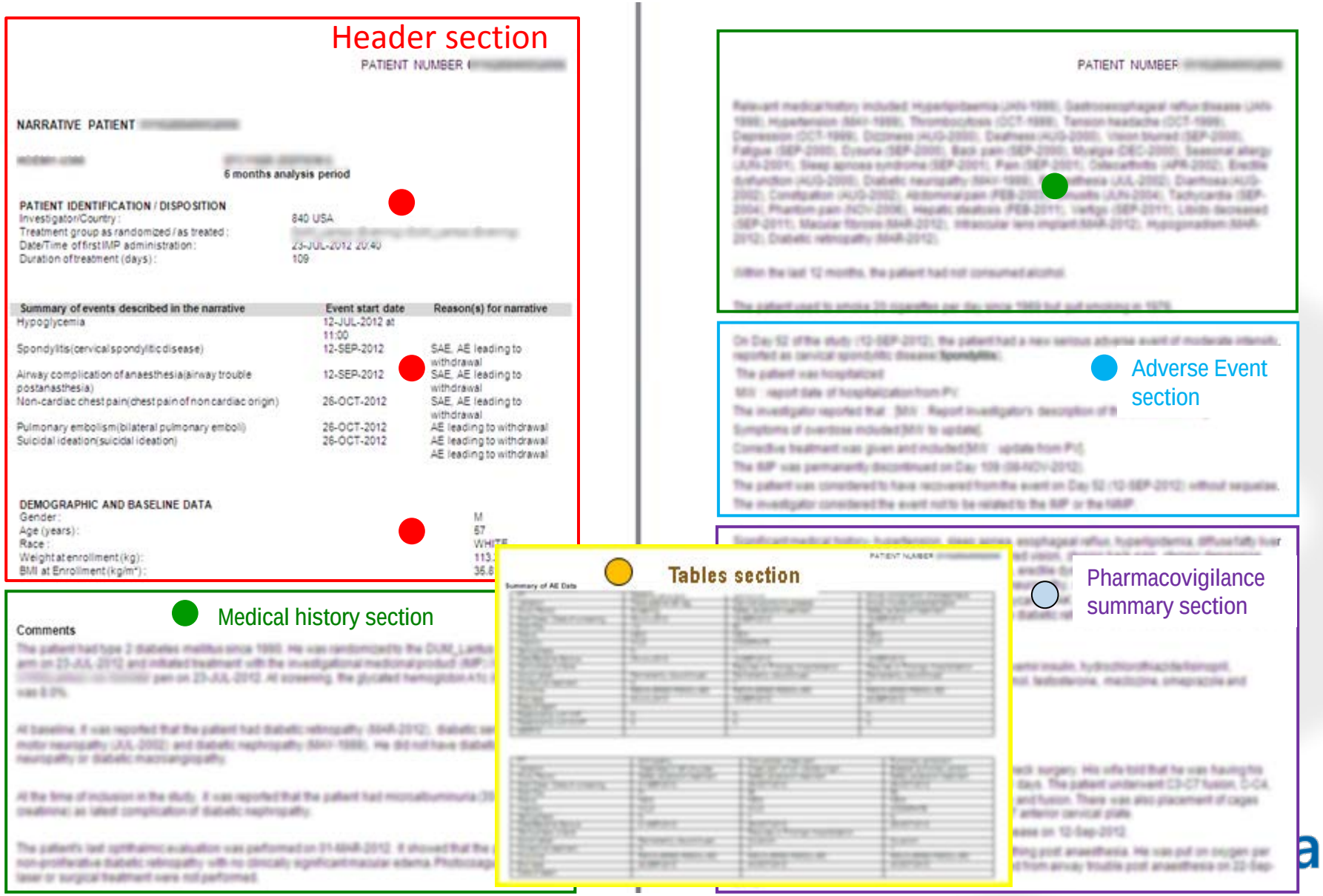
Structure of patient narratives (2/2)



Calculating Savings

- ClinDoc time: 0.8h/narrative (This includes training; MW prepare first draft; Comment Integration; QC; Coordination; ClinDoc meetings)
- CRUISE technical development time: 0.15h/narrative
- Total cost with manual process without CRUISE @ 8h / narrative- $100 (per hr cost of resources) * 8 (number of Hours/narrative) * 2140 (number of narratives) = 1.7 M USD
- Total cost with CRUISE @ 0.95h (0.8 + 0.15h) / narrative - $100 (per hr cost of resources) * 0.95 (number of Hours/narrative) * 2140 (number of narratives) = 203K USD

Manual Effort: 8 Hrs./ narrative
EnCORE: 0.95 Hrs./ narrative

Production costs without EnCORE: $1.7M
EnCORE Enabled: $203K

Results Delivered & The Future

- Narratives @ Sanofi
  - Delivered narratives for 16 studies
  - Time reduction in QC process
  - Use of industry standard data model as input for Narratives process
  - Additional time benefits for on-demand narratives
  - Partnering with FDA to develop standardized output (HL7)
- Time Savings
  - For 4,000 clinical documents
    - 24,000 hours -> 2,000 hours
- Cost Savings
  - For 1,000 narratives
    - $275,000
  - For 7,500 narratives
    - $2,000,000
- The Big Win
  - Faster time to market

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