PAT – Turning Data into Knowledge

Chris Hobbs
GDCh PAT Colloquium Basel
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Turning Data Into Knowledge

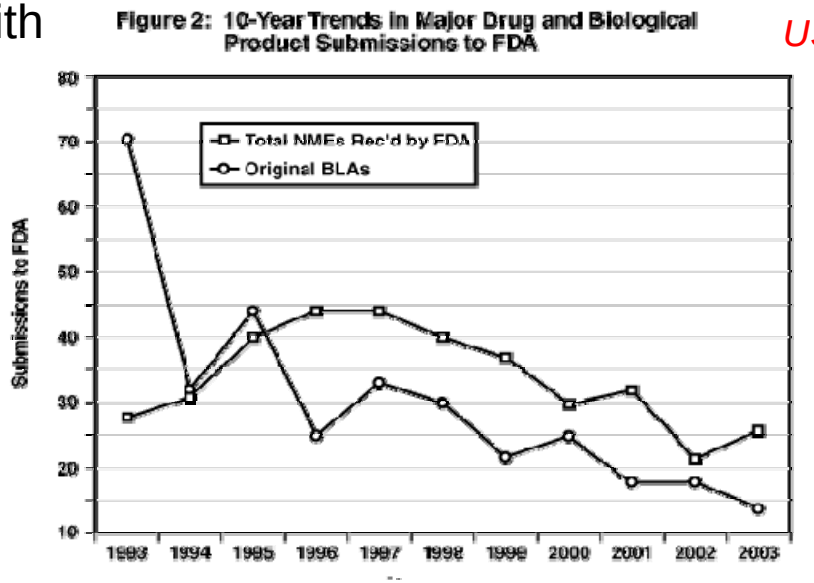
- Why QbD and Why PAT ?
- What are the Data Handling Challenges ?
- Managing Analyzers
- Managing Process and Analytical Data

Why QbD and Why PAT ?

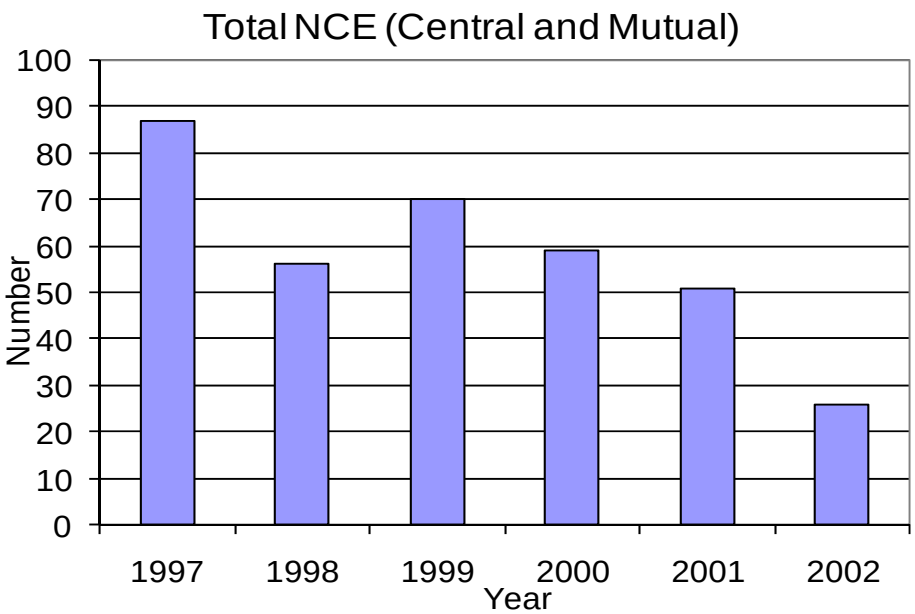
Times are changing in pharma manufacturing

- Increased pressure on cost, time and innovation with fewer and fewer new drugs issued
- Companies have to re-invent the balance between quality and compliance
- Most regulator agencies work with industry to reinvent innovation and ensure more affordable drugs

USA



EMEA



- Slow down in R&D innovation combined with patent expiration on 19 blockbusters
- Projected $40 Billion in lost revenue for the top 10 pharmaceutical manufacturers

Why QbD and Why PAT ?

Manufacturing Objectives

- Produce
  - The right quality
  - In the shortest time
  - At the lowest cost
  - Predictable fashion
- Life Science Manufacturing
  - Does not always meet all criteria
  - Efficiency is lower than comparable industries
  - Higher variability than what is desired
    - PWC, Deming, etc
    - Stop inspecting, correct problem at its root
  - Lots of room for improvement that requires a new way of working.

Why QbD and Why PAT ?

- A change in the guidance issued by the FDA, allows pharmaceutical companies to take a quantified science and risk based approach to drug manufacture by the use of online analytical technology.
- This allows
  - Better understanding of the process
  - Reduces the time to market
  - Reduces production costs
  - Flexibility in product production and pricing

Why QbD Why PAT ?

A more flexible approach

- Understand Process Variations
  - A process is well understood when:
    - All critical sources of variability are identified and explained
    - The resulting process upset from input variability is recognized
    - Product output based on inputs and process can be accurately and reliably predicted
- Control outputs from input variability by:
  - Identifying and measuring Critical Quality Attributes (CQAs)
    - Measure of product properties such as identity, strength, potency, purity, particle size, homogeneity and moisture
  - Identifying and controlling Critical Process Parameters (CPPs)
    - Parameters that have affect on CQAs such as valve set points, agitator speed and pump speed

Why QbD Why PAT ?

Objectives

- Encourage innovation and efficiency improvement
- Improve the understanding of manufacturing processes by implementing analytical solutions at/on/in-line

Economic Benefits

- Reduced cycle times
- Increased equipment utilization
- Reduction in warehousing requirements (quarantine)
- Reduced time to market
- Change purely batch process into continuous manufacturing process
- Reduced QA/QC costs

Quality Benefits

- Higher product inspection rate
- Reduced process errors
- Decreased product exposure for operators
- Improved product consistency
- Promotes continuous improvement in a regulated process

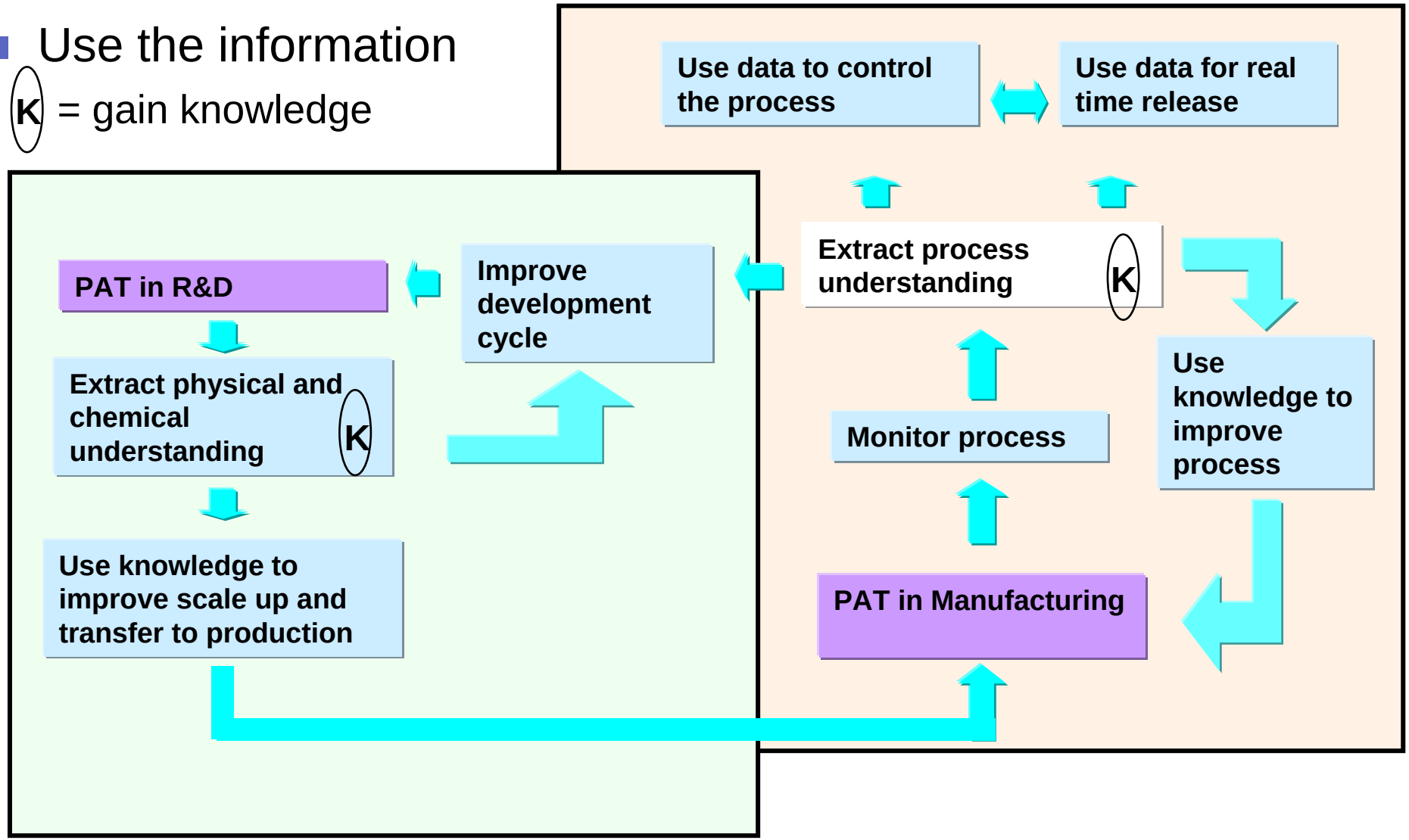
Turning Data Into Knowledge

- Why QbD and Why PAT ?
- What are the Data Handling Challenges ?
- Managing Analyzers
- Managing Process and Analytical Data

What are the Data Handling Challenges ?

- Use the information

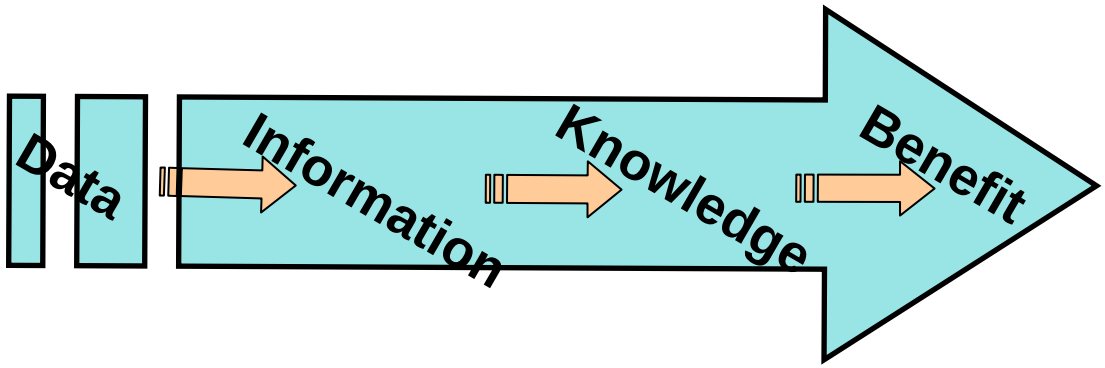
(K) = gain knowledge



What are the Data Handling Challenges ?

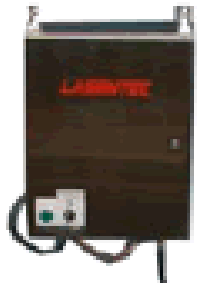
The three stages of PAT

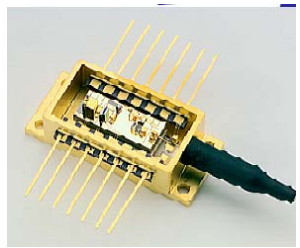
- LEARN – Gather data from analysers and process instruments to better understand the process
- PREDICT – Create a model which will predict *Quality Attributes*. Use the predicted value to advise operators when quality deviation occurs or when a process is complete. Validate with lab tests
- CONTROL – Directly control the process according to the predicted *Quality Attribute*. Validate with lab tests



What are the Data Handling Challenges ?

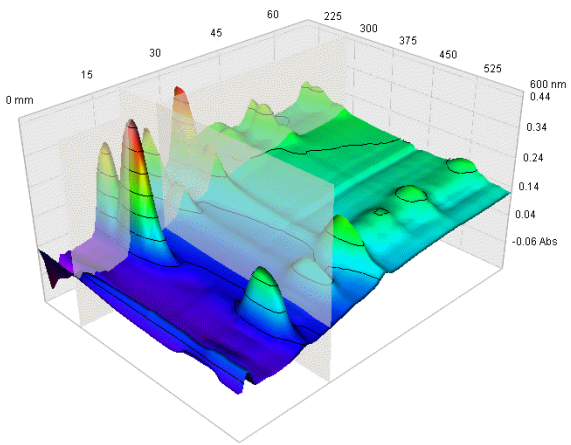
- There are many Analyzer manufacturers
- Each Manufacturer has their own interface and client software
- Analyzers can be used to perform more than one type of analysis
- Multiple analyzers may be required in order to control product quality.
- Analyzer data needs to be synchronized with other analyzers and or the control system.
- The quality prediction and its raw data needs to be associated with batch of pharmaceutical being manufactured according to FDA rules. (Electronic signatures, long term storage, common formats etc….)

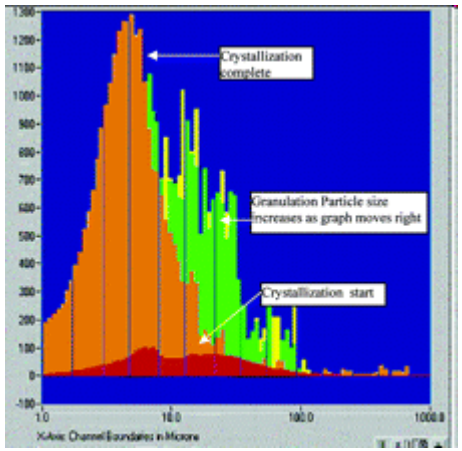


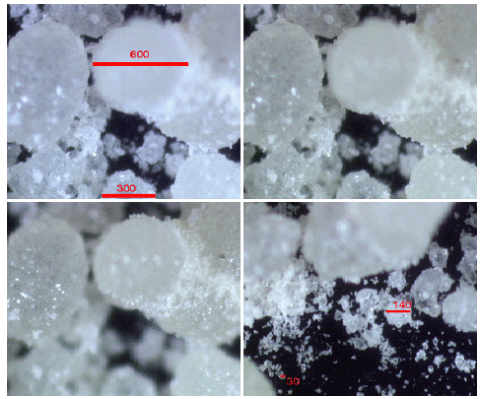


What are the Data Handling Challenges ?

- Analyzers produce multiple disparate formats e.g. Spectra, Bar Graphs, Chromatographs, Images etc.
- An analyzer model can be used to predict many different properties.
- Not all analyzer measurements are in real time.
- In order to interpret data from multiple analyzers the measurements need to be correlated.
- Data collected needs to be made available to various offline platforms e.g. modelling packages, LIMS, EBRS etc







What are the Data Handling Challenges ?

“Configure, Manage, Execute, Store and Analyze”

- Key Concepts for Data Management
  - Multi-Analyzer Management
    - Analyzer configurations for multiple analyzers are stored in one location and integrated with PAT Method
    - Provides a Platform for executing multi-instrument models.
    - Diagnostics and Reference information to be stored
  - Structured Data Storage (Batch ID, Note Book No., Stock Unit, Order No.)
    - Univariate and Multivariate data from multiple Instrument platforms
    - SCADA/DCS process data.
    - Method Execution provide Audit Trail, Alarm and Event
    - Central Model Management
  - Data Integrity
    - PAT Method Data to be archived by PAT Method reference number.
    - Off-line storage based on reference number
  - Data Access
    - Local client for Method management and Method execution
    - Make data available to existing operator screens. (SCADA / DCS)
    - Remote Client support for data analysis and display using purpose built data applications
    - Data may be extracted by different off the shelf standards. (OPC, ODBC, ODA, SQL)
    - Standard tools available for visualization

Turning Data Into Knowledge

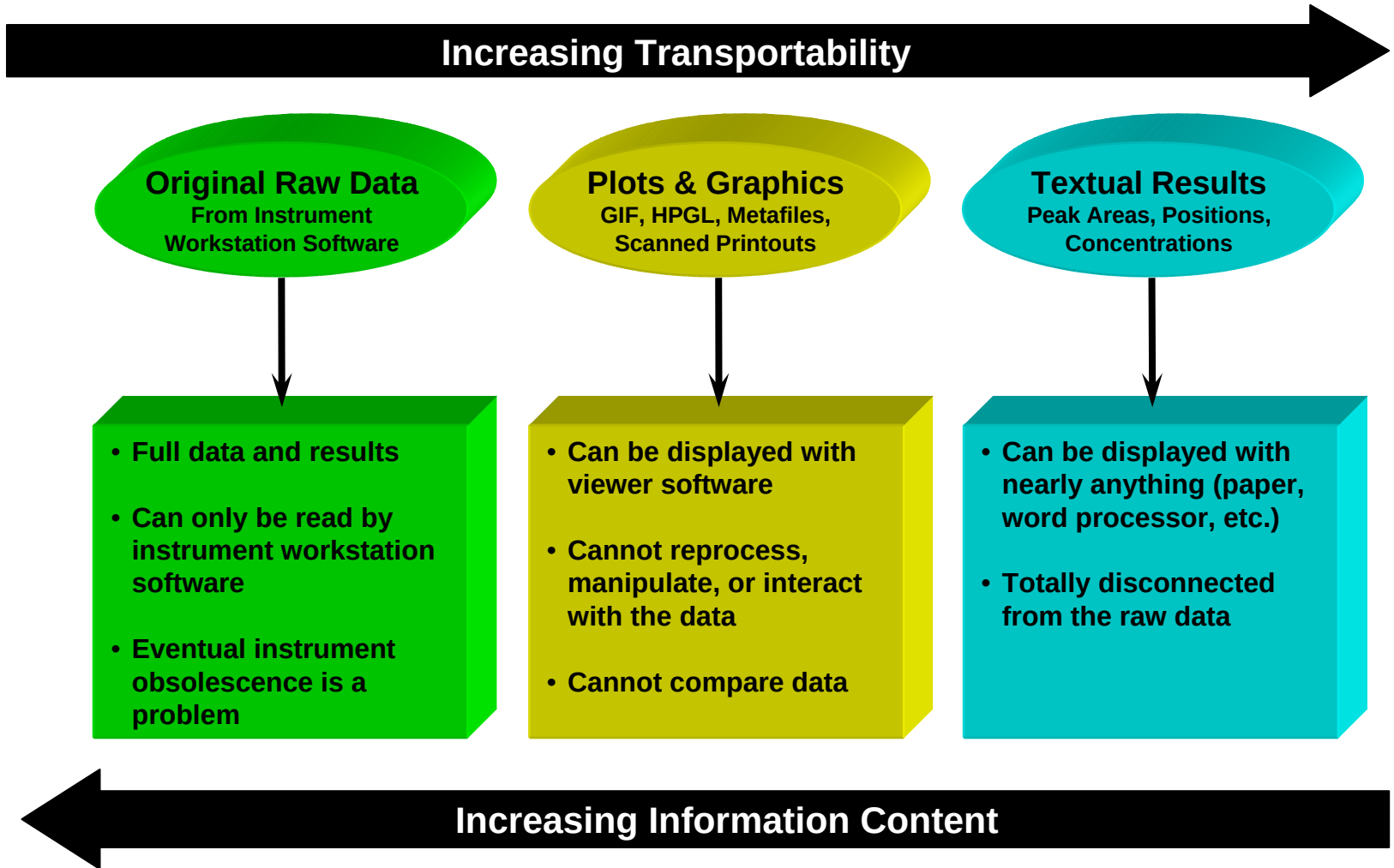
- Why QbD and Why PAT ?
- What are the Data Handling Challenges ?
- Managing Analyzers
- Managing Process and Analytical Data

Managing Analyzers

- Analyzer integration for solutions such as the Process Analytical Technology (PAT) Initiative presents a unique set of integration challenges for data exchange and control.
  - There is a large variety of analyzers types, from various vendors with many different types of data, including complex arrays and structures.
  - There are many different ways to integrate analyzers and execute control from external systems.
  - New process optimization opportunities exist that require unit and system level coordination and control of multiple analyzers from different vendors.
  - No standard data model exists for different classes of analyzer. All solutions are purpose-built.
  - Standard interfaces drive down the validation costs for project implementation in the pharmaceutical industry.
  - Initiatives such as PAT are driving analyzer integration and the best way to accomplish this is via open standards.

Managing Analyzers - Existing Standards for analyzers

- Data exchange standards
  - Driven by the need to store analytical data for laboratory instruments

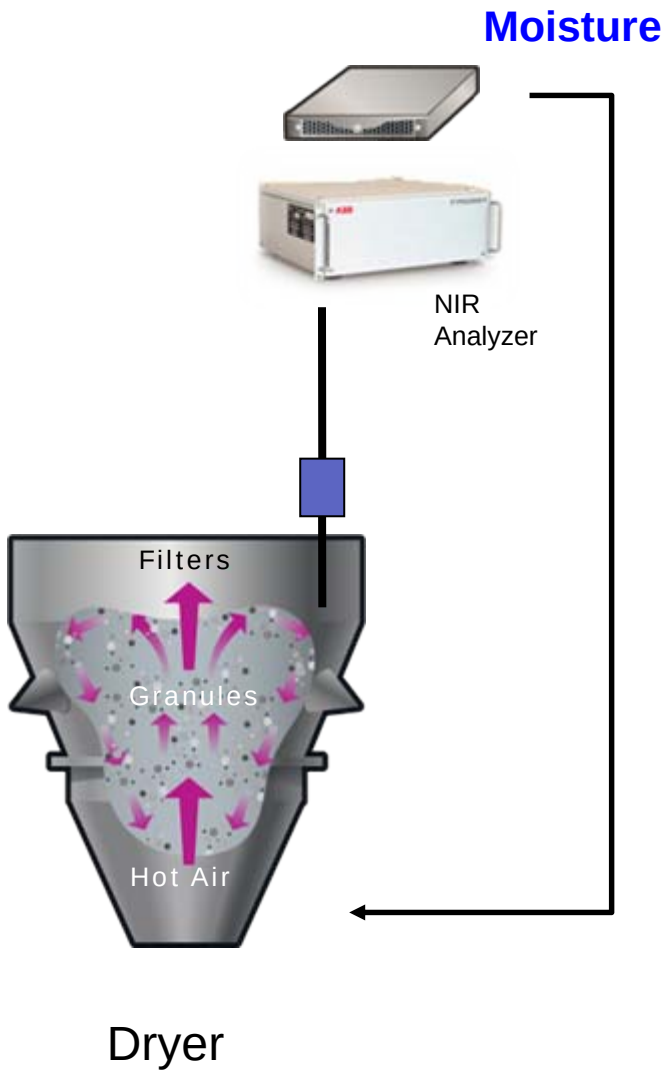


Managing Analyzers – Examples of Current Interfaces

- ABB FTIR: Provides a DLL that gives access to instrument functionality with a series of method calls
- Bruker Matrix-F: Provides a DLL that gives access to instrument functionality through a generic 3 letter ASCII command code
- Mettler-Toledo FBRM: No DLL or driver of any form, need to use proprietary RS232 protocol or full laboratory FBRM software
- CDI Diode Array: Provides an OPC/DA interface with tags for array data, scalar data and instrument control
- Mettler-Toledo MonARC: Embeded computer provides access to commands and data through SQL server databases

Typical Dryer Application

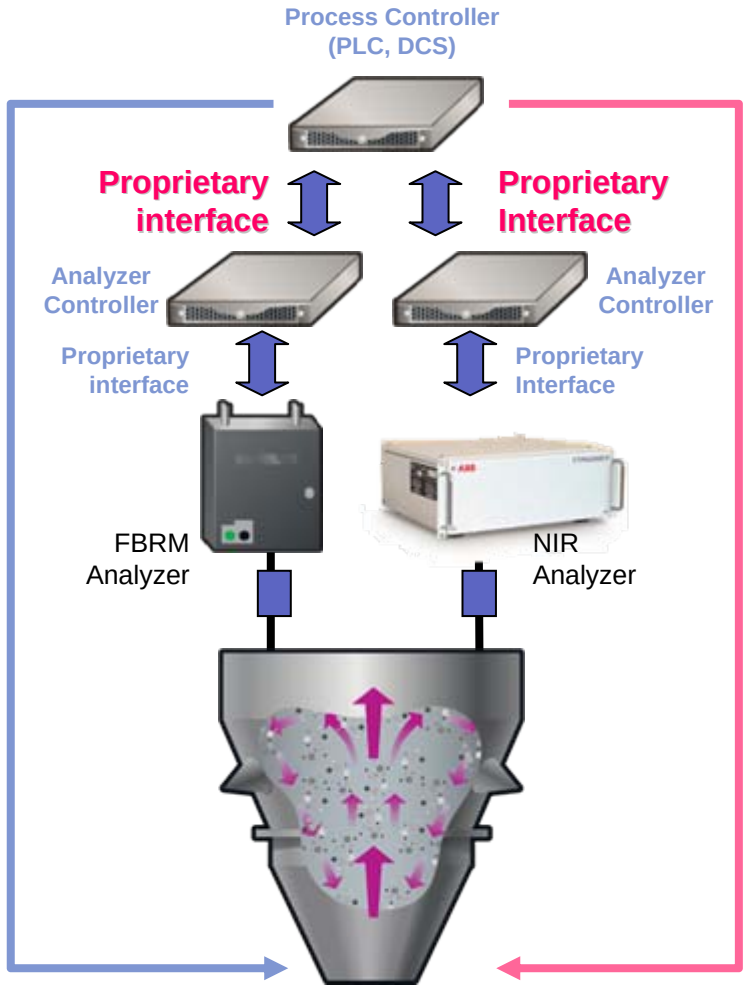
- Learn: What is happening while we dry
- Predict: Use the data to get moisture
- Control: Change the process to get what we want



Current Analyzers in the Process

Proprietary Interfaces – Non Standard Data

- FBRM used to monitor particle size
  - Detect prevent clumping
  - Detect presence of fines that can clog filters
  - Provide data to allow closed loop control to optimize drying



- NIR used to monitor moisture
  - Determine end-point
  - Moisture profile used for asset monitoring
  - Provide data to allow closed loop control to optimize drying
- **Integration at Process Controller is expensive and proprietary**
  - **Limited data types from analyzer controller to process controller in non-standard format**

Managing Analyzers

- The current status quo is unsustainable
  - Analyzers show too much variation in their interfacing capabilities
  - Validation of software with this level of variability is difficult
- We need a new standard for Analyzer Interfaces. A standard which
  - Provides a consistent way to create interfaces
  - Allows the interfaces to be reused by multiple software packages
- Desired Characteristics
  - Define the notion of analyzer class (Spectrometer, Liquid Chromatograph, Particle size, Mass Spectrometer, …)
  - Within a class should be entirely data driven (no code changes In the base platform)
  - Needs to support high data volumes on a Network (imaging)

Managing Analyzers – OPC-ADI

OPC Foundation Announces Support for Analyzer Devices Integration into OPC Unified Architecture Platform

Press Release dated January 12, 2008

The OPC Foundation has announced support for Analyzer Devices Integration into the OPC Unified Architecture. The OPC Foundation has created a working group composed of end-users: **Abbott , GSK ,Pfizer** and vendors: **ABB, Mettler-Toledo, Umetrics** representing both Process Analytical Technology (PAT) and laboratory industries to develop the information model for all analyzer devices facilitating plug-and-play multivendor interoperability. The Analyzer Device Integration Working Group will develop a common method for data exchange and an analyzer data model for process and laboratory analyzers. The model will be developed as a logical extension of the OPC UA specifications. Analyzer integration based on standards will offer unique opportunity in Data Management & Integration for solutions such as Process Analytical Technology (PAT).

Managing Analyzers – OPC-ADI

Vision

- In the same way that field device standards have driven the widespread adoption of intelligent field devices in the process industries, the ADI standard will promote the use of high level analyzers in manufacturing processes.
- The ADI standard will provide a single model for analyzer vendors to create and distribute device drivers that expose the capabilities of process and laboratory analyzers using the universally accepted, platform-neutral OPC UA standard.
- These drivers shall allow complete access to all low level and high level analyzer data and be compatible with regulated manufacturing environments.
- OPC UA is being adopted as the basis for the ADI standard because
  - It is a platform neutral standard. Drivers can be implemented on any operating system or embedded in any networked device
  - It is designed to support complex data types and object models
  - Designed to achieve high speed data transfers using efficient binary protocols.
  - It has broad industry support beyond process automation and is being used in support of other industry standards such as S95, S88, EDDL, MIMOSA, OAGiS
  - Toolkits are available to support the creation of OPC UA drivers and applications.

Managing Analyzers – OPC-ADI

"An Architecture for Integration"

Level 1 – Univariate data integration

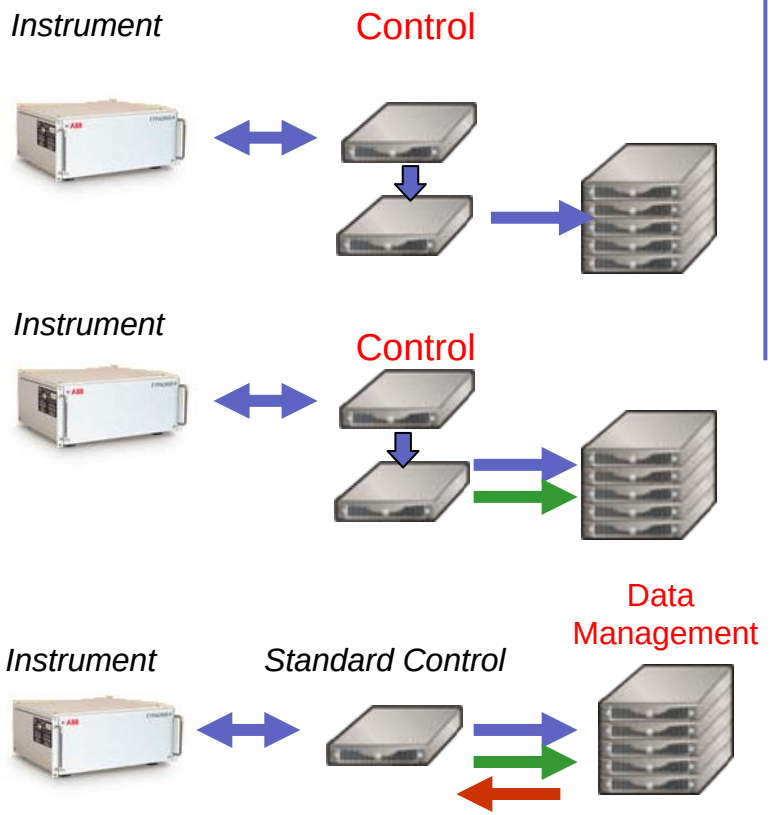
- In this model only predicted properties are collected

Level 2 – Multivariate data integration

- In this model predicted properties and raw data are collected (spectra, chromatograms, histograms)

Level 3 – Full Instrument control

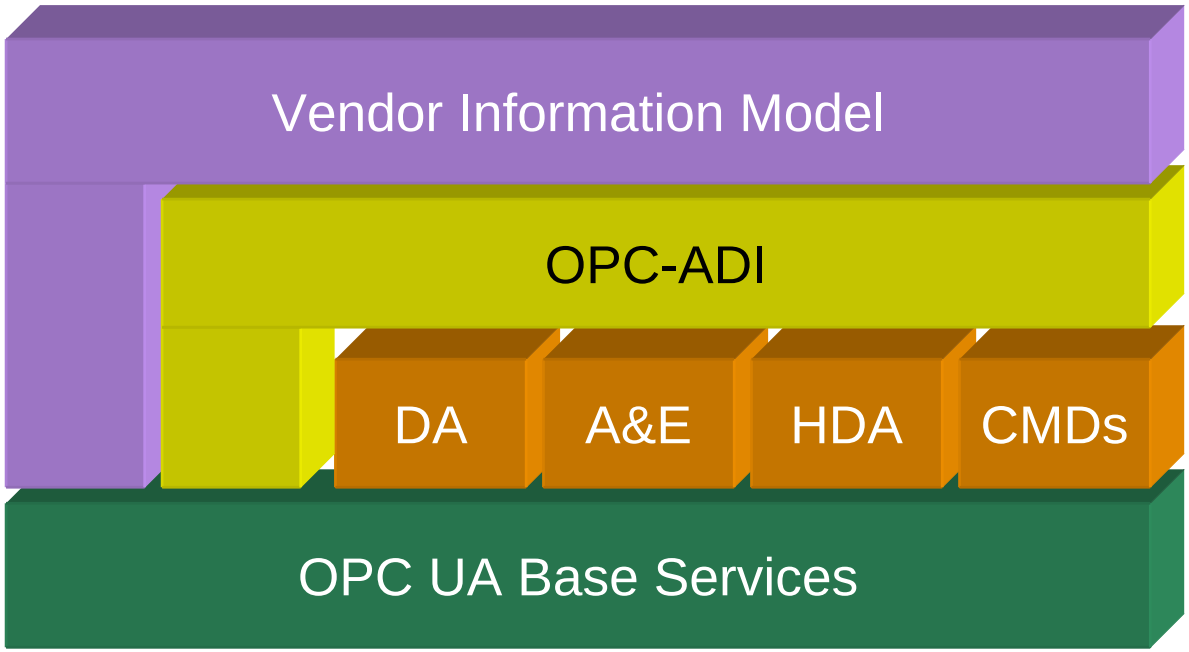
- In this model the central system holds the analyzer configuration



Level 3 is the enabling technology for integration of high level analyzers

- Provides central coordination/control of all analyzers
- Provides a single validated interface to all analyzers
- Provides central storage of all RAW analytical data

Managing Analyzers – OPC-ADI



Analyzer Device Interface

OPC Information Model

All Necessary Services

OPC-ADI is one of many OPC UA Information Model Extensions

Managing Analyzers – OPC-ADI

OPC-ADI Analyzers in the Process
Standard Interfaces – Standard Data

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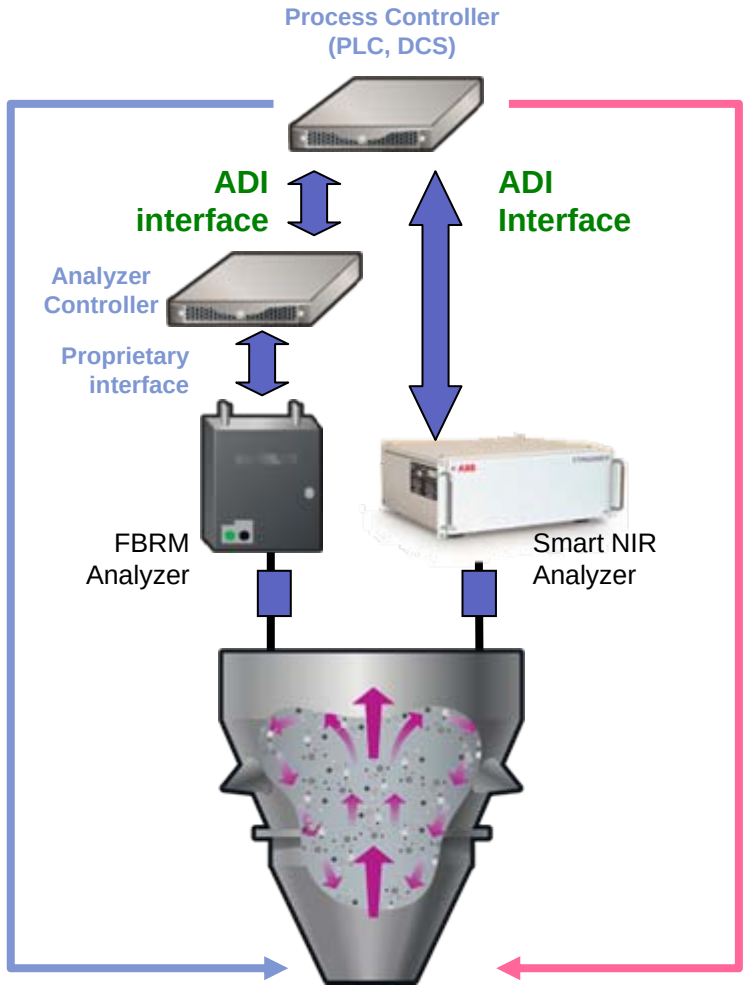

- NIR used to monitor moisture
  - Determine end-point
  - Moisture profile used for asset monitoring
  - Provide data to allow closed loop control to optimize drying

- **Integration at Process Controller is standard and easier**
  - **Complex data types available from analyzer controller to process controller in a standard format**

Current Members

- ABB
- Abbott
- Arla Foods
- BR&L Consulting
- CAS
- FOSS
- GlaxoSmithKline
- Kaiser Optical Systems
- Malvern Instruments
- Mettler-Toledo Autochem
- Novartis
- OPC Foundation
- Pfizer
- Siemens
- Software Toolbox
- Sympatec GmbH
- Thermo Fisher Scientific
- Umetrics
- Yokogawa

Timeline

- February 2008 – kickoff
- Scheduled meetings

Date	Location	Host
April 15-17, 2008	Cleveland, OH, USA	ABB
June 24-26, 2008	Raleigh, NC, USA	BR&L / ISA
August 12-14, 2008	London, UK	GSK
September 23-25, 2008	Chicago, IL, USA	Abbott
November 4-6, 2008	Malvern, UK	Malvern
December 9-11, 2008	Brussels, Belgium	Siemens

- December 2008 - planned draft release
- June 2009 – planned first release
- Reference implementation Q1

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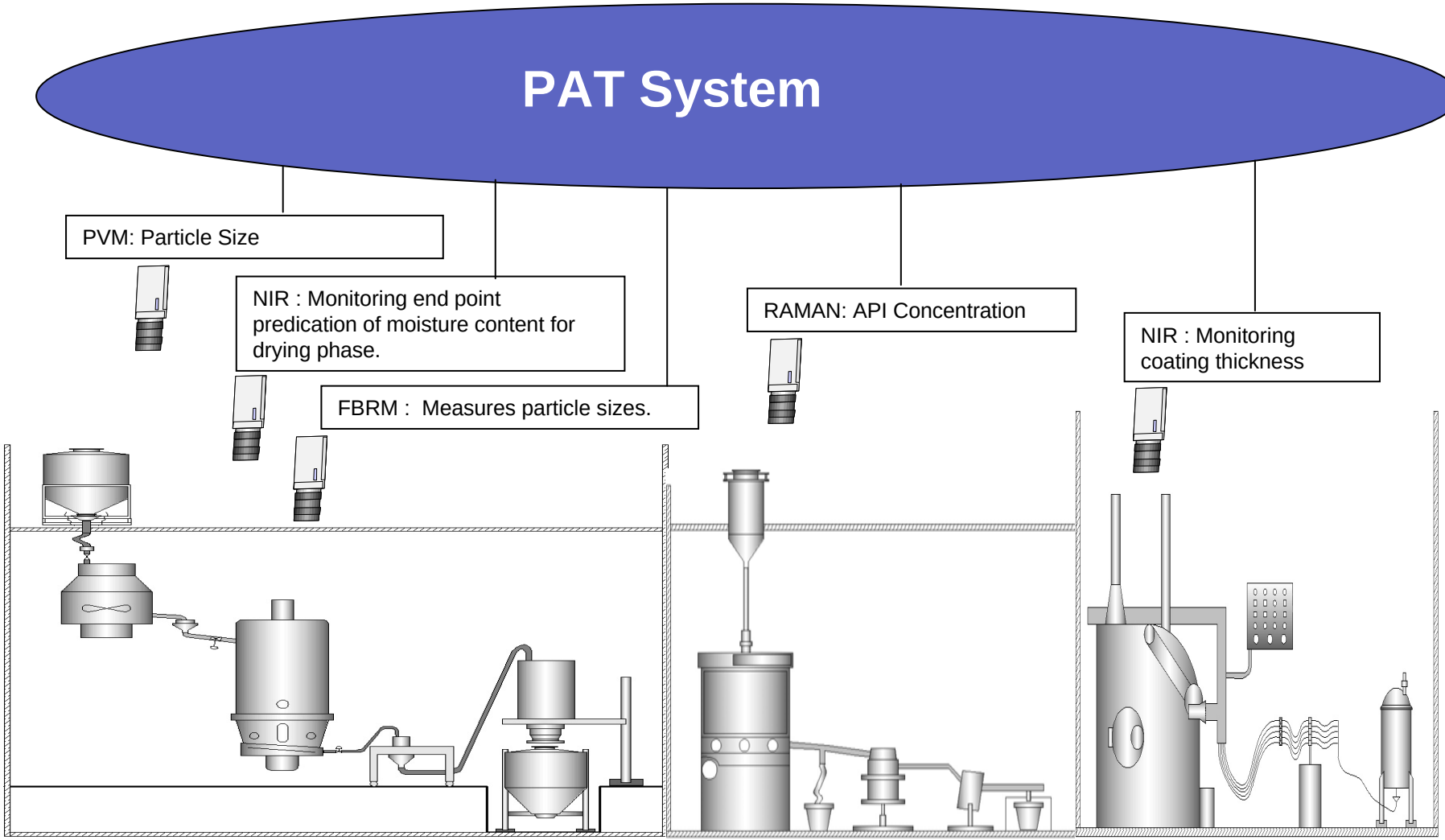
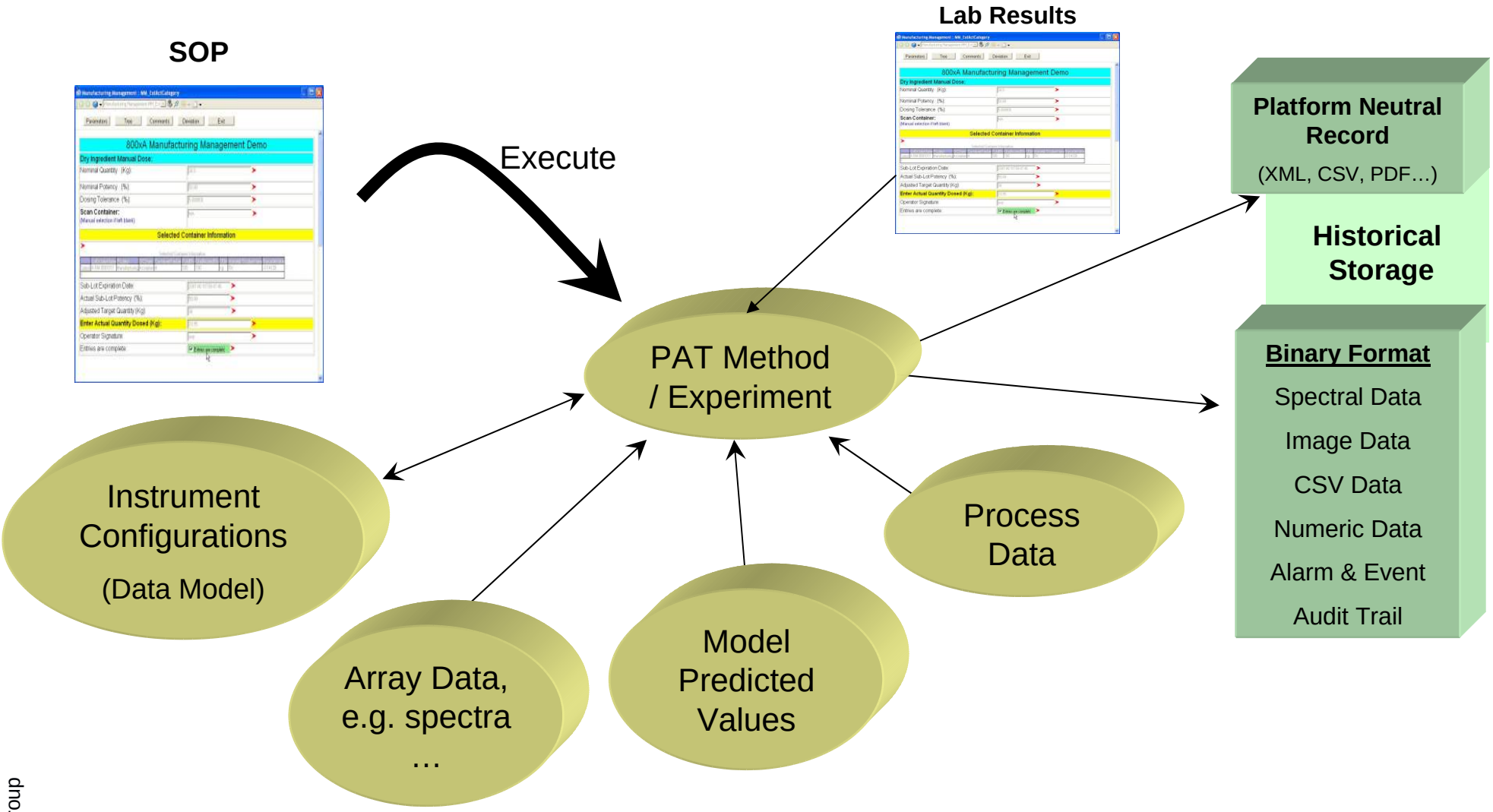
Managing Process and Analytical Data

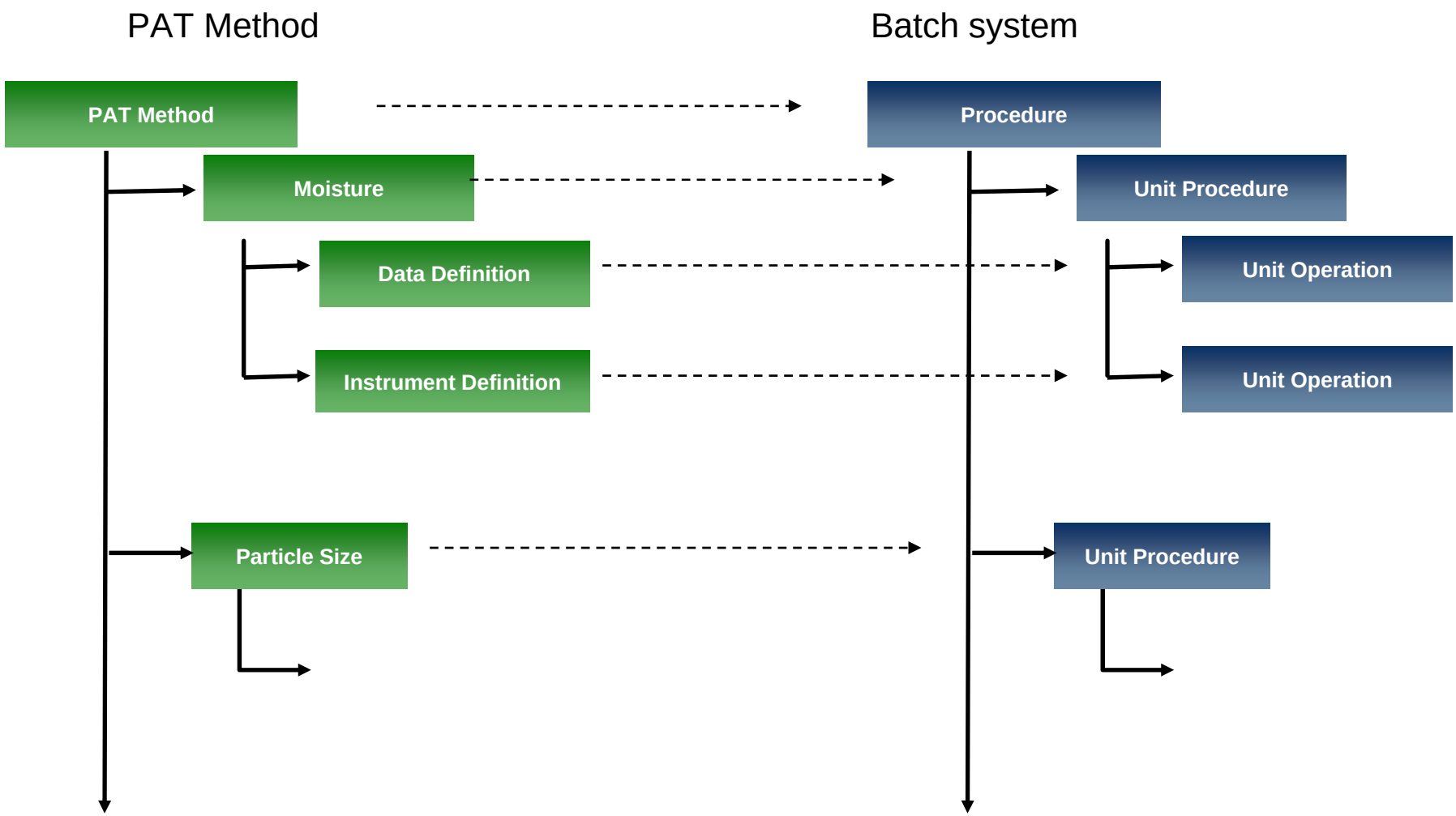


Managing Process and Analytical Data - Structured Data



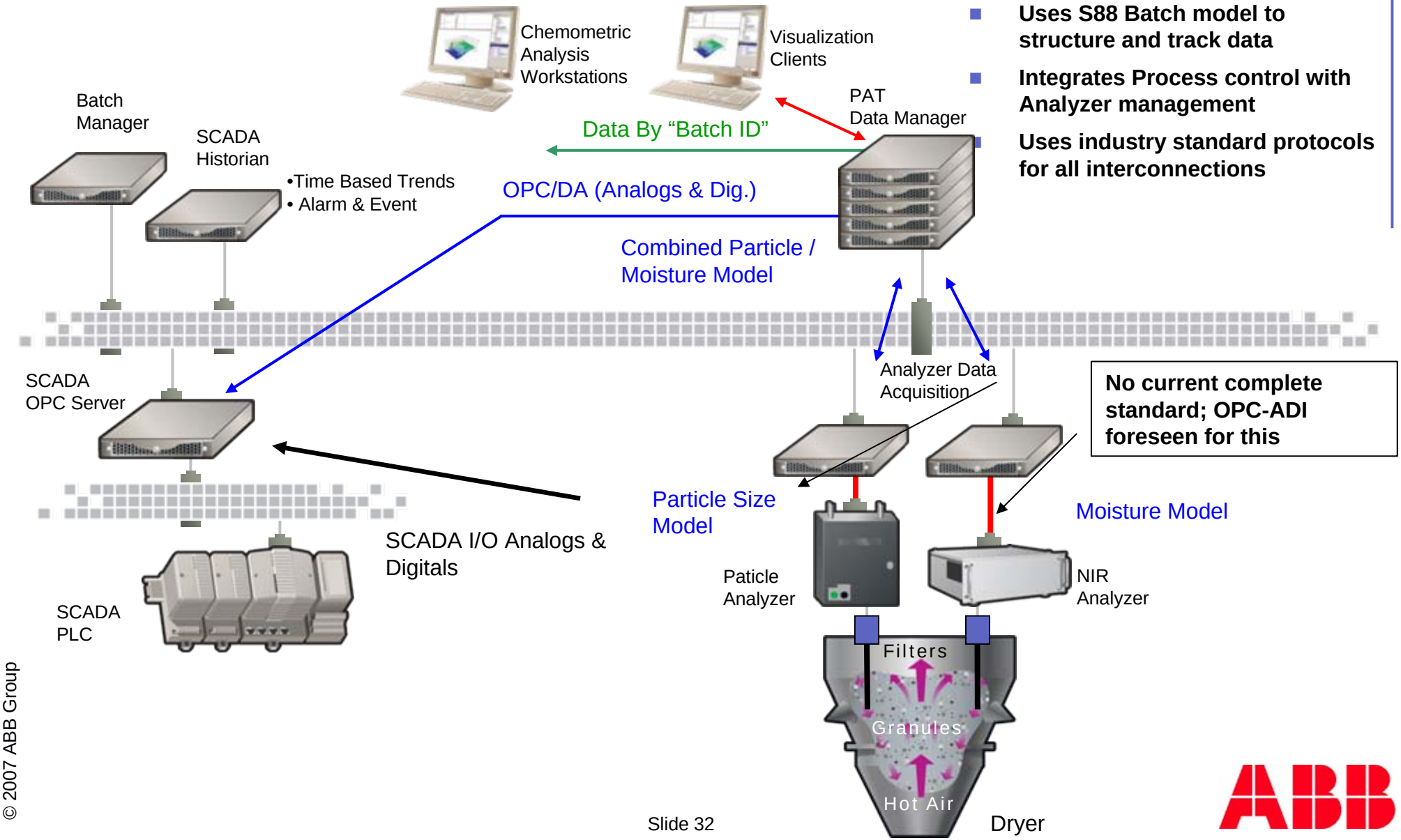
"PAT Method Data"

Managing Process and Analytical Data - Structured Data



"Use S88 Batch Model to structure data"

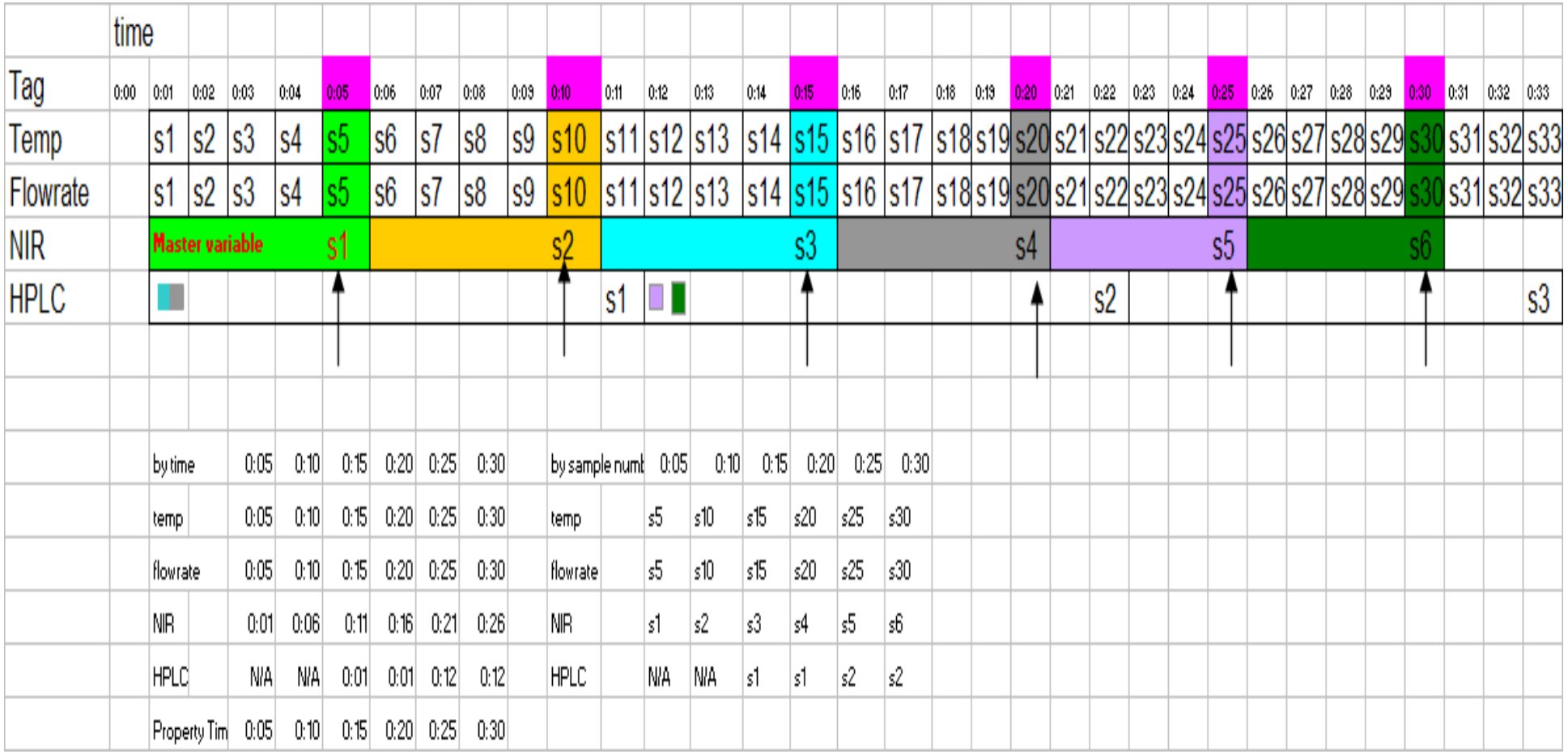
Managing Process and Analytical Data – Data Access



- **Uses S88 Batch model to structure and track data**
- **Integrates Process control with Analyzer management**
- **Uses industry standard protocols for all interconnections**

No current complete standard; OPC-ADI foreseen for this

Managing Process and Analytical Data – Data Access



by time	0:05	0:10	0:15	0:20	0:25	0:30
temp	0:05	0:10	0:15	0:20	0:25	0:30
flowrate	0:05	0:10	0:15	0:20	0:25	0:30
NIR	0:01	0:06	0:11	0:16	0:21	0:26
HPLC	NA	NA	0:01	0:01	0:12	0:12
Property Tim	0:05	0:10	0:15	0:20	0:25	0:30

by sample numb	0:05	0:10	0:15	0:20	0:25	0:30
temp	s5	s10	s15	s20	s25	s30
flowrate	s5	s10	s15	s20	s25	s30
NIR	s1	s2	s3	s4	s5	s6
HPLC	NA	NA	s1	s1	s2	s2

"Data must be correlated"

Managing Process and Analytical Data – Data Access

PAT Data Export Tool

Select Batches and Logs

Select the desired information to export from the tree display, or select a batch and enter manual timeslice information.

Name	Start Time	End Time
WTS_inst_01	09/11/2007 16:53:33	09/12/2007 09:04:54
FiltrationSkid	09/11/2007 16:57:14	09/12/2007 09:04:54
Feed/Filtration	09/11/2007 16:57:15	09/12/2007 09:04:54
ABB-01	09/11/2007 16:57:17	09/12/2007 09:04:54
ABB-01Ch1	09/11/2007 16:57:18	09/12/2007 09:04:53
SolventExtractor	09/11/2007 16:57:14	09/12/2007 09:04:54
Solv.Extract.Procedure	09/11/2007 16:57:17	09/12/2007 09:04:54
FBRM01	09/11/2007 16:57:17	09/12/2007 09:04:54
FBRM01Ch1	09/11/2007 16:57:18	09/12/2007 09:04:53
FBRM01Ch1PreProcess00	09/11/2007 16:57:20	09/12/2007 09:04:52
FBRM01Ch1Sample00	09/11/2007 16:57:20	09/12/2007 09:04:52
FBRM01Ch1St01:H_Action_1	09/11/2007 17:06:42	09/12/2007 08:55:48
FBRM01Ch1St01:H_Warn_1	09/11/2007 17:06:42	09/12/2007 08:55:48
FBRM01Ch1St01:Value_1	09/11/2007 17:06:42	09/12/2007 08:55:48
FBRM01Ch1St02:H_Action_1	09/11/2007 17:06:46	09/12/2007 08:55:52

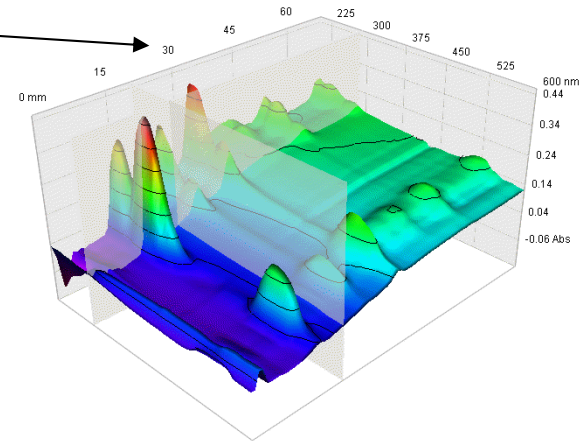
Currently Running	False
Time	
Time Period	09/11/2007 16:53:33 - 09/12/2007 09:04:54
Timeslices	**1 selection**
Timeslice 1	**09/11/2007 16:57:20 - 09/12/2007 09:04:52**
Manual Sampling Interval	1
Manual Sampling Reference Time	**09/11/2007 16:57:20**
Reference Log	
Sampling Mode	HighestDensity

Timeslices

Allows for a time-based selection of data to export, and provides options for specifying data sampling rates.

UTC

Set Defaults | < Back | Next > | Close



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