How the PI System helps Sandoz to cope with regulatory compliance

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Agenda

- Sandoz – a Novartis company
- PI-System at Sandoz
- The role of a health agency
- Regulative aspects

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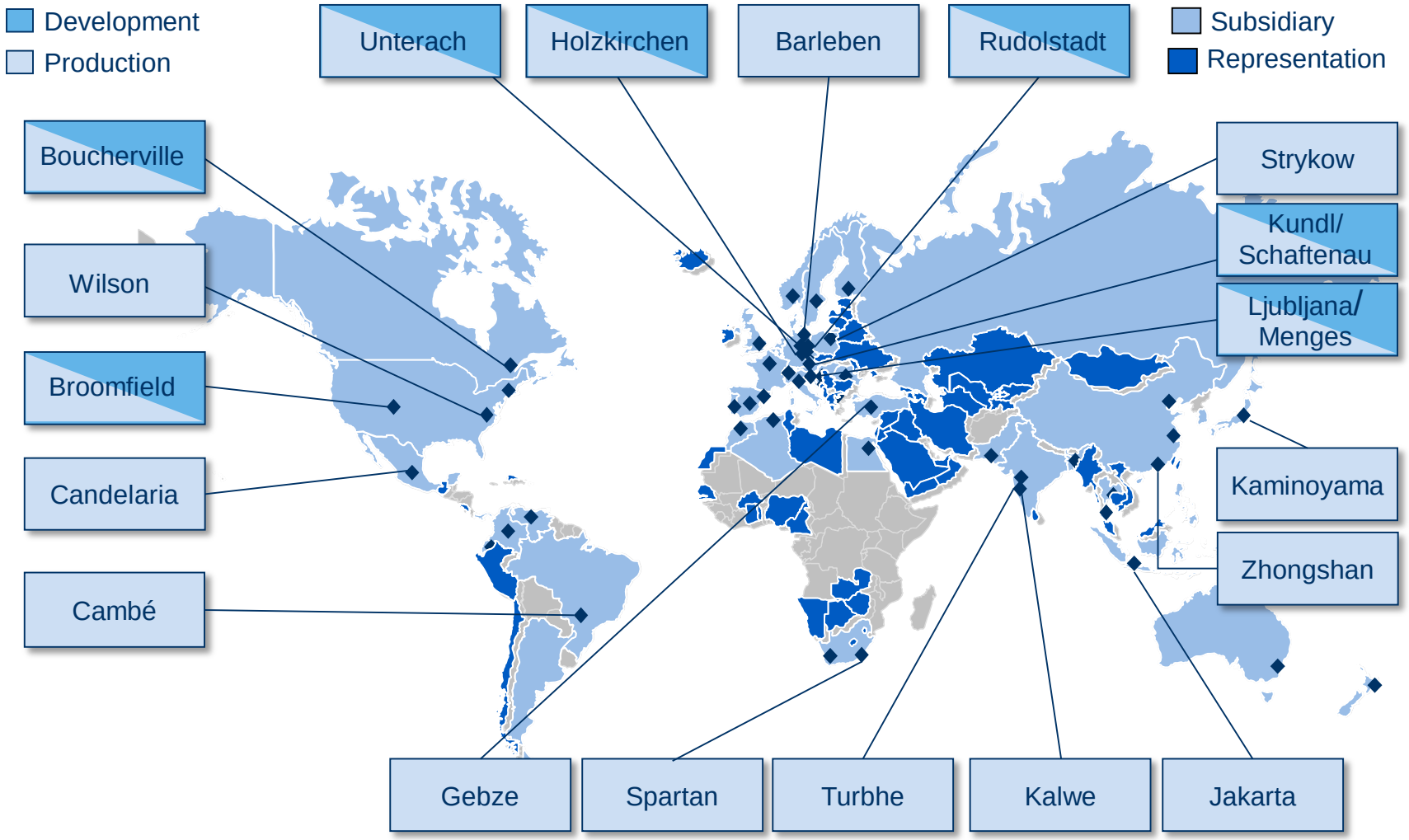
Generics – good news for everyone

Significantly increase global access to high-quality and affordable medicines

Enable enormous cost savings for patients and healthcare systems

Free up funds for patent-protected medicines and drive further innovation

Sandoz is active in more than 160 countries worldwide



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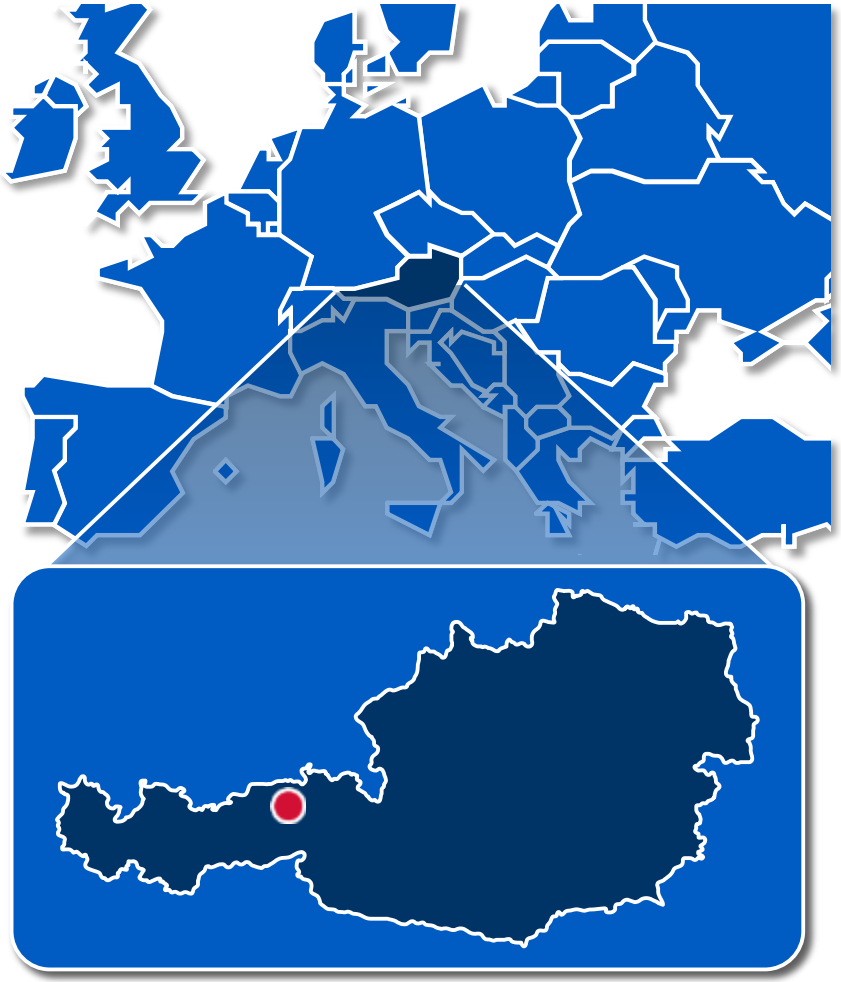
Sandoz GmbH, Kundl

Largest research and development site of Sandoz worldwide



Kundl (Tyrol, Austria)

- Fermentation
- Synthesis (ß-lactam antibiotics)
- Sterile precipitation (ß-lactam antibiotics)
- Enzymes
- Recombinant proteins
- FDFs
- Pilot plants (fermentation, downstream and chemical synthesis)

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Sandoz GmbH, Schaftenau

Center of Competence for modern cell culture technology

Schaftenau (Tyrol, Austria)

- Synthesis (non-ß-lactams)
- Sterile precipitation
- Lyophilization
- Hormones, anticoagulants
- Recombinant proteins (cell culture technology)
- FDFs

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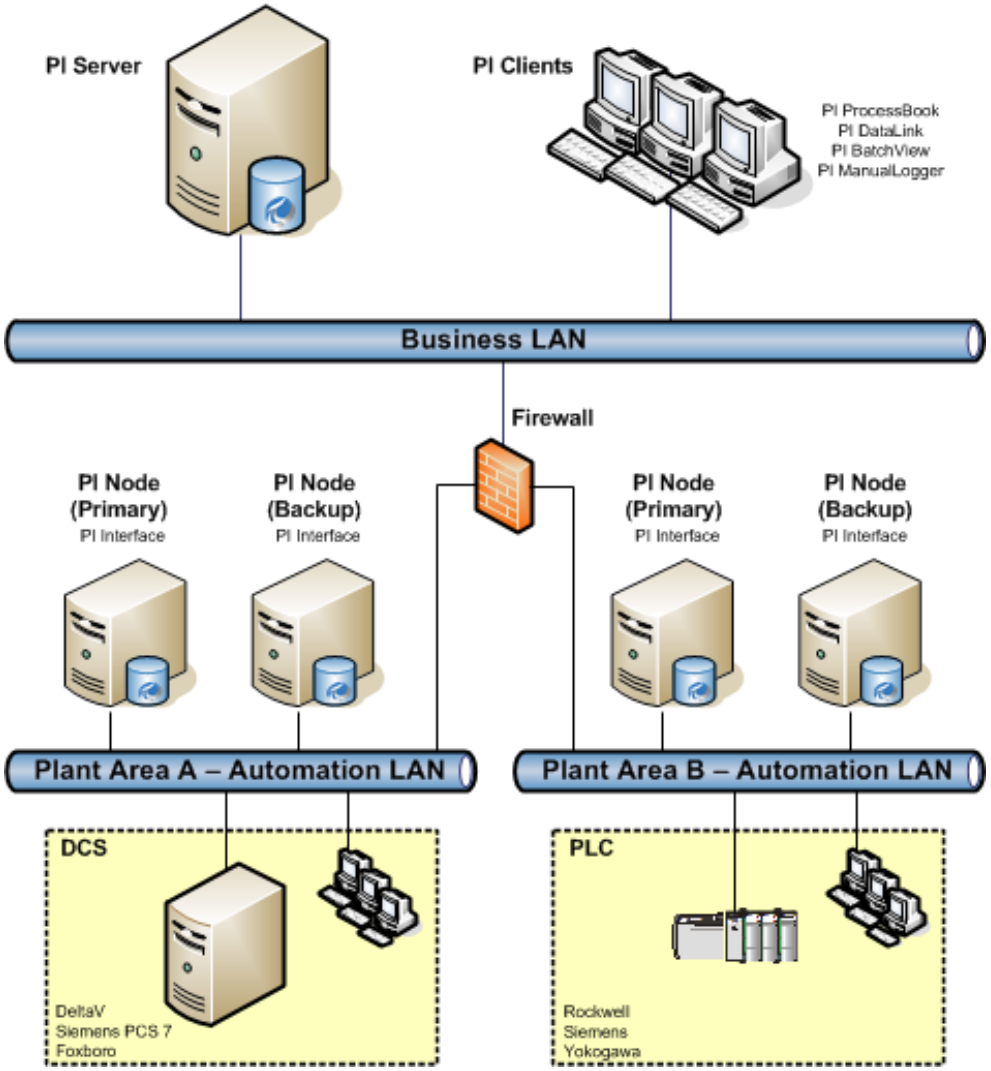
PI-System at Sandoz Kundl/Schaftenau

Infrastructure Schematic



Area of operation:

- Data Archiving
- Process Monitoring
- Data and Fault Analysis
- Batch Data Recording (EBR)
- Calculations
- Monitoring (e.g. Refrigerators)

Key data:

- First Installation 1996
- >150.000 PI Tags on 5 PI-Servers
- >1500 Users at Site
- 60 PI Interfaces

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The role of a health agency
Food and Drug Administration

Mission statement

The agencies mission is to **ensure** the **safety** and **effectiveness and security** of the products under its jurisdiction.

- The Food and Drug Administration (FDA) is an agency within the U.S. Department of Health and Human Services.
- It is protecting the public health by **assuring the safety, effectiveness, and security** of human and veterinary drugs, vaccines and other biological products, medical devices, nation's food supply, cosmetics, dietary supplements, and products that give off radiation.
- FDA attempt to ensure compliance by adverse reporting, field alert reports, inspections, market sampling, recall oversight and analyzing industry, technology and trends.
- FDA focuses on risks and GMP (Good Manufacturing Practice) concerns.

The role of a health agency
Types of inspections

Routine Surveillance Inspections

- **Periodic**

  frequency (usually 2 years) inspections are carried out by the regulatory agency to ensure continued compliance after a product has been launched or for complex production site

- **Risk Assessment Model**

  , i.e. Center for Drug Evaluation and Research: Risk value assigned (date since last inspection, classification of last 3 inspections, recalls, therapeutic significance)

Directed Inspections

- **Pre-Approval Inspections (PAI)**

  The New Drug Application (NDA, ANDA) is the registration file sent to the FDA for marketing of a new drug product in the USA. The Biologics License Application (BLA) is the equivalent to an NDA for biopharmaceutical and biotechnology products.

- **For-cause-inspections**

  can be made, if there is awareness of the agency about a non-compliance situation e.g. follow-ups of previous inspection findings, recalls, complaints or any product related incidents

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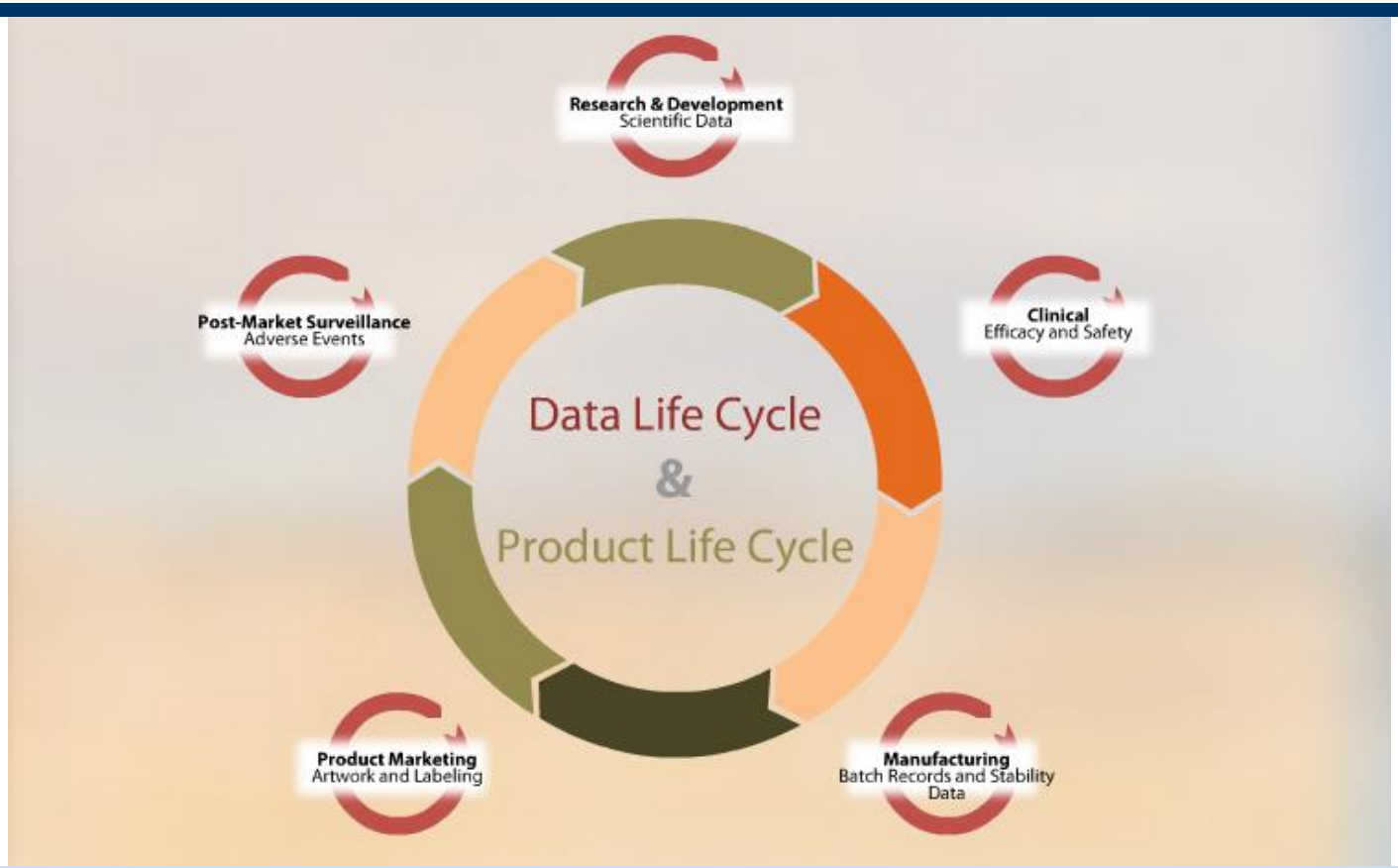
Data Integrity
Data Lifecycle & Product Lifecycle



- Data are the evidence to our patients and health authorities that our products are safe and effective.
- Data tells the story of a product long after it is shipped.

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Data Integrity
PI-System and Data Integrity

Example scenario:

Periodic Inspection of a FDF production line (Finish Dosage Forms) by a regulative authority.

Expectation:

Generated data need to be complete, accurate, consistent and secure.

Does the QA review data matches the electronic data?

- Regulators want to see the data directly in the system

How did you get the data?

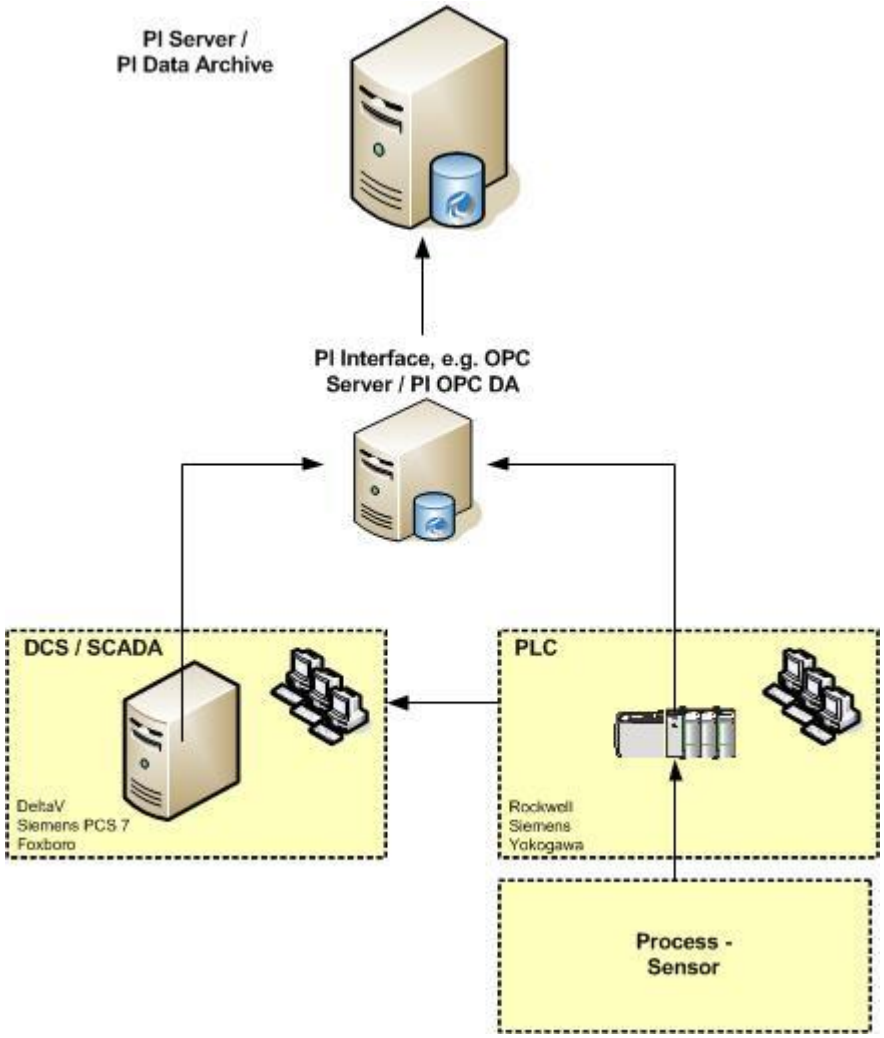
What data are changed (Audit Trail)?

What was the flow of data?

- Regulators don‘t want to only see the end result anymore:

  - Audit Trail for configuration and data changes
  - Security Management
  - Segregation of duties

Data Integrity
PI-System Data Exception & Compression



- Develop a clear philosophy on how you are archiving data.

  Can you explain your story to an auditor?

- First priority is not to loose GxP Data due to too much filtering.

- Do not miss any excursions in the process and record it as DCS/SCADA does.

- Terms for data archival:

  - *Exception:* filtering at interface node
  - *Compression:* filtering at PI Data Archive

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Archiving
PI-System for Longtime – Data Archive

Example scenario:

Raw data archiving of particle sensor in a FDF sterile filling unit (Finish Dosage Forms).

Expectation:

Production relevant data is archived and accessible for a specific time period. Raw data (PI-System data) is part of electronic batch record.

How do you know that access to data archive is ensured?

- Regulators ask for Backup and Recovery procedures for the system

System access ensured for the next years?

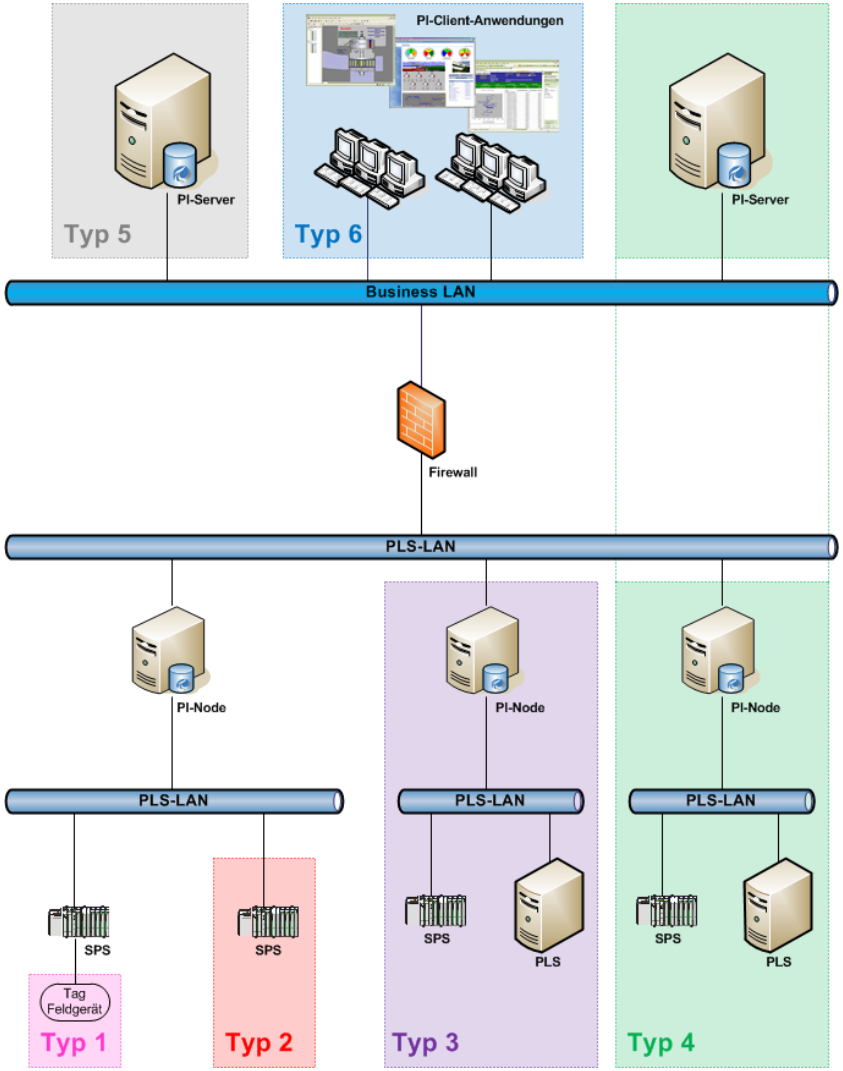
Archived data complete?

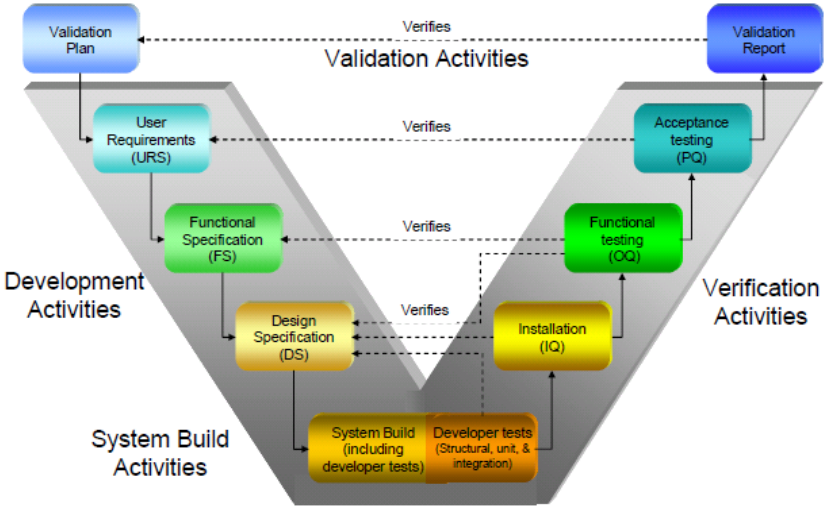
Are there any deviations?

- Regulators want to see documented evidence e.g. of:

  - Incident management
  - Deviation handling
  - Product impacts

Validation
CSV – Computer System Validation





Note that the grey-shaded background represents the classical boundaries of the V-model

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Validation
PI-System CSV – Lifecycle Management

Scenario:

Monitoring of particles in the sterile filling line of non-solid FDFs (Finish Dosage Forms).

- Function Risk Assessment (FRA) for the identification of potential risks

  - GxP criticality
  - impact/failure consequences
  - probability of occurance
  - probability of non-detection

- Change Management

  (traceability, production impact)

- Incident and Deviation Management

  (Impact analysis on product)

- User Management

  (access rights, segregation of duties)

- Disaster & Recovery procedure/tests

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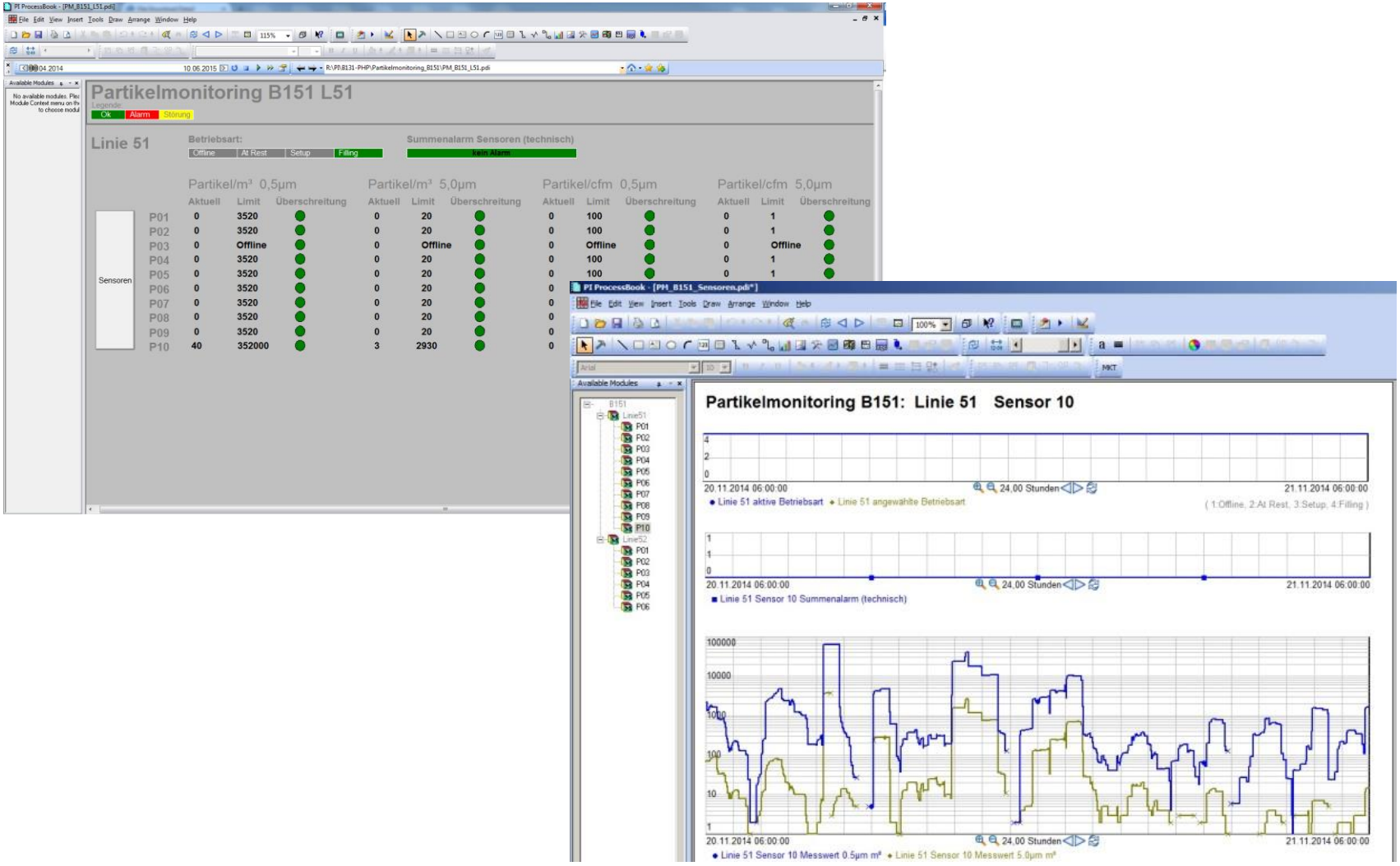
Validation

PI-System CSV – Lifecycle Management



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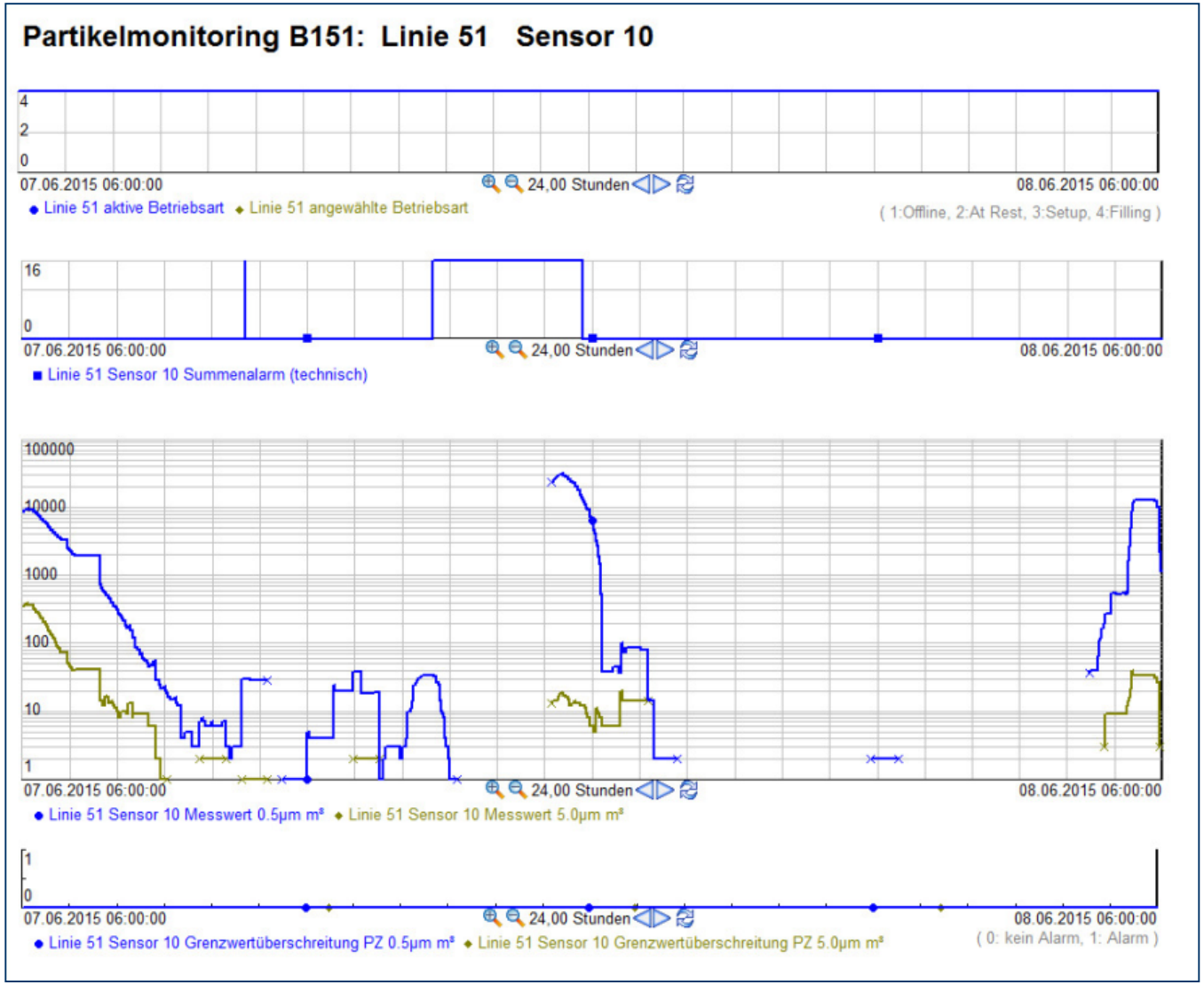
Validation

PI-System CSV – Lifecycle Management



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How the PI System helps Sandoz to cope with regulatory compliance

In the regulated production environment, data are the evidence to your patients and health authorities that your products are safe and effective.

Therefore, IT-System are an integrated part for the development, release, production and post-market surveillance within a product life cycle.

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Business Challenges

A. Continuous increase of regulation requirements, also for IT-Systems (e.g. Data Integrity).

B. Frequent and deep involvement of IT-Systems for production decisions and inspections. Data are part of the batch record.

C. Only one archive for GxP data archiving at site is recommended.

Solution(s)

A. PI-System as the Data Historian implemented.

B. Defined data archive strategy.

C. Sophisticated and stable technology, processes and systems deployed wit PI-System.

Results and Benefits

- System with good standing within our GxP production environment.
- Standard for raw data archiving on a large production site
- As a consequence, good inspection results because of a clear story.

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THANK YOU

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