Theory 8

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PDA EU
Freeze – Drying In Practice

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Osterode am Harz, Germany

Company portrait

With almost 15 years of experience Pharmbiocon GmbH in Bad Endbach is a reliable partner of the pharmaceutical and medical devices industry.

The company can draw from its resource pool of technical engineers (biotechnology, pharmatechnology, life science technology, process engineering and mechanical engineering) and natural scientists (biologists, chemists).

Main business areas are project leads, engineering, management and consulting services for international projects, planning and surveillance of technical transfer projectes in fill / finish facilities, GMP quality assurance as well as engineering of complex processes.
Furthermore, Pharmbiocon GmbH can be contracted as a general planer. The benefit for the customer will be the pooling of the ordering process with a single person of contact on site, combined with high fexibility and a reduced risk of down time.

In addition, we offer a fully equiped bio safety level II laboratory to our costumers. A pilot plant lyophilisation facility can be use here to develop or optimize your processes or performe failure mode analyses (production galenics).

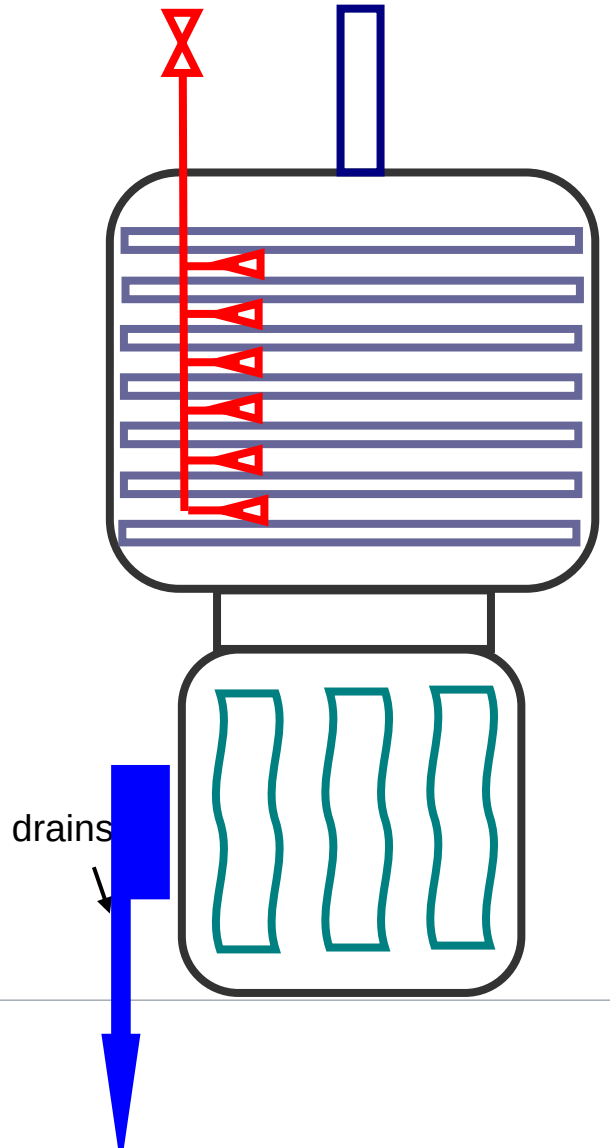
Pharmbiocon
Life Science Engineering

Cleaning and sterilisation

Theory 8:
Cleaning and sterilisation

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

CIP / SIP systems

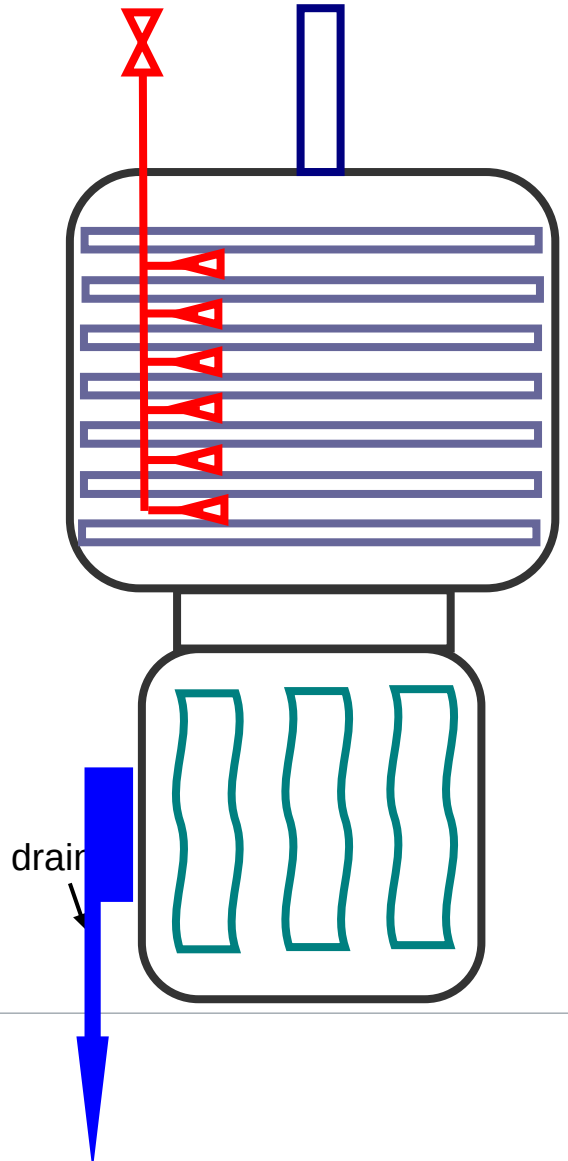


The aim of a CIP / SIP system is to clean the system and to sterilize the Freeze Dryer according to Specification.

GMP guidelines:

- 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



Prozess of CIP / SIP:

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

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

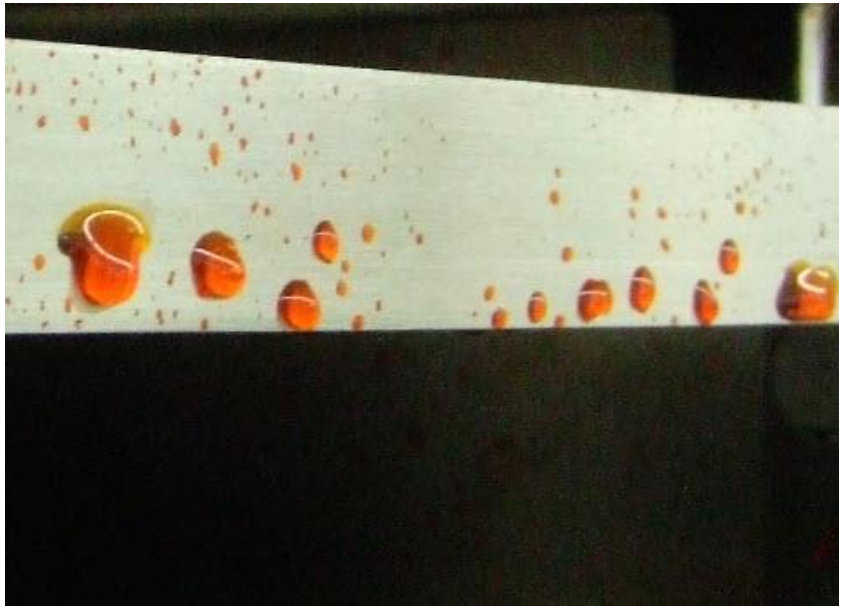
CIP / SIP systems ensure sufficient and qualitative supply of media for machines.

The Media supply for a CIP / SIP system, depends on other Equipments e.g. clean steam generators, WFI generators and distribution Loops.

CIP / SIP systems

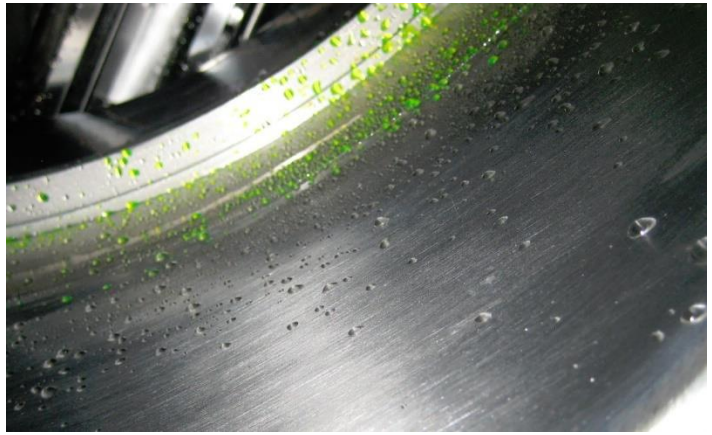
The riboflavin test can used as proof of solid design of a the CIP system.

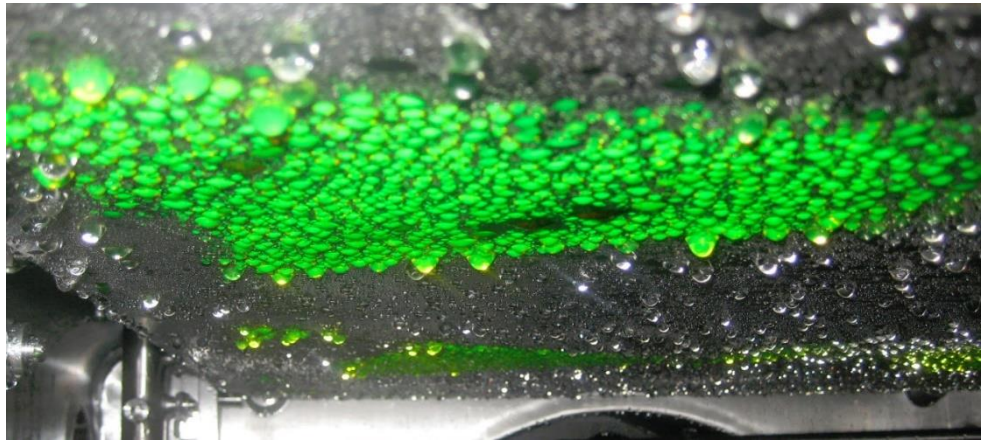
- the riboflavin test shows potential weakness of the CIP system (spray shadows)
- demonstrate cleaning success
- spray shadows can help to setup the CIP System

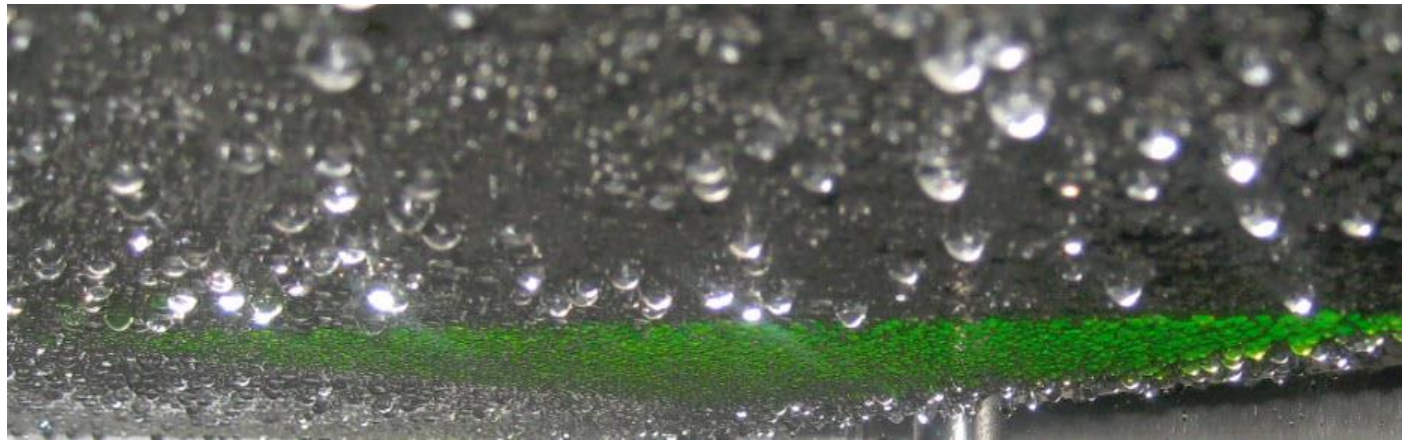


CIP / SIP systems

Examples of spray shadows:







CIP / SIP systems

Cleaning validation:

After verification of good design of CIP system, the cleaning validation (CV) can be stared. The CV of the cleaning process demonstrate the Process is valid to do the same each Run and also that the Process have the expacted cleaning success.

Testmethods are e. g.:

- do the cleaning cycle three times, all three cycles should have the same result and be reproducible
- proof of cleaning success with bioindicators
- test samples from surfaces (Swap)

In cases of validation the automation Part should also checked, If an automated process is used the process should be validated (Software Validation).

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

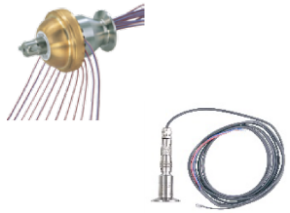
Sterilisation qualification

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

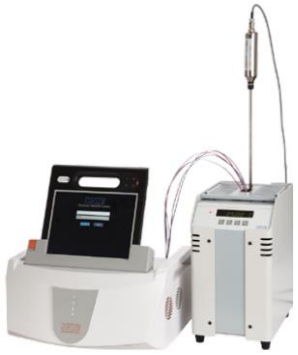
Before each run the Equipment should be calibrated, as well as after each run a system check should be carried out.

Calibration system with oil

Calibration system dry block



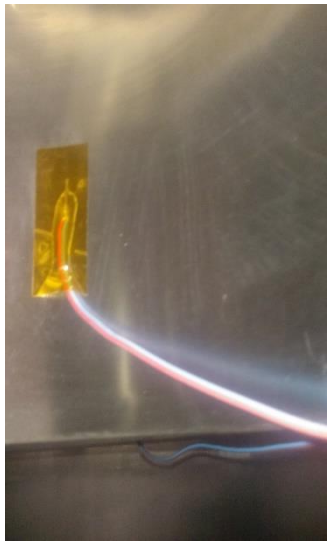
Qualification pout / absolute pressure tube

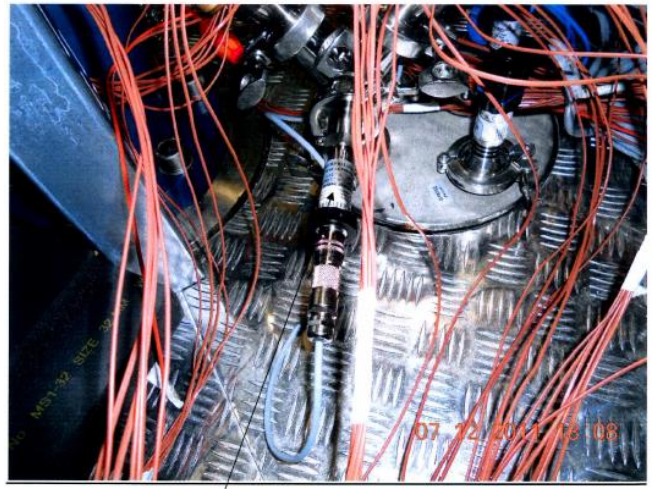


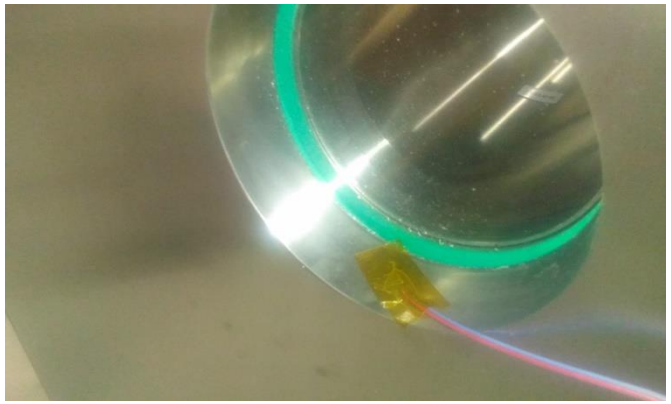
Construction of a recorder system including a temperature standard

CIP / SIP systems

Examples:



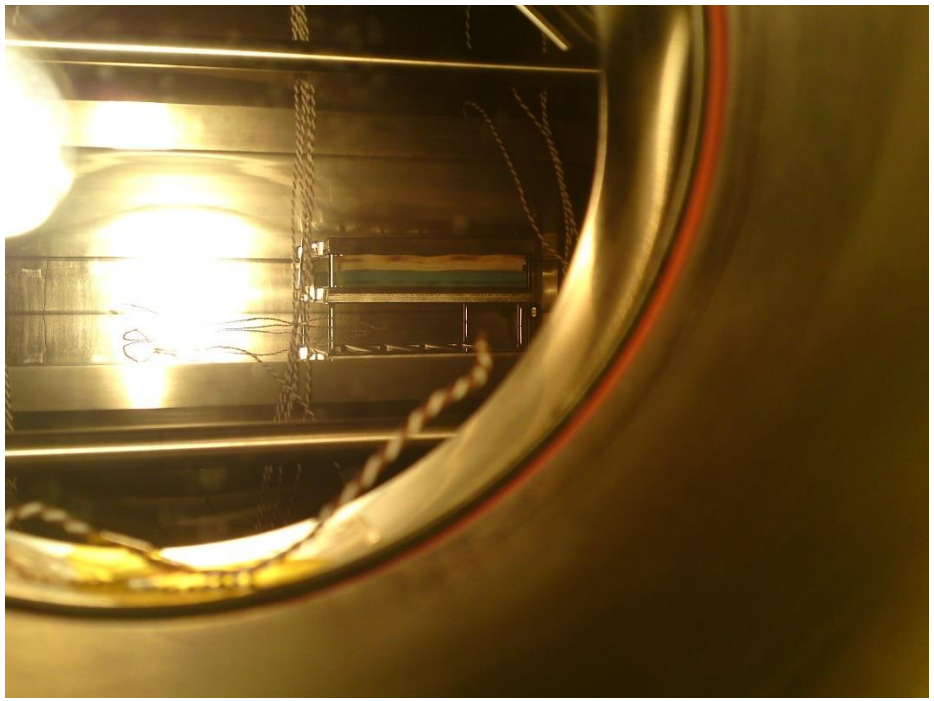




CIP / SIP systems

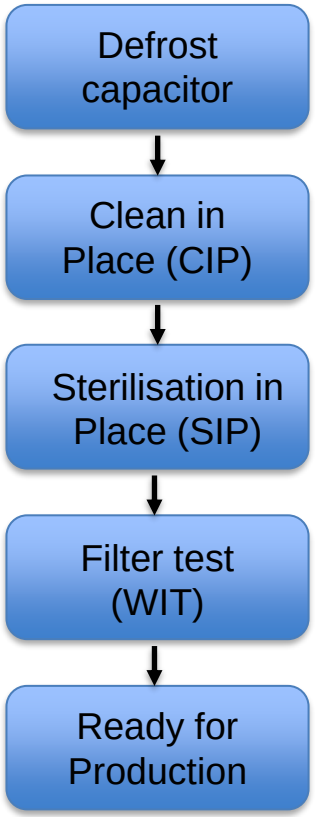
Special Tests for sterilization process are:

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



CIP / SIP systems

Turnaround - process:



The turnaround process includes different processes like defrost / CIP / SIP / WIT.

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

Attention:

After the turnaround process the system is not endlessly sterile. A 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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