Saint-Gobain Bioprocess Bags Demonstrate Compatibility with Vaporized Hydrogen Peroxide (VHP)

Vaporized Hydrogen Peroxide (VHP) is an increasingly common sterilizing agent in pharmaceutical manufacturing processes, particularly in final fill applications. For this reason, it is important that the single-use materials used in final fill processes are able to withstand exposure to VHP. Through rigorous testing, Saint-Gobain has demonstrated that their 5-layer, single-use bioprocess bags are well-suited for use in applications where VHP is employed for decontamination purposes.

VHP DECONTAMINATION IN THE FINAL FILL PROCESS

Hydrogen peroxide (H_2O_2) is a very reactive and oxidative chemical. However, due to its high sterilization efficiency and clean process (with water and oxygen as the only byproducts), VHP has been increasingly used for the sterilization and decontamination of materials used in pharmaceutical & food production processes. Signaling the safety of its usage, VHP as a sterilizing agent has been approved by both the US Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA).

In pharmaceutical processes, VHP decontamination has been especially used for the sterilization of final fill isolators and Restricted Access Barrier Systems (RABS). The general process involves the following steps (see Figure 1):

1. Dehumidification: dry air is introduced to reduce the relative humidity in the isolator;
2. Conditioning and decontamination: introducing the VHP for decontamination and maintaining the concentration of VHP and relative humidity at required level for the whole decontamination process;
3. Aeration: introducing aseptic air and exhausting VHP to the required level (usually under 1 ppm).

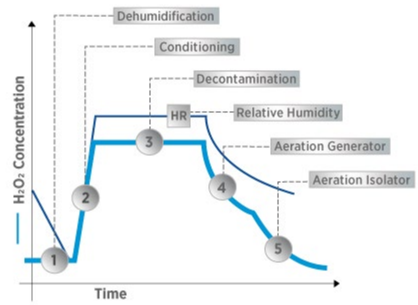


Figure 1. The process of a Vaporized Hydrogen Peroxide (VHP) decontamination cycle.

Although VHP is convenient and effective for the decontamination of the isolator, it is necessary to consider the influences of VHP on the sterilized materials, both physically and chemically. VHP can be physically absorbed into the materials and then released slowly after the decontamination process, which can be potentially destructive to the final pharmaceutical products. In another case, if the sterilized materials are not compatible with VHP, they could be broken down by its oxidative properties causing impurities leaking into final products or the failure of components during the final fill process. Therefore, it is important that the single-use materials selected for final fill applications are capable of withstanding VHP exposure or that protective packaging is used to protect final fill during VHP decontamination.

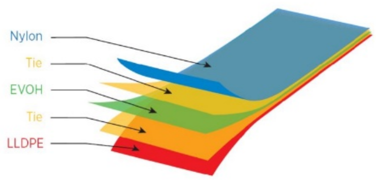
MATERIAL USED IN SAINT-GOBAIN BIOPROCESS BAGS

Saint-Gobain's single-use, bioprocess bags are comprised of a 5-layer film (see Figure 2) optimized for bioprocess production applications. The layers of Saint-Gobain's film, from the outermost to the product-contact layer, are as follows:

1. Nylon – providing impact and tear resistance for toughness while being handled.

2. Tie structure – multiple materials providing bonding between layers and add to the overall performance of the bag.
3. Ethyl Vinyl Alcohol (EVOH) – an excellent gas barrier against the transmission of oxygen and carbon dioxide.
4. Tie structure – another bonding layer.
5. Linear Low Density Polyethylene (LLDPE) – product contact layer with broad chemical compatibility.

Through testing explained below, the materials and structure of Saint-Gobain's bioprocess bags are proven to be extremely capable of ensuring that VHP does not permeate through to the bioprocessing fluid where it could contaminate and damage sensitive pharmaceutical products.



TESTING METHODOLOGY/APPROACH

Materials – Polymeric packaging

In addition to Saint-Gobain's film for its bioprocess bags, several other materials were selected for VHP exposure testing as a useful benchmark. Due to the limited existing data on hydrogen peroxide permeation in commercially available polymers, water vapor permeation was used to advise material selection according to the data in Table 1. While water is not the perfect model for hydrogen peroxide, its similar molecular structure and size make it a reasonable initial reference.

Materials	Water vapor permeation	Hydrogen peroxide liquid permeation [2]	Hydrogen peroxide vapor permeation [2]
	Test Condition: 90% RH at 30 - 40°C Unit (@ 25 µm²/24h)	Test Conditions: 90% H_2O_2 at 74°C Unit (g H_2O_2/0.001 inch/100 inch²/24h)	Test Condition 90% H_2O_2 at 25°C Unit (g H_2O_2/0.001 inch/100 inch²/24 h)
Aluminum foil laminate	-0[3]	-	-
Teflon	7.0 [4]	001-0.09	-
HDPE	5.9 [5]	0.04	-
PP	6.5-10.7 [5]	-	5.5×10^{-9}
LLDPE	17.7 [5]	9	0.1
PVC	46.5 [5]	2.5-8	2.5-8
PET	18.6-20.2 [5]	-	-
Nylon 6	18 [5]	-	-
EVOH	22-124 [6]	-	-

With the above data, and due to practical considerations, the final materials tested were:

1. Saint-Gobain's 5-layer bioprocess film (7 mil, Nylon/Tie/EVOH/Tie/LLDPE)
2. Saint-Gobain's monolayer LLDPE used in tank liner applications (5 mil)
3. Aluminum foil laminate (6.3 mil, PET/LLDPE/Aluminum/Nylon)
4. Multi-layer PE (4.5 mil)
5. HDPE (3 mil)
6. LLDPE (6 mil)
7. LLDPE (4 mil)
8. Laminated LLDPE (5 mil, Nylon/LLDPE)
9. Nylon (3 mil)

Testing the accumulative hydrogen peroxide after the decontamination process

During the VHP decontamination process, hydrogen peroxide can slowly permeate through the packaging material. In order to collect the hydrogen peroxide, we developed two methods for the analysis – a "water balloon" and a "gas detection tube" method.

"Water Balloon" Method
The first method is to fill the package fully with water for a "water balloon". Once the hydrogen peroxide diffuses into the bag (Figure 3A), it will be absorbed and dissolved in water. Therefore, the accumulative hydrogen peroxide could be indicated by its concentration in the water.

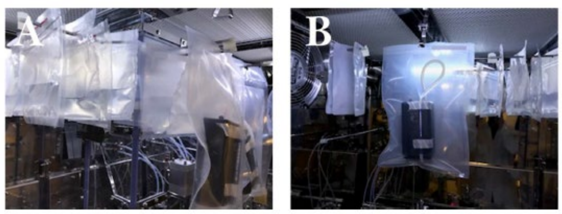
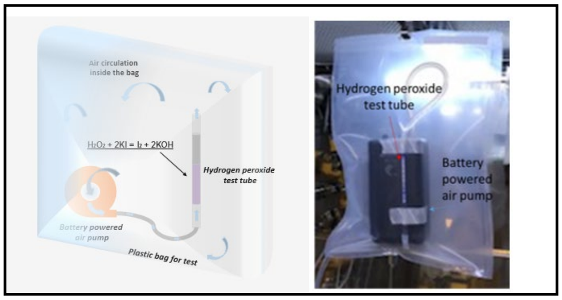


Figure 3. A) "Water balloons" and B) "gas detection tube" hanging inside the isolator for the decontamination.

"Gas Detection Tube" Method
The second method utilizes a gas detection tube (Figure 4). The tube is assembled with an air pump inside the sealed bag, and the pump circulates the air through the tube during the test. The gas detection tube is a column containing chemicals that can absorb and react with hydrogen peroxide ($2H_2O_2 + 2KI \rightarrow I_2 + 2H_2O + O_2$). The reaction with hydrogen peroxide causes a color change in the tube indicating the level of hydrogen peroxide present. In contrast with the first method, this method allows the level of hydrogen peroxide to be monitored in real time.



The VHP decontamination process

Temperature in the isolator	75 - 86°F	
Dehumidification	~30 min	
Conditioning	~10 min	VHP from 0 to 1000 ppm
Decontamination	120 min	VHP maintain at >1000 ppm
Aeration	>30 min	VHP less than 0.5 ppm

RESULTS AND ANALYSIS

As shown in Table 2 and Table 3, Saint-Gobain's 5-layer bioprocess bags, along with aluminum as a benchmark, had the best results with virtually no permeation of hydrogen peroxide.

Hydrogen peroxide permeation through different polymers

Due to differences in density, crystallinity and polarity, the hydrogen peroxide permeation in the materials varies. Aluminum foil laminate is impermeable to hydrogen peroxide, therefore, barely any hydrogen peroxide could be detected in the "Foil" bag by any method (Table 2). By contrast, "Nylon", due to its high polarity, is highly permeable to hydrogen peroxide. More than 30 ppm hydrogen peroxide is detected in the "water balloon" after the decontamination cycle (Table 2). Polyolefin is much more permeable than Nylon; however, there are still about 3 to 10 ppm hydrogen peroxide found in both "water balloon" (Table 2) and "gas tube" (Table 3).

Hydrogen peroxide permeation through different laminated structure

The hydrogen peroxide permeation of the polymer film is significantly improved when the lamination contains a less permeable material. The aluminum layer enables the low permeation of "Foil". Similarly, the "Saint-Gobain 5-layer" also demonstrates very low permeation to hydrogen peroxide.

	Bag	Polymer & structure	Thickness (mil)	Hydrogen peroxide (ppm)		
				Test kit #1	Test kit #2	Test kit #3
#1	Foil Bag	PET/ LLDPE/ Foil/Nylon	6.3	~0	0.05-0.30	0.0-0.3
#2	Saint-Gobain 5-Layer bag	Nylon/Tie/ EVOH/Tie/ LLDPE	7	<1	0.05-0.30	0.0-0.1
#3	Multi-layer PE Bag	PE	4.5	~3	1-2	3-4
#4	Saint-Gobain LLDPE Bag	LLDPE	5	~3	1-2	4-5
#5	HDPE bag	HDPE	3	3-10	2-4	6-8
#6	LLDPE bag	LLDPE	6	3-10	2-4	6-8
#7	Laminated LLDPE bag	Nylon/ LLDPE	5	3-10	2-4	5-8
#8	LLDPE bag	LLDPE	4	3-10	2-4	7-10

Table 2. Packaging made from different polymers and different structure, and the hydrogen peroxide permeation results tested by the "water balloon" method. (note the three colorimetric analysis tests were employed for confirmation, the results were not exactly the same values but falling into the same range with the different testing methods).

	Bags	Manufacturer of test tube	Detection range/level	Thickness (mil)	Hydrogen peroxide (ppm)
#2	Saint-Gobain 5-Layer bag	Draeger Gastec	0.1 to 3.0 ppm 0.5 to 10.0 ppm	7	0.1-3 no reading
#3	Multi-layer PE bag	Draeger	0.1 to 3.0 ppm	4.5	0.1-3
#5	HDPE bag	Gastec	0.5 to 10.0 ppm	3	8-10
#7	Laminated LLDPE bag	Gastec	0.5 to 10.0 ppm	5	8-10
#6	LLDPE bag	Draeger	0.1 to 3.0 ppm	6	>3

Table 3. Packaging made from different polymers and different structure, and the hydrogen peroxide permeation results tested by the "gas detection tube" method. VHP concentration is low, the color change is very light to identify the exact reading for #2 and #3 bags.

CONCLUSION AND SUMMARY

With VHP so commonly used in final fill applications, it is important to select materials that are capable of withstanding exposure to and restricting permeation of hydrogen peroxide. Our testing successfully identified Saint-Gobain's 5-layer film bioprocess bags as a suitable material for use in final fill applications with VHP exposure.

REFERENCES

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ABOUT

SAINT-GOBAIN

The Bioprocess Solutions business unit of Saint-Gobain supplies the bioprocessing, pharmaceutical, cell therapy, and laboratory industries with high performance assemblies and fluid path components.

Its industry-leading product portfolio and material expertise provide customers with the answers and assurance they need when processing pharmaceutical products.