Sistemi di Automazione con architettura Modulare e Distribuita:

Corretta progettazione a supporto della Data Integrity

Alessandro Ferroni

Engineering Director Dompé farmaceutici S.p.A.

Dompé

www.dompe.com

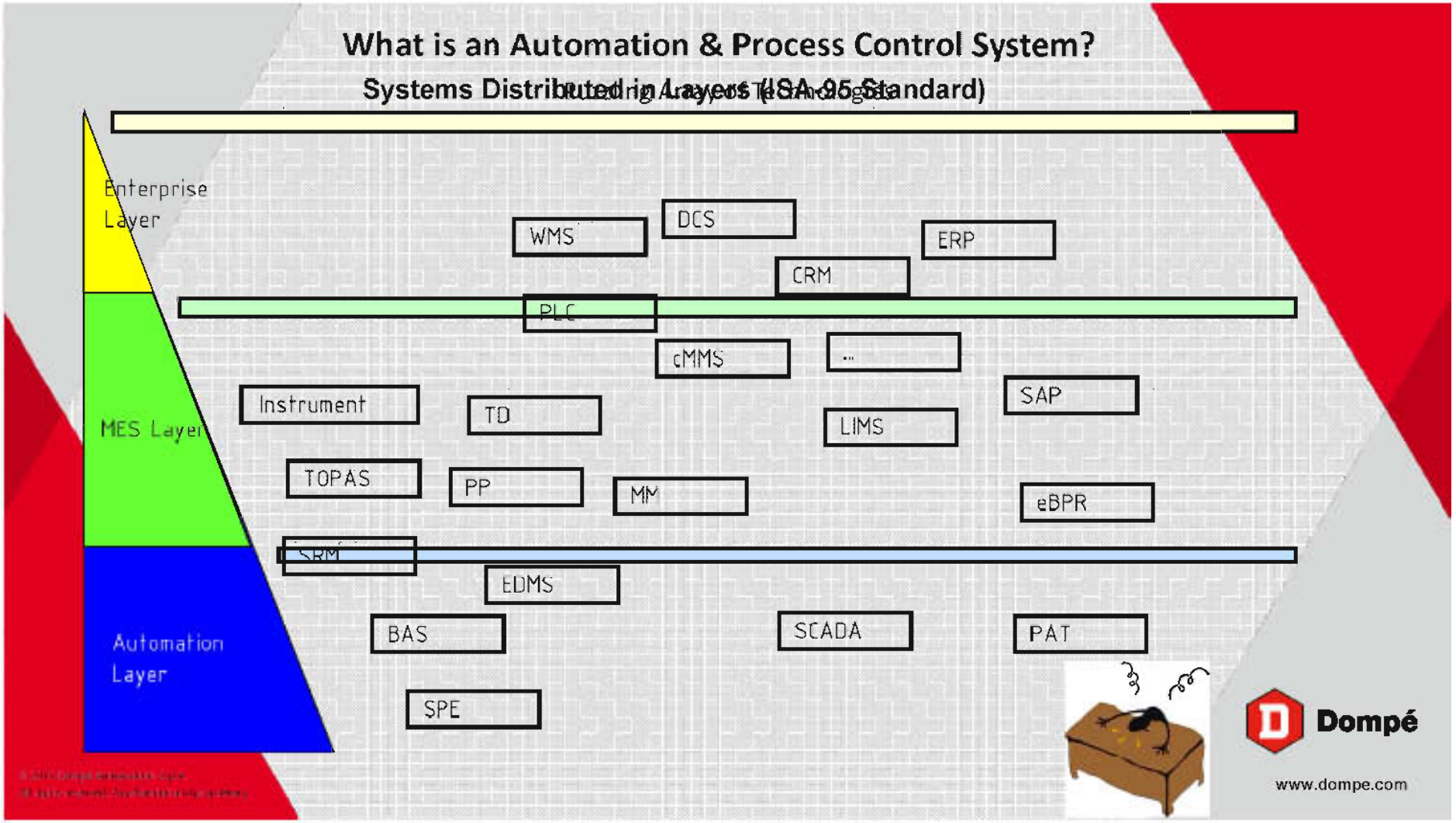
- What is an «Automation & Process Control System» ?
- MHRA Data Integrity Requirements Impact on Control Systems
- Design Starting point: Impact Assessment / Risk Analysis (key 1)
- A Crystal Clear «Site Automation Strategy» (key 2)
- MODULAR Architecture & Libraries (key 3)
- Ease of New Requirements implementation

Dompé

www.dompe.com

What is an Automation & Process Control System?

Systems Distributed in Layers (ISA-95 Standard)



Dompé

www.dompe.com

MHRA Data Integrity Requirements impact for Control Systems

What is REALLY new in MHRA Guidance? Not much but…

1) Discourage reverting from computer to **MANUAL/PAPER**

2) Focus on Data **MANIPULATION** risks (Fraudulent / Mistake)

3) **RISK BASED** approach (ICH Q9) expected

4) Formal **Restore Testing** as part of System Validation

5) **Audit Trail REVIEW** required for Product Release

6) System **Administrator ROLE and account use** clarified

Stand-alone systems Clock Synchronization

Internal clocks of several computers may differ. Even when initially set accurately, real clocks will differ after some amount of time due to clock drift, caused by clocks counting time at slightly different rates.

SOP for periodical verification and adjustment. Reference to a verified standard (GSM, IT Network).

OR: Automatic synchronization:

DCF77 USB Clock

Design Starting Point:
Impact Assessment / Risk Analisys (key 1)

Assessment at SYSTEM LEVEL

is complementary to the assessment at **PROCESS LEVEL** (ICH-Q9)

1) Identification by Risk Analisys/**Impact Assessment for each single System COMPONENTS:**

- GMP Instruments (Temperature, Pressure, Humidity, Process flow, …)
- GMP Parameters (Process and Equipment Setpoints)
- GMP Sequences (Automated Recipes)
- GMP Reports (Raw Data trend, Alarms, Events, Audit Trail, Parameter changes,..)

2) Implementation of Data Integrity Requirements **ONLY ON IDENTIFIED COMPONENTS** !!

3) System Validation by GAMP 5 Guideline

Design Starting Point:
Impact Assessment / Risk Analisys (key 1)

Dompé	UPSTREAM BIOTECH Assessment Strumentazione Critica	IOQR-AH9001/EF9001-2012 Allegato "A" Pag. 2/6

Criterio di identificazione della Strumentazione critica

In accordo a quanto previsto nel VMP-001-BIOT-2011 "Biotech Manufacturing Validation Master Plan ", per ognuno dei sistemi /apparecchiature /utilities ad Impatto Diretto viene identificata la strumentazione critica attraverso le seguenti domande:

Strumentazione Critica	
Numero domanda	Domanda
1	Lo strumento è utilizzato per dimostrare conformità con un Processo Registrato?
2	La normale Operatività dello strumento ha un effetto diretto sulla qualità del prodotto?
3	Un Malfunzionamento o un Allarme associato allo strumento ha effetto diretto sulla qualità o efficacia del prodotto?
4	Le informazioni prodotte da questo strumento sono registrate come parti di un Batch Record, dati di rilascio di un lotto o altra documentazione GMP?
5	Lo strumento controlla elementi di un Processo Critico che possano impattare la qualità del prodotto, senza verifiche indipendenti delle performance del Sistema?
6	Lo strumento è utilizzato per creare o preservare lo Stato Critico del Sistema?

Se la risposta è SI ad almeno una delle domande, lo strumento è classificato come strumento critico e deve essere inserito nel piano di taratura periodica di stabilimento definendo la corrispondente Frequenza di Taratura.

Design Starting Point:
Impact Assessment / Risk Analisys (key 1)

Example: Biotech SCADA supervise Upstream & Downstream HVAC, PW, WFI, Refolding Process.

On a Total of 387 Instruments assessed, 60% has been identified to be GMP Instruments (!).

Each of them required Implementation and Validation of Electronic Signature, Audit Trail and all other Data Integrity requirements.

Elenco della strumentazione

Impianto di condizionamento downstream AH9001-EF9001

IDENTIFICAZIONE STRUMENTO				CARATTERISTICHE DELLO STRUMENTO						Domande						Criticità			
N.	Item	Strumento	Matricola	Range	Accuratezza	Sensibilità	Campo di taratura	Campo di lavoro	Limiti di accettazione	1	2	3	4	5	6	GMP	Sicurezza	Data taratura	Frequenza Taratura
1	C91.TT01	Temperatura canale ingresso aria esterna (Sonda Combinata)	H1440091	-20/+80 °C	±0,2 °C	N/A	-15 – 45 °C	-15 - 45 °C	±1 °C	N	N	N	N	N	N	-	-	25/06/2012	Manutenzione
2	C91.MT01	Umidità relativa canale ingresso aria esterna (Sonda Combinata)		0/100 % u.r.	±2% u.r.	N/A	35 - 80 %	35 - 80 %	±3 %	N	N	N	N	N	N	-	-	25/06/2012	Manutenzione
3	C91.TT03	Temperatura canale mandata aria (Sonda Combinata)	H1440090	-20/+80 °C	±0,2 °C	N/A	5 - 40 °C	5 - 40 °C	±1 °C	N	S	S	N	S	S	☑	-	25/06/2012	Annuale
4	C91.MT02	Umidità relativa canale mandata aria (Sonda Combinata)		0/100 % u.r.	±2% u.r.	N/A	35 - 80 %	35 - 80 %	±3 %	N	S	S	N	N	S	☑	-	25/06/2012	Annuale
5	C91.TT04	Temperatura canale estrazione aria (Sonda Combinata)	H1140031	-20/+80 °C	±0,2 °C	N/A	5 - 40 °C	5 - 40 °C	±1 °C	N	N	N	N	N	N	-	-	25/06/2012	Manutenzione
6	C91.MT03	Umidità relativa canale estrazione aria (Sonda Combinata)		0/100 % u.r.	±2% u.r.	N/A	35 - 80 %	35 - 80 %	±3 %	N	N	N	N	N	N	-	-	25/06/2012	Manutenzione
7	C91.TT13	Temperatura locale UP-29	N.D.	-20/+60 °C	±0,2 °C	N/A	23 °C	5 - 40 °C	±1 °C	N	N	N	N	N	N	-	-	17/07/2012	Manutenzione
8	C91.TT14	Temperatura locale UP-31	N.D.	-20/+60 °C	±0,2 °C	N/A	23 °C	5 - 40 °C	±1 °C	N	N	N	N	N	S	-	-	17/07/2012	Manutenzione
9	C91.TT05	Temperatura ripresa locale UP-14	058712-01/04	-10/+50 °C	±0,2 °C	N/A	5 - 40 °C	5 - 40 °C	±1 °C	N	S	S	N	S	S	☑	-	25/06/2012	Annuale
10	C91.TT02	Temperatura UTA AH9001	151012-01/01	-10/+50 °C	±0,2 °C	N/A	5 - 40 °C	5 - 40 °C	±1 °C	N	N	N	N	N	N	-	-	25/06/2012	Manutenzione
11	C91.TT15	Temperatura UTA AH9001	058712-02/01	-10/+50 °C	±0,2 °C	N/A	5 - 40 °C	5 - 40 °C	±1 °C	N	N	N	N	N	N	-	-	25/06/2012	Manutenzione
12	C91.TT06	Temperatura ripresa locale UP-13	058712-01/09	-10/+50 °C	±0,2 °C	N/A	5 - 40 °C	5 - 40 °C	±1 °C	N	S	S	N	S	S	☑	-	25/06/2012	Annuale
13	C91.TT07	Temperatura ripresa locale UP-11	058712-01/02	-10/+50 °C	±0,2 °C	N/A	5 - 40 °C	5 - 40 °C	±1 °C	N	N	N	N	N	N	-	-	25/06/2012	Manutenzione

Cristal Clear «Site Automation Strategy» (key 2)

Sitewide Standardization and Integration in

ONE UNIFIED SITE ARCHITECTURE

developed as a prerequisite to Data Integrity implementation

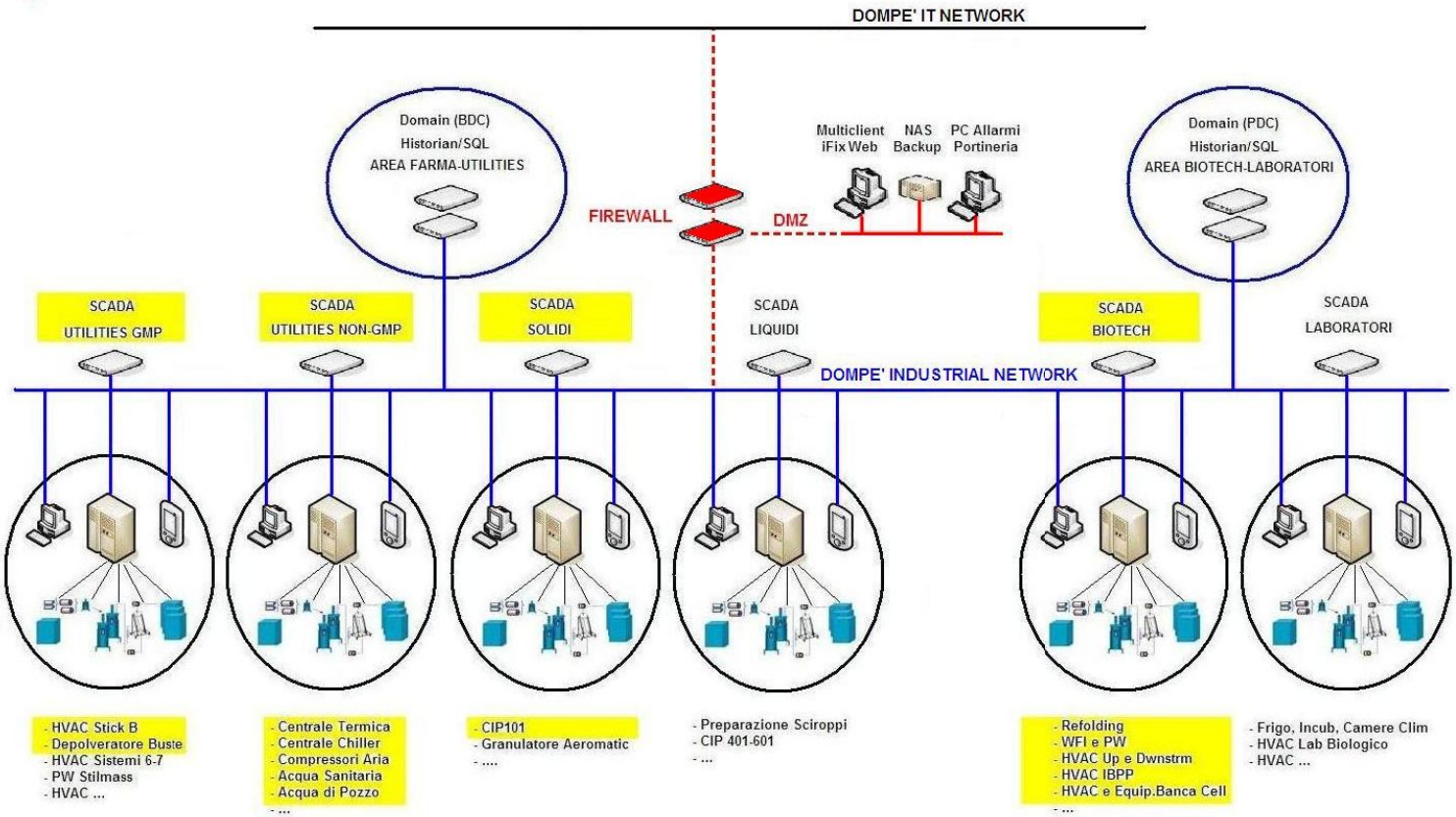
Definition of **One Unified Hardware and Software** Architecture for:

- Process Controls,
- Raw Data Collection, Trending & Archiving
- Alarms & Events,
- Process Parameters and related Reporting
- Equipment & Machines automation,
- Controlled Environments Supervision (Cold Rooms, Freezers, Incubators, ..)

Unified for all areas:

- Pharmaceutical Production Site
- Biotech Production Site
- Central Utilities and WWTP
- Quality Control and Development Labs

Crystal Clear «Site Automation Strategy» (key 2)



MODULAR Architecture & Libraries (key 3)

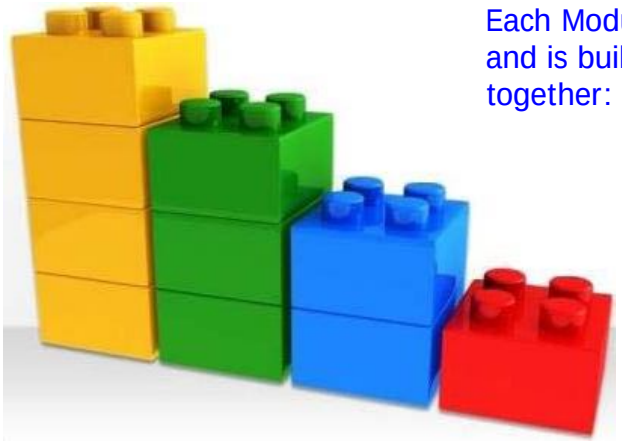
1) Definition of the Key Functional Block required.
2) Development of the corresponding sw Library Module with System Integrator support
3) Module Testing and Validation by first deploy Project

The Control Module library Components are the same for all processes, independently form application and area.

MODULAR Architecture & Libraries (key 3)

"The wall is made by bricks"

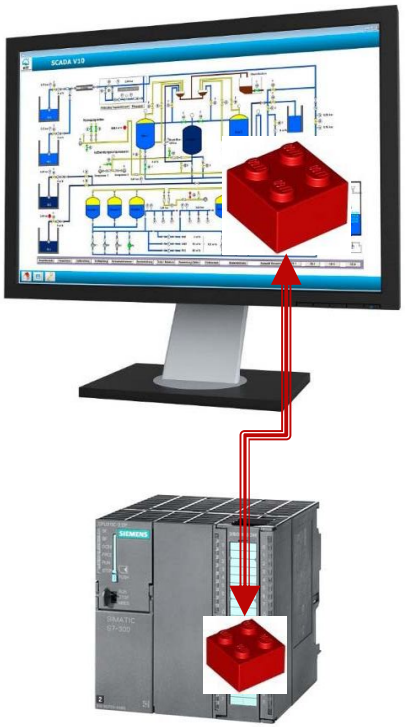
The system is fully modular, each module is a brick in the wall. This approach makes easy to Introduce in the system a new functionality, Modify it and Track the Changes.



Each Module has its own Version and is built by two parts operating together:

PLC code part

VBA code part



MODULAR Architecture & Libraries (key 3)

The Process Control Systems implemented after 2011 have been realized by Modular Software Architecture.

A New Module is Developed, Implemented and Validated as part of a Project (s.a. New Biotech Upstream Plant Project) and then with a very **LOW RISK** and **LOW COST** it can be deployed to all other Plants and Equipment of the Site.

Example: Temperature faceplate module. It has its own Version and can be istantiated in all HVAC and process equipment.

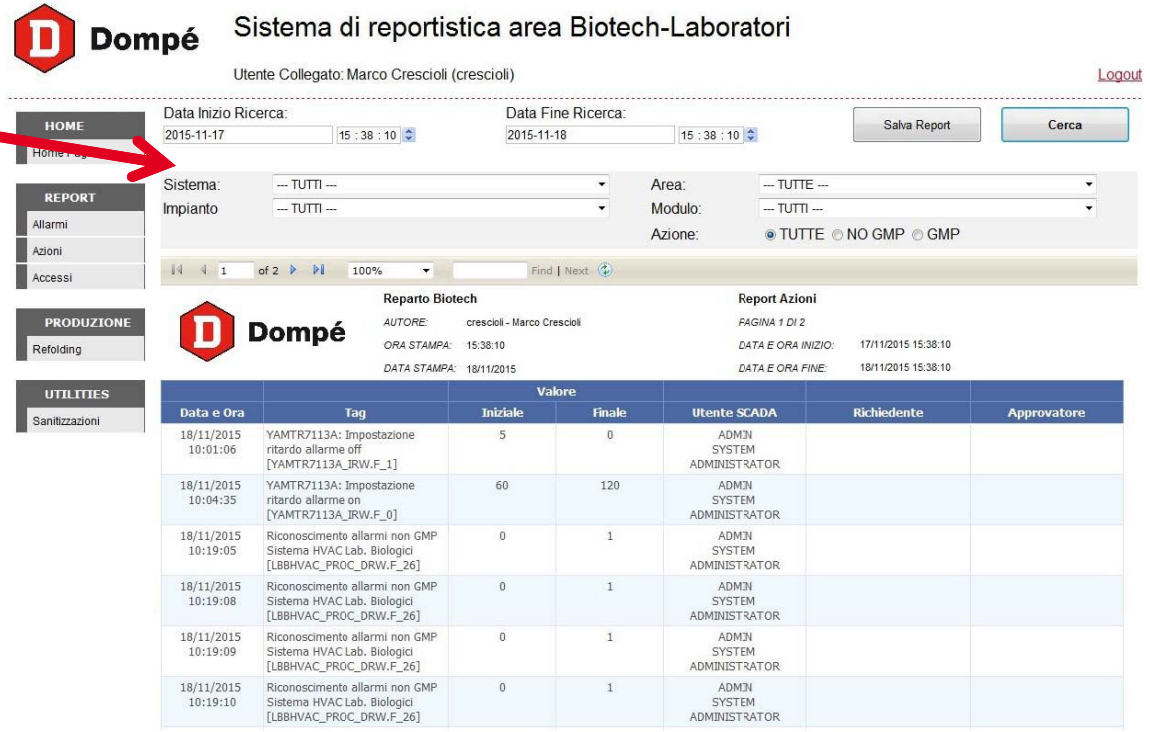
For each single implementation, in case it is assessed to be a GMP Critical instrument, it is sufficient to flag it with the Electronic Signature checkmark and all Data Integrity Software Modules will be activated.

Ease of New Requirements Implementation

The Modular Architecture **makes easy the deploy of New Requirements** to all Integrated Control Systems of the entire Dompé Site.

Example: Following an AIFA inspection focused on Data Integrity a new **Audit Trail Reporting Module** has been implemented, which includes a **Filter Menu Structure** to create clear and «easy to read» Reports to allow Audit Trail Review to be part of Product Release process.

The New Reporting Module, developed and validated in less than 1 month from the previous version, can now be easily deployed to all GMP critical supervision systems of the Site.



MODULAR Architecture & Libraries (key 3)

- Library Validation

Each new Library Module is implemented and first tested by the System Integrator and than released with its own validation package.

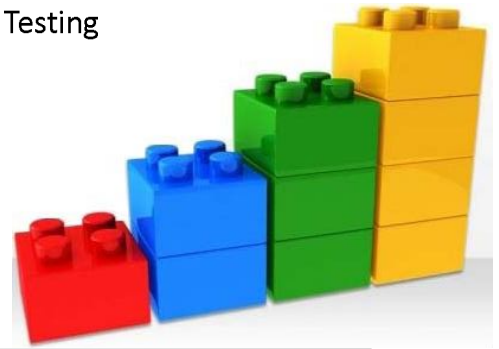
Validation of the Module is executed and documented by the first Project Team implementing the new functionality in the first Control System.

- Library Deploy

Deploy of the new Library Module to other Control Systems onsite allows simplified IQ-OQ of the Module as instantiated in the new system.

Deploy is done by Change Control Procedure with simplified Configuration & Functional Testing

Implementation Validation can be reduced from GAMP category 5 to category 4 ?



MODULAR Architecture & Libraries (key 3)

- Added Value

- Easy to maintain and deploy
- Fast validation
- Flexibility conjugated with clear Tracking
- Powerful and flexible Reports configurable by the operator with filters engine (different reports for different users)

- Data Integrity

The data integrity is guarantee handling appropriately Data and Libraries.

Each library module is "closed" and the operator has only the controlled configurations available. All actions are tracked and stored in system database. The only way to reach the data is to use the Report web site, if you have the rights....

Filters Engine for Audit Trail Reports made possible the required **Audit Trail Review by the Qualified Person for Batch Release**.

Proprietary Systems

Not all Process Control and Plant Automation Systems could be integrated in the new Dompé Standard Site Architecture. Some Production Equipment and Machines are realized with their **own Vendor Proprietary Control System**. In this case Dompé provides the Vendor with a similar Documentation and Implementation Requirements to follow a similar implementation process (User Requirements, Impact Assessment, Risk Analysis).

Examples:

- Applikon Fermenters supervision and control system
- GEA Centrifuge control system
- GE Chromatography Unicorn system
- Pall Filter Skid control system
- Fedegari Autoclaves

The centralized Infrastructure provides anyway **CENTRALIZED SERVICES validated as part of the Infrastructure Validation** that can be used also for low Impact Equipment (s.a. Secondary Packaging Lines).

(Note: Different approach from IT Infrastructure Validation

Deep customization not required, implementation of the Basic Data Integrity Requirements:

- User Access Groups with appropriate Password levels
- Centralized system and parameters backup (no data trending)
- Raw Data and Pdf reports archiving

Thank you and ….

Questions?