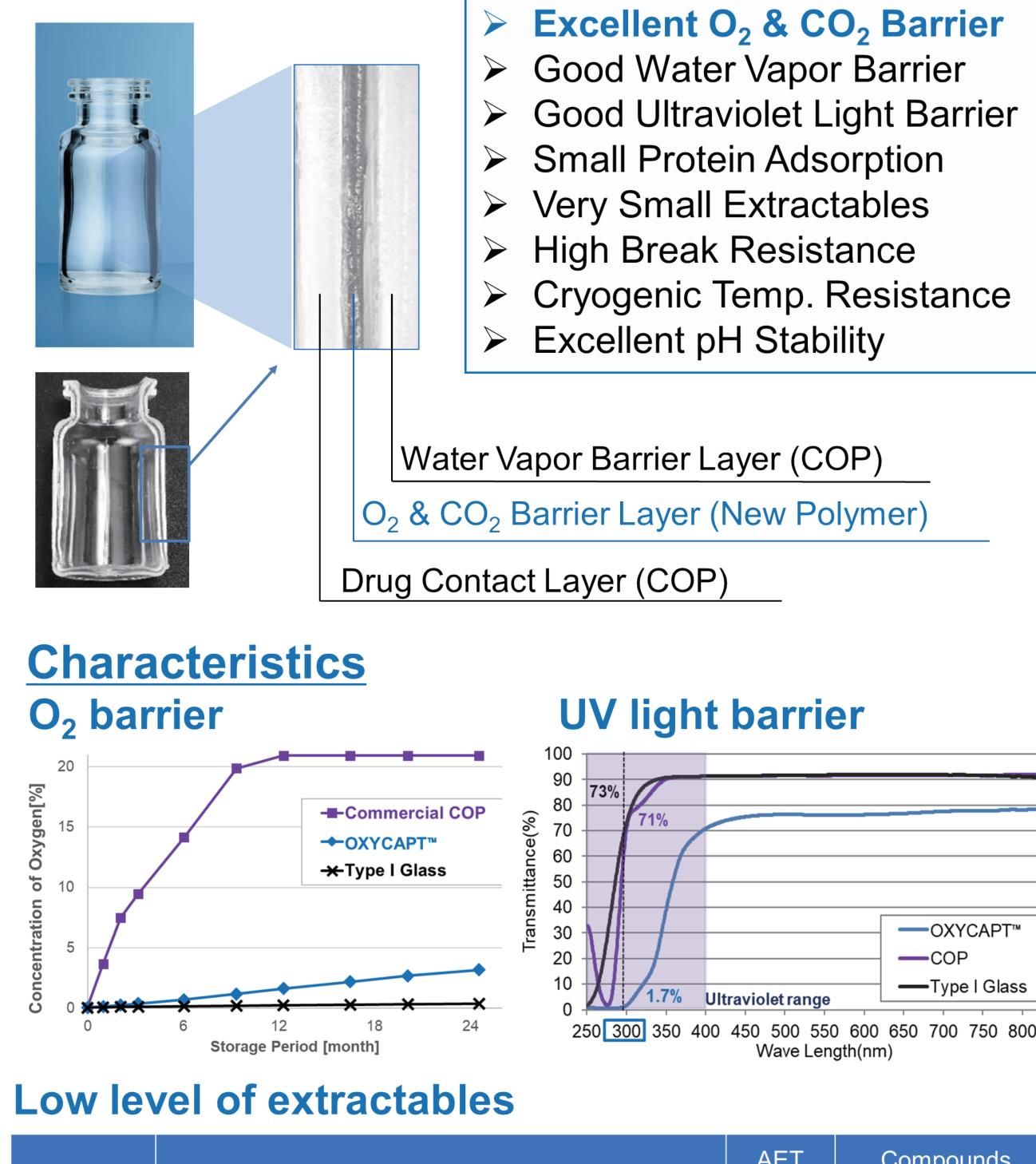
Container Closure Integrity Test of OXYCAPT Multilayer Plastic Vial with Dry Ice at -80°C Yoshiko Sakuma Mitsubishi Gas Chemical Company, Inc.

MITSUBISHI GAS CHEMICAL

1. About our plastic vial

OXYCAPT[™] is a multilayer plastic primary container based on our polymer and molding technology.



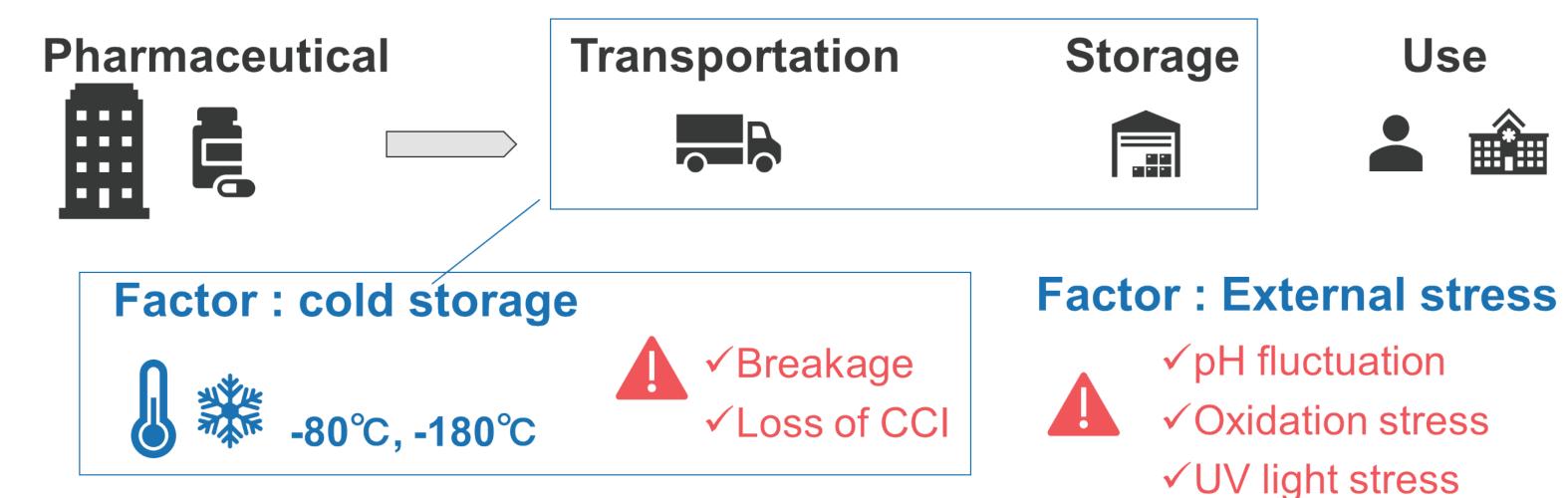
	Method	Solution	AET (ppm)	Compounds found above AET		
	HS-GC-MS	0.1 % PS-20 , pH 3 buffer, pH 10 buffer	0.3	Not detected		
	GC-MS	0.1 % PS-20 , 50% EtOH, pH 3 buffer, pH 10 buffer	1.5	Not detected		
	LC-UV-MS	0.1 % PS-20 , 50% EtOH, pH 3 buffer, pH 10 buffer	1.5	Not detected		
Incubation condition : 50°C/ 48h						

3. Conclusion

- OXYCAPT[™] is a multilayer plastic container intended for biologics and gene/cell therapy.
- OXYCAPTTM has good O_2 and CO_2 barrier.
- The experimental data shows that OXYCAPT[™] vial is very suitable for medications stored or transported at cold temperature because it has an excellent durability.
- OXYCAPT[™] greatly has a low risk of contamination of organic and inorganic extractables, and contributes to a stability of biologics and cell and gene therapy.

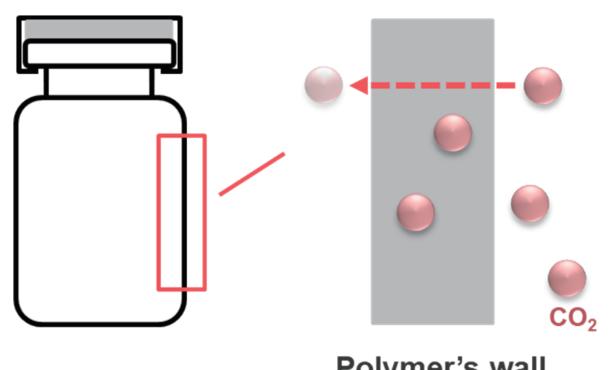
2. Experimental data

In general, in the process of transportation, storage and use, biologics and gene/cell therapy are potentially exposed to various risks including breakage, loss of container closure Integrity, and fluctuation of pH. The experimental data demonstrates an efficiency of OXYCAPTTM vial against such the risks.



2-1. Study on carbon dioxide barrier at room temperature

Carbon dioxide molecules permeate through polymers' wall and get into the headspace and its transmission rate(CO2TR) is different among each material. MGC compared the carbon dioxide barrier of OXYCAPT[™] and COP.



Sample and method

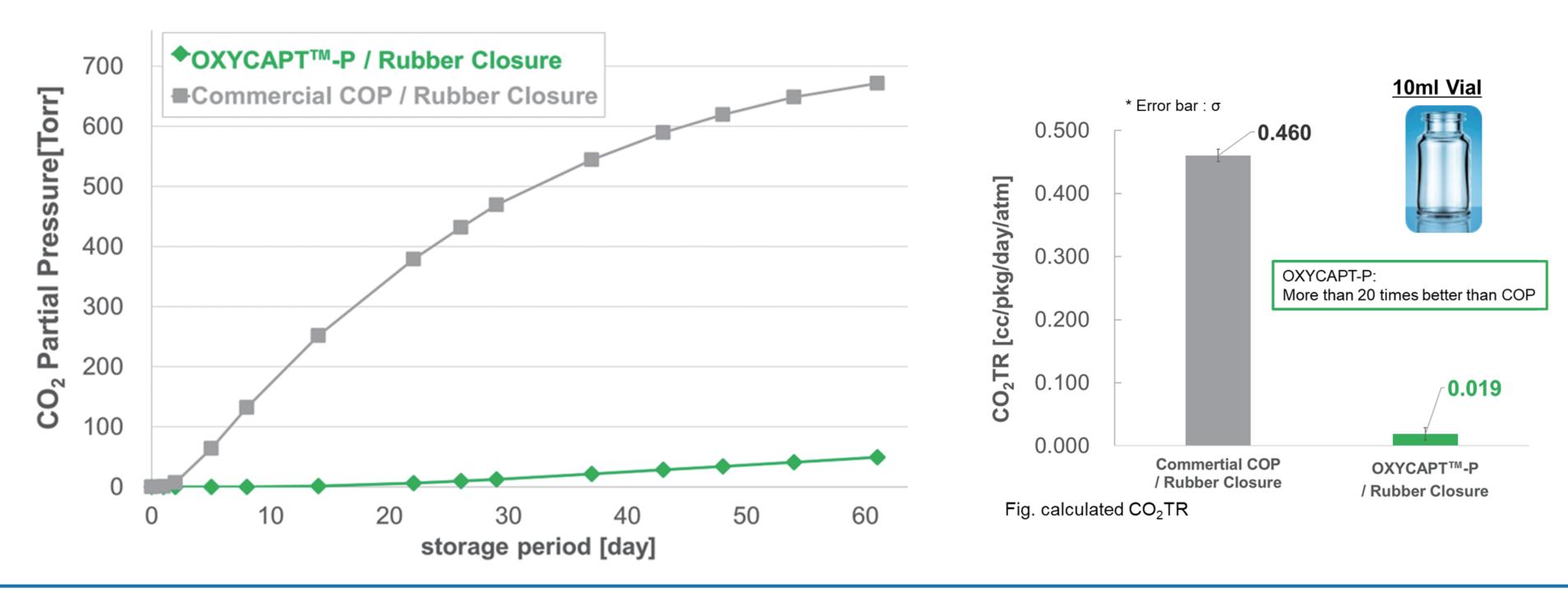
10 pcs of 10mL OXYCAPT vials, closure and aluminum seals were placed into a chamber with nitrogen and stored at 23° C. Concentration of CO2 in headspace gradually rises.

Table 1: Samples of Carbon Dioxide Barrier test at Room Temperature

Vial	Closure	Crimp	
OXYCAPT™ 10mL	Bromo butyl rubber	Aluminum seal	23°C CO ₂ Ga
COP monolayer 10mL	Bromo butyl rubber	Aluminum seal	

Result

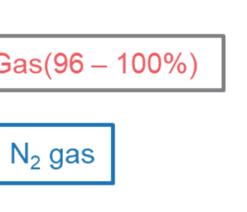
OXYCAPT[™] has very good CO2 barrier performance as material and CO2 barrier of OXYCAPTTM vial is more than 20 times better than COP.



Use



Polymer's wall



2-2. Study on carbon dioxide barrier after thawing process

The state-of-the-art drugs such as cell & gene therapy products are usually stored at deep cold temperature and often transported with dry ices. As the glass transition temperature of rubber is around -65 $^\circ\,$ C and the coefficient of thermal expansion is much different from the glass, it is important to choose the proper vials and rubbers in terms of container closure integrity (CCI). Instead of glass vials, COP vials are often used for such drugs recently to achieve good CCI, but we have found CO2 gasses eventually permeate into the COP vials after thawing process.

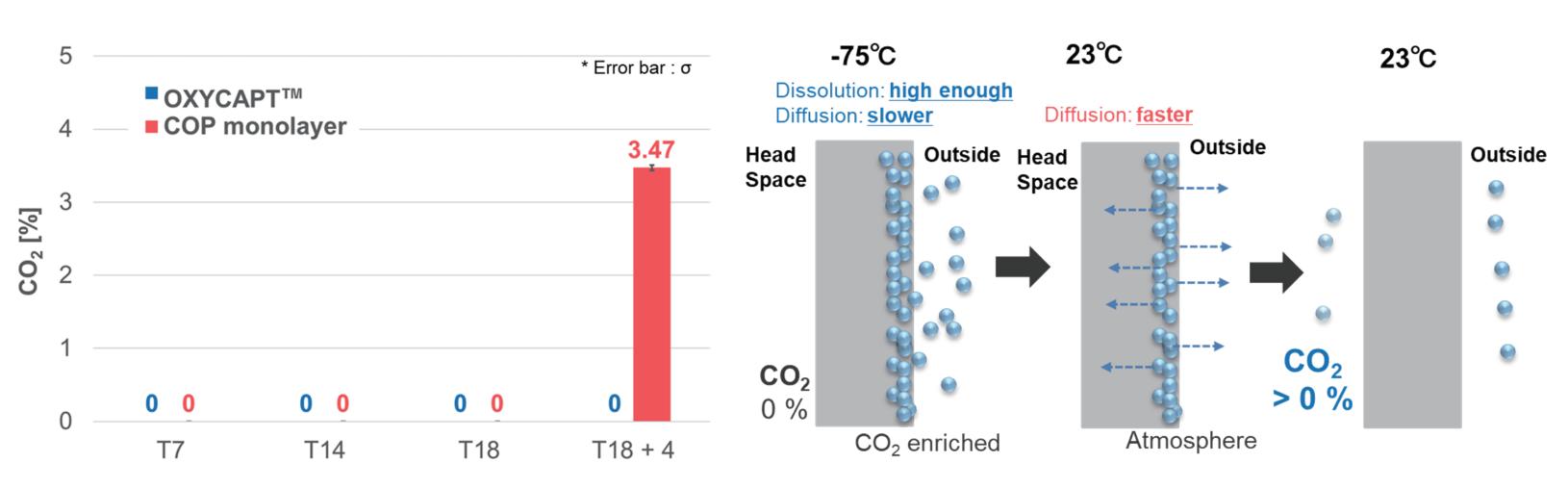
Sample and method

10 pcs of OXYCAPT and COP vials were placed into a chamber with nitrogen and stored at -75 $^{\circ}$ C for 18 days and CO2 concentration in head space were measured. After that, the vials were transferred to atmospheric environment and stored at 23° C for 4 days and CO2 concentration were measured again.

Table 2: Samples of Carbon Dioxide Barrier test after thawing process

Vial	Closure	Crimp
OXYCAPT [™] 10mL	Bromo butyl rubber	Aluminum seal
COP monolayer 10mL	Bromo butyl rubber	Aluminum seal

Result



2-3. pH stability test

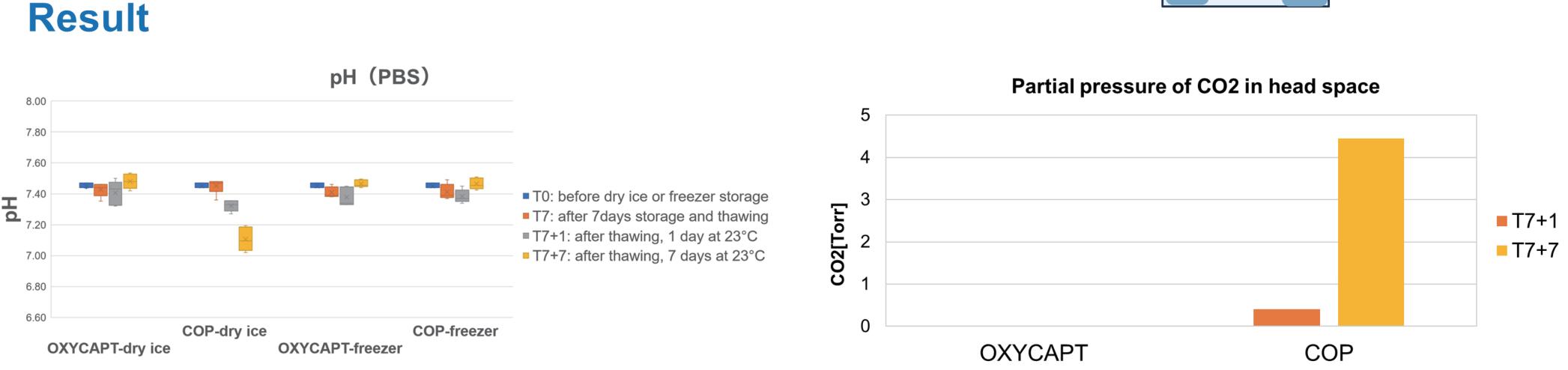
The cell & gene therapy products are often transported with dry ices. The pH shift caused by CO2 ingress during transportation have been pointed out. MGC compared the pH stability of OXYCAPT[™] and COP.

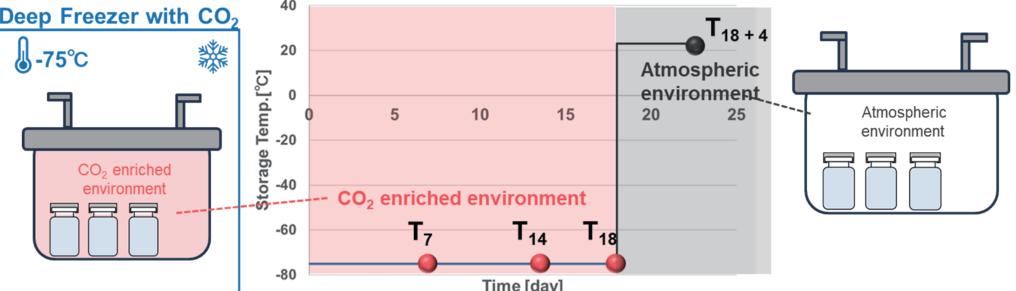
Sample and method

5mL of PBS(pH7.4) were filled in OXYCAPT[™] and COP vial under an atmosphere of N2. The vials were placed into a -80° C freezer or an insulated box with dry ice. After 1 week storage, the vials were thawed in a 37 $^{\circ}$ C hot water bath for 10 minutes. After thawing, the vials were left at 23° C and pH level of PBS were measured. The sample number is 5.

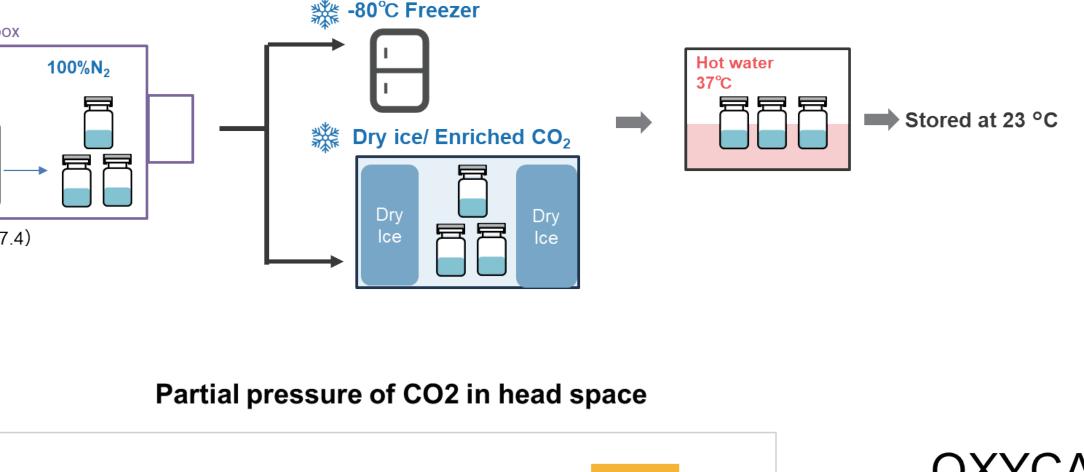
Table 3: Samples of pH stability test Crimp Closure Vial

OXYCAPT™ 10mL	Bromo butyl rubber	Aluminum seal
COP monolayer 10mL	Bromo butyl rubber	Aluminum seal





OXYCAPTTM vials could keep 0% of CO_2 in head space even after storage for 18 days under CO₂ enriched environment and additional storage for 4 days at room temperature. There are 2 phenomena of gas molecule permeation through plastics, dissolution and diffusion. This result is attributed to the temp. dependence of dissolution and diffusion of OXYCAPT[™] polymer.



OXYCAPT[™] vials could keep stable pH of PBS and can be met by cell & gene therapy.