In-line UV/DUV Spectroscopy

for Cleaning Control in Biopharmaceutical Manufacturing

Instant Results: Real-time data acquisition

No Sampling: Non-destructive in-line measurement

No Consumables: No reagents required

No Moving Parts: Long-term reliability and minimal maintenance assured

No Dilutions: Measure highly concentrated samples without pretreatment

NIST Traceable: Simplified verification and regulatory compliance

cGMP Compliant: Streamlined IQ, OQ, and PQ protocols for rapid validation

Effective cleaning control is essential for safeguarding product quality, preventing contamination, and maintaining compliance with stringent regulatory frameworks. The Kemtrak Spectra industrial process photometer utilizes multi-wavelength ultraviolet (UV) and deep ultraviolet (DUV) technology to provide highly sensitive, non-invasive detection of trace level residues directly within CIP/SIP processes and cleaning verification workflows *(Schallom et al. 2025; Chullipalliyalil et al. 2020)*.

As regulatory agencies increasingly promote science- and risk-based approaches aligned with Process Analytical Technology (PAT) and Quality by Design (QbD) principles, UV/DUV spectroscopic methods enable real-time feedback to verify and optimize cleaning performance. Consequently, UV/DUV spectroscopy is emerging as a foundational technology for modern cleaning validation programs and advanced Pharma 4.0 manufacturing strategies *(Provenzano et al. 2022)*.

Operational Efficiency

Continuous in-line UV/DUV monitoring enables data-driven cleaning decisions:

- **Dynamic cycle endpoints:** Cleaning cycles can be terminated as soon as a validated UV absorbance baseline is reached, replacing fixed-duration cycles with evidence-based endpoints that adapt to actual soil load.
- **Reduced resource consumption:** Avoid over-cleaning by terminating cycles at the verified clean endpoint, reducing water, energy, and chemical usage and lowering the environmental footprint of manufacturing operations.
- **Real-time trending:** Continuous UV absorbance profiles generate a complete, time-stamped record of each cleaning event, supporting verification of validated cleaning states and providing audit-ready documentation for regulatory review.
- **Residue characterization:** Each residue type produces a characteristic absorbance signature across the UV/DUV spectrum, allowing the system to distinguish between intact proteins, degraded biologics, and alkaline or acidic cleaning agents simultaneously.
- **Regulatory alignment:** Continuous in-line monitoring supports process verification requirements outlined in EU GMP Annex 15 (Qualification and Validation) and Annex 1 (Manufacture of Sterile Medicinal Products), reinforcing a science- and risk-based contamination control strategy.

(Provenzano et al. 2023; Rathore et al. 2008; Schallom et al. 2025)

High-Sensitivity Residual API Detection

UV/DUV spectroscopy provides rapid, selective detection of biologic residues during cleaning:

- **A220 monitoring:** At 220 nm provides broad-spectrum detection of proteins, peptides, nucleic acids, and degraded product fragments, as well as UV-absorbing cleaning agent residues, making it the primary wavelength for general cleaning verification.
- **A280 kinetics**: At 280 nm provides selective monitoring of intact proteins and antibodies, enabling real-time evaluation of protein removal dynamics and estimation of the remaining cleaning time required to reach acceptance limits.
- **Aggregation insights:** DUV excitation (below 250 nm) can reveal aggregated or denatured protein species — materials that are typically the most difficult to remove during cleaning and that conventional TOC or conductivity methods may fail to distinguish from intact product.

By delivering direct absorbance data throughout the entire cleaning cycle, in-line UV/DUV enables continuous verification rather than reliance on sporadic grab samples.

(Aitken et al. 2009; Rathore et al. 2008; Schallom et al. 2025)

Detection of Acidic and Alkaline Cleaning Chemicals

In-line UV/DUV systems support robust monitoring of detergent clearance:

- Spectral analysis can differentiate detergent signatures from protein residues, allowing simultaneous monitoring of both soil removal and cleaning agent clearance within a single measurement cycle.
- Cleaning agents may be formulated or spiked with UV-traceable markers for enhanced specificity, enabling unambiguous confirmation of detergent presence and removal even in complex biopharmaceutical matrices.
- Enables rinse optimization by confirming detergent clearance at the earliest verifiable point, reducing rinse volume and cycle time while maintaining full regulatory compliance.

(Gillespie et al. 2015; Schallom et al. 2025; Westman et al. 2000)

Enabling PAT, QC Efficiency, and In-line Release

UV/DUV spectroscopy delivers actionable analytical data suitable for PAT frameworks:

- Provides continuous, science-based visibility into cleaning performance, generating a complete spectroscopic record of each CIP cycle that can serve as primary evidence of a validated cleaning state.
- Real-time decision support strengthens contamination control strategies by enabling operators to act on live data rather than waiting hours or days for off-line laboratory results.
- In-line verification reduces reliance on off-line laboratory assays such as TOC and HPLC, lowering QC workload, compressing equipment release timelines, and supporting a transition toward real-time or parametric release strategies.

By minimizing manual sampling and accelerating data availability, UV/DUV instrumentation reduces QC workload and supports faster equipment turnaround. In many workflows, UV/DUV can replace or complement non-specific off-line assays such as TOC when proteins degrade and become difficult to quantify *(Schallom et al. 2025; Provenzano et al. 2023)*.

Variable-Wavelength Performance

Advanced multi-wavelength UV/DUV instruments, such as the Kemtrak UV Spectra, significantly expand traditional detection capabilities by enabling users to:

- Select optimal wavelengths and corresponding molar absorption coefficients for each specific residue or cleaning agent, allowing the method to be tailored to the chemistry of each application
- Maintain linear measurement performance across a wide concentration range, from trace-level residues at the limit of quantitation up to high-concentration cleaning agent solutions
- Avoid signal saturation that is common with fixed single-wavelength UV sensors, by dynamically selecting a wavelength suited to the current concentration in the process stream

This enhanced flexibility supports robust and reliable detection under highly variable cleaning and rinsing conditions.

Continuous Evidence of Cleanliness

UV/DUV spectroscopy provides critical, real-time data demonstrating a sustained state of control in biochemical cleaning processes. Rather than relying exclusively on discrete laboratory assays, manufacturers gain continuous, time-resolved confirmation that cleanliness limits are consistently achieved, supporting emerging regulatory expectations for in-line or hybrid release strategies.

About the Author

Matthew Rice holds a PhD in Process Analytical Chemistry from The Royal Institute of Technology, Stockholm, and a degree in Chemical Engineering from the University of Sydney. Matthew is the founder and CEO of Kemtrak AB, a high-tech Swedish company developing and manufacturing high-performance industrial process instrumentation.

Under his leadership, Kemtrak has achieved global recognition through innovation, quality, and international growth. Matthew also serves on multiple boards, contributing to Sweden's industrial and technology sectors.

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For detailed specifications on the Kemtrak Spectra please visit southforkinstruments.com to download a product sheet.

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