Ensure Ultra-Low Residual Hydrogen Peroxide Levels for GMP Pharmaceutical Production

with the Picarro PI2124 Gas Concentration Analyzer

PICARRO

THE CHALLENGE

Why PPM Isn't Enough for Drug Protection

Isolated Aseptic Pharmaceutical Production

High-potency active pharmaceutical ingredient (HPAPI), large-molecule (biologic) drugs, and aseptic fill and finish require isolated, sterile production environments. VHP (vaporized hydrogen peroxide) is the principal treatment for decontamination in isolated pharmaceutical manufacturing. But if the residual VHP level is too high after decontamination and aeration, or anytime during the production process, the drug product can oxidize and degrade. As a result, vaporized hydrogen peroxide bio-decontamination in isolators is treated as a critical process that must be scientifically understood, monitored, and governed as part of a facility's contamination control strategy.

VHP Concentration Control

The recommended exposure limit (REL) of VHP by workers in general industry is 1 part-per-million (ppm), codified in 29 CFR 1900 by the National Institute for Occupational Safety and Health (NIOSH). Other applicable standards my vary based on a specific industry and exposure time, but they are generally in the ppm range. While sufficient for human health and safety, ppm levels are too high to prevent drug oxidation and to sustain efficacy, safety, and stability. In aseptic pharmaceutical manufacturing, residual VHP levels are commonly controlled at the parts-per-billion (ppb) level to protect product quality. Some biologic drug producers are setting levels as low as 30 ppb to avoid oxidation. Health and safety monitors that measure exposure limits in ppm cannot ensure VHP levels are low enough to avoid drug product oxidation.

Continuous VHP Monitoring

As shown in **Figure 1**, the Picarro PI2124 gas concentration analyzer has almost five orders of linear dynamic range, and it can continuously measure VHP levels. This enables users to:

- Measure VHP levels as low as 3 ppb to avoid oxidation and help sustain drug efficacy, safety, and stability.
- Monitor the residual VHP level from early in the aeration cycle to determine when it is low enough to reliably begin production operations.
- Monitor residual vaporized hydrogen peroxide continuously to detect excursions and support ongoing process control.

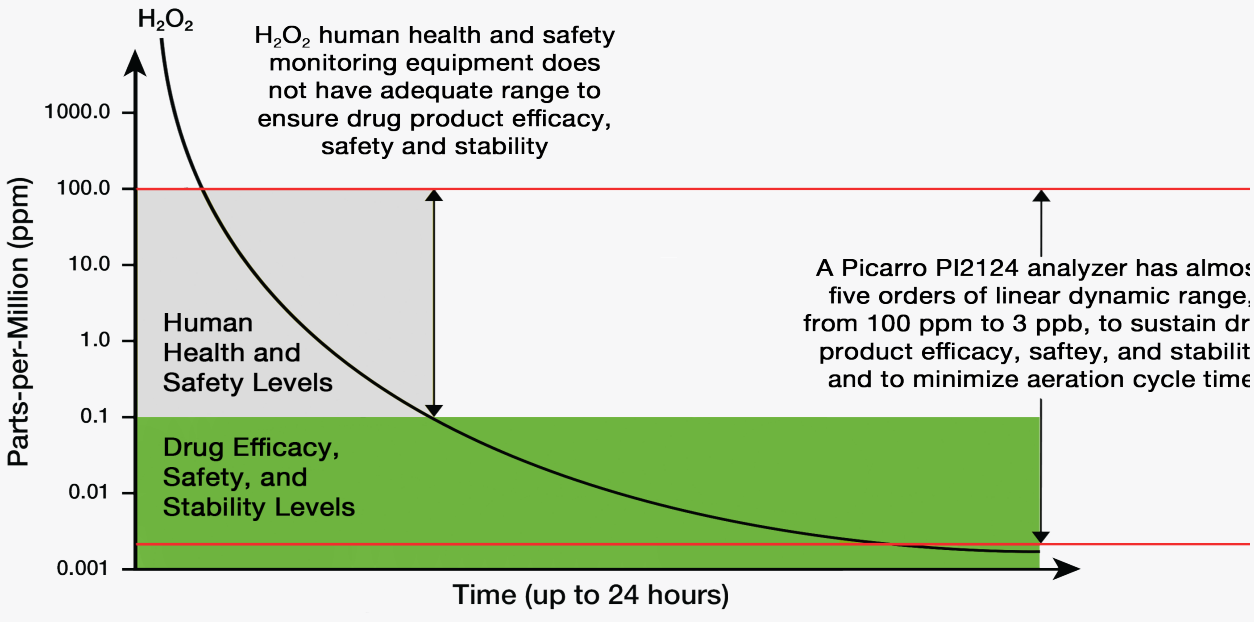

Figure 1. Monitoring residual H_2O_2 levels across the VHP clearance profile

CONTINUOUS MONITORING - THREE OPERATING PHASES

VHP Process Monitoring Across Aeration, Production, and Process Development

As illustrated in **Figure 1**, VHP concentration changes dynamically over time and must be understood at both ppm and ppb levels to protect sensitive pharmaceutical products and enable efficient operations. The PI2124 Analyzer provides continuous, real-time measurement of VHP, delivering actionable insight across critical phases of isolator operation.

Aeration Cycle Monitoring

During post-decontamination aeration, continuous VHP measurements can be used to verify clearance to site-defined ppb targets before initiating production. Rather than relying solely on fixed aeration times, operators can use measured concentration data to identify the aeration end-point dynamically, helping minimize unnecessary downtime while maintaining product protection.

Production Campaign Monitoring

The same measurement capability shown in **Figure 1** can be applied beyond aeration. Continuous monitoring during production enables detection of unexpected VHP sources, such as off-gassing from materials or components in the isolator. Measurement data can be used to document that VHP levels remain within acceptable limits throughout the production campaign and support investigation if excursions occur.

Process Development and Optimization

VHP concentration data collected over time can support development and optimization of aeration cycles for sensitive products, materials, and isolator configurations. Comparing concentration profiles across cycles and campaigns helps assess process consistency and supports data-driven improvement efforts.

PERFORMANCE SNAPSHOT

PI2124 Analyzer Specifications

Measurement range	0–100 ppm
Lower detection limit	~3 ppb
Measurement interval	~10 seconds
Response time	< 1 minute
Precision	~1 ppb-class (typical)

Operational Value

The PI2124 analyzer provides continuous VHP measurements without wet chemistry or consumables and requires infrequent calibration and maintenance. Its wide dynamic range enables monitoring from high ppm levels during decontamination through low-ppb levels relevant to product efficacy, safety, and stability.

Data Integration

Measurement data can be output digitally or via optional analog outputs to secure SCADA systems or data-logging devices, allowing integration into existing control, review, and documentation workflows.

Designed for GMP Pharmaceutical Manufacturing

GMP Data Integrity and Qualification Support

The PI2124 analyzer supports GMP pharmaceutical manufacturing when qualified, validated, and operated under site procedures. Its software supports 21 CFR Part 11–compliant electronic records and signatures, including role-based access control, and can interface with secure SCADA or data-logging systems. The analyzer supports monitoring and verification activities but does not replace VHP cycle validation, biological indicators, or required risk assessments.

Analyzer Validation and Verification

The PI2124 analyzer rarely requires calibration or maintenance. However, GMP guidelines do require that users periodically validate system performance. While Picarro does provide a protocol for validation by VHP total evaporation, it requires wet chemistry and from 8 to 24 hours to complete.

As an alternative, Picarro has developed a validation protocol that uses methane as a surrogate gas. Compared to the VHP total evaporation method, the surrogate gas method enables easier and faster validation of the analyzer's accuracy, and includes a report with e-signature capability.

Picarro also provides an installation qualification (IQ) and operation qualification (OQ) check list, so that the analyzer can be installed and put it into operation quickly and easily with GMP compliance.

"Compliance, robustness of processes, and efficiency will need to be squared in one equation."

A report entitled, "Rapid Growth in Biopharma: Challenges and Opportunities," by McKinsey & Company discusses critical drug development and production considerations. In regards to meeting quality requirements, the report states that, "Compliance, robustness of processes, and efficiency will need to be squared in one equation." The Picarro PI2124 analyzer is designed to help companies address all three challenges simultaneously to ensure ultra-low levels of residual VHP in GMP pharmaceutical production environments.

About Picarro

Picarro is a leading provider of gas concentration and isotope analyzers, with over 5,000 instruments across 100 countries. Major pharmaceutical, CMO, and isolator companies have used Picarro hydrogen peroxide analyzers for over a decade. Picarro analyzers and systems are used in a wide range of other applications, natural gas distribution, commercial sterilization, fenceline monitoring, pharmaceutical manufacturing, and scientific research. Our PhD scientists and optical engineers design and produce instruments in our headquarters located in the heart of Silicon Valley, California.

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