borer

advanced cleaning solutions

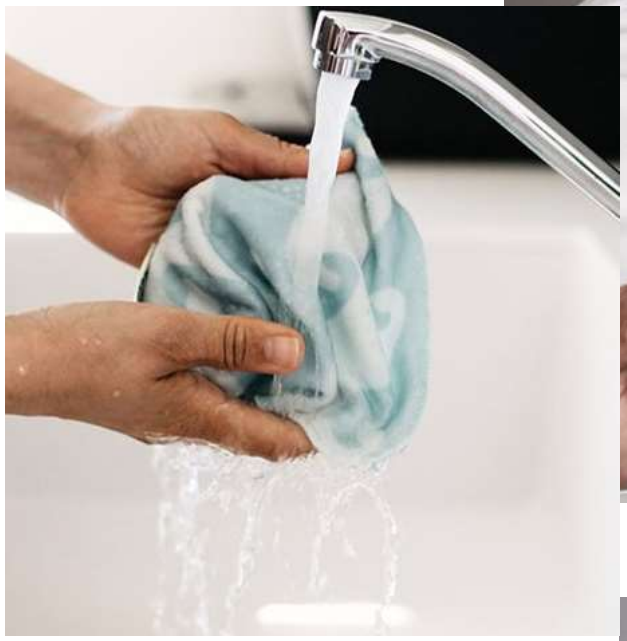
Wie bestimme ich die «cleanability»? Erfahrung und Lösungen für validierte Reinigungsprozesse.

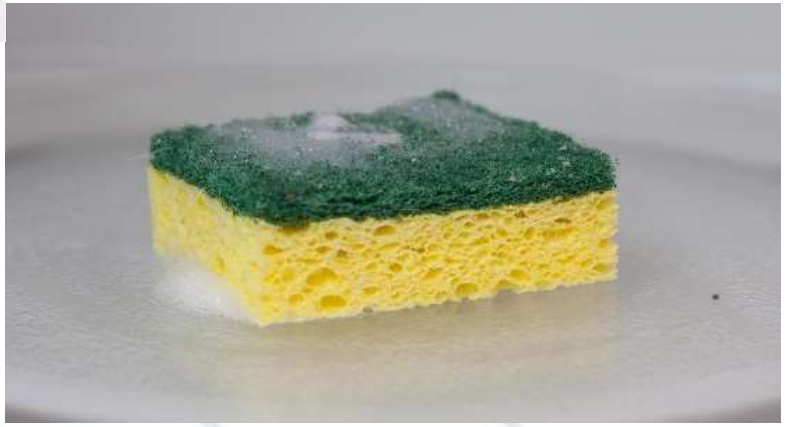
Gionatan Turacchio

International Sales Manager Life Sciences

04. November 2019

…und jetzt?!





Definition

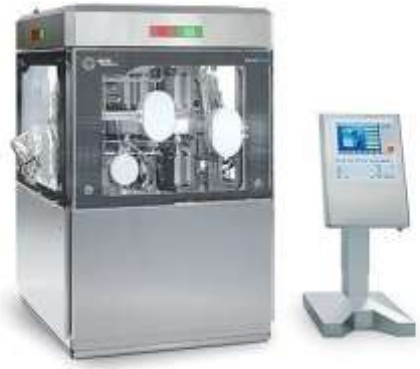
Wie lässt sich „Reinigbarkeit“ beschreiben?

10.10. Where a worst case product approach is used as a cleaning validation model, a scientific rationale should be provided for the selection of the worst case product and the impact of new products to the site assessed. Criteria for determining the worst case may include solubility, cleanability, toxicity and potency.

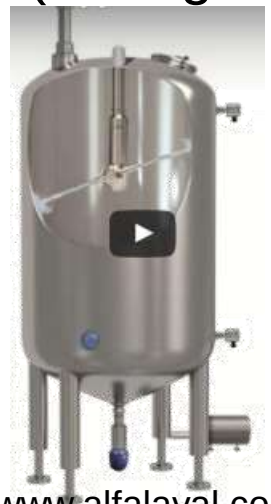
(EU GMP Annex 15: Qualification and Validation)

Reinigungsarten – produktberührende Flächen

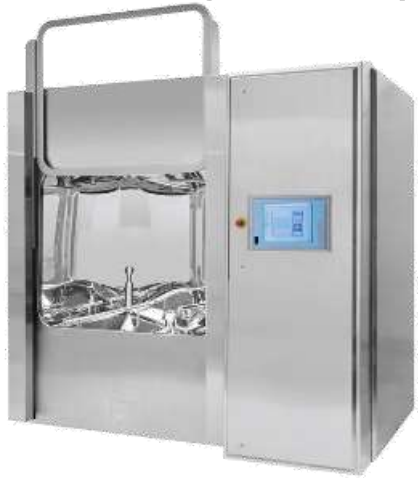
- Trocken (Staubsauger)
- CO_2 Strahlen
- Wässrig basierte Reinigung mit/ohne Reiniger
- Lösungsmittel (z.B. Methanol) basierte «Reinigung»
- WIP washing in place (primär Dekontamination)
- CIP cleaning in place (keine Demontage vor Reinigung)
- COP cleaning out of place (Reinigung demontierter Anlagenteile)



www.fette-compacting.com



www.alfalaval.com



www.muellercleaning.com

Auswahl des geeigneten Reinigers

- Optimales Wirkungsspektrum
- Materialverträglichkeit
- Vollständige Dokumentation
- Analytik: Verfügbarkeit geeigneter Analysenmethoden
- Entsorgungs- und Umweltbetrachtungen
  - pH, Temperatur
  - Detergenzienverordnung EU
  - Abbaubarkeit der Inhaltsstoffe
- Arbeitsplatzsicherheit
- Toxikologie (Grenzwerte basierend auf PDE-Dokumentation)
- Langfristige Verfügbarkeit
- Informationen zu Änderungen (Change Control)
- Kompetenter Anbieter/Hersteller: **Borer Chemie AG**

Wieso rückstandsfrei?

Verschiedene Regularien

- Regularien
  - **21 CFR 211.63**: equipment design, size, and location shall be appropriate to facilitate operations for its intended use and for its cleaning and maintenance.
  - **21 CFR 211.67(a)**: equipment and utensils shall be cleaned, maintained, and, as appropriate for the nature of the drug, sanitized and/or sterilized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product.
  - **Regulatory Agency Challenge**… prove that you can clean production equipment adequately, such that residues from the production of one product will not carry over an cross-contaminate the next product…

(FDA, OECD)

Wieso rückstandsfrei? II

Patientensicherheit, optimale Produktivität

- Reinheit & Unbedenklichkeit des Medikamentes
  - Vorbeugung von Kreuzkontamination
    - Produktrückstände
    - Aktivstoffrückstände
    - Hilfsstoff-, Reinigungsmittel-, etc.. Rückstände
    - Rückstände chemischer oder mikrobiologischer Natur
  - Die Integrität des Endproduktes aufrechtzuerhalten

Wieso rückstandsfrei? III

Werterhaltung, Produktivität und Wirtschaftlichkeit

- Erhöhung der Lebensdauer von Produktionsanlagen
  - Anwendungen mit NaOH/KOH über längere Zeit bei höheren Temperaturen können zu Korrosion/Verfärbungen von Edelstahl sowie Korrosion/Glas führen
- Erhöhung der Produktivität (Wartung Unterhalt, Ausfälle)
- Das Verhältnis Kosten / Leistung

Was „sagt“ der neue Annex 15?

„Life Cycle Approach“

without introduction of additional requirements to EudraLex, Volume 4, Part II. It is a GMP requirement that manufacturers control the critical aspects of their particular operations through qualification and validation over the life cycle of the product and process. Any planned changes to the facilities, equipment, utilities and processes, which

General

A quality risk management approach should be applied throughout the lifecycle of a medicinal product. As part of a quality risk management system, decisions on the scope and extent of qualification and validation should be based on a justified and documented risk assessment of the facilities, equipment, utilities and processes. Retrospective

Warning letters…

https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/newton-laboratories-inc-dba-newton-homeopathics-559612-04232019

Fundamental GMP defects at ... | Newton Laboratories Inc DB...

the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).

You failed to demonstrate that your cleaning practices are sufficient to remove potential contaminants from your equipment product contact surfaces.

nt to remove potential

ufacturing equipment
d from your equipment
s greater than 300 CFU/mL and total organic carbon (TOC) with test results as high as 896,692 parts per billion (ppb). These manufacturing conditions present a significant cross-contamination risk between drug products. They also pose a potential contamination risk of drug products with microbes, cleaning agents, and drug residues.

In your response, you state that you will perform cleaning validations in a timely manner. However, your response cannot be fully evaluated because you did not provide the results of any validation studies to support the effectiveness of your cleaning practices.

In response to this letter, provide the following:

• A comprehensive plan to evaluate cleaning procedures and practices, and validation studies for each piece of manufacturing equipment used to manufacture more than one product.

o ensure that your cleaning
eaning validation protocol
uld include, but not be limited

o Evaluating drugs of the highest toxicity;
o Assessing drugs of the lowest solubility in their cleaning solvents;
o Evaluating drugs with characteristics that make them difficult to clean; and,
o Swabbing equipment locations that are most difficult to clean.

solvents;
fficult to clean; and,
clean.

• A summary of updated standard operating procedures (SOP) that ensure an appropriate program is in place for verification and validation of cleaning procedures for new products, processes, and equipment.

Firm Name	City	State	Country/Area	Inspection En	Program Are	CFR/Act Number	Short Description	Long Description
Austarpharma	Edison	NJ	United States	05.01.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent malfunctions and cc
CMIC CMO U	Cranbury	NJ	United States	11.01.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent malfun
Cape Drugs	Annapolis	MD	United States	22.01.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
Wasserburge	Wasserburg a. Inn		Germany	23.01.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent contamination that v
Recro Gaines	Gainesville	GA	United States	24.01.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contam
Botanic Beau	Las Vegas	NV	United States	02.02.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
The Original E	West Warwic	RI	United States	02.02.2018	Drugs	21 CFR 211.67(b)(2	Cleaning SOPs/schedules	Procedures for the cleaning and maintenance of equipment are deficient regarding maintenance
Vista Pharma	Nalgonda District		India	09.02.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent malfun
Patheon Phar	Cincinnati	OH	United States	14.02.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent contamination that v
Amol Pharma	Sanganer, Jaipur		India	16.02.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
Aurobindo Ph	Medak District, Hyderabad		India	20.02.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
Aurobindo Ph	Medak District, Hyderabad		India	20.02.2018	Drugs	21 CFR 211.67(b)(3	Cleaning SOPs/instructions	Procedures for the cleaning and maintenance of equipment are deficient regarding sufficient det
Denver Solutio	Englewood	CO	United States	23.02.2018	Drugs	21 CFR 211.42(c)(1	Cleaning System	Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the ro
BioDiagnostic	Brea	CA	United States	27.02.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
MSN Laborat	Rangareddy District		India	28.02.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
AmLion Tooth	Petaling Jaya		Malaysia	02.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
DJB Gas Ser	Salt Lake City	UT	United States	07.03.2018	Drugs	21 CFR 211.67(b)(3	Cleaning SOPs/instructions	Procedures for the cleaning and maintenance of equipment are deficient regarding sufficient det
Jiangsu Provi	Changzhou		China	09.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent contamination that v
Juzen Chemi	Toyama		Japan	09.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned at appropriate intervals to prevent contamination that wou
Sun Pharmac	Cranbury	NJ	United States	09.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent contamination that v
Tomita Pharm	Naruto		Japan	09.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent malfun
Piramal Phar	Lexington	KY	United States	14.03.2018	Drugs	21 CFR 211.42(c)(1	Cleaning System	Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the ec
Mylan LLC.	Caguas	PR	United States	15.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned at appropriate intervals to prevent contamination that wou
Mylan LLC.	Caguas	PR	United States	15.03.2018	Drugs	21 CFR 211.67(b)(3	Cleaning SOPs/instructions	Procedures for the cleaning and maintenance of equipment are deficient regarding sufficient det
California Pha	Camarillo	CA	United States	23.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
Alkem Labora	Daman		India	27.03.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not at appropriate intervals to prevent that would alter the safety, ident
ABCO Labora	Fairfield	CA	United States	11.04.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamin
Mylan Pharma	Morgantown	WV	United States	12.04.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
Mylan Pharma	Morgantown	WV	United States	12.04.2018	Drugs	21 CFR 211.67(b)(6	Cleaning SOP/inspection	Procedures for the cleaning and maintenance of equipment are deficient regarding inspection of
New Era Natu	Durango	CO	United States	13.04.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned at appropriate intervals to prevent contamination that wou
Q A Laborato	Kansas City	MO	United States	19.04.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contam
Aurobindo Ph	Mahabubnagar	District	India	04.05.2018	Drugs	21 CFR 211.42(c)(1	Cleaning System	Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the ro
Bayer de Mex	Lerma		Mexico	11.05.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent malfunctions and cc
Eriochem SA	Parana		Argentina	22.05.2018	Drugs	21 CFR 211.42(c)(1	Cleaning System	Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the ro
Germiphene (	Brantford		Canada	24.05.2018	Drugs	21 CFR 211.67(b)(6	Cleaning SOP/inspection	Procedures for the cleaning and maintenance of equipment are deficient regarding inspection of
Farmaqro, S.	Santiago De Queretaro		Mexico	25.05.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamin
Mission Hills,	San Jose Iturbide		Mexico	25.05.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
Apotek Produ	Kungens Kurva		Sweden	01.06.2018	Drugs	21 CFR 211.67(b)(6	Cleaning SOP/inspection	Procedures for the cleaning and maintenance of equipment are deficient regarding inspection of
Pekana Natur	Kislegg		Germany	01.06.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamin
Selder S.A. d	Ciudad De Mexico		Mexico	01.06.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamin
Parfums Chri	St Jean de Braye		France	08.06.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not at appropriate intervals to prevent that would alter the safety, ident
Hale Cosmeci	Bloomington	IL	United States	20.06.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamin
American Pha	Fort Worth	TX	United States	21.06.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contam
Genentech, Ir	Hillsboro	OR	United States	05.07.2018	Drugs	21 CFR 211.67(b)(2	Cleaning SOPs/schedules	Procedures for the cleaning and maintenance of equipment are deficient regarding maintenance
Aizant Drug R	Rangareddy District, Hydera		India	13.07.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamin
Tec Laborato	Albany	OR	United States	13.07.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
Andapharm, L	Fort Lauderda	FL	United States	18.07.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contam
Actavis Labor	Davie	FL	United States	19.07.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned at appropriate intervals to prevent malfunctions that would
Laboratorios I	Pueblo Yecapixtla		Mexico	20.07.2018	Drugs	21 CFR 211.67(b)(2	Cleaning SOPs/schedules	Procedures for the cleaning and maintenance of equipment are deficient regarding maintenance
LifeSouth Cor	Gainesville	FL	United States	24.07.2018	Drugs	21 CFR 211.42(c)(1	Cleaning System	Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the ro
Medical Chen	Torrance	CA	United States	16.08.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamin
Ohm Laborato	New Brunswic	NJ	United States	17.08.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not maintained at appropriate intervals to prevent contamination that v
Aidance Skin	Woonsocket	RI	United States	31.08.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev
American We	Williamsport	PA	United States	13.09.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned and maintained at appropriate intervals to prevent contam
Kumho Denta	Geumceon		Korea (the Re	13.09.2018	Drugs	21 CFR 211.67(a)	Cleaning / Sanitizing / Maintenance	Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prev

…weitere Themen…

- Sichtbare Reinheit (Visually clean)
- Akzeptanzkriterien

Gerne erläutern wir die wichtigsten Vorteile, welche unsere Kunden schon heute schätzen

- grosse Erfahrung mit kritischen Rückständen und den Anforderungen im cGMP Bereich
- hervorragendes Prozessverständnis

„Eine Sorge weniger!“

überwiegend tensidfreie Produkte, die den neusten Anforderungen (REACH) und gesetzlichen Richtlinien (Detergenzienrichtlinie, Biozidverordnung) entsprechen

- Erstklassige Performance bei vergleichsweise niedrigen Arbeits/ Anwendungskonzentrationen

…wichtigste Vorteile…

- deconex® CLEAN : kundenspezifische Entwicklung von Reinigungsverfahren mit ressourcenoptimierten Parametern (Zeit, Temperatur, Konzentrationen)
- deconex® CLEAN bietet den Kunden einen konkreten Verfahrensvorschlag
- deconex® CLEAN dient als *Rationale* für die Reinigungsverfahren im Routinebetrieb vollständige und umfassende Dokumentation
- Support vor Ort bei der Implementierung von Reinigungsprozessen
- Spezifische und validierte analytische Methoden zum Nachweis von Reinigungsmittelrückständen.
- Unterstützung bei der Reinigungsvalidierung

deconex® CLEAN

deconex® CLEAN - Evaluation und Definition optimaler Reinigungsverfahren

Eine Sorge weniger - deconex® CLEAN ist Ihre Lösung für integrierte Reinigungsprozesse!

deconex® CLEAN berücksichtigt die technischen Möglichkeiten Ihrer Prozessausrüstung sowie die Betriebsbedingungen. deconex® CLEAN eignet sich für Ihre Reinigungsaufgaben im cGMP-Umfeld und liefert eine wichtige Basis für die Reinigungsvalidierung.

Ihre Vorteile mit deconex® CLEAN

Wissenschaftlich

- Praxisnahe Labortests
- Umfassende Anwendungsdatenbank
- Vollständig dokumentiert (deconex® CLEAN Report)

Compliant*

- Teil der *Rationale* nach cGMP
- Grundlage für Reinigungsverfahren (SOP)
- Basis für die Reinigungsvalidierung

Kostensparend

- Verfahrensentwicklung in kurzer Zeit
- Kein Produktionsunterbruch
- Schneller Transfer in den Routinebetrieb

*Annex 15 EU-GMP Guidelines

*ASTM E3106-2018 Standard Guide for Science-Based and Risk-Based Cleaning Processes Development and Validation

borer
advanced cleaning solutions

Finden Sie Antworten!

Welches sind die wirklich wichtigen Faktoren bei der Reinigung?

Wie komme ich zum optimalen Reinigungsprozess?

Kommen Sie am Borer Stand vorbei und besprechen zusammen die Möglichkeiten!

Vielen Dank für Ihre Aufmerksamkeit!