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Product Knowledge Management (PKM)

Providing product and process data across an enterprise

ACHEMA – June 2006

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PKM – What is it?

- **PKM is a visionary approach to how product and process data is shared across the enterprise and across the entire product lifecycle (Development → Commercialization → Retirement)**
- **First hand experience with 6 of the top 10 pharmaceutical companies has shown that PKM is a vision shared by all but none have achieved**

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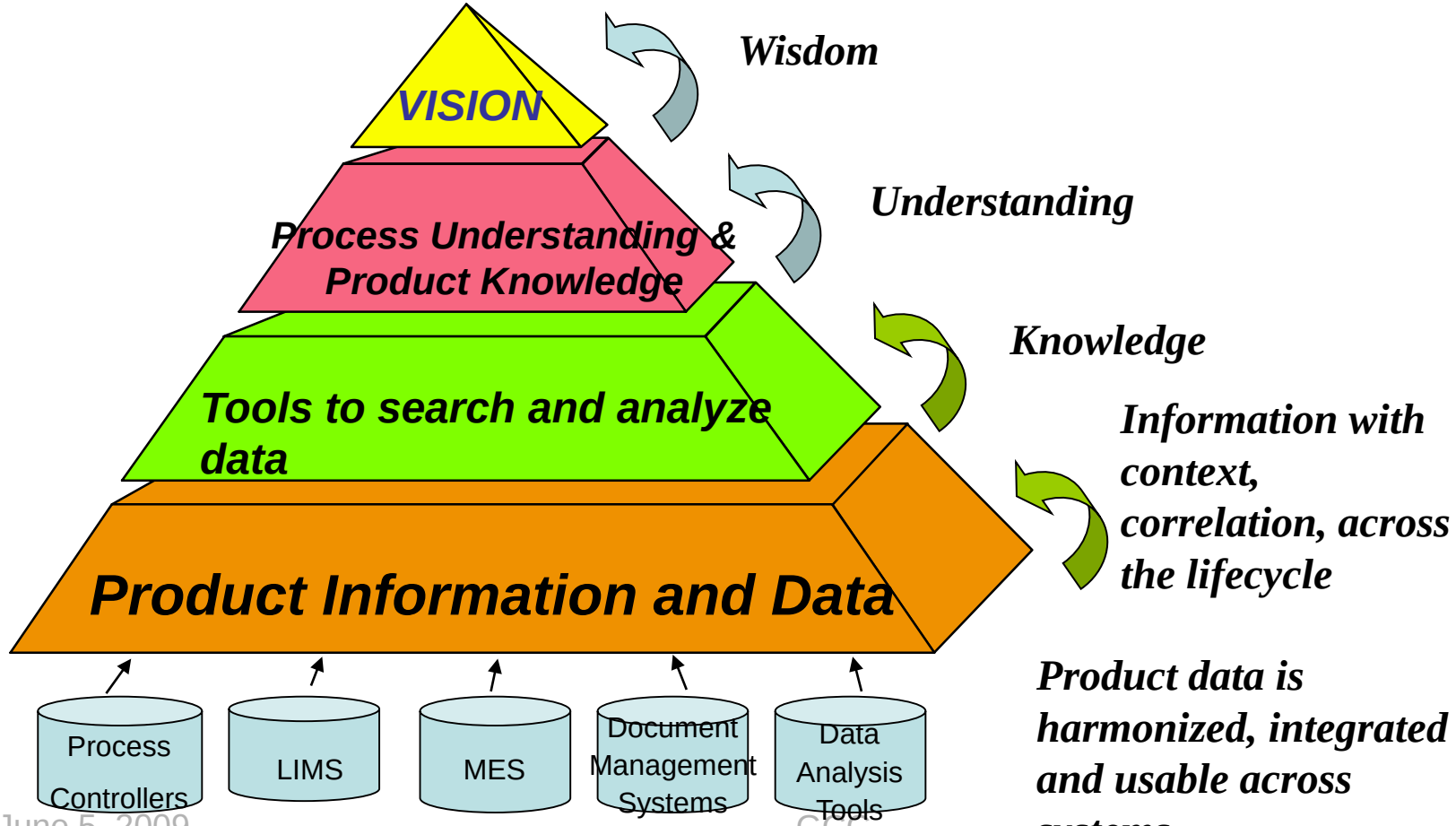
PKM is about transforming product data and information into product "Wisdom"



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PKM - Summary of AS IS landscape at most Pharma companies

- **Product Information (both data and documents) resides in many disparate electronic systems and some manual systems**
- **A common global data model across Research and Manufacturing is not well developed**
- **There is very little standardization of application platforms across the enterprise (ERP, MES, LIMS, ERP, EDMS)**
- **There is little or no standardization of integration platforms across the enterprise**

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PKM - Vision

Provide rapid and comprehensive access to product and process knowledge to maximize performance, assure quality and optimize resource utilization…through information systems that are fully and securely networked across all of R&D and Operations.

- **Provide real-time access on a common user interface to data and documents anywhere in the network.**
- **Develop tools for data mining, robust searching and analysis that can convert output into information → knowledge → understanding → wisdom which allows for data-driven decisions.**
- **Development of products and processes utilizing quality by design principles to meet emerging regulatory requirements**
- **Use the common information model, the Enterprise Service Bus (ESB) and global data standards that enable data transformation and translation across systems**

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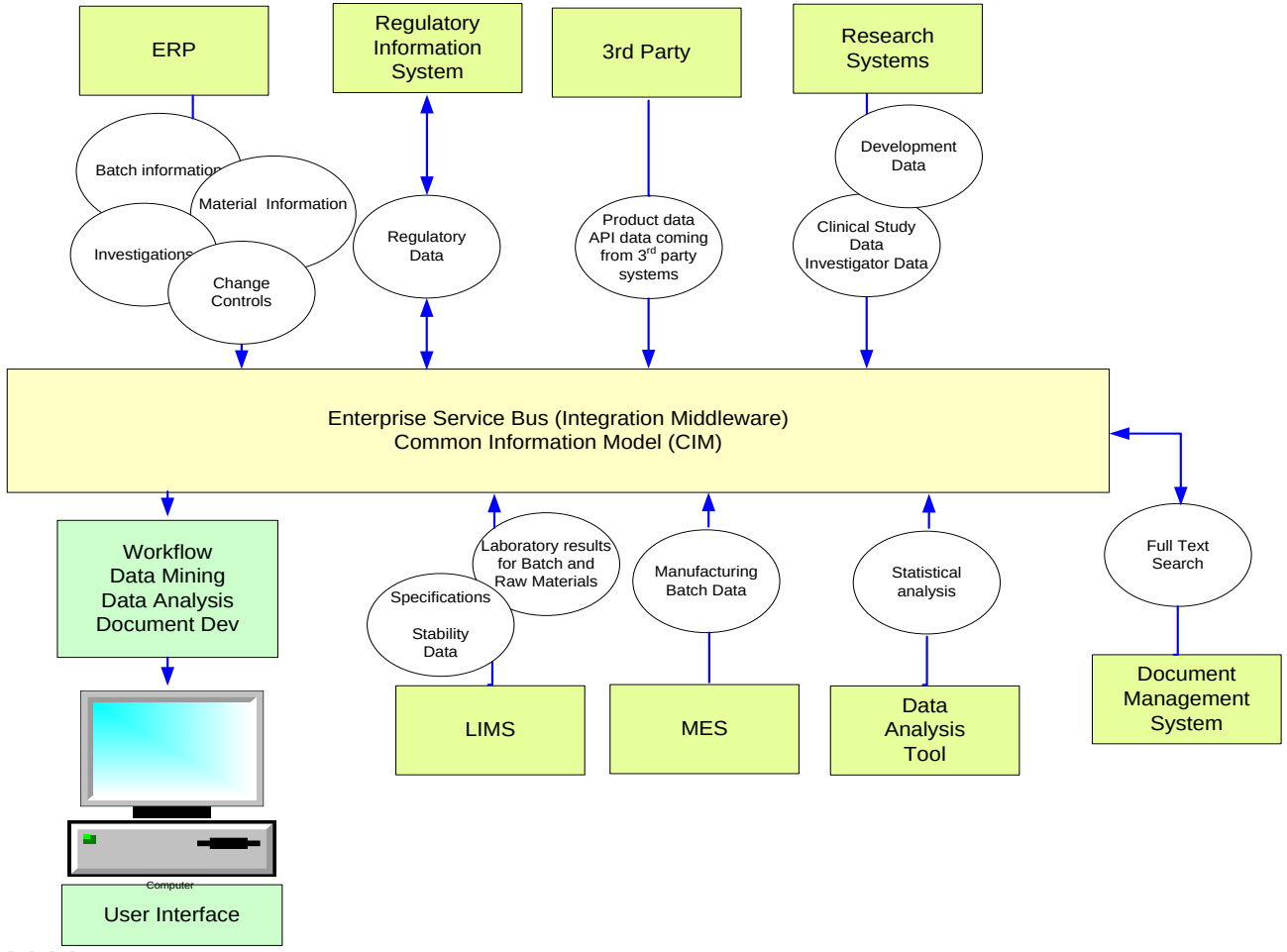
PKM – Conceptual Integration Architecture



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What are the benefits if the vision is reached?

What if you could ask the following questions and get a "real-time" response:

- **Has Product X ever had a problem (in Development or post launch) with black specs on the surface of the tablet after coating?**
- **Do any Development documents and/or Validation documents for Product Y identify a problem with stability failures at elevated temperatures?**
- **Did the Development group ever experience a problem with an unidentified peak at wavelength 725nm for Raw Material Z?**
- **What is the most current (best practice) template for an IQ/OQ Validation Protocol for a new syringe filling machine?**
- **Has there ever been a Laboratory Investigation Report (LIR) for the Agilent 1200 series HPLC unit for detector drift?**
- **How can I get a statistical summary of all manufacturing and laboratory data for the 3 validation batches of Product M so I can write my Validation report?**
- **What formulation of Product D is registered in China?**
- **Does tablet hardness for Product Z exhibit a seasonal trend if hardness data from the last 3 years is analyzed?**

Use Cases

- **Product data & information from Development Sites, Manufacturing Sites and the Laboratories can be compared and analyzed**
  - **Including the ability to perform full text searches of Development & Validation documents in DMS for key words**
- **Traceability of a reoccurring product problem across the entire lifecycle of the product**
  - **Ability to merge information from Development documents into a database with manufacturing and laboratory data and perform statistical trending**
- **3rd party manufacturing**
  - **Get manufacturing and lab data from 3rd Party systems (MES and LIMS) and bring it into a database. Ability to analyze and correlate the 3rd Party data with Development, Manufacturing and Laboratory data**
- **Validation Reports**
  - **Retrieve all relevant manufacturing and laboratory data needed to generate Validation Reports**
  - **Get the most current Global template for a Validation report**
- **Root Cause Analysis**
  - **Compile and analyze Development, Manufacturing and Laboratory data to assist in RCA**

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PKM Roadmap – What are the phases?

- **Phase 1 – Requirement Gathering**
  - **Description of the AS IS environment**
    - What systems exist?
    - Does integration middleware exist?
    - Data standards and harmonization?
  - **User Requirements Specifications**
  - **Project checkpoint:**
    - Project concept
    - Project justification
    - Proposed budget
    - Proposed timeline for design, build and test
- **Phase 2 – Design, Build and Test**
- **Phase 3 – Deploy and Maintain**


PKM - AS IS - V1


PKM - URS V1


PDR - PKM

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A Strategic Vision for Manufacturing Science

How Process Analytical Technology, Product Robustness, Data Acquisition & Recording Technology can revolutionize how we manufacture pharmaceuticals

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Definition of Manufacturing Science

- **It includes**
  - ***PAT (Process Analytical Technology)***
  - ***PR (Product Robustness) Methodologies such as: 6 Sigma, SPC, Cpk, Black Belt, etc.***
  - ***DA+EBR (Data Analysis & Data Acquisition System + Electronic Batch Record)***
- **It may also include concepts like:**
  - ***Risk Based approach to compliance***
  - ***Different process technologies (make the technology fit the process instead of the process fit existing technology)***
  - ***Development Robustness (using PR methodology during the product development process in R&D)***

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Pharma Manufacturing

	Today	Future
Quality	2 sigma	6 sigma
Technology	Islands of automation	Integrated automation
Data	Static	Dynamic
Documentation	Paper based	Electronic
New technology	Conservative	Aggressive
PR Tools	Some	SPC, Cpk, 6σ, Black Belt
Data Analysis	As needed	Real-time

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Vision

"PAT uses Data Acquisition/Analysis tools and the Electronic Batch Record platform and integrates Product Robustness methodology to achieve Manufacturing Science"

Ideally we would apply Manufacturing Science to both new products (process design) and existing products.

Objectives of Manufacturing Science

- Regulatory processes are optimized
- Real-time control of processes
- Management of variability
- Control the parameters that control the Quality
- All relevant data is stored and available for analysis using a strong set of data analysis tools
- Analysis of data leads to process understanding that leads to making changes that IMPROVE our processes

Expectations from implementing MS

- **Shifting quality control from off-line lab based "testing to document quality" to on-line, real-time continuous quality assurance and control that prevents quality deviations at the source.**
- **Enhancement of Quality Assurance achieved through a broad application of various PAT applications**
- **Electronic acquisition, storage, retrieval and analysis of batch processing data instead of the current paper based systems**
- **Standardized hardware and software tools for storage, retrieval and analysis of processing data**
- **Standardized tools and methodology for the assessment of processing data**
- **Standardized tools and methodology for use of processing data to improve our products and processes**

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Economic Justification

- **Better control of our processes and products = few, if any, batch difficulties = lower costs = better regulatory compliance = no adverse findings from Regulatory agencies**
- **On-line in-process testing & release = reduction of manufacturing cycle time = reduction of in-process material inventories = lesser need for plant capacity, improved cash flow**
- **Reduced off-line testing = reduced costs**
- **More robust processes and products = 100% customer service and no shortages**
- **Very tight processing limits = shorter time to market = more difficult for products to be copied by someone else = extended product life cycle**
- **Fewer re-work and scrap = less risk of product recall**
- **No operator contact = improved EHS**
- **Efficient quality systems facilitate oversight and investigation**

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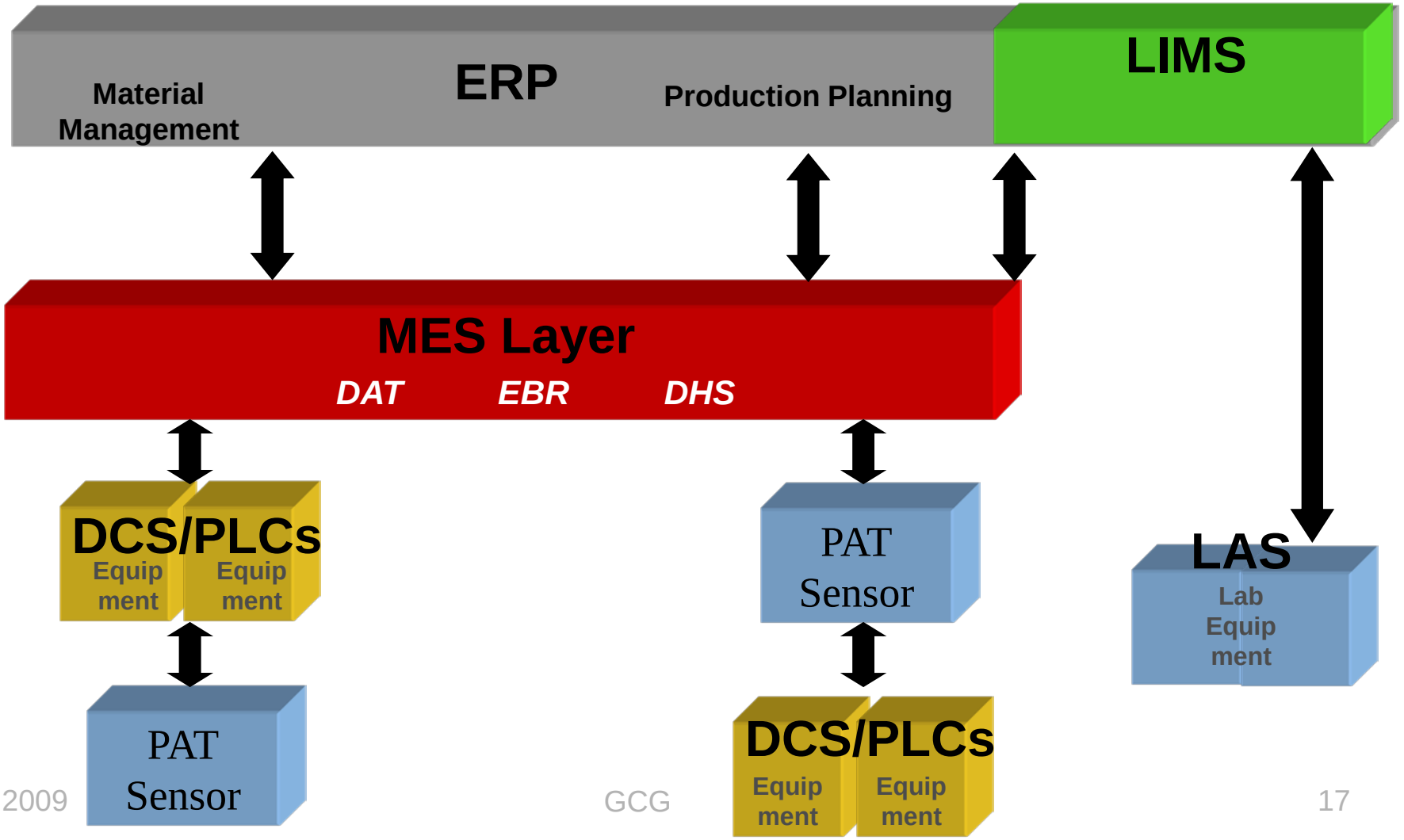
Architecture



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What would a MS Project look like?

- **Could be a large project (Millions of EURO…many months)**
  - ***Multiple systems at once (EBR & DA) + PAT initiative + PR methodologies training***
  - ***Multiple sites***
  - ***Multiple products***
- **Or it could be a pilot project of one product and one site**

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Important Factors

- Organization
- Standardization
- Regulatory Philosophy, Strategy & Principles
- Pre-requisites
- Milestones and project plan
- Education and Change Management

Potential pitfalls for a large MS project

- **Need to have TOTALLY SEPARATE headcount for: Development Team…Implementation Team…Support Team**
- **Not enough exposure with and/or commitment from Senior Management**
- **Communication mechanisms (both up and down) need to be started early and be consistent**
- **The time needed to create and execute Test Scripts can be underestimated**
- **Need to find a good way to track the tasks of separate (but connected) parts of the project…coordinated task and resource planning across multiple systems is really hard**
- **The FAT (Factory Acceptance Test) not "rugged" enough…therefore you find too many bugs during the SAT (Site Acceptance Test) testing**
- **Changes in the membership of Steering Committee and Site Management**
- **Future support organization not evaluated at the start of the project**
- **Business processes are not challenged, harmonized or streamlined enough**
- **Working from multiple locations makes communication hard**

What might it look like if we achieve Manufacturing Science?

A vision of pharma manufacturing

- Annual Product Reviews are completed (start to finish) in 2 hours per product
- A supervisor faced with a problem batch can sit at his/her desk, extract data on..compression hardness..60 minute dissolution..granulation moisture..raw material moisture for the last 20 batches and find a recent trend of increasing dissolution rates that is perfectly correlated with moisture levels of raw material and tablet hardness.
- A Manufacturing Engineer can collect data from the last 50 production batches of a product and do statistical trending and analysis using data from BOTH the API Plant and the DP Plant.
- In order to release batches you no longer perform wet chemistry analysis but rather, release based on real-time statistical analysis of 2 key parameters collected from NIR sensors during the process. And you have a 100.0% confidence level that this defines acceptable product.
- The Supervisors and Lab Managers can go home ON TIME because the product processes are predicable, reproducible and “in statistical process control”

THANK YOU
for your attention

Are there any questions?

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For one large Pharma company the vision and scope are:

VISION: **To develop and implement product information standards, integrated business processes and supporting technology to enable efficient sharing and access to product information across Research and Manufacturing**

SCOPE: **Product Information (documents and related data) from development track through product divestiture across Research and operations in the Consumer, Nutri and Pharma businesses. (Regulatory and compliance processes that extend to affiliates are in scope.)**