Make the Switch

A Guide to Getting Ahead of Changing Cleanroom Disinfectant Regulations and Building a Forward-Thinking Program

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Introduction:

EPA PTAP Data Call-In: Signaling A Global Trend

The EPA's December 2018 Data Call-In (DCI) of para-tertiary amylphenol (PTAP), an active ingredient found in some registered cleanroom disinfectants in the U.S., will require U.S. suppliers to discontinue selling PTAP-based products. Pharmaceutical manufacturers currently using PTAP-based products – those with operations in the U.S., as well as global operations wanting to maintain a globally compliant cleanroom portfolio – will be required to switch to an alternative, broad-spectrum biocide when their existing PTAP-based product supply runs out following the vendor phase-out date. However, the wide-angle view shows the EPA DCI as just one part of a larger, global trend of changing regulations and restrictions on cleanroom disinfection products and practices.

Taken in this context, the PTAP switch becomes a critical inflection point: An opportunity to think long-term and begin building a forward-thinking cleanroom disinfection program. This short e-book provides an overview of global trends in cleanroom regulation and details a strategy for getting ahead of these regulatory changes – minimizing change-management costs, mitigating compliance uncertainty and the potential for audit findings, and enabling pharmaceutical manufacturers to focus their resources on their core business.

Overview of the Data Call-In

What & Why

PTAP, or para-tertiary amylphenol, is an active ingredient with antimicrobial activity that can be found in some registered cleanroom disinfectants in the U.S. The U.S. Environmental Protection Agency (EPA) has issued a Data Call-In (DCI) for the active ingredient PTAP. Through the DCI, EPA is requiring additional data from the active ingredient manufacturers to support the continued use of this active in registered disinfectants. The amount of data requested by the EPA is significant and PTAP manufacturers have decided not to support the generation of the additional studies.

U.S. Impacts

Pharmaceutical manufacturers currently using disinfectant products containing PTAP in the U.S. will have to find alternative solutions. .

Global Impacts

Global pharmaceutical manufacturers wanting to maintain a harmonized, global program will need to shift away from PTAP-based disinfectant use across major markets.

Seeing the Big Picture: The Future of Cleanroom Regulation

As forward-thinking pharmaceutical manufacturers look to minimize the costs, risks and other pains of managing the change control process associated with a switch away from PTAP-based products, they are considering changes in the regulatory landscape that signal future contamination control requirements:

TREND #1:

The global move to restrict phenolic actives

The EPA PTAP DCI reflects a global trend: regulatory agencies around the world are moving to reduce the use of many common active ingredients in the cleanroom environment.

- **EU BPR considering chlorophene-based product restriction:** The European Chemicals Agency (ECHA) has identified chlorophene, another phenolic active, as fulfilling the interim criteria as a biocide with endocrine-disrupting properties, meaning the active is not foreseen for long-term support for use in hard-surface disinfectant products in the cleanroom space. The final outcome will either be completely disallowing the use of chlorophene-based products (off the market within 12-24 months), or significantly limiting their approval for a limited period and for small-scale applications requiring additional operator PPE.

- **Phenolic actives not widely available in Asia-Pacific:** Phenolic biocides are not widely approved as a biocidal active in China, Australia or Korea. With the change to more restrictive regulations in Asia-Pacific regions, the use of these actives in disinfectants is likely to become a bigger challenge for cleanroom manufacturers.

KEY TAKEAWAY:

As regulators increasingly restrict active ingredients, products containing phenolic actives - including PTAP and chlorophene — do not represent a long-term solution for globally compliant cleanroom disinfection.

TREND #2:

Residues Matter

The landmark draft changes to EU GMPs for Sterile Medicines, i.e., Annex 1, indicate a major new focus for global regulators: surface residues that may inhibit effective disinfection and/or introduce product or quality risks. In particular, the draft changes to Annex 1 include a new requirement that relates to surface residues:

- **Distinct cleaning and disinfection steps:** Chapter 5.31 of the EU GMP Annex 1 draft states, "For disinfection to be effective, cleaning to remove surface contamination must be performed first, while chapter 6.5 stipulates a cleaning protocol that "a) Removes any residues that would otherwise create a barrier; b) Prevents chemical and particulate contamination of the product."

  This separation of cleaning and disinfection ensures that surface matter does not disrupt disinfectant efficacy. In particular, the common practice of using a disinfectant with a surfactant to achieve "one-step" cleaning presents the risk that the disinfectant active is reduced or impeded by the surface matter.

KEY TAKEAWAY:

While the Annex 1 draft will soon become official EU regulation with global implications, any pharma manufacturer selling into the EU will also need to comply with these new requirements. Annex 1 also represents widely accepted best practices, and regulatory agencies in major global markets may soon follow the EU's lead in adopting specific and strict residue-removal requirements. Even those organizations not immediately impacted by Annex 1 should consider compliance with these best practices.

Making the Switch: Evaluating Your Options

For organizations immediately impacted by the EPA PTAP DCI, the initial challenge is finding an alternative broad-spectrum biocide. Several products exist that deliver comparable performance.

Evaluating PTAP alternatives through the long-term lens of global regulatory changes reveals critical shortcomings that may lead to additional cost, risk and operational disruptions down the road.

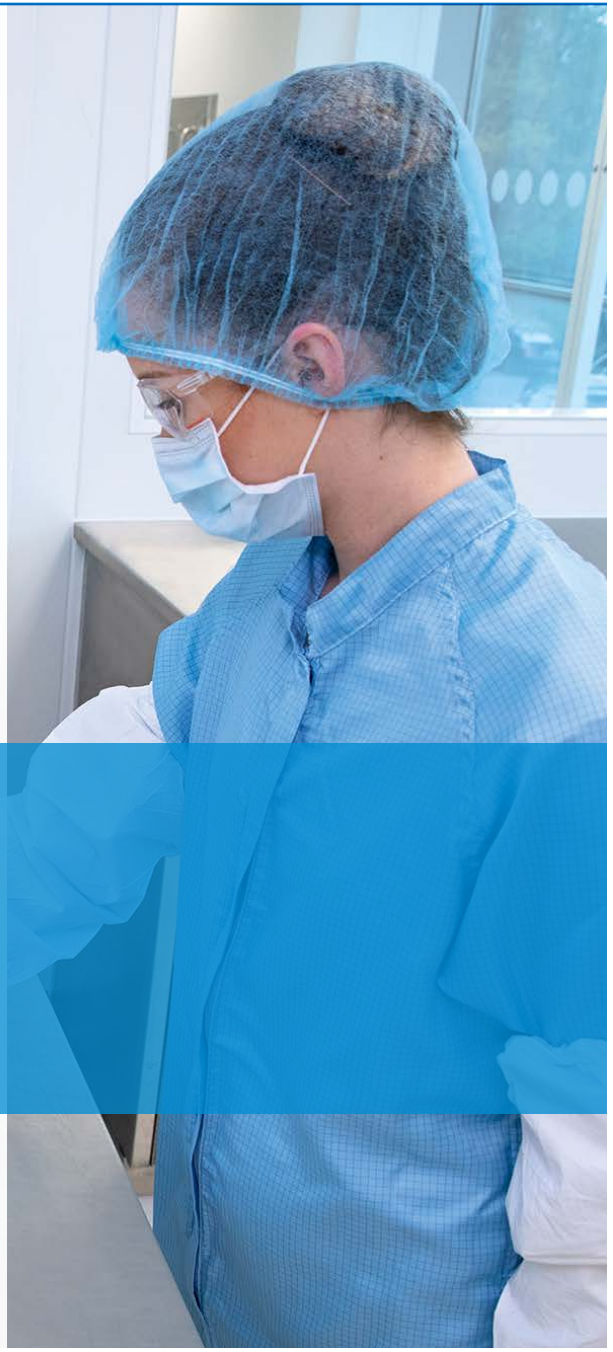
4 OPTIONS FOR MANAGING THE DCI

Delaying the Pain
Stockpiling PTAP-Based Products

The "Easy" Switch
Chlorophene-Based Products

The Conventional Alternative
Traditional Quat-Based Products

A Smarter Switch
Reduced-Residue Quat-Based Products



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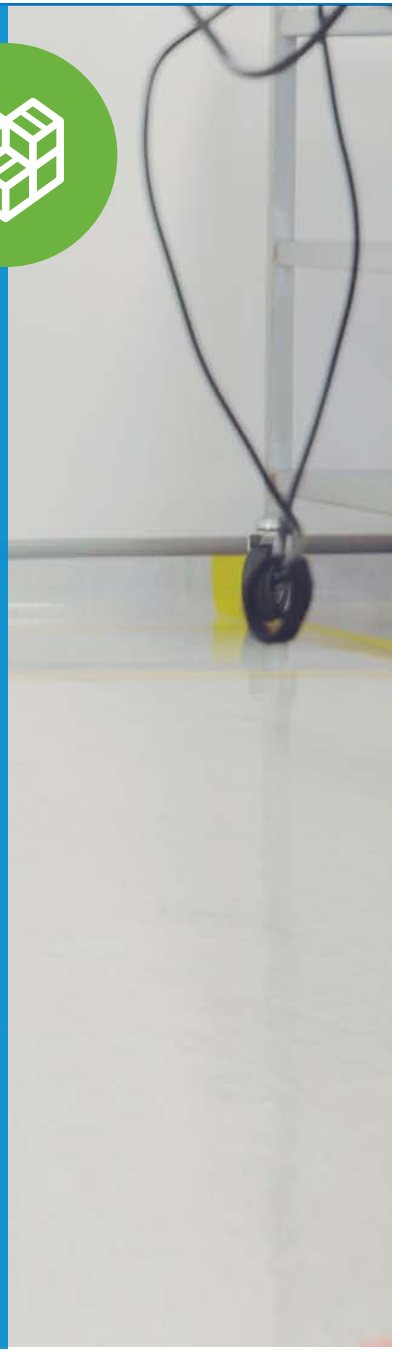
Option #1: Delay the Pain

Stockpiling PTAP-Based Products

Availability of PTAP-based disinfectants will soon end. The tempting solution is to stockpile PTAP-based products and delay the pain of the switch.

Key Challenges

- **Potential supply shortages:** As pharmaceutical manufacturers stockpile PTAP-based products, supply may become less reliable. Running out of a disinfectant product before validating a replacement could mean significant production downtime.
- **Potential re-validation delays:** Delaying the switch means delaying validation. Securing a spot with a trusted independent lab to execute validation testing may become increasingly challenging as the deadline for PTAP removal nears. Again, potential re-validation delays (e.g., retesting) could lead to production downtime.



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Option #2: Make the "Easy" Switch

Switching to Chlorophene-Based Products

One option cleanroom disinfectant suppliers are presenting as a PTAP alternative are chlorophene-based products – a lateral switch to another phenolic-based product.

Key Challenges

- **Chlorophene-based products still require re-validation:** The key hurdle in the PTAP switch is the time-consuming and cost-intensive process of re-validating a new product – a hurdle which even "similar" chlorophene-based disinfectants must clear.
- **Chlorophene-based products are not globally compliant:** With restrictions in the EU and limited approval in Asia-Pacific, chlorophene-based products are not globally viable.
- **Health & safety concerns:** Under EU CLP regulations, chlorophene-based products have been classified as having potential carcinogenic and reproductive toxicity concerns.

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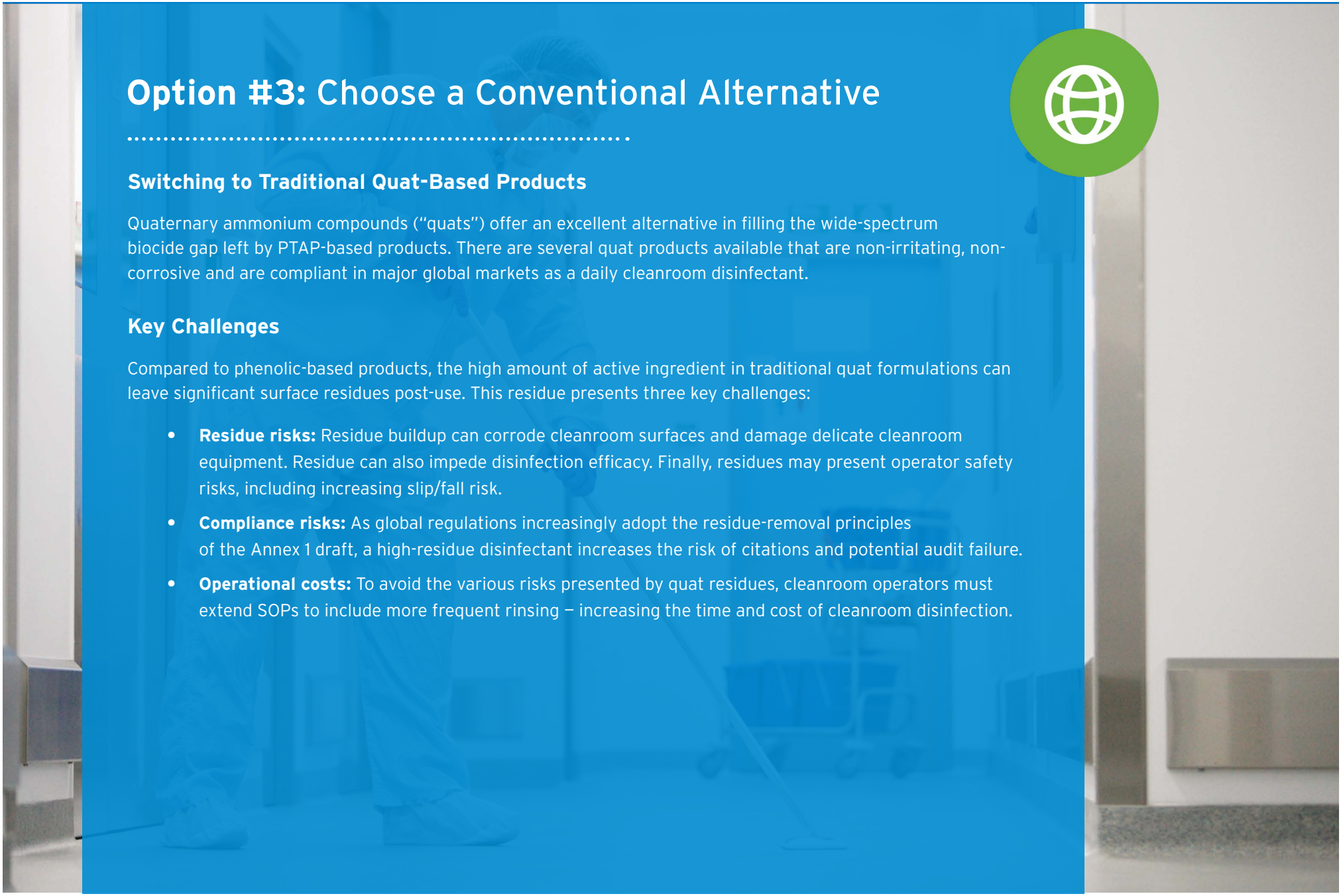

Option #3: Choose a Conventional Alternative

Switching to Traditional Quat-Based Products

Quaternary ammonium compounds ("quats") offer an excellent alternative in filling the wide-spectrum biocide gap left by PTAP-based products. There are several quat products available that are non-irritating, non-corrosive and are compliant in major global markets as a daily cleanroom disinfectant.

Key Challenges

Compared to phenolic-based products, the high amount of active ingredient in traditional quat formulations can leave significant surface residues post-use. This residue presents three key challenges:

- **Residue risks:** Residue buildup can corrode cleanroom surfaces and damage delicate cleanroom equipment. Residue can also impede disinfection efficacy. Finally, residues may present operator safety risks, including increasing slip/fall risk.
- **Compliance risks:** As global regulations increasingly adopt the residue-removal principles of the Annex 1 draft, a high-residue disinfectant increases the risk of citations and potential audit failure.
- **Operational costs:** To avoid the various risks presented by quat residues, cleanroom operators must extend SOPs to include more frequent rinsing – increasing the time and cost of cleanroom disinfection.

A Smarter Choice: Achieve Global Compliance – Drive Operational Efficiency

Recent Ecolab studies show residues from traditional disinfectant and sanitizing products can interfere with cleanroom operations, including the ability of contact plates to neutralize excess residues post application. This can result in overconfidence that cleanroom contaminate levels are under control. Ecolab® Klercide® Cleanroom Quat is a next generation quaternary ammonium compound biocide that directly aligns with global regulatory standards. Unlike traditional quaternary ammonium compounds, the low concentration active in Klercide Cleanroom Quat leaves minimal residue behind on surfaces, helping ensure sanitization while reducing the requirement for routine rinsing.

The Unique Value of a Minimal Residue Quat

Reliable

Ecolab Klercide Cleanroom Quat has been proven to deliver cleanroom-relevant sanitization in controlled environments.

Ensure product quality & safety

Less harsh on surfaces

Like traditional quats, this product is significantly less less corrosive than phenolic-based products – protecting expensive and sensitive cleanroom equipment.

Protect your assets

Minimal residue – less frequent rinsing

Ecolab Klercide Cleanroom Quat usage results in less accumulative residue. Less residue leads to lower frequency of rinsing.

Streamline SOPs – drive efficiency

Globally compliant

Ecolab Klercide Cleanroom Quat is approved for use in major markets and can be a cornerstone of a globally harmonized cleanroom program.

Build a long-term solution – reduce future compliance issues

Turning a Forced Change into a Value-Add Opportunity:

Building a Forward-Thinking Cleanroom Portfolio

For those facing the required switch away from PTAP products, a holistic assessment recognizes that the greatest hurdle – re-validation – is unavoidable. Moreover, failing to consider the broader, global context of the EPA PTAP DCI presents the risk of selecting an alternative that may leave manufacturers facing the same re-validation burden just a few years down the road.

Instead, forward-thinking pharmaceutical manufacturers are using the EPA PTAP DCI as an opportunity to look beyond traditional options and short-term strategies. New, minimal-residue quat chemistry provides cleanroom operators with a safe, reliable PTAP alternative. Moreover, this new option enables cleanroom operators to meet increasing compliance standards while streamlining the required SOPs related to residue-removal – mitigating risk while enhancing operational efficiency and controlling costs. Going forward, cleanroom operators must look for solutions like this – ones that address immediate pain points as well as big-picture challenges – in order to build an efficient, effective and streamlined cleanroom program that meets U.S. regulatory standards – and aligns with the global regulatory trends of tomorrow.

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An Expert Partner Supporting Your Success

Cleanroom Disinfection Solutions
Ecolab provides pharmaceutical manufacturers with complete cleaning and disinfection programs, including the full Ecolab® Klercide® portfolio. Our complete contamination control portfolio is designed specifically for the pharmaceutical industry to help you deliver your promise of patient safety.

Validation Support
Ecolab can assist in navigating the complex validation processes and change controls. Ecolab validation support provides a complete package to ensure successful validation of Ecolab products in line with global regulatory expectations and acceptance criteria, including a global method, supporting data set and supporting expertise – all tailored for the cleanroom environment.

Technical Lab Support
Ecolab offers support to identify the right cleaning procedures for your specific processes and products, including solubility tests, dipping tests and material compatibility tests.

Regulatory & Quality Guidance
Ecolab leverages deep industry expertise to deliver insights and guidance on regulatory expectations, regulatory trends and available tools to ensure compliance for product safety and quality.

Assessment, Recommendations & Reporting
Ecolab offers site-survey services from our International Register of Credited Auditors (IRCA) to assess the cleaning and disinfection requirements within your controlled environments.

Customer Training
Ecolab develops and delivers comprehensive, in-person training programs to address a full range of topics related to cleanroom disinfection.

SEE HOW ECOLAB CAN HELP YOU BUILD A HIGHLY EFFICIENT, FORWARD-THINKING CLEANROOM OPERATION.

Visit www.ecolab.com/maketheswitch