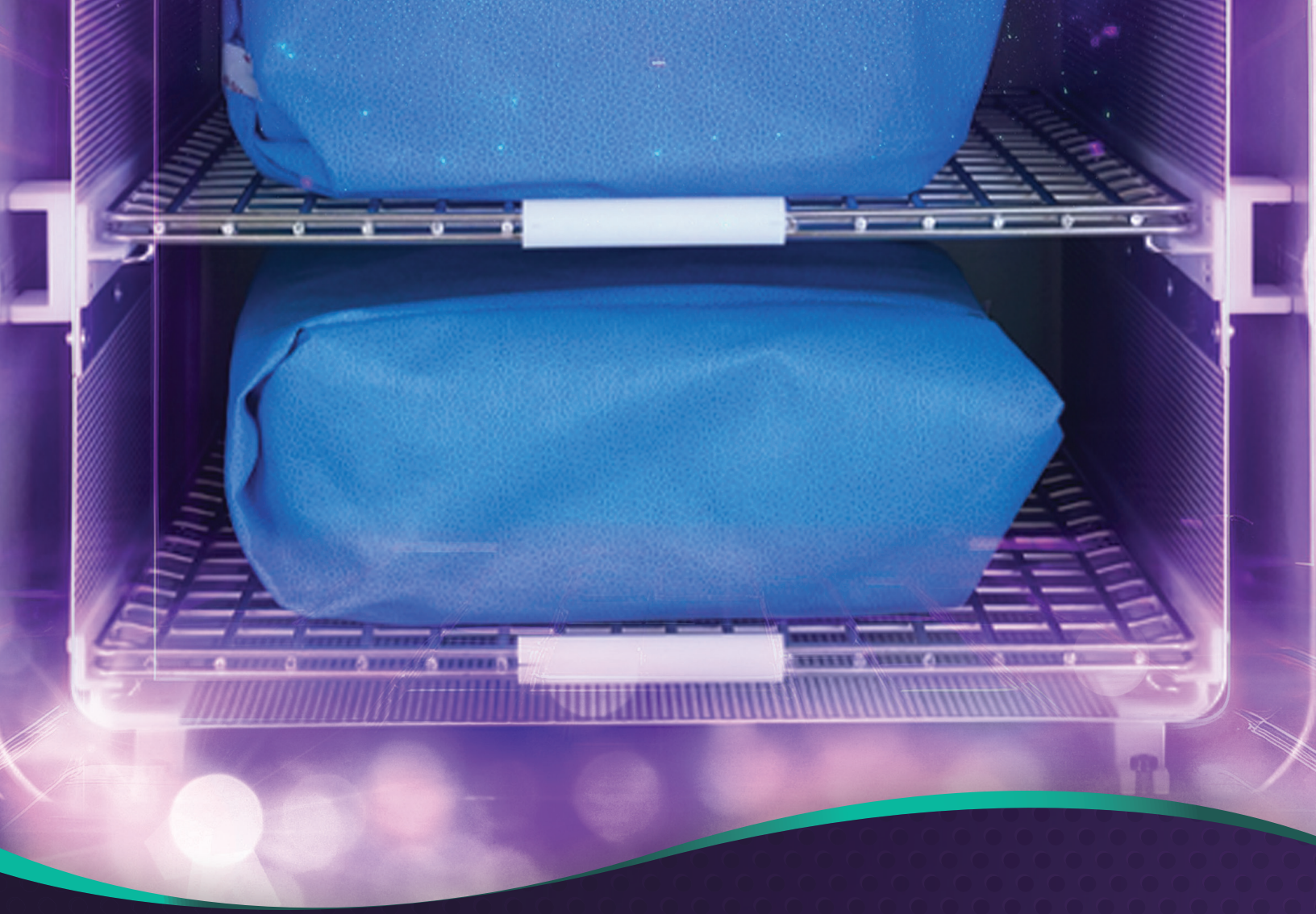

Advanced Sterilization Products™

The Power of Plasma

for Effective Low-Temperature Sterilization

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The Importance of Sterilization in Healthcare

In the ever-evolving healthcare landscape, the importance of effective sterilization cannot be overstated. **The stakes are high—patient safety hinges on the assurance that every surgical instrument and medical device is free from infectious pathogens.** The healthcare industry faces growing challenges in infection control, the adoption of technologies to support both sterilization Margin of Safety and environmental safety is essential.

Patients worldwide place immense trust in surgeons and hospital staff to ensure their safety during surgical procedures. A critical component of this trust is the assurance that medical devices and instruments are free from infectious pathogens. Equally important is maintaining environmental safety for staff providers.

As the healthcare industry faces growing challenges in infection control, the adoption of hydrogen peroxide gas plasma (HPGP) technology is a crucial step forward in safeguarding both patients and healthcare workers while advancing sustainability goals.

Each year, approximately 310 million major surgical procedures take place globally, with 40 to 50 million occurring in the United States and 20 million in Europe. Given these high numbers, the potential for surgical complications is significant. While the global surgical mortality rate ranges from 1-4%, this seemingly low percentage still results in a considerable number of deaths. More concerning is the fact that 5-15% of patients experience serious postoperative complications, impacting millions of individuals annually. This underscores the need for rigorous sterilization standards to minimize the risks associated with surgical interventions and improve patient outcomes. [1]

It's estimated that approximately half of surgical site infections (SSIs) are preventable. The financial burden of an SSI can range from $10,000 to $90,000, particularly when prosthetic joints are involved. To address this, various medical management strategies are in place, including surgical antimicrobial prophylaxis. Perioperative and intraoperative measures to reduce the risk of SSIs include maintaining proper patient glycemic control, ensuring normothermia, providing adequate oxygenation, and conducting full-body antisepsis prior to surgery. [2]

FINANCIAL BURDEN OF SSIs **$10K TO $90K**

Role of Sterile Processing Departments (SPDs) and the Consequences of Inadequate Sterilization

Effective sterilization practices, coupled with comprehensive infection prevention measures, are critical for minimizing the impact of surgical site infections (SSIs) and improving patient outcomes. **At the heart of this process is the Sterile Processing Department (SPD), which serves as a critical, yet often underappreciated, component of the healthcare system.** SPDs are responsible for the meticulous cleaning, disinfection, and sterilization of medical devices and surgical instruments that are vital for patient care. These unsung heroes of healthcare ensure that equipment is free of harmful microorganisms, thereby playing a crucial role in preventing healthcare-associated infections (HAIs).

The importance of rigorous attention to detail and repeatable, standardized processes in SPD operations cannot be overstated. Even minor lapses can lead to serious consequences. For example, retained biodebris in complex, hard-to-clean instruments such as cannulated drills may not be fully sterilized after standard autoclave cycles, potentially leading to infection. Additionally, delays in the reprocessing of surgical instruments can increase the likelihood of contamination with resistant pathogens, heightening the risk of infection transmission during subsequent procedures.[3]

To effectively address the high incidence of HAIs and mitigate the risks associated with improper instrument sterilization, healthcare facilities must implement and maintain stringent infection control measures at every stage of patient care. This includes focusing on timely and thorough reprocessing of surgical instruments to eliminate any retained biological debris that could carry infectious agents.[4]

> Sterilization of medical devices is not merely a box to be checked; it is **a critical and complex process that requires a robust, multi-faceted approach**.

Achieving complete sterilization involves the elimination of all microorganisms, including bacteria, viruses, and fungi, which requires precision, advanced technology, and strict adherence to best practices in sterile processing. Without proper sterilization protocols, healthcare facilities face an increased risk of infection outbreaks, potentially leading to severe patient outcomes, extended hospital stays, and higher healthcare costs.

Reprocessing Modalities [5]

Most Difficult to Kill ↑ Less Difficult to Kill

Organism	Sterilization	High-Level Disinfection (HLD)
Bacterial Spores	✓	X
Mycobacteria	✓	✓
Fungi	✓	✓
Vegetative Bacteria	✓	✓
Enveloped Viruses	✓	✓

SPDs, through their meticulous work, contribute directly to patient safety, infection prevention, and overall healthcare quality. By preventing the transmission of infectious diseases, they support better clinical outcomes and reduce the burden of SSIs and HAIs on both patients and healthcare systems. Their role is vital in maintaining the delicate balance between technological innovation in medical care and the foundational principles of cleanliness and sterility that are essential for successful patient treatment.

Regulatory Guidelines and Compliance:

Why Margin of Safety in Sterilization is Important

In the context of medical device sterilization, the term "Margin of Safety" refers to the built-in buffer designed to ensure an extremely high probability of eliminating all microorganisms on the device. This concept goes beyond simply achieving sterility; it acknowledges the inherent variability within sterilization processes.

A high Margin of Safety is critical and is directly linked to the Sterility Assurance Level (SAL) achieved during sterilization. SAL, expressed as a probability (e.g., 1 in a million or 10^{-6}), represents the likelihood of a single microorganism surviving sterilization on a single device.[6] A lower SAL (i.e., a smaller probability of microorganism presence) indicates a higher level of sterility assurance. **A high Margin of Safety exceeds the minimum required lethality, building in a buffer that ensures a very high probability of achieving sterility, even with minor process variations.**

Achieving and maintaining a high Margin of Safety in sterilization is paramount to preventing healthcare-associated infections and safeguarding patient health. To effectively implement these critical sterilization processes, healthcare facilities rely on dedicated departments such as the sterile processing department and Infection Prevention (IP) departments and standardized hospital sterilization protocols and device manufacturers' instructions for use.[7] Adherence to stringent guidelines and regulations is essential in achieving this critical objective. Organizations such as Association for the Advancement of Medical Instrumentation (AAMI) and The Joint Commission (JC) have established comprehensive frameworks to guide healthcare facilities in implementing effective sterilization processes.[7]

The JC emphasizes the importance of fostering a culture of safety, prioritizing sterilization and environmental exposure. The concept of Margin of Safety is central to discussions about sterilization, especially in situations where cleaning processes may be imperfect.

> Higher concentrations of hydrogen peroxide (HP) during sterilization can **address challenges to Margin of Safety** by ensuring **effective sterilization**, even in suboptimal conditions.[11]

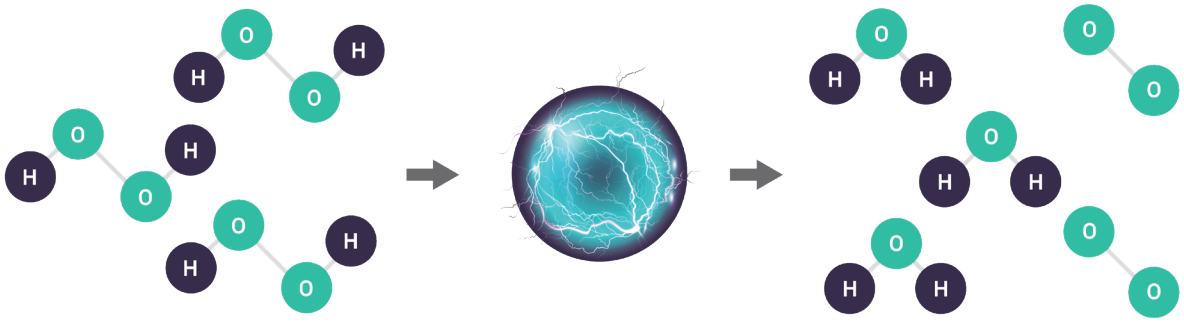
The JC's Sentinel Event Database reveals that leadership's failure to create an effective safety culture is a key factor in various adverse events, from wrong-site surgeries to delays in treatment.[8]

Research conducted by Ofstead et al. has shown that even under observation, technicians sometimes fail to follow complete sterilization processes. This lack of adherence highlights the importance of having a robust Margin of Safety in place, ensuring that sterilization methods can compensate for human error and maintain patient safety.[9]

Hydrogen Peroxide Gas Plasma (HPGP) Technology and the Margin of Safety

Complex medical devices with intricate designs and the potential for damage from use pose significant challenges to cleaning and subsequent sterilization. Therefore, choice of sterilization technology must consider these factors to ensure adequate microbial reduction.

Hydrogen Peroxide Gas Plasma (HPGP) is a subset of low-temperature sterilization (LTS). This technology is designed to maximize the effectiveness of the sterilization process while ensuring the safety of both patients and healthcare personnel. Central to this system is the role of plasma, which facilitates the breakdown of hydrogen peroxide (HP)—a potent sterilizing agent—into harmless byproducts. **This breakdown not only enhances the sterilization process but also mitigates the risks associated with residual peroxide exposure at the cycle's end.** This enhances safety by making the contents safe for handling and use.[10] This process enables higher concentrations of HP as a safety factor during the sterilization cycle, which is essential for achieving thorough penetration. At the same time, plasma ensures that HP is effectively broken down at the end of the cycle, reducing the risk of residual peroxide on sterilized items.[11]



Research has demonstrated that HPGP systems offer a higher Margin of Safety compared to VHP without gas plasma technology, particularly in the presence of challenging contaminants such as salt and blood plasma.[4] To explore these issues further, an independent study assessed how different sterilization processes could mitigate risks associated with residual proteins or salts on medical instruments, evaluating both vegetative bacteria and spores, including multidrug-resistant organisms.

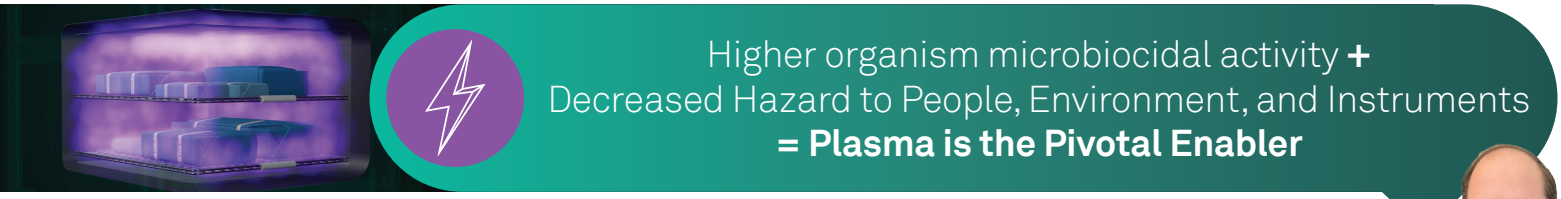
> Research has demonstrated that **HPGP systems offer a higher Margin of Safety** compared to VHP, particularly in the presence of challenging contaminants such as salt and blood plasma.[4]

Although this does not negate the need for strict adherence to sterilization protocols, it highlights the importance of establishing a robust Margin of Safety in an imperfect world.[11] As noted in peer-reviewed literature, not all sterilization technologies used in healthcare are equally robust.[5,11] While FDA-cleared technologies are designed to kill a broad range of microorganisms, their effectiveness can be compromised if instruments are not adequately cleaned before sterilization. Even the most advanced technology may fail if instruments are burdened with contaminants due to inadequate cleaning.[4]

As found in the efficacy study by Rutala et al., the higher concentration of HP in the HPGP sterilizer (25.6 mg/L) compared to VHP (9.1 mg/L) was considered by the authors to be a potential safety buffer, providing an explanation for the significantly higher Margin of Safety for HPGP (1.9% sterilization failure rate) versus VHP (76.3% sterilization failure rate).[11] Another way to view this is a 98.1% Margin of Safety for HPGP compared to 23.7% for VHP. When comparing VHP to steam and HPGP, Rutala et al. noted:

> "**VHP [without plasma technology] has a significantly narrower margin of safety** in killing vegetative bacteria and spores in the presence of a salt and serum challenges."[4]

The study's findings have significant implications for the choice of sterilization methods in healthcare settings. While steam sterilization remains the most effective method, HPGP offers a viable alternative for heat-sensitive instruments, particularly when used with plasma technology to enhance safety and reduce environmental impact.



Higher organism microbiocidal activity **+**
Decreased Hazard to People, Environment, and Instruments
= Plasma is the Pivotal Enabler

Environmental and Occupational Safety

Dr. Ivan Salgo, MD, MS, MBA
ASP VP, Chief Medical and Scientific Affairs Officer

As outlined by the Joint Commission, ensuring the control of airborne contaminants in critical areas through the use of appropriate ventilation systems is essential. Beyond the immediate effectiveness of sterilization methods, the environmental impact of these processes is an increasingly important consideration. Hydrogen peroxide (HP) is generally considered a safer sterilizing agent compared to others, such as ethylene oxide, which is known for its acute irritant and carcinogenic effects.[13]

Reducing HP exposure is critical for several reasons, including its potential to act as an airway irritant, particularly for individuals with pre-existing pulmonary conditions such as asthma and chronic obstructive pulmonary disease (COPD). These conditions are common, and even brief exposure to excess HP can trigger significant respiratory reactions.

In addition to its health impacts, the reduction of environmental emissions of HP aligns with global Environmental, Social, and Governance (ESG) initiatives, which prioritize sustainable and responsible practices across all sectors, including healthcare. Hospital sterile processing departments (SPDs) and other healthcare sterilization facilities must be well-ventilated to minimize harmful exposures. However, real-world conditions are often imperfect, and there is always the potential for residual HP to remain on instruments after the sterilization process. This residual peroxide poses a risk not only to the instruments, which may undergo further chemical interactions but also to the healthcare workers who handle them.[14]

A study published in the peer-reviewed *Journal of Occupational and Environmental Hygiene* examined the HP concentrations measured near different models of sterilizers.[14] The authors looked beyond the 8-hour time weighted average (TWA) to observe individual fugitive vapor emissions throughout the workday. The study suggested that a short-term exposure limit (STEL) for HP is warranted. Many governments both in the United States and abroad, have established STEL of 2 to 3 ppm.[14]

"Ensuring proper control of airborne contaminants in critical areas through the use of appropriate ventilation systems is **essential for maintaining a safe hospital environment**." [12]

The study noted that of the seven sterilizers observed over four years, **peak exposure without plasma technology was almost 19 times higher than a low-temperature sterilizer using plasma to reduce emissions.**

The authors stated,

> "The American Conference of Governmental Industrial Hygienists Threshold Limit Value for hydrogen peroxide is 1 ppm, 8-hr TWA, and according to these guidelines, **the maximum exposure to hydrogen peroxide should be no more than 5 ppm**. Clearly, some of the exposures recorded here exceed this value, and even though the TWA exposures do not exceed the legal permissible exposure limits, the exposures **should be flagged as potentially harmful to employees**." [14]

In real-world settings, such as a busy hospital SPD with five (5) vaporized hydrogen peroxide (VHP) sterilizers running five (5) loads a day, five (5) days a week, operators could face approximately 125 additional exposure events when removing a load from the VHP sterilizer.

In contrast to the VHP without plasma technology models used in the study, other sterilizers, including certain Hydrogen Peroxide Gas Plasma models, demonstrated lower emission levels. These results suggest that **the design and engineering of sterilization equipment can provide a statistically significant impact on the level of HP vapor released into the environment.** [14]

Higher HP Exposure in Non-Plasma Technology Sterilizers [14]

Benefits of Plasma Technology

Hydrogen Peroxide (HP) has emerged as a preferred sterilization method due to its **effectiveness, safety, and environmental friendliness.** While both Vaporized Hydrogen Peroxide (VHP) and Hydrogen Peroxide Gas Plasma (HPGP) utilize HP as a sterilant, HPGP technology offers superior performance in several key areas.

Rutala et al. identify three potential advantages of plasma technology in HPGP, not found in non-plasma VHP platforms, as outlined in their study on sterilization effectiveness:[11]

- **Quick Breakdown of Residual HP:** Plasma technology enables the rapid breakdown of residual HP, whereas VHP without plasma technology has a gradual release.
- **Reduced HP Vapor Release:** Plasma breaks down HP into benign components (H_2O and O_2), preventing a burst of HP vapor when opening the sterilization chamber door and subsequent release into the environment.
- **Higher Cycle Concentrations of HP:** Plasma allows for higher cycle concentrations of HP, increasing the Margin of Safety compared to VHP platforms. Rutala's study showed a 76.3% sterilization failure rate for VHP versus only a 1.9% failure rate for HPGP under conditions of salt and serum residual. This represents an over four-fold advantage in Margin of Safety under conditions where cleaning is not complete prior to sterilization.

Moreover, the benefits of a HPGP system extend beyond just the immediate sterilization process. By incorporating plasma technology, this system aligns with broader healthcare goals of **enhancing safety, reducing environmental impact, and improving the overall quality of patient care**. The reduction in HP exposure achieved through plasma technology not only protects healthcare workers and patients but also contributes to the sustainability goals of healthcare institutions.

In an era where environmental responsibility is increasingly recognized as a key component of healthcare quality, the ability to reduce emissions and protect the environment is a significant advantage.

Differentiating HPGP and VHP without Plasma Technology: A Comparative Analysis

Uses vaporized HP technology to achieve sterilization effect:

HPGP ✓ VHP ✓

SIMILAR

Both use vaporized HP but a **higher HP concentration is achieved in HPGP** vs VHP.

HP concentration measurement method:

HPGP – Direct VHP – Indirect

DIFFERENT

HPGP + UV Spectroscopy is better able to accurately determine HP concentration in the chamber.

Margin of Safety | **Sterilization robustness under conditions of suboptimal cleaning:**

98.1% (HPGP) 23.7% (VHP without Plasma)

DIFFERENT

Under conditions of residual salt and serum, **HPGP had a significantly higher Margin of Safety** (98.1% sterilization success for HPGP) vs VHP (only 23.7% sterilization success).[4]

Margin of Safety | **HP Residual Elimination Method:**

HPGP
Gas Plasma + Vacuum (Lower peak emissions upon opening chamber door)

VHP
Vacuum only (Peak Emissions)

DIFFERENT

Using both vacuum and gas plasma, **HPGP provides a higher Margin of Safety** by minimizing residuals on the product and reducing fugitive emissions when the chamber is opened.[14]

Summary

In conclusion, the **Hydrogen Peroxide Gas Plasma (HPGP) Low-Temperature Sterilization (LTS) system, with its innovative use of plasma technology and additional safety mechanisms, offers a powerful and effective solution for medical sterilization.** The system enhances the efficacy of Hydrogen Peroxide (HP) as a sterilizing agent while simultaneously reducing the risks associated with residual peroxide exposure, providing a critical **Margin of Safety** in healthcare settings for both patients and staff. Furthermore, the environmental benefits of plasma technology align with global efforts to promote sustainability and protect the health of both patients and healthcare workers. HPGP systems represent not only a technological advancement in sterilization but also a significant step forward in **ensuring the safety, sustainability, and efficiency of healthcare practices.**

Effective sterilization is a cornerstone of patient safety, crucial for preventing the transmission of healthcare-associated infections (HAIs). The meticulous cleaning, disinfection, and sterilization processes undertaken by Sterile Processing Departments (SPDs) are critical to this effort.

A high Margin of Safety in sterilization is essential to ensure the elimination of virtually all viable microorganisms, including resistant strains. HPGP sterilization has emerged as a superior technology in achieving this standard. Compared to Vaporized Hydrogen Peroxide, HPGP offers a significantly enhanced Margin of Safety, evidenced by its superior efficacy in inactivating a broader spectrum of microorganisms, including spores, while being less affected by the presence of organic matter and salts.

Moreover, HPGP demonstrates a gentler profile on both patients and instruments. Its compatibility with a wide range of medical device materials and its environmentally-friendly byproducts contribute to its overall safety and efficacy.

As healthcare continues to evolve, the need for advanced sterilization technologies becomes increasingly evident. By prioritizing HPGP and other innovative sterilization methods, healthcare institutions can **significantly enhance patient outcomes, reduce the risk of HAIs, and contribute to a safer healthcare environment.**

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