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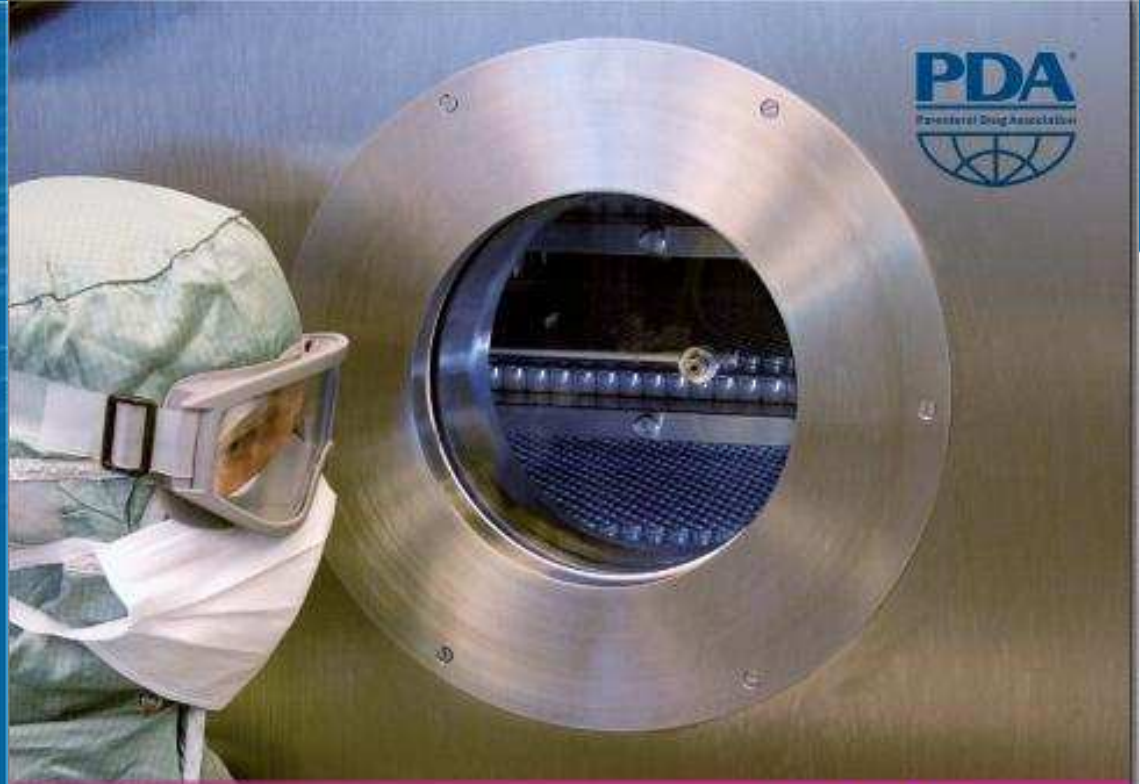


2018 PDA Europe

Freeze Drying in Practice

23–27 April 2018 | Training Course

23–27 April 2018

Martin Christ Gefriertrocknungsanlagen GmbH
Osterode (Harz) | Germany

www.pda.org/URL

Company portrait

Lyo Engineering is your partner in pharmaceutical industry and medical engineering in the areas of management / quality assurance / engineering with more than 10 years of experience in pharmaceutical plant engineering and construction in the fields of project handling and quality assurance.

Among other things our business activities include project management for international freeze drying projects in pharmaceutical industry, planning and monitoring of technical transfer projects of fill- / finish areas and all aspects of GMP quality assurance, for instance classification of equipment components in accordance with GMP risk analysis as qualification basis, GMP-based employee training, performance of external and internal audits, planning and monitoring of acceptance tests (FAT / SAT) and qualification phases (DQ / IQ / OQ / PQ), as well as the creation of the pharmaceutical technical documentation.

We gladly support you in the successful implementation of projects in regulated environments from the URS to the handover to the production.

Lyo Engineering

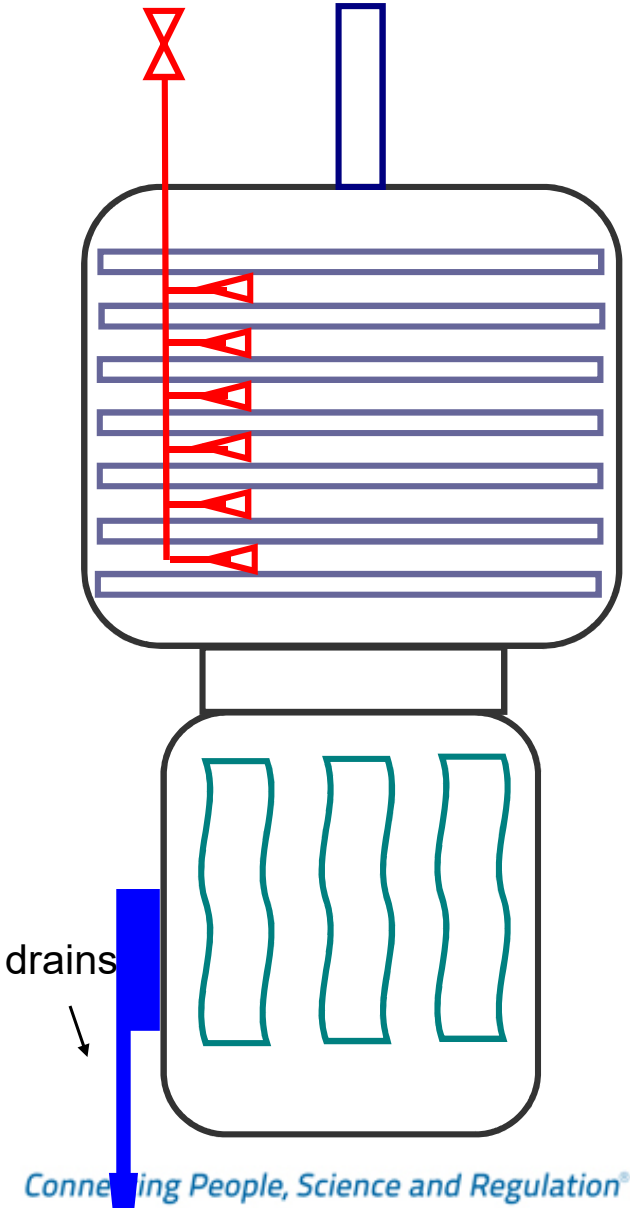
GMP is our passion!

Cleaning and sterilisation

Theory 7:
Cleaning and sterilisation

- CIP / SIP systems
- acceptance of CIP / SIP systems
- cleaning validation
- sterilisation qualification
- turnaround process

CIP / SIP system

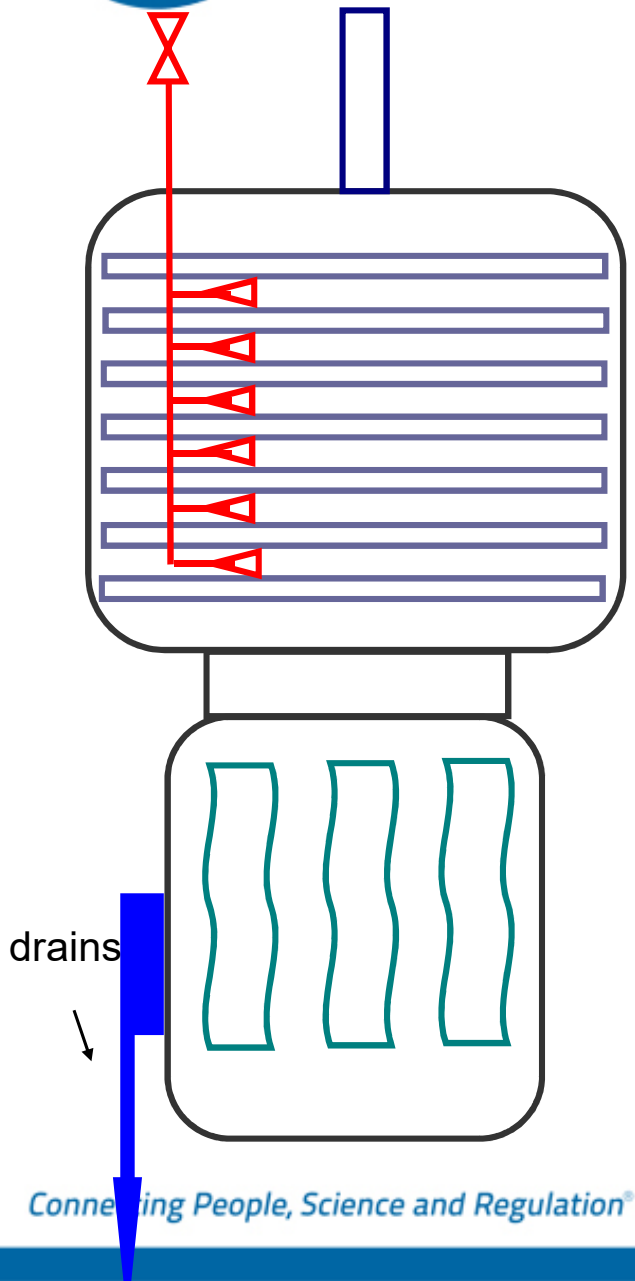


The tasks of a CIP / SIP system consists of cleaning and sterilisation of a machine according to the applicable rules.

In accordance with the GMP guidelines there should be noted the following things:

- assignment of responsibility of cleaning
- creation of cleaning time schedule
- description of cleaning
- define the acceptance criteria of cleaning
- proof of successful system cleaning (validation)

CIP / SIP systems



Technical procedure of CIP / SIP systems:

The system to be cleaned must be easy to clean in accordance to the applicable rules (e. g. no dead spaces, corners should be rounded, etc.).

CIP / SIP systems can be integrated in a freeze dryer or created as stand-alone machine.

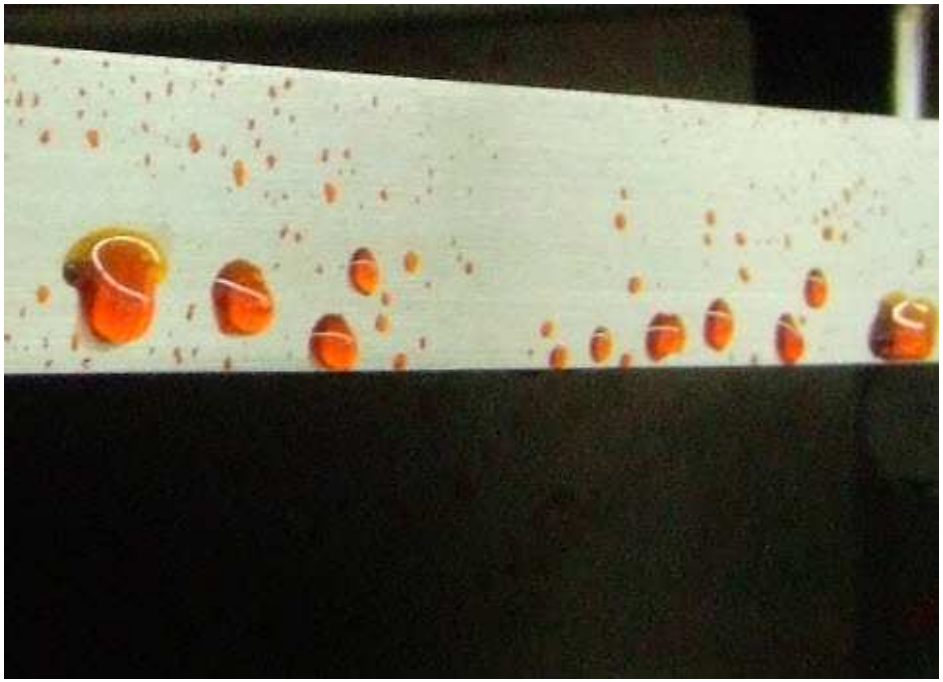
CIP / SIP systems ensure sufficient and qualitative supply of media for machines.

Upstream systems for a CIP / SIP systems are, among other things, clear steam generators, WFI generators and distribution networks (Loops).

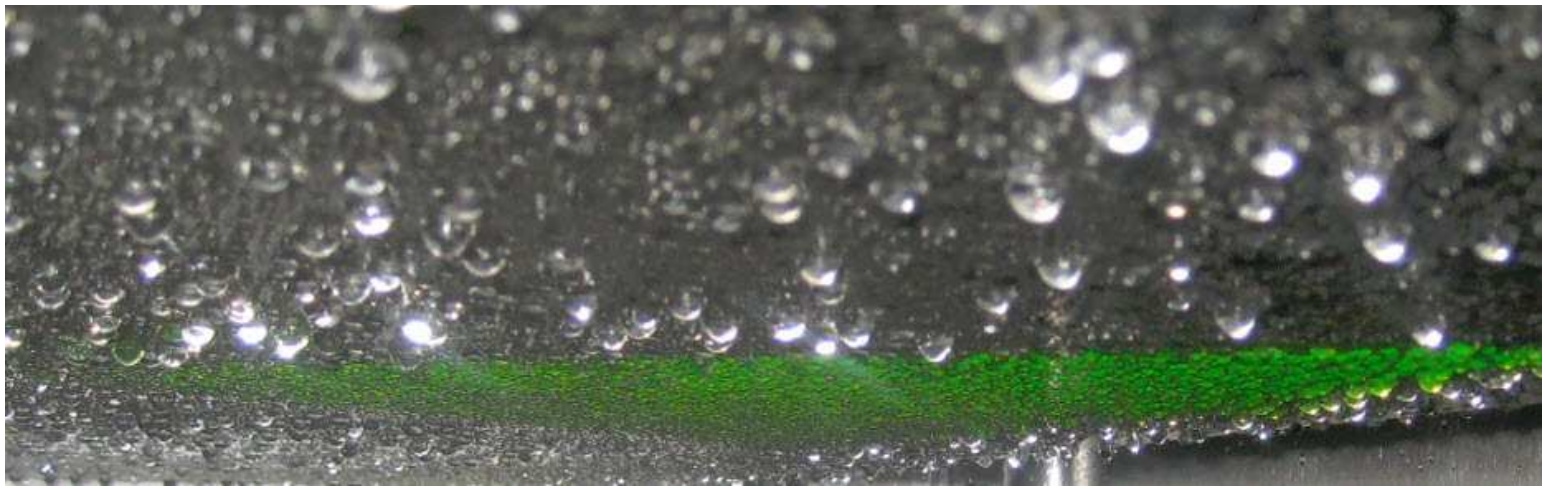
CIP / SIP systems

The riboflavin test can used as proof of solid design of a CIP system.

- the riboflavin test shows potential weakness of system (spray shadows)
- point out cleaning success
- spray shadows quickly shows up



Examples of spray shadows:



CIP / SIP systems

Cleaning validation:

After verification of good design of CIP system, subsequent validation of the cleaning process proves that the process also achieves the necessary cleaning success.

The proof is provided by e. g.:

- cleaning cycles three times, all three cycles should lead to the same result and be reproducible
- proof of cleaning success with bioindicators
- test samples from surfaces

In cases of validation the degree of automation should also take into account. If an automated process is used, it should be specified and validated.

If a manual cleaning takes place, it must also be validated and revalidated at defined time intervals. The employees for this purpose must be appropriately trained.

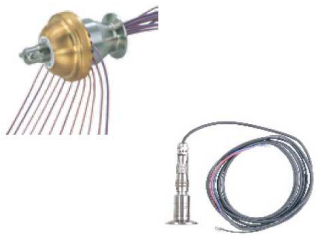
Sterilisation qualification

The qualification of sterilisation generally takes place with extern build-in equipment (recorder). The recorder e. g. can be wired system with thermocouples (online measuring system) or a wireless system (logger).

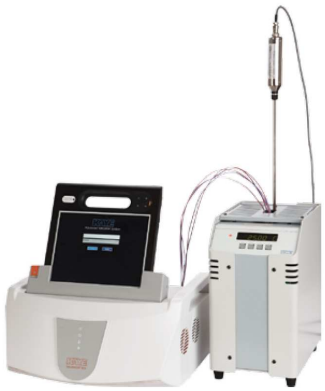
It does not matter what system one happens to be dealing with, before each run there should be an appropriate calibration, as well as after each run a check of the system.

Calibration system with oil

Calibration system dry block



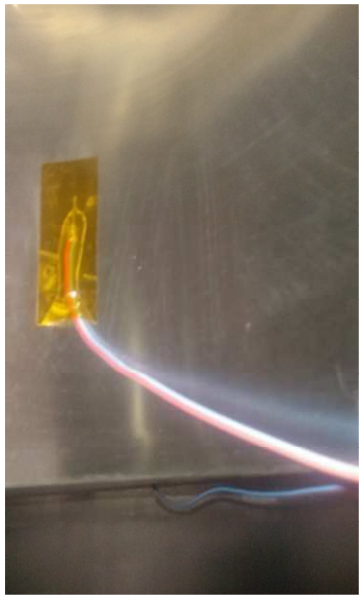
Qualification pout / absolute pressure tube

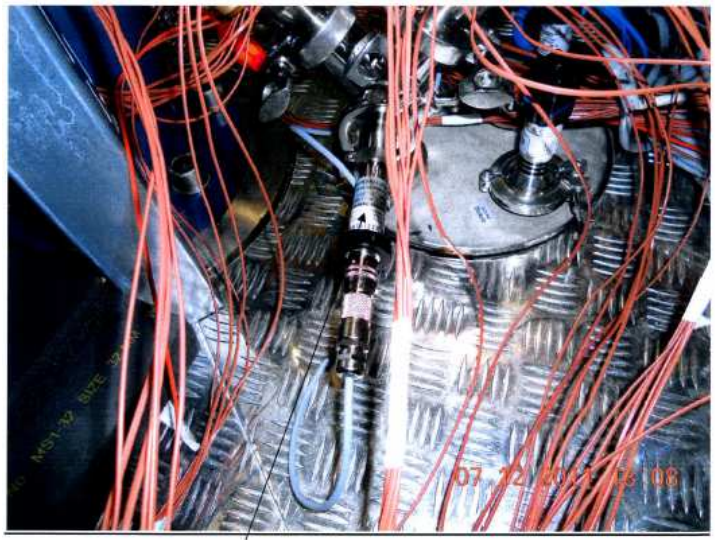


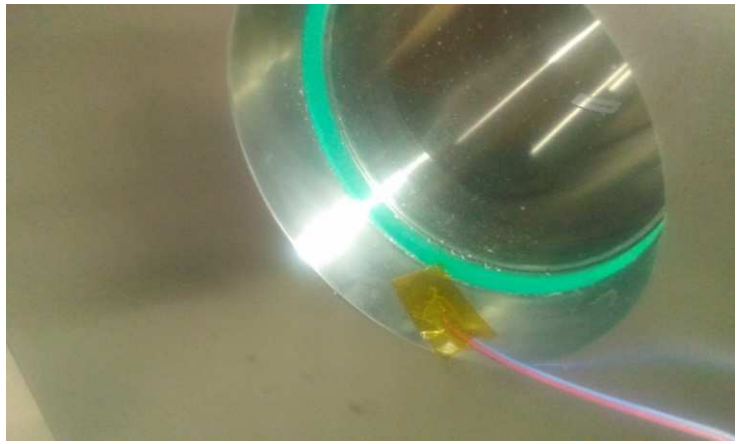
Construction of a recorder system including a temperature standard

CIP / SIP systems

Examples:



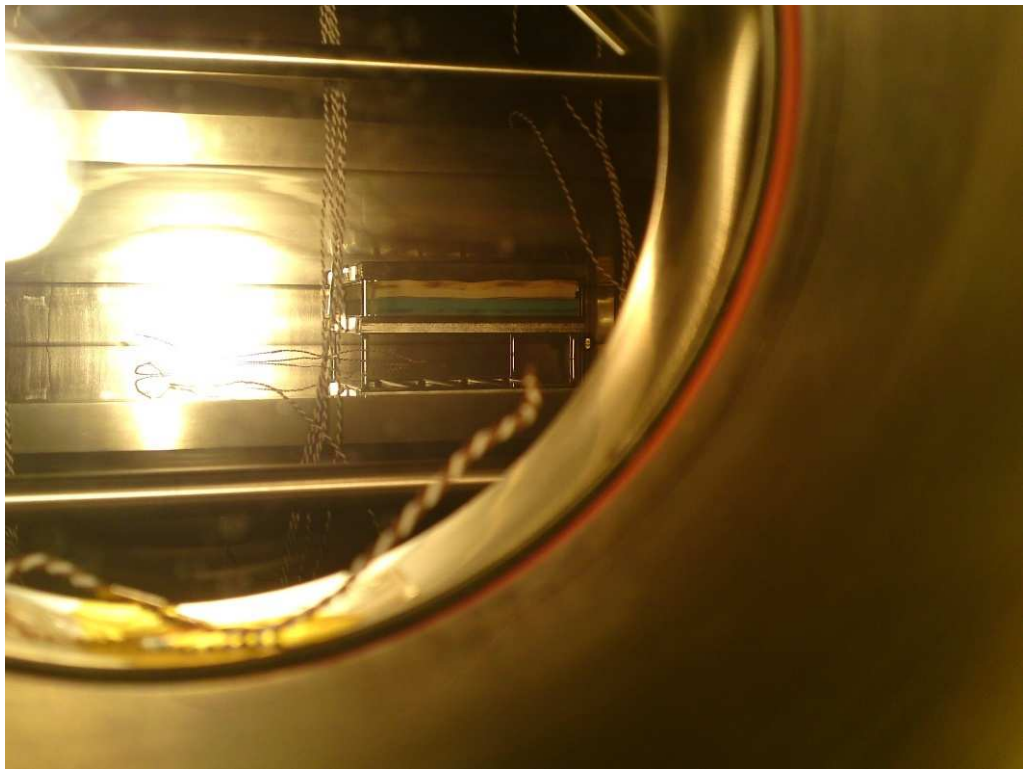




CIP / SIP systems

Addition to the qualification and the sterilisation process:

- use of bioindicators
- use of Bowie-Dick-Test



CIP / SIP systems

BACKUP:

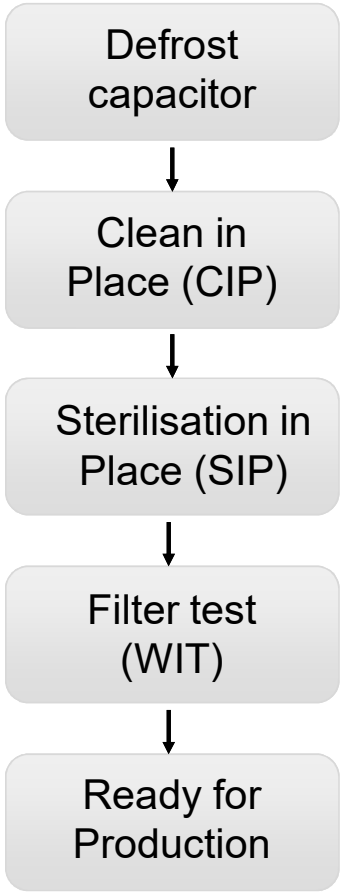
- The Fluids (e.g. sodium hydroxide, acetic acid) are injected with dosing valves into the suction line of the CIP-circulation pump. A conductivity sensor is required in circulation system to monitor the dosing.
- After cleaning the dosing fluids must be completely removed from the chamber. These include that the complete system must be rinsed with WFI The rinsing process is controlled with a second conductivity sensor at drain.

Condumax

Indumax (both Endress+Hauser)

CIP / SIP systems

Turnaround - process:



The turnaround-process is a machine involving several processes like defrost / CIP / SIP / WIT).

The turnaround-time shows the time from the end of production (unloading GT) till the start of a new production batch.

Attention:

After the turnaround process the system is not endlessly sterile. Here the form of validation of a sterile hold time has to be determined. This time should be fixed at relevant machines (e. g. as sterile bit).

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