

# GUIDING THE TRANSITION FROM EtO STERILIZATION



We are strategic partners in sterilization and bio-decontamination solutions for major players in the biotechnological, pharmaceutical and Medical Device industries.



**With 70 years of experience,**  
Fedegari is committed to the future  
with an ever-relevant vision.

# A new perspective changes the way we see the world

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A different sterilization paradigm is emerging.  
Navigating it demands process ownership.

Medical device sterilization is entering a new phase: **materials, complexity, regulatory** evolution and alternative sterilization methods require a structured and validated approach.

**Fedegari governs** this transition through experimental process development and deep knowledge of sterilization principles.

## How we govern the transition:

- 🕒 **Guiding** you in selecting the most appropriate sterilization pathway based on material compatibility.
- 🕒 **Working alongside** you in our Tech Centers to experimentally evaluate each specific application.
- 🕒 **Developing and validating** tailored vH<sub>2</sub>O<sub>2</sub> sterilization processes for highly complex devices, ensuring safe and reliable outcomes.

**Start this new  
adventure** →

# WHAT IF MAKING DEVICES SAFE WAS ALSO A DANGER?

For more than 50 years, ethylene oxide has been the reference sterilization method for heat-sensitive medical devices.



**2019**

The U.S. EPA identifies **EtO** as a significant **cancer risk**



**2019**

The U.S. FDA calls for development of a **SAFER** sterilization process

# Replacing EtO IS NOT a technology decision

Sterilization feasibility begins with the device.

Material composition, geometry and packaging configuration determine which sterilization principles can be applied.

The transition from EtO requires a **process-driven** approach.



\* Ref. Biomedical Instrumentation & Technology, Volume 54 • Number s1- Pages: 6 - 14, PubMed: 34169981

# Sterilization methods IN COMPARISON

At Fedegari, we selected Moist Heat and vH<sub>2</sub>O<sub>2</sub> for transitioning from EtO.

By adopting these technologies, we support Medical Device manufacturers with safer, more competitive and high-productivity sterilization solutions, designed to meet modern regulatory expectations while ensuring uncompromised process control and product integrity.

	EtO	Steam	vH <sub>2</sub> O <sub>2</sub>
<b>Exposure temperature (°C)</b>	37 ÷ 63	110÷125	30 ÷ 60
<b>Cycle time (hours)</b>	> 20	2-5	2-8 *
<b>Quarantine</b>	Mandatory	Not Applicable	Not Applicable
<b>Residual limits</b>	1 ppm	Not Applicable	1ppm
<b>Environment</b>	Hazardous	Friendly	Friendly
<b>Toxic</b>	YES	NO	NO
<b>Explosive</b>	YES	NO	NO
<b>Material Compatibility</b>	High	Medium	High

\* Depending on loads characteristics (refer to the case study for further insight)

Steam sterilization is applied whenever possible.

For sensitive materials, Fedegari develops vaporized hydrogen peroxide sterilization pathways.

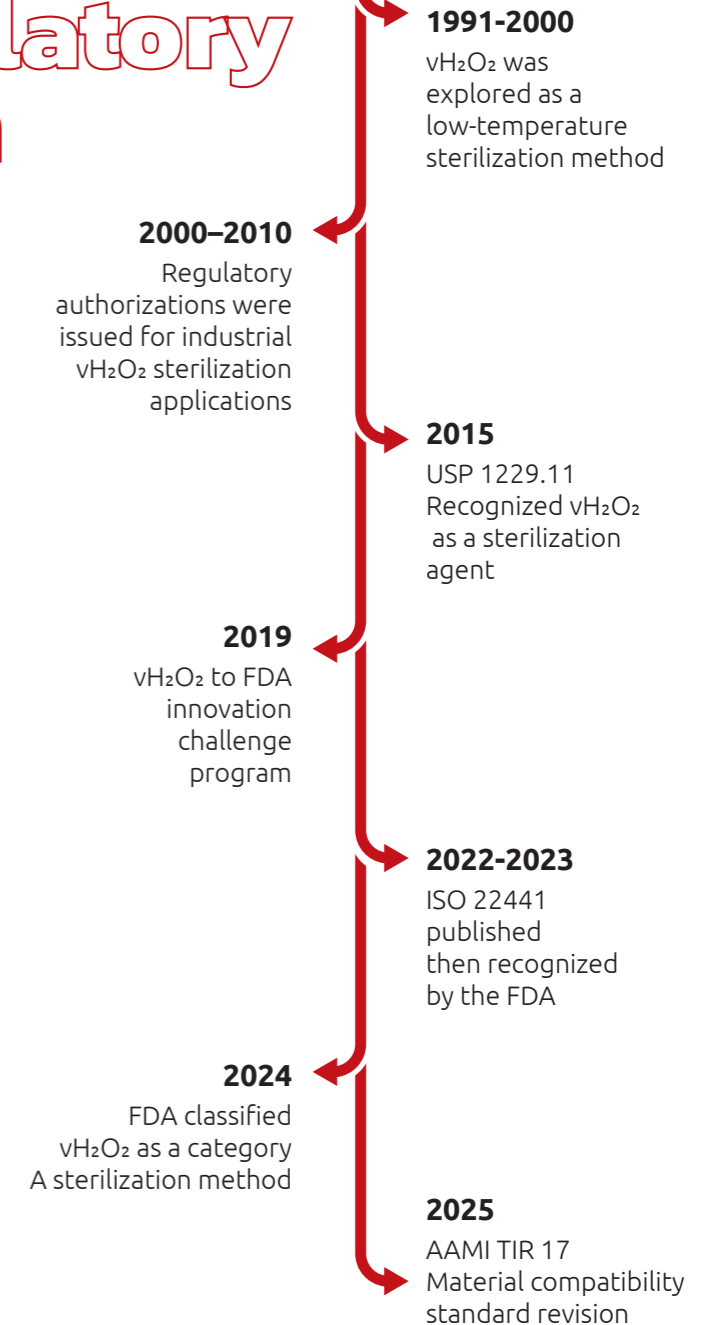
## vH<sub>2</sub>O<sub>2</sub> Regulatory recognition

The regulatory framework surrounding vaporized hydrogen peroxide sterilization has evolved rapidly over the last decade.

Standards development and regulatory recognition have established vH<sub>2</sub>O<sub>2</sub> as a credible sterilization pathway for heat-sensitive medical devices.

The focus is now shifting from technology exploration to process development and industrial validation.

## Industrial Adoption



The evaluation of alternative sterilization methods requires more than equipment.

It **requires** experimental validation, deep understanding of materials and control of sterilization principles.

## FEDEGARI TECH CENTERS

develop and verify sterilization processes for complex medical devices with challenging geometries and multi-material assemblies, ensuring sterilization efficacy while safeguarding product safety.

# KNOWLEDGE AS THE CORE

### Process Knowledge

Understanding sterilization mechanisms, material compatibility and microbial inactivation principles.

### Experimental Infrastructure

Controlled environments for material testing, process optimization and sterilization studies.

### Industrial Validation

Translation of experimental evidence into scalable sterilization processes.

## ASSOCIATION WORKING GROUPS

**KILMER KILMER**

vH<sub>2</sub>O<sub>2</sub> KILMER modality Team  
KILMER material group

**AFI**   
Associazione Farmaceutici Industria  
Società Scientifica

Parental product study group

**PDA** 

PDA sterile processing parental drug  
manufacturing

**ISPE**  **ISPE** | SHAPE THE FUTURE  
OF PHARMA

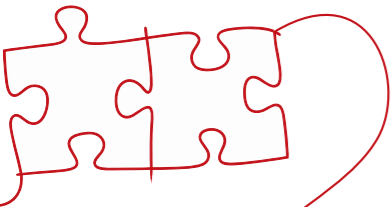
GAMP - IT manager & infrastructure qualification  
Medical device  
Design in life science  
Aseptic and biologics manufacturing facilities

Knowledge drives business growth.

# Scientific approach

A **structured development pathway**, from pilot phase to final validation, supported by comprehensive testing and robust data consolidation.

**MATERIAL COMPATIBILITY**



**RESIDUAL EVALUATION**



**CQA VERIFICATION**



**BI WORST-CASE MAPPING**



**PROCESS OPTIMIZATION**












**Our experts work with you to develop a strategic transition plan, tailored to your specific needs and products.**

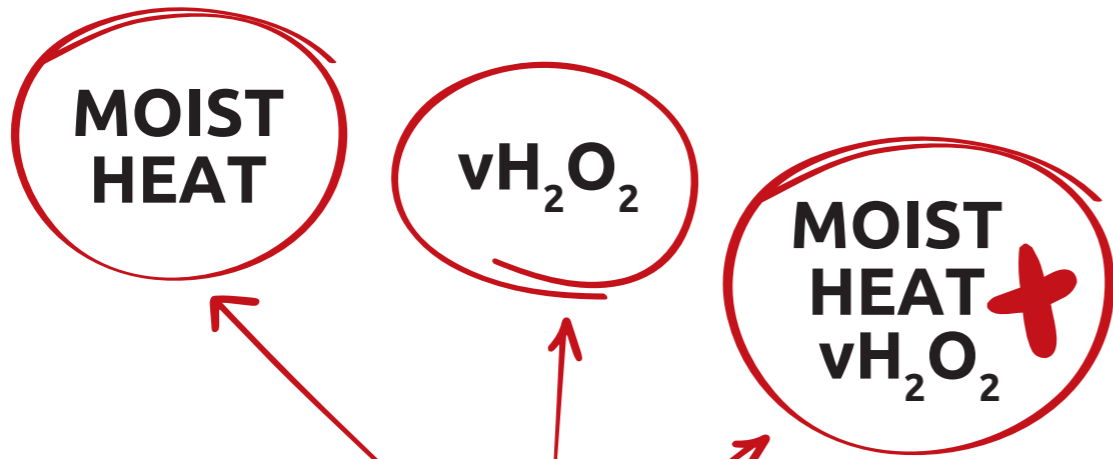
The future of patient safety and product efficacy depends on making the right choices today. The future of collective well-being depends on this too.

# THE PRODUCTS WE CAN SAFELY HANDLE

Scan me to stay up to date



Product	Class / Description	Materials
 <b>Empty syringe</b>	MD, Class IIa	PP, LDPE, PI, Medical-grade paper, PA/PE film
 <b>Vitrectomy system</b>	MD, Class III	PC, Tyvek®, PP
 <b>Suture Kit</b>	MD, Class IIb	PA, Tyvek®, PET
 <b>PFS with ophthalmic drug</b>	Combination Product	Glass, PI, Tyvek®
 <b>RTU vials</b>	Primary container - MD Class IIa	Glass, Tyvek®/LDPE
 <b>Pacemaker</b>	MD, Class III	Various materials
 <b>Filter</b>	Single Use Technology	PES, PSU, PP, PU, PC
 <b>Hemodialysis Tubing set</b>	MD, Class IIb	PVC, PP, Medical Paper/ LDPE
 <b>Oxygenator</b>	MD, Class III	PU, PET, PVC, PC, Tyvek®/LDPE









## Why limit your process to one technology?

Moist heat and vH<sub>2</sub>O<sub>2</sub> are available either individually or combined within the same equipment, ensuring the optimal process for every material.



## QUALITY BECOMES SCIENCE

## SCIENCE BECOMES DESIGN

-  Pressure **2 - 3 bar**
-  **121 °C - 134 °C**
-  **Cycle Time:** Tailored process based on product characteristics
-  **Cycle Time:** Tailored process based on product characteristics, with deep vacuum facilitating vH<sub>2</sub>O<sub>2</sub> penetration and improving aeration
-  **30 - 60°C** during the process
-  Deep vacuum down to **1mbar**

Fits for All

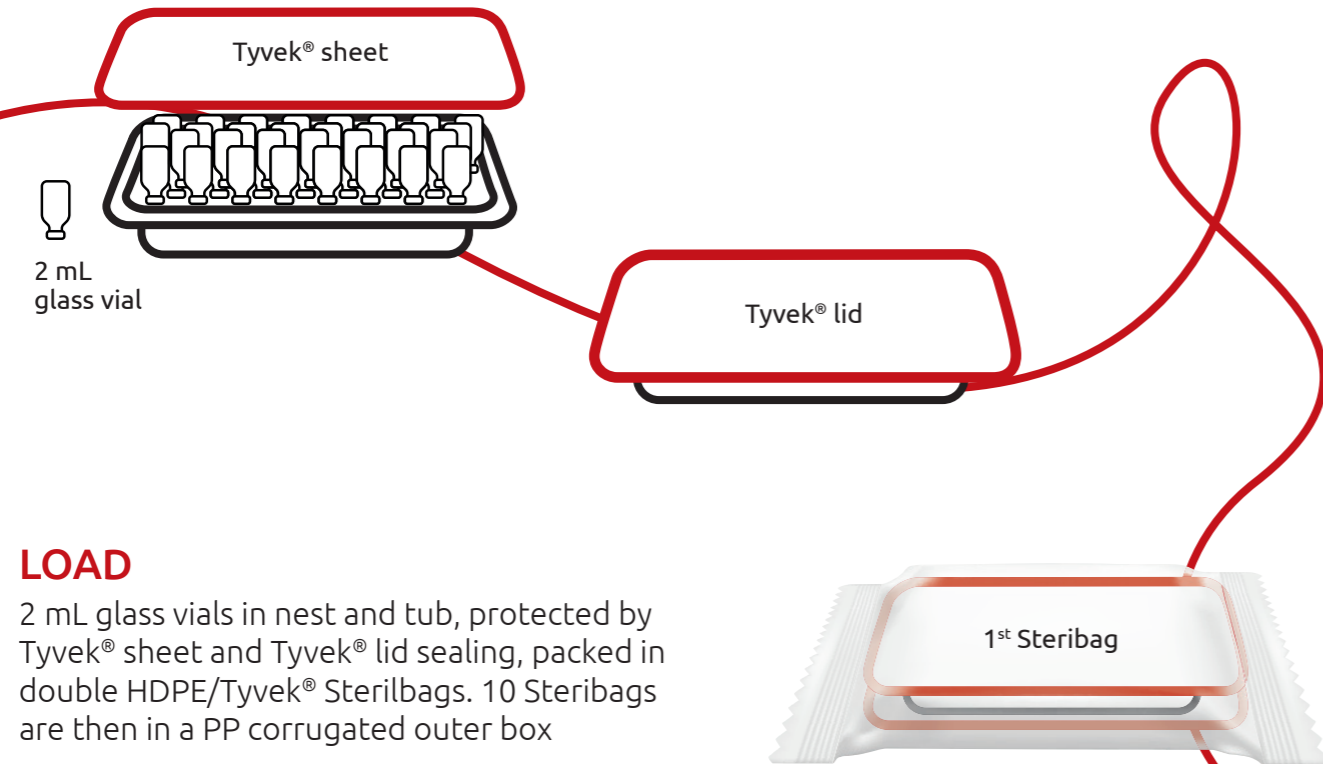
Material sensitivity defines the sterilization strategy

Regardless of device complexity

# PRIMARY CONTAINERS IN MULTIPLE PACKAGING

## Fedegari Tech Centers

develop and verify sterilization processes for complex medical devices with challenging geometries and multi-material assemblies, ensuring sterilization efficacy while safeguarding product safety.



### LOAD

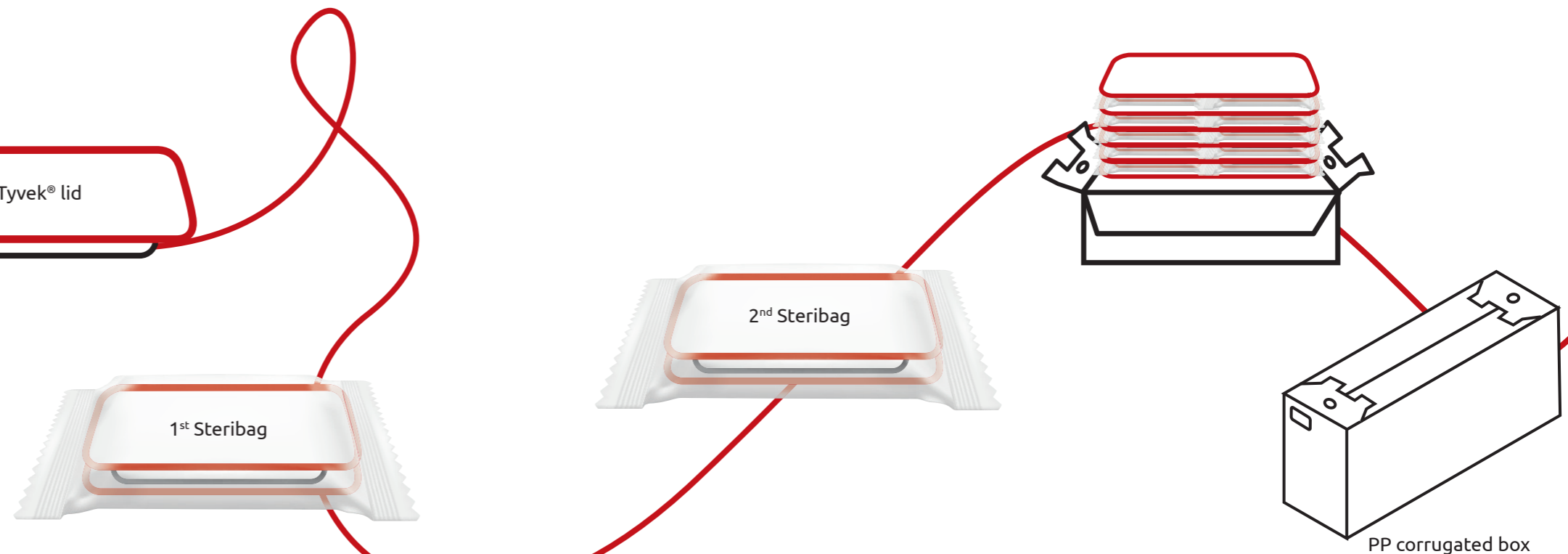
2 mL glass vials in nest and tub, protected by Tyvek® sheet and Tyvek® lid sealing, packed in double HDPE/Tyvek® Sterilbags. 10 Steribags are then in a PP corrugated outer box

## STERILIZATION PROCESS

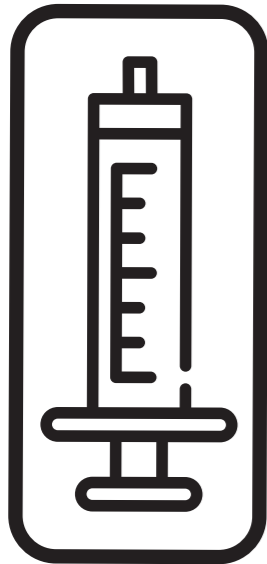
The process was designed to achieve a Sterility Assurance Level (SAL) equal to or greater than  $10^{-6}$ , while preserving the integrity of both primary and secondary packaging materials. A specific focus was placed on the evaluation of residual hydrogen peroxide levels inside the vials.

## RESULTS

- Multilayer device complexity requires controlled sterilization development.
- Ensured effective  $vH_2O_2$  penetration across all layers while preventing residual accumulation
- Achieved faster cycles and eliminated post-process storage



# EMPTY PLASTIC SYRINGE



## LOAD

60 mL syringe packaged within Tyvek®/plastic blister configuration

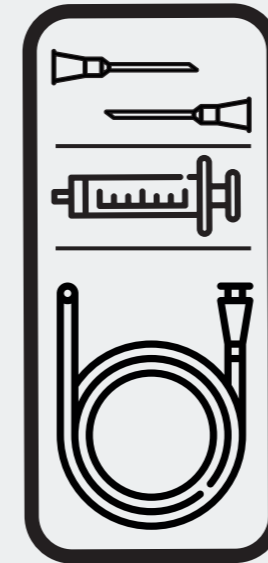
## STERILIZATION PROCESS

The cycle includes a conditioning phase, followed by sterilization through vH<sub>2</sub>O<sub>2</sub> injection combined with deep vacuum pulses. The final aeration phase was optimized to ensure effective removal of vH<sub>2</sub>O<sub>2</sub>

## RESULTS

- ☞ Validated vH<sub>2</sub>O<sub>2</sub> distribution and sterilization efficacy confirmed by BIs (SAL 10<sup>-6</sup> or 12 SLR)
- ☞ vH<sub>2</sub>O<sub>2</sub> residues lower than 1 ppm measured using KMnO<sub>4</sub> titration method
- ☞ Total cycle time 3.5 hours

# VITRECTOMY SYSTEM



## LOAD

Open tube (2 m) with an inner diameter of 4 mm, syringe, plunger, and needle packaged in a plastic/Tyvek® blister.

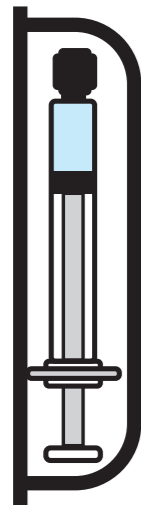
## STERILIZATION PROCESS

The cycle includes a conditioning phase, followed by sterilization through vH<sub>2</sub>O<sub>2</sub> injection combined with deep vacuum pulses. The final aeration phase was optimized to ensure effective removal of vH<sub>2</sub>O<sub>2</sub>

## RESULTS

- ☞ Validated vH<sub>2</sub>O<sub>2</sub> distribution and sterilization efficacy confirmed by BIs (SAL 10<sup>-6</sup> or 12 SLR)
- ☞ vH<sub>2</sub>O<sub>2</sub> residues lower than 1 ppm measured using KMnO<sub>4</sub> titration method
- ☞ Total cycle time 4 hours

# PFS WITH OPTHALMIC DRUG



## LOAD

Glass PFS filled with an ophthalmic drug product, enclosed within Tyvek®/plastic blister packaging

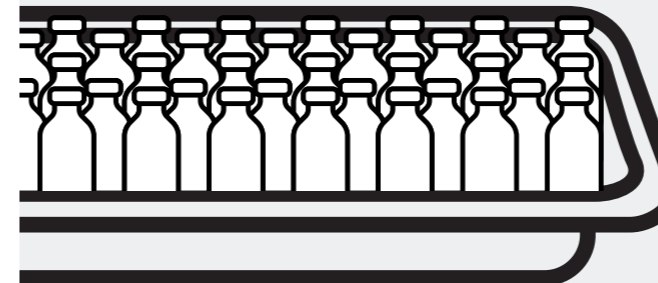
## STERILIZATION PROCESS

The cycle includes a conditioning phase, followed by sterilization through vH<sub>2</sub>O<sub>2</sub> injection combined with deep vacuum pulses. The final aeration phase was optimized to ensure effective removal of vH<sub>2</sub>O<sub>2</sub>

## RESULTS

- vH<sub>2</sub>O<sub>2</sub> sterilization process parameters were optimized to achieve a SAL of 10<sup>-6</sup> while balancing sterilant dose
- Residual vH<sub>2</sub>O<sub>2</sub> levels (measured using UV visible method) comply with the Guidelines for Drinking-water Quality (4th ed., World Health Organization, 2011) and with Directive (EU) 2020/2184
- Total cycle time 3 hours

# READY TO FILL GLASS VIALS



## LOAD

2 mL glass vials arranged in a nest and placed in a tub, covered with a Tyvek® sheet and sealed with a coated Tyvek® lid (1073B®). The complete assembly is configured as a closed system and double-bagged in an HDPE/Tyvek® sterilization bag

## STERILIZATION PROCESS

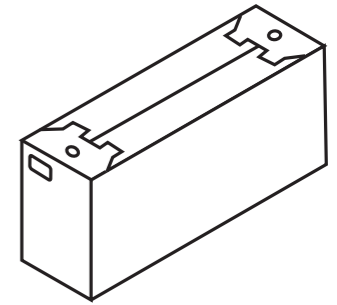
The cycle includes a conditioning phase, followed by sterilization through vH<sub>2</sub>O<sub>2</sub> injection combined with deep vacuum pulses. The final aeration phase was optimized to ensure effective removal of vH<sub>2</sub>O<sub>2</sub>

## RESULTS

- vH<sub>2</sub>O<sub>2</sub> sterilization process parameters were optimized to achieve a SAL of 10<sup>-6</sup> while balancing sterilant dose
- vH<sub>2</sub>O<sub>2</sub> residues lower than 1 ppm measured using UV- visible method
- Total cycle time 3.5 hours

# HAEMODIALYSIS BLOOD TUBING SET

# NEW CHALLENGES AHEAD



## CAN VAPORIZED HYDROGEN PEROXIDE STERILIZE MULTIPLE SECONDARY PACKAGING LAYERS?

**With Fedegari, yes.** Because sterilization performance is defined by how the process is controlled.

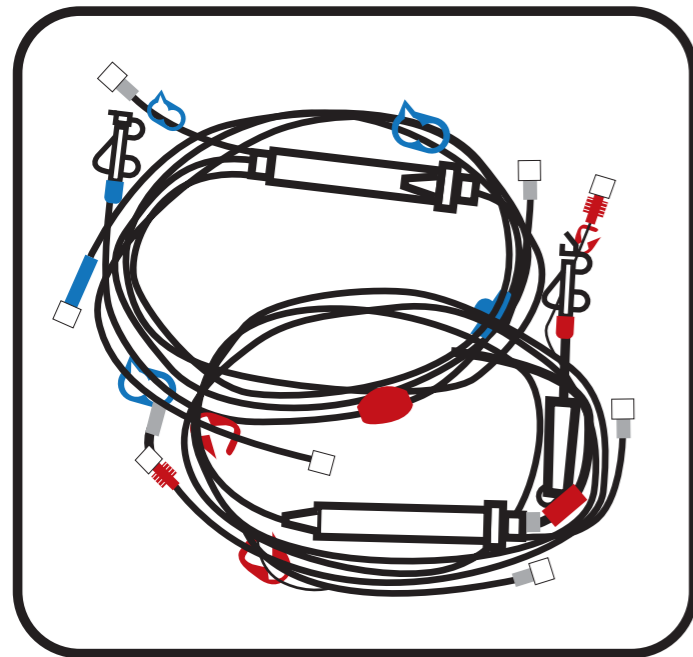


## CAN STERILIZATION EFFICACY BE ACHIEVED THROUGH CELLULOSE SECONDARY PACKAGING WHILE PRESERVING PRODUCT INTEGRITY?

Get in touch and find out.

More questions.  
Let's explore them together. →

Scan me to know more  
about our processes  
and experiences



## LOAD

Hemodialysis blood tubing set, characterized by very long tubes (295-385 cm) with an inner diameter of 5 mm, not all vented

## STERILIZATION PROCESS

The cycle includes a conditioning phase, followed by sterilization through vH<sub>2</sub>O<sub>2</sub> injection combined with deep vacuum pulses. The final aeration phase was optimized to ensure effective removal of vH<sub>2</sub>O<sub>2</sub>

## RESULTS

- Validated vH<sub>2</sub>O<sub>2</sub> distribution and sterilization efficacy confirmed by BIs (SAL 10<sup>-6</sup> or 12 SLR)
- vH<sub>2</sub>O<sub>2</sub> residues lower than 1 ppm measured using KMnO<sub>4</sub> titration method
- Total cycle time 8 hours

# Q&A

## WHICH STERILITY ASSURANCE LEVEL IS ACHIEVED USING THIS TECHNOLOGY?

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A 12-log spore reduction is reached.

## WHAT IS THE MAXIMUM CHAMBER SIZE AVAILABLE FOR vH<sub>2</sub>O<sub>2</sub> STERILIZATION?

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Since Fedegari manufactures all vessels in-house, there are no specific size limitations. Chambers up to 40 m<sup>3</sup> have already been delivered.

## HOW COMPLEX IS THE EQUIPMENT COMPARED TO EtO, SPECIFICALLY REGARDING THE INVESTMENT COST?

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The equipment investment is comparable. However, vH<sub>2</sub>O<sub>2</sub> sterilization process performs shorter cycle times and does not require quarantine at the end of the cycle. This consequently results in savings in both time and building space.

## WHAT IS THE ACCEPTABLE RESIDUAL LEVEL? ARE THERE ANY REGULATORY RECOMMENDATIONS?

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Currently, there are no specific guidelines or regulations that set an allowable vH<sub>2</sub>O<sub>2</sub> residue inside the product. There are only general references in ISO 22441:2022.

To define these limits, manufacturers should perform a toxicological risk assessment in accordance with ISO 10993-17.

## WHERE HAVE BIOLOGICAL INDICATORS BEEN PLACED WHEN TESTING THE PRODUCTS?

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Always in the worst case scenario, challenging hidden points.

**For any further information, please contact us**

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