Strategies for Cleaning Process Validation in the Pharmaceutical Environment

Enabling automated cleaning of complex machine parts for an efficient validation

Melich Dietrich Seefeldt & Dr. Olaf Neuschaefer-Rube

20th April 2021

FEDEGARI GMBH

Outline

„Enabling automated cleaning of complex machine parts for an efficient validation“

1	Regulative definitions & automated cleaning	6
2	Complex parts’ cleaning & validation	9
3	Customer trials & cases	11

This is us – Fedegari

Company overview

- Fedegari founded in Pavia, Italy in **1953**
- Global provider of machines & integrated solutions for the **Contamination Control** in the **Bio-/ Pharmaceutical industry**
- Globally acting, family-owned group with 7 international subsidiaries and **550** employees world-wide

FEDEGARI GMBH

Fedegari portfolio

Turn-key solutions & required services for the techno-economic production of innovative sterile drugs

FEDEGARI GMBH

1. Regulative definitions & automated cleaning

Regulative definitions & automatic cleaning

Global regulatory bodies define cleaning validation similarly & state concerns about manual cleaning to deliver insufficient scientific data

Source	Definition validation	Automatic vs. manual application
FDA Guide to Inspections of Validation of Cleaning Processes (1993)	*„In the end, the test of any **validation** process is whether **scientific data** shows that the system **consistently does as expected** and produces a result that consistently **meets predetermined specifications**“*	***„How variable are manual cleaning processes from batch to batch and product to product?“***
Annex 15: Qualification and Validation (2015)	*„Cleaning validation is documented evidence that an approved cleaning procedure will reproducibly remove the previous product or cleaning agents used in the equipment below the scientifically set maximum allowable carryover level.“*	***„10.15. Where manual cleaning of equipment is performed, it is especially important that the effectiveness of the manual process should be confirmed at a justified frequency.“***
PIC/S 006-3 – Validation Master Plan (2007)	*„7.1.3 …Cleaning Validation is documented evidence that an approved cleaning procedure will provide equipment which is suitable for processing of pharmaceutical ingredients (APIs)“*	***„How many times need a manual cleaning process be applied to ensure adequate cleaning of each piece of equipment?“***

Complex parts' cleaning & validation

Within the life cycle concept of the 2011 FDA guidance the design of the key-equipment-to-be-cleaned is an important factor, to reach a validatable cleaning procedure, but…

Stage 1: Process Design
- Define the Knowledge Space
- Identify Critical Process parameters
- Determine Control Strategy

Stage 3: Process Monitoring
- Monitoring of Critical Process Parameters as Part of APR and Other Monitoring Programs

Stage 2: Process Qualification
- Equipment / Utility / Facility Qualification
- Process Performance Qualification

*„The **functionality** and limitations of commercial **manufacturing equipment** should be **considered** in the **process design**, as well as predicted **contributions to variability** posed by different component lots, production operators, environmental conditions, and measurement systems in the production setting.“*

*“…The results of **DOE studies** can provide **justification** for establishing **ranges** of incoming component quality, **equipment parameters**, and in-process material quality attributes…“*

FEDEGARI GMBH

2. Complex parts’ cleaning & validation

Complex machine parts

…many complex machine parts often cannot be cleaned automated, compared to standard ones

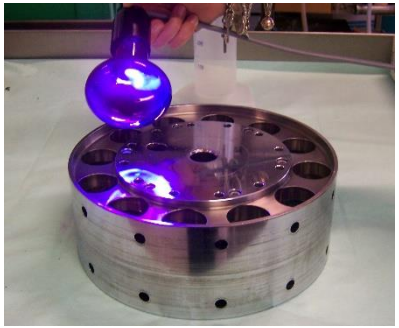
Complex machine parts

Examples:

- Tabletting devices,
- Multi-port containers
- Custom-made production devices
- …

Influencing factors on complexity:

- Accepted functional design,
- Residue acceptance criteria,
- Product quality expectations
- Production efficiency.
- …



- *Specifically **custom-engineered devices** in automatic washers can guarantee **full coverage** of most **complex load surfaces.***

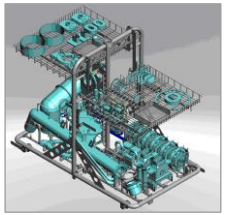
- *They can **treat** defined peculiarities and **enable standardization** and **proven reproducibility of procedures** and therefore the required "scientific data" for process validation.*

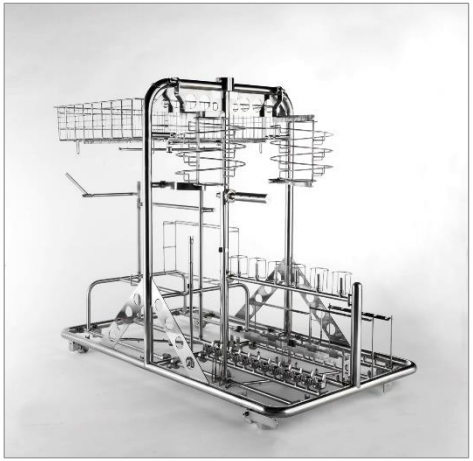
FEDEGARI GMBH

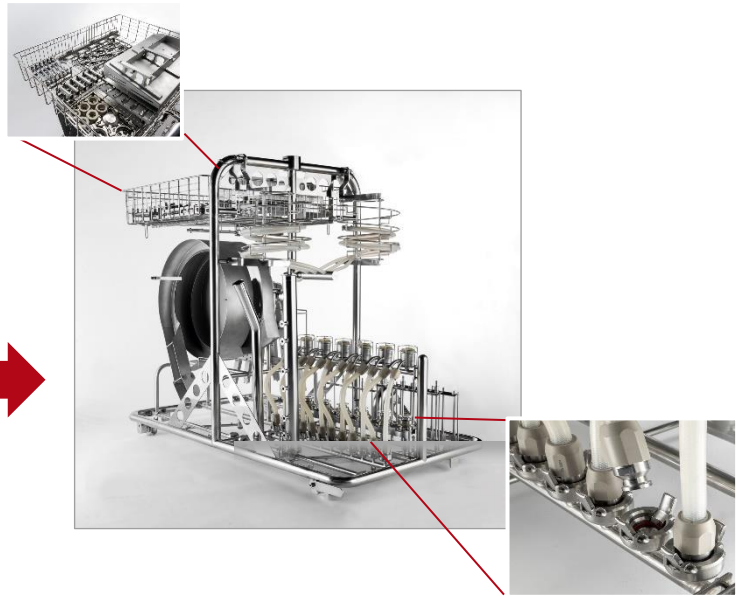
3. Customer trials & cases

Reaching validated cleaning process through design & quality

Flexible & module-engineered design of washing racks for dedicated loads







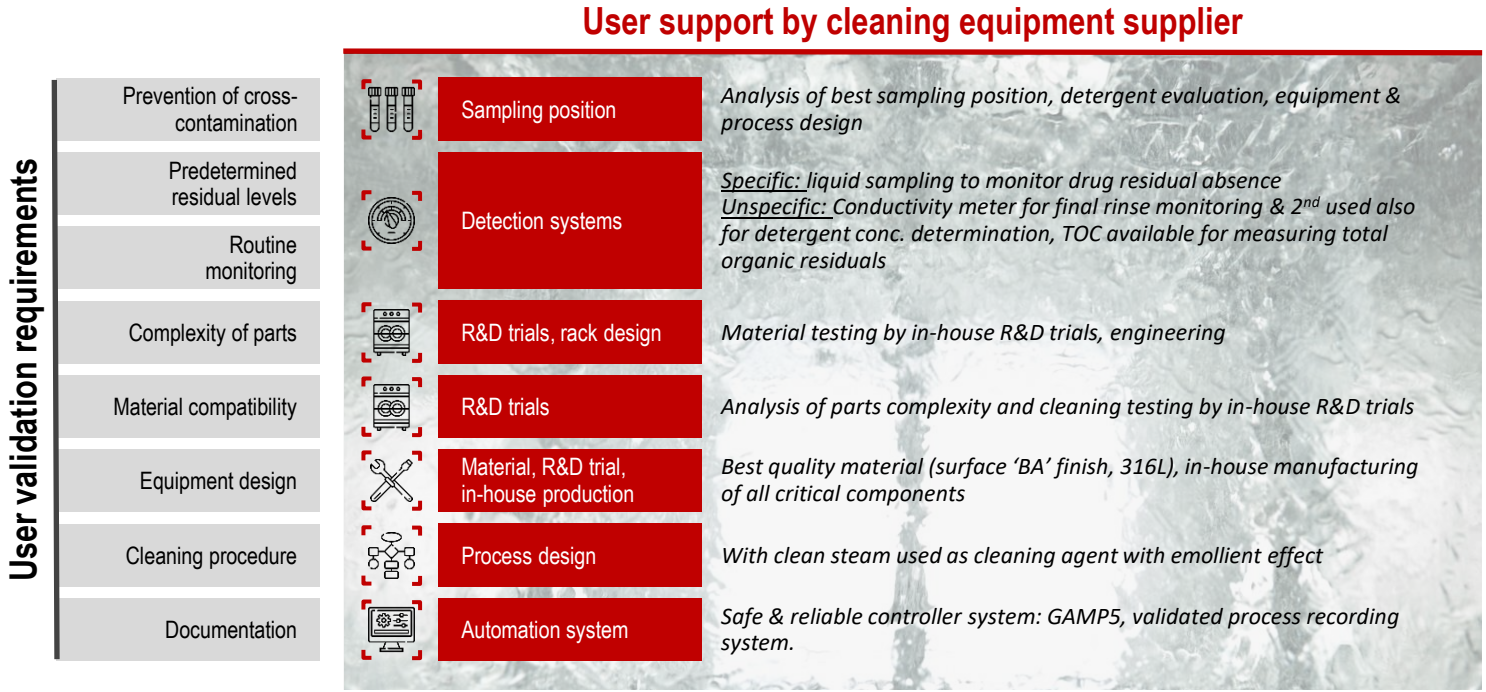
The washing racks can include:

- Nozzles
- Spray arms
- Rotating spray balls
- Water blades
- Orifices

FEDEGARI GMBH

Automated equipment solutions for customer cleaning validation

Collaborative activities to fascilitate verifiable cleaning strategies: Overview



FEDEGARI GMBH

Case 1: Reaching cleaning requirements using design & quality

Collaborative activities to fascilitate verifiable cleaning strategies: R&D trials

Removal of pharmaceutical drug (cytotoxic)
Manufacturer requirements: parts visual clean and dry

Identification of critical parts & areas for automated cleaning trials using Mannitol as ‚placebo' contamination (shows similar properties as drug)

Identification of the worst part for automated cleaning

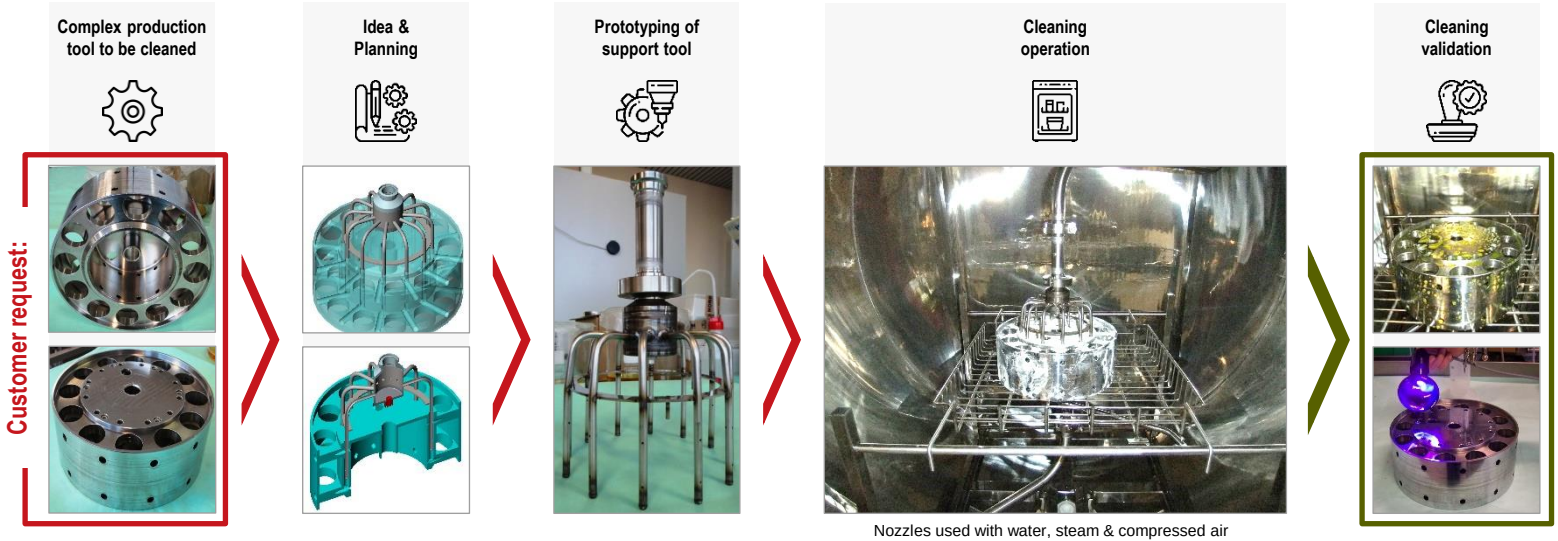
FEDEGARI GMBH

Case 1: Reaching cleaning requirements using design & quality

Collaborative activities to fascilitate verifiable cleaning strategies: R&D trials

Removal of pharmaceutical drug (cytotoxic)

Trial activities simplify cleaning process verification tasks for routine cleaning process



Nozzles used with water, steam & compressed air

FEDEGARI GMBH

Case 2: Reaching cleaning requirements using design & quality

Collaborative activities to fascilitate verifiable cleaning strategies: R&D trials

Gelatine removal from capsule manufacturing part
Manufacturer requirements: Reducing microbial contamination (< 30 cfu/ml) and parts visual clean

Assembled production part

'Placebo' contamination simulation, using "coloured" gelatine for R&D cleaning trials

Artificially 'contaminated' production part ready to perform 1st cleaning trials

FEDEGARI GMBH

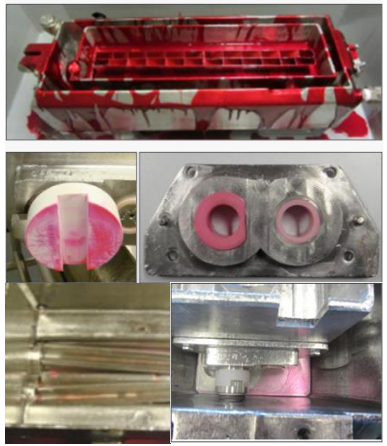
Case 2: Reaching cleaning requirements using design & quality

Collaborative activities to fascilitate verifiable cleaning strategies: R&D trials

Gelatine removal from capsule manufacturing part

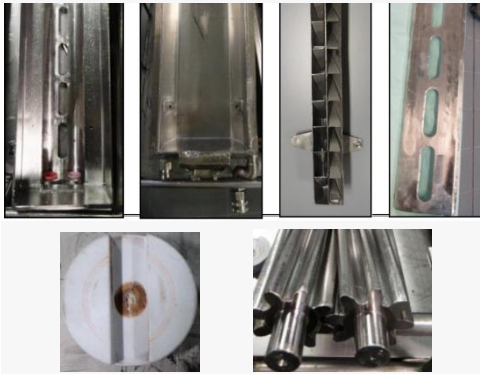
Cleaning trials leads to engineered solutions towards automated cleaning process

Identifying critical areas during initial cleaning trials



Testing design: simultaneous steam injection (100°C) and mechanical action by air bubbling

Test resulting in ‚visible clean' parts and microbial reduction is possible through subsequent sterilisation



FEDEGARI GMBH

Washer-Steriliser: Validated ‘cleaning’ & ‘sterilization’ in one unit

Automated cleaning & subsequent sterilization can be performed as validated processes with just a single equipment

FOWS Washer-Sterilizer features:

- Automated cleaning as validated process
- Saturated steam sterilization as validated process

- Joint (and single) validated and automated cleaning & sterilization processes
- Saving of installation space
- Increased efficiency & time saving
- Cost savings (in investment & maintenance)

FEDEGARI GMBH

FEDEGARI GMBH

www.fedegari.com/de

Ihr Full-Service Partner für Sterilisationslösungen

Wir sind für Sie da:

Dr. Olaf Neuschäfer-Rube

- Technischer Vertrieb Industriemaschinen
- Prozessdesign
- Projektentwicklung

Melich Dietrich Seefeldt

- Leitung Niederlassung
- Vertriebs-, Angebots & Vertragsmanagement
- Investitionsberatung

Igor Vidari

- After-Sales zuständig
- Installation & start-up
- Validation Techniker

+49 (0)69 9074 66-200

Labor@de.fedegari.com

Industrie@de.fedegari.com

Ersatzteile@de.fedegari.com

Thank you

www.fedegari.com

FEDEGARI GMBH