




***COP Cleaning:
Difficult Residues and Cleaning
Challenges
Will begin shortly***



product quality
cleaning workshops

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COP Cleaning: Difficult Residues and Cleaning Challenges

Featuring Alconox



The PQCW offers practical, hands-on and independent, training in cleaning.



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9/14/2021
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Hosts: The Product Quality Cleaning Workshop Team



Barbara and Ed Kanegsberg - "The Cleaning Lady and the Rocket Scientist"

- BFK Solutions - Consultants in Critical Cleaning
- Authors and Editors of the two-volume CRC Handbook for Critical Cleaning
- Independent evaluations and recommendations
- Co-chairs of the Product Quality Cleaning Workshops
- barbara@bfksolutions.com and ed@bfksolutions.com



Darren Williams - "The Professor"

- Professor of Physical Chemistry at Sam Houston State University
- Leader of the Cleaning Research Group
- Co-chair of the Product Quality Cleaning Workshops
- Performs cleaning trials and formulates cleaning chemistries
- williams@shsu.edu

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PQCW - Workshops for Terrific Products

- ▶ "While I would prefer to have been at in-person laboratories so I could have hands-on experiences with cleaning processes, I really liked the two-week virtual PQCW.
- ▶ "People with different functions within our company, including Strategic Sourcing, Project Management, and Manufacturing Engineering, attended.
- ▶ "We learned a lot; and we have made changes. We are refining our own cleaning requirements and putting together training programs.
- ▶ "For example, we used the workshop to develop **black light testing and fixtures**; and we have already set up a one-hour "Parts Washing 101" training course.
- ▶ "The section about **EPA amended TSCA** had useful, timely information."
 - ▶ Christian Johnson, Engineer, Yaskawa, participant, PQCW21




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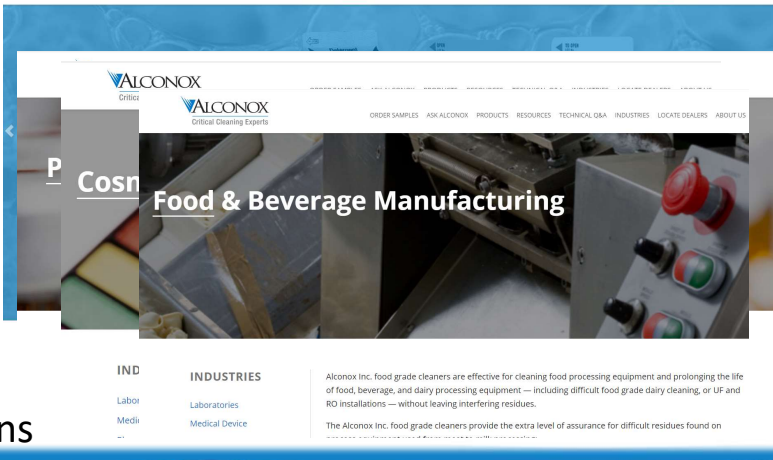
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Today's Talk

- ▼ Introduction
- ▼ Basic detergency
 - ▼ Critical Cleaning
 - ▼ Cleaning Chemistry
- ▼ Aqueous Cleaners
 - ▼ Methods (COP/Manual)
 - ▼ Detergent Selection
 - ▼ Optimization
- ▼ Cleaning Validation
- ▼ Case Study
- ▼ Discussion and Questions



The screenshot shows the Alconox website with a navigation menu: ORDER SAMPLES, ASK ALCONOX, PRODUCTS, RESOURCES, TECHNICAL Q&A, INDUSTRIES, LOCATE DEALERS, ABOUT US. The main content area features a large image of industrial machinery with the text 'Food & Beverage Manufacturing'. Below this, there are sections for 'INDUSTRIES' including Labor, Medical, and Medical Device, and a paragraph of text describing Alconox's food grade cleaners.


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Introduction

- ▼ Michael Moussourakis
- ▼ 20+ yrs, biopharm and medical device, process optimization, troubleshooting, training, critical cleaning, filtration
- ▼ Alconox Inc. (New York, USA)
- ▼ mmoussourakis@alconox.com
- ▼ ++(914)610-3057
- ▼ Senior Director, Strategic Affairs
- ▼ Not the model in this picture ----->



The photo shows two individuals, a man and a woman, both wearing white lab coats and blue gloves. They are standing next to two large industrial cleaning containers: a white one on the left and a tan one on the right. The background is a plain, light-colored wall.

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Introduction

- Privately held 75+ yr. old company
- Third generation family ownership
- Detergent manufacturer serving
 - Laboratories
 - FDA: biopharma, medical device, healthcare, food, cannabis, cosmetic
 - Precision manufacturing: solar, aerospace, electric
- Over half a century of global distribution
- Over 50 countries – and all 7 Continents
- Expert technical support – Our pride

75 YEARS



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Define Critical Cleaning

What is critical cleaning?

- Cleaning that impacts the value of the finished output from whatever is being cleaned
- Typically some observation, measurement or validation is done related to precision critical cleaning
- Critical cleaning in FDA or USDA regulated industries of components or substrates is the complete removal of undesirable contaminants to a desired preset level
- The preset level is normally the minimum level at which no adverse effects take place in a subsequent operation.


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Chemistry of Cleaning

- Organic solvents
 - Alcohols
 - Ethers
 - Petrochemical
- Only clean residues that are soluble in them
- Volatile Organic Carbon Concerns
- Flammability Concerns
- Waste Disposal Concerns



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Chemistry of Cleaning

Water

- Only cleans things soluble in it
- Excellent where water alone will work

Commodity chemicals (aqueous)

- Caustic soda and potash (NaOH & KOH)
- Phosphoric and nitric acid
- Single cleaning mechanisms of alkaline or acid attack
- Require high concentrations, no synergistic cleaning
- Waste disposal concerns

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Chemistry of Cleaning

Detergent for Critical Cleaning

- ▽ Aqueous – blend
- ▽ Surfactant – anionic, nonionic, cationic
- ▽ Builders – chelation, anti-re-deposition, silicates
- ▽ Additives – enzymes, rinse aids

HOW ALKALINE CLEANERS WORK

Source: Praetler Cleaning Magazine, June 1997.

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Cleaning Methods (COP focused)

- ▽ Soak
- ▽ Scrubbing
- ▽ Agitated Immersion
 - ▽ Ultrasonic
 - ▽ Bubbled
 - ▽ Pump under immersion



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Manual Cleaning

- ▼ COP Cleaning Processes
 - ▼ Soak
 - ▼ Low cost of capital equipment
 - ▼ Easy to perform
 - ▼ No Computer System Validation (CSV)
 - ▼ Ultrasonic
 - ▼ Cavitations release massive energy at the surface residual interface
 - ▼ Usable on a wide variety of materials of construction
 - ▼ Usually 40+ kHz

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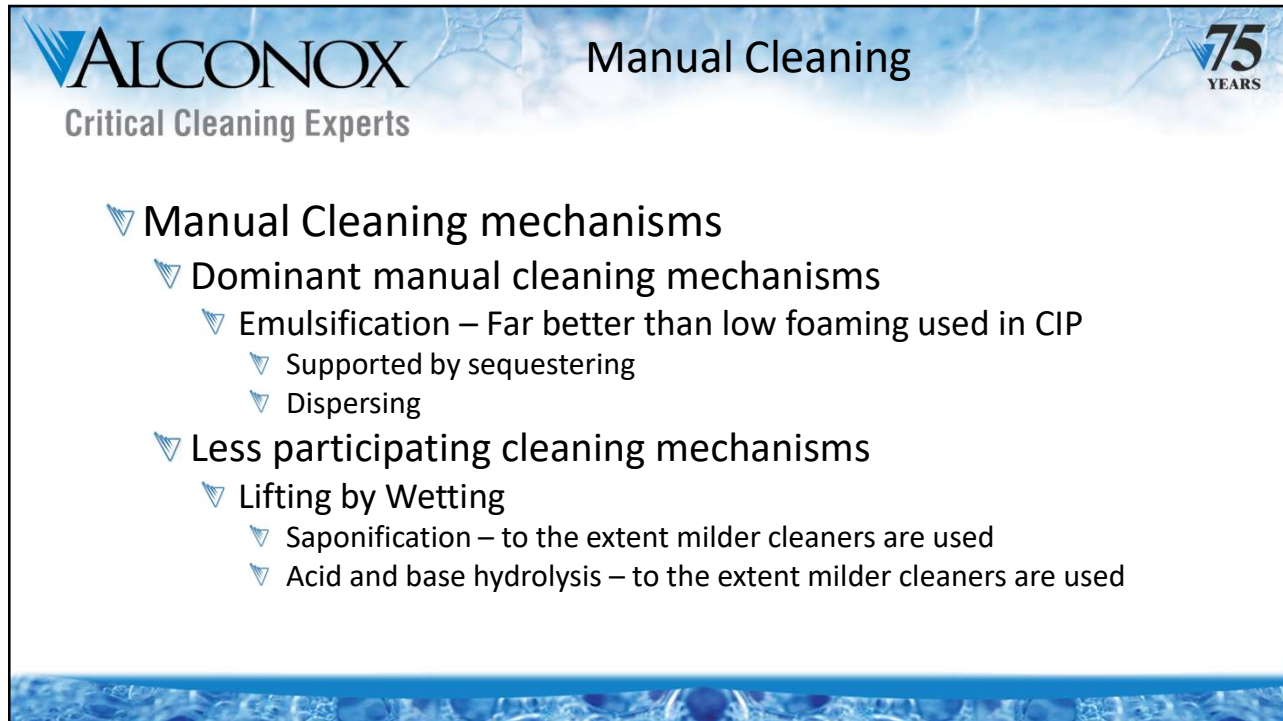
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Manual Cleaning

- ▼ Scrub
 - ▼ Wipes – especially single use and should be non shedding
 - ▼ Brushes (nylon may be degraded by alkaline cleaners) – smooth cleanable brushes of polypropylene can be more desirable
 - ▼ Non abrasive pads (best to use robust pads that do not degrade and leave insoluble fibers)
 - ▼ Abrasives (may be undesirable due to harming equipment and potentially leaving insoluble solid abrasive residues)
 - ▼ Sponges – sometimes not desirable due to leaching compounds and harboring microbes

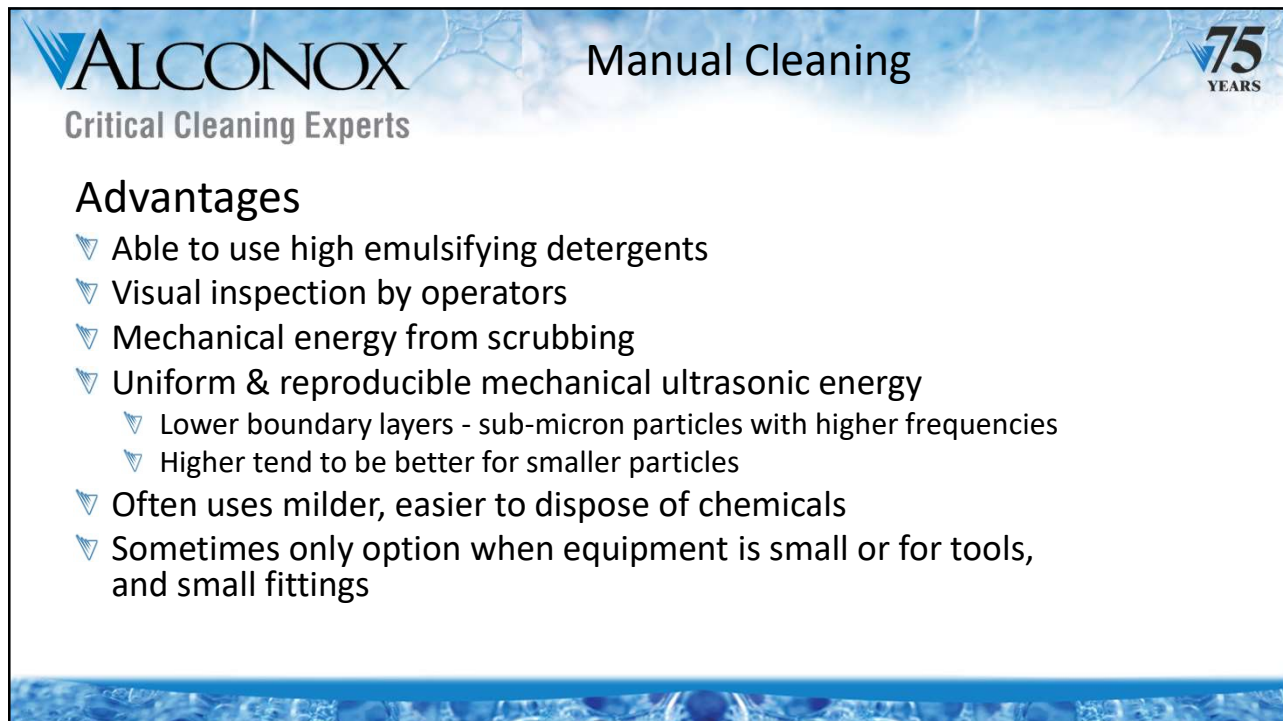
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ALCONOX Manual Cleaning **75 YEARS**
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- ▼ Manual Cleaning mechanisms
 - ▼ Dominant manual cleaning mechanisms
 - ▼ Emulsification – Far better than low foaming used in CIP
 - ▼ Supported by sequestering
 - ▼ Dispersing
 - ▼ Less participating cleaning mechanisms
 - ▼ Lifting by Wetting
 - ▼ Saponification – to the extent milder cleaners are used
 - ▼ Acid and base hydrolysis – to the extent milder cleaners are used

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ALCONOX Manual Cleaning **75 YEARS**
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Advantages

- ▼ Able to use high emulsifying detergents
- ▼ Visual inspection by operators
- ▼ Mechanical energy from scrubbing
- ▼ Uniform & reproducible mechanical ultrasonic energy
 - ▼ Lower boundary layers - sub-micron particles with higher frequencies
 - ▼ Higher tend to be better for smaller particles
- ▼ Often uses milder, easier to dispose of chemicals
- ▼ Sometimes only option when equipment is small or for tools, and small fittings

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Manual Cleaning

- Disadvantages
 - Requires labor
 - Needs appropriate PPE
 - Safety issues
 - Soak cleaning volume vs. automated CIP cleaning
 - May have variability

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Detergent Selection

Hard to Choose Which Cleaner

- Over 3000 Cleaner suppliers
- Quality levels ranging from appearance grade to semiconductor quality
- There are formulations for gross soil removal and fine trace soil removal
- Formulations change for economy, performance or marketing claims

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Detergent Selection

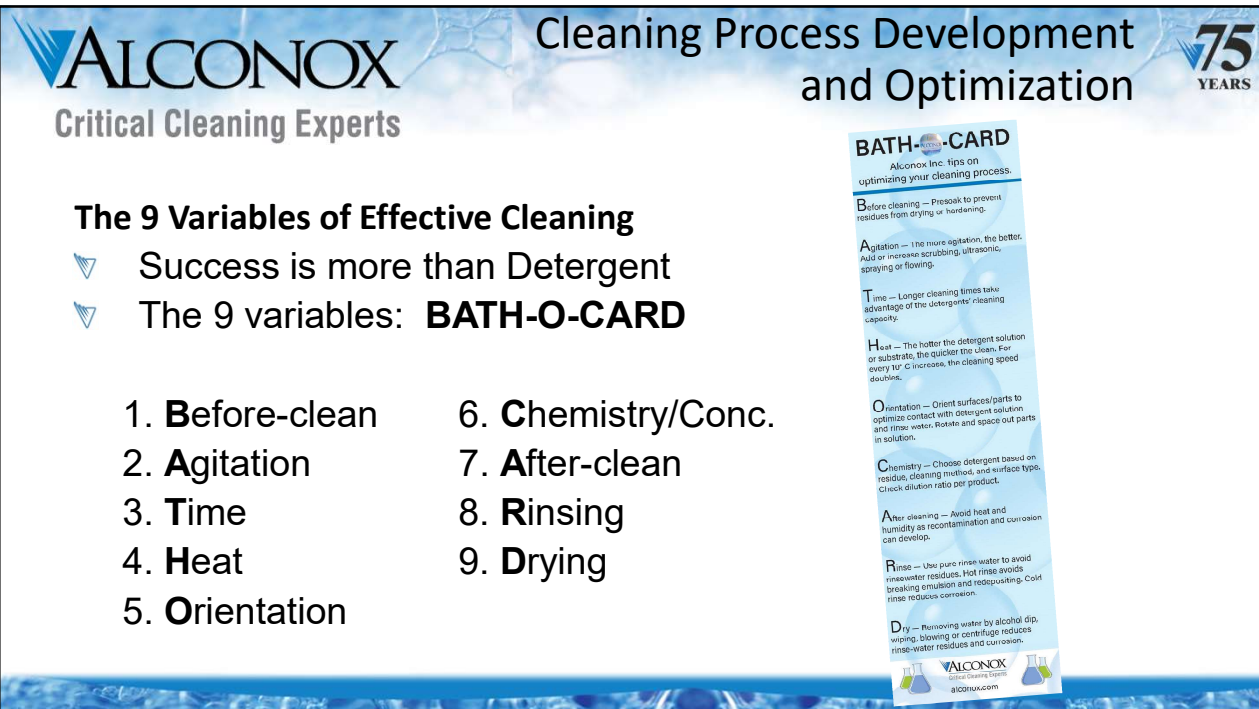
Regulatory Support

- ✔ One should choose brands that are cGMP compliant:
 - ✔ Precise formulations & quality control
 - ✔ Lot-specific COA, technical bulletins & SDS should be available

Comprehensive cGMP compliance support

- ✔ Documentation available
- ✔ Lot traceability of cleaners
- ✔ Toxicity data
- ✔ Ingredient reactivity information
- ✔ Cleaner shelf-life testing
- ✔ Cleaning validation support
- ✔ Written cleaning procedures

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Cleaning Process Development and Optimization

The 9 Variables of Effective Cleaning

- ✔ Success is more than Detergent
- ✔ The 9 variables: **BATH-O-CARD**

1. Before-clean	6. Chemistry/Conc.
2. Agitation	7. After-clean
3. Time	8. Rinsing
4. Heat	9. Drying
5. Orientation	

BATH-O-CARD
Alconox Inc. tips on optimizing your cleaning process.

Before cleaning — Presoak to prevent residues from drying or hardening.

Agitation — The more agitation, the better. Add or increase scrubbing, ultrasonic, spraying or flowing.

Time — Longer cleaning times take advantage of the detergent's cleaning capacity.

Heat — The hotter the detergent solution or substrate, the quicker the clean. For every 10° C increase, the cleaning speed doubles.

Orientation — Orient surfaces/parts to optimize contact with detergent solution and rinse water. Rotate and space out parts in solution.

Chemistry — Choose detergent based on residue, cleaning method, and surface type. Check dilution ratio per product.

After cleaning — Avoid heat and humidity as recontamination and corrosion can develop.

Rinse — Use pure rinse water to avoid rinse-water residues. Hot rinse avoids breaking emulsion and redepositing. Cold rinse reduces corrosion.

Dry — Removing water by alcohol dip, wiping, blowing or centrifuge reduces rinse-water residues and corrosion.

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ALCONOX Critical Cleaning Experts **Cleaning Process Development and Optimization** **75 YEARS**

Process Conclusion – A Lifestyle Approach


- ▼ Selecting the right cleaner is easier if you understand the 9 variables that effect cleaning performance
- ▼ Match your cleaner to the cleaning method, substrate, and type of residue
- ▼ Then evaluate health and environmental safety
- ▼ The 9 variables intrinsic to cleaning process
 - ▼ → cleaning validation → clean product

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ALCONOX Critical Cleaning Experts **Cleaning Validation/Verification** **75 YEARS**

Validating the use of a cleaner:

- ▼ Identify Cleaner Residues
- ▼ Select a Residue Detection Method
- ▼ Choose a Sampling Method
- ▼ Validate a Residue Detection Method
- ▼ Construct Recovery Studies
- ▼ Set Residue acceptance criteria
- ▼ Validate the cleaning process with the new cleaner
 - ▼ Including design of experiments for optimal process
 - ▼ Including three consecutive cleaning trials
 - ▼ Including and Creating the Validation Report
- ▼ Write procedures and train operators



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Critical Cleaning Experts Cleaning Validation/Verification

Validating the use of a cleaner:
Detergent Residue Detection - Specific vs. non-specific

- ▽ Specific ingredients:
 - ▽ high performance liquid chromatography (HPLC)
 - ▽ ion selective electrodes
 - ▽ flame photometry
 - ▽ UV spectroscopy
 - ▽ enzymatic detection
 - ▽ Titration
- ▽ Blend of ingredients:
 - ▽ total organic carbon
 - ▽ pH
 - ▽ Conductivity
 - ▽ Visual inspection
 - ▽ Contact Angle (portabl)

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Critical Cleaning Experts Cleaning Validation/Verification

Summary

- ▽ Critical cleaning steps effecting the quality, safety or manufacture
 - ▽ “Hot Spot” or worst-case locations
- ▽ Validation is achieved by proving that a process operates within predetermined parameters
- ▽ Manual Cleaning ---- consider both detergent and product residues
 - ▽ ADE/PDE as detergent limits
 - ▽ Limits for the active drug
 - ▽ Excipients
 - ▽ Degradation products
 - ▽ Cleaning agents
 - ▽ Bioburden
 - ▽ Endotoxins

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COP Cleaning Case Study

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Pharmaceutical Company Case Study

- ▼ Progesterone/estrogen combination therapy
- ▼ highly water insoluble nature of progesterone/estrogen steroid structure
 - ▼ Cleaning doesn't scale "nicely"
 - ▼ Inconsistency at large scale
- ▼ Move away from their typical CIP low foaming?

Progesterone

CC(=O)C12CC[C@H]3[C@@H]1CC[C@@H]2[C@]34CCCC(=O)C4

Estrogen

CC12CC[C@H]3[C@@H]1CC[C@@H]2[C@]34C=C5C(=C)C=C(O)C5O4

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COP Cleaning Case Study

75 YEARS

Pharmaceutical Company Case Study

- ▼ More than just a residual
- ▼ Very low level requirement
- ▼ Cytotoxic, antibiotic, and hormones

Progesterone

CC(=O)C12CC[C@H]3[C@@H]1CC[C@@H]2[C@]34CCCC(=O)C4

Estrogen

CC12CC[C@H]3[C@@H]1CC[C@@H]2[C@]34C=C5C(=C)C=C(O)C5O4

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COP Cleaning Case Study

75 YEARS

▼ **Pharmaceutical Company Case Study**

- ▼ Consideration of more aggressive CIP detergent
- ▼ Consideration of a new CIP system
- ▼ Consideration of a higher foaming, COP process
 - ▼ Ultrasonic/soak of parts
 - ▼ Scrubbing of equipment that can't be soaked/sonicated
 - ▼ Flowing water rinse

Progesterone

CC(=O)C12CC[C@H]3[C@@H]1CC[C@@H]2[C@]3(O)CCC4=CC(=O)CC[C@]4(C)C

Estrogen

CC12CC[C@H]3[C@@H]1CC[C@@H]2[C@]3(O)CCC4=CC(O)C=C4

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COP Cleaning Case Study

75 YEARS

▼ **Pharmaceutical Company Case Study**

- ▼ Able to consistently meet cleaning requirements
- ▼ Validate using a “manual” higher foaming detergent
 - ▼ Both specific and non specific used
- ▼ High emulsifying ability to more easily remove Progesterone/Estrogen

Progesterone

CC(=O)C12CC[C@H]3[C@@H]1CC[C@@H]2[C@]3(O)CCC4=CC(=O)CC[C@]4(C)C

Estrogen

CC12CC[C@H]3[C@@H]1CC[C@@H]2[C@]3(O)CCC4=CC(O)C=C4

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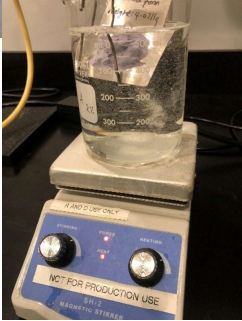
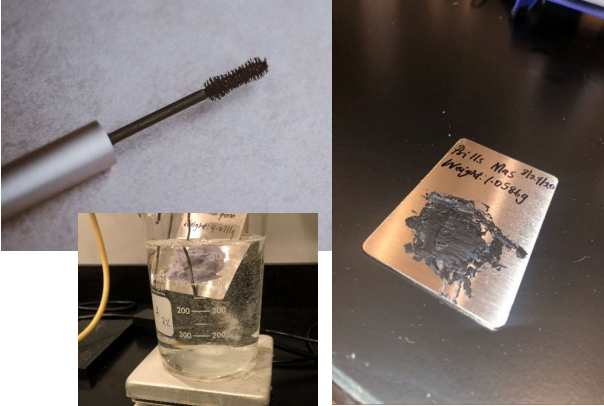
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COP Cleaning Case Study 2

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OTC Skin Product

- Adherent, waterproof compound – mascara
- Customer looking to COP
 - Instruments and small parts/vessels
- Experience indicates using Keylajet detergent and optimizing parameters



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COP Cleaning Case Study 2

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OTC Skin Product

- KJ worked to some degree...
- It was noted the oily remained – add emulsification
- 85/15 % blend of roughly 3% KJ/LQ.
- Powerful concept of detergent blends
 - When manual/COP involved with proper PPE, foaming or non foaming not the issue, best chemistry is



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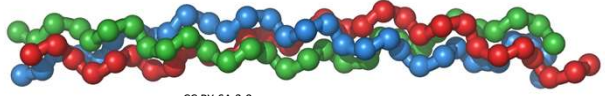

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COP Cleaning Case Study 3

75 YEARS

Nutraceutical

- ▼ Turmeric, acidic components, collagen
- ▼ Needs oxidation, acid cleaner, protease?
- ▼ What we know –
 - ▼ Collagen swells in presence of alkaline
 - ▼ Acid cleans acid
 - ▼ Turmeric aromatic compounds cleaned by oxidation



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COP Cleaning Case Study 3

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Nutraceutical

- ▼ Determine if Citranox (acidic detergent) cleans alone
 - ▼ Removes most collagen and acid residues
 - ▼ Rust colored residue remaining – aka turmeric
- ▼ Follow with alkaline + oxidative detergent – Detojet
- ▼ Typical alkaline then acid reversed
- ▼ Follow the science - Verified on full scale



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Product Quality Cleaning Workshops

FIND OUT MORE

- ▶ Hands-on, practical
- ▶ Online, on-demand, on campus, or on-site
- ▶ More Info?

www.shsu.edu/pqcw

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Q: What was most valuable about the workshop?
A: "The general overview of cleaning and the importance of cleaning procedures - a 2018 attendee's perspective from their processes."
• Solvent properties, cleaning verification, soil analysis, microbiology

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This Product Quality Cleaning Webinar was brought to you by the **PQCW Team** and the generous support of our sponsors. For more information on Critical Cleaning **Contact Us!**



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Have a great
rest of your day



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