MITSUBISHI GAS CHEMICAL

MULTILAYER PLASTIC VIALS & SYRINGES FOR BIOLOGICS

In this article, Shota Arakawa, Researcher, and Tomohiro Suzuki, Associate General Manager, both of Mitsubishi Gas Chemical, discuss OXYCAPT™ Plastic Vial and Syringe, the company's proprietary material, made of multilayered cyclo-olefin polymer and a novel polyester, which provides a product with all the advantages of plastic, coupled with strong oxygen and UV barrier properties.

Although essential for humans, oxygen is basically unnecessary for processed foods and drugs. Over 40 years ago, Mitsubishi Gas Chemical (MGC) developed an oxygen absorber called AGELESS® which prevents the oxidation of foods. Since then, AGELESS® has been used for in a variety of food products worldwide and MGC has been a leading company in the oxygen-absorber field. AGELESS® has also been used for

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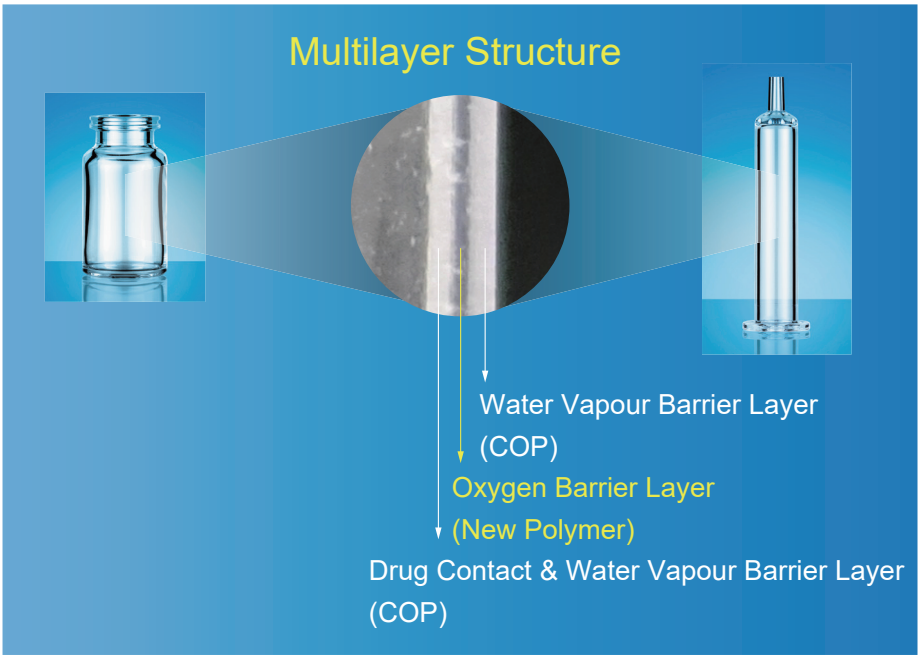

Figure 1: Multilayer Structure of OXYCAPT™.

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	Glass	Cyclo Olefin Polymer (COP)	OXYCAPT™
Oxygen Barrier	Excellent	Not Good	Excellent
Water Vapour Barrier	Excellent	Good	Good
Resistance to Breakage	Bad	Good	Good
Inorganic Extractables	Not Good	Excellent	Excellent
Organic Extractables	Excellent	Excellent	Excellent
Protein Adsorption	Not Good	Good	Good
pH Stability	Not Good	Good	Good
UV Barrier	Bad	Bad	Good
Weight	Bad	Excellent	Excellent
Disposability	Bad	Good	Good

Table 1: Comparison of the strengths and weaknesses of glass, COP and OXYCAPT™.

"Although about 70% of 300 nm UV light transmits through glass and COP, only 1.7% transmits through OXYCAPT™."

drug products, such as intravenous (IV) solutions, prefilled syringes, ampoules and tablets, for many years, especially in the Japanese market. It significantly contributes to stabilising the efficacy of drugs and extending their shelf-life. However, the use of an oxygen absorber is not common so much in the US or Europe, because additional items, including dispensing machinery, sealing equipment and secondary packaging with high gas barrier, are needed to apply the absorber.

Therefore, MGC began developing alternative technologies to the oxygen absorber. Firstly, MGC developed a new oxygen-absorbing polymer, which featured a very low level of extractables and demonstrated no degradation, even after absorbing oxygen. Secondly, MGC sought an improvement on the existing multilayer-moulding technology which has been used frequently in the beverage industry to enhance the oxygen and carbon dioxide barrier provided by the packaging. By combining these two technologies, MGC has successfully developed a multilayered plastic vial and syringe called OXYCAPT™.

OXYCAPT™ Vial & Syringe consists of three layers. The inner and outer layer are made of cyclo-olefin polymer (COP), the most reliable polymer used by the pharma industry. The middle layer is made of a novel polyester that has been developed by MGC (Figure 1). The COP layers give OXYCAPT™ the traditional characteristic advantages of polymer vials and syringes while the new polyester plays a role as an oxygen and UV barrier to address the weaknesses inherent to using COP alone.

Current syringe primary packaging materials all come with their own problems: glass suffers from breakage and delamination, whereas plastic is not a sufficient oxygen and ultraviolet light (UV) barrier. Particularly with glass, the US FDA has pointed out these problems, which have led to more than 50 incidents of recall. To address the problems associated with glass, some suppliers have launched plastic alternatives, however the oxygen barrier provided by these products has failed to meet the demands of customers. However, OXYCAPT™ has overcome both the weaknesses of glass and of COP (Table 1). MGC believes that OXYCAPT's achievements, including a strong oxygen barrier, very low extractables, good UV barrier and high break resistance will bring

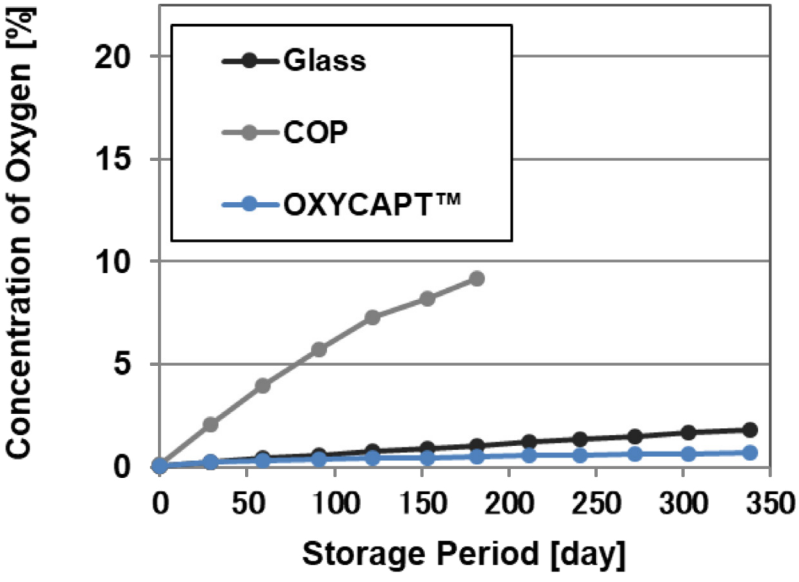

Figure 2: Concentration of oxygen over time inside vials of glass, COP and OXYCAPT™ originally filled with nitrogen.

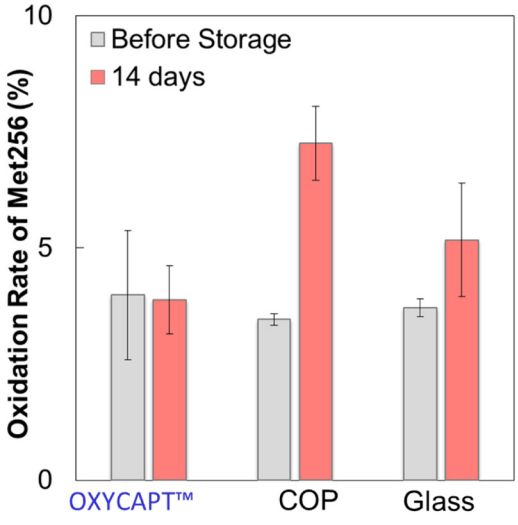

Figure 3: Oxidation rate of an antibody, stored in containers of glass, COP and OXYCAPT™ at 25°C, under a light source of 2000 lx for 14 days.

substantial benefits to the pharma industry.

A study showed that the oxygen barrier quality of OXYCAPT™ is superior to that of glass and far better than COP. The air in vials of glass, COP and OXYCAPT™ was completely replaced with nitrogen and were then stored at 25°C and 60% relative humidity (RH). The oxygen concentration in the COP vial immediately rose, because oxygen transmits through the wall of the vial and the surface of the rubber stopper. The glass vial with a perfect barrier property also rose up gradually, as oxygen transmits through the rubber stopper. On the other hand, OXYCAPT™ kept very low oxygen concentration for a long time, since OXYCAPT™ gradually absorbs the oxygen that permeates through the rubber stopper, as well as the vial itself (Figure 2).

OXYCAPT™ also provides an ultraviolet (UV) barrier. Although about 70% of 300 nm UV light transmits through glass and COP, only 1.7% transmits through OXYCAPT™. This further contributes to biologic stability. MGC conducted studies to confirm the efficacy of OXYCAPT™ as a UV and oxygen barrier. An antibody stored in containers of glass, COP and OXYCAPT™ was exposed to a light source of 2000 lx and stored at 25°C for 14 days. The oxidation rate of methionine 256 was measured by peptide mapping. The results show that the oxygen and UV barrier of OXYCAPT™ can contribute to the stability of antibodies (Figure 3).

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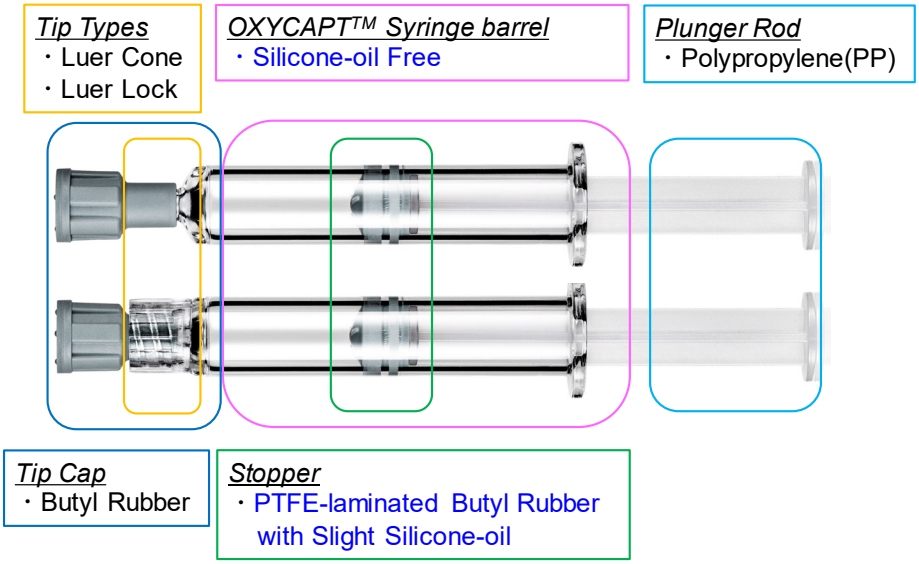


Figure 4: Components of the OXYCAPT™ syringe.

The OXYCAPT™ Syringe consists of tip cap, barrel, PTFE-laminated stopper and plunger rod (Figure 4). Although a very small amount of silicone-oil is coated on the stoppers, no silicone-oil is baked on the barrel. According to MGC's internal studies using antibodies, it has found this feature noticeably reduces instances of protein aggregation, compared with existing Type I glass syringes. In addition to Luer Cone and Luer Lock, MGC has tackled the development of staked-needle syringes.

Studies have shown that OXYCAPT™ generates extremely low levels of extractables. One study was conducted to measure volatile, semi-volatile and non-volatile impurities from OXYCAPT™. Water and four solutions (50% ethanol, NaCl, NaOH and H_3PO_4) were used and impurities were measured by gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-UV spectroscopy-mass spectrometry (LC-UV-MS) after 70 days at 40°C. Compared with the control, no impurities were detected in any of the OXYCAPT™ containers. A second study was conducted to measure inorganic extractables from OXYCAPT™. The level of extractables was similar to those from COP, which is well-known as an extremely pure polymer, and less than that of Type I glass.

MGC can offer bulk vials, ready-to-use (RTU) vials and syringes, provided in ISO-compliant nest and tub formats (Figures 5 and 6). The nest and tub are primarily sterilised using gamma rays. There are 2, 6 and 10 mL variants for vials, and 1 mL long and 2.25 mL variants for syringes.

Each polymer meets the requirements

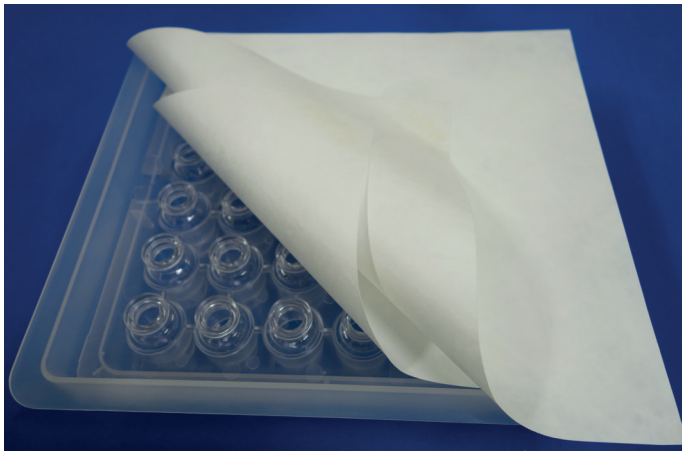


Figure 5: ISO-compliant nest and tub format for vials.

Figure 6: ISO-compliant nest and tub format for syringes.

of USP661, USP87, USP88, EP and has been filed in the FDA's drug master file (DMF). The vials and syringes are also compliant with each pharmacopoeia and have been filed in the DMF. The syringes are produced and controlled in accordance with ISO 13485.

In conclusion, OXYCAPT™ Plastic Vial and Syringe was developed to overcome the weakness of glass and plastic currently in use. In addition to the special features of COP, such as a strong water vapour barrier, high breakage resistance, very low extractables and low protein adsorption, OXYCAPT™ provides a strong oxygen and UV barrier. MGC anticipates that OXYCAPT™ will be used for oxygen- and UV-sensitive drugs, particularly in the rapidly growing biologics market.

ABOUT THE COMPANY

Mitsubishi Gas Chemical does business in a wide range of fields, from basic chemicals to fine chemicals and functional materials. MGC established its Advanced Business Development Division in 2012 as a centre for continually creating new businesses, and developed OXYCAPT™ Plastic Vial & Syringe as an alternative to glass containers.

ABOUT THE AUTHORS

Shota Arakawa is a Researcher in the Advanced Business Development Division of Mitsubishi Gas Chemical. He gained a Diploma in Science in 2007 and a Master Degree of Science in 2009 from Osaka University (Japan). Since April 2009 he has been in charge of macromolecular science, especially the synthesis of polymers and material development, for MGC. In 2012 he joined the development team for OXYCAPT™.

Tomohiro Suzuki is an Associate General Manager at Mitsubishi Gas Chemical, having joined the company in 1998. He belonged to the Oxygen Absorbers division until 2011, and was transferred to the Advanced Business Development Division in 2012 to be a member of OXYCAPT™ development team. Since then, he has been in charge of marketing OXYCAPT™ Plastic Vial & Syringe.

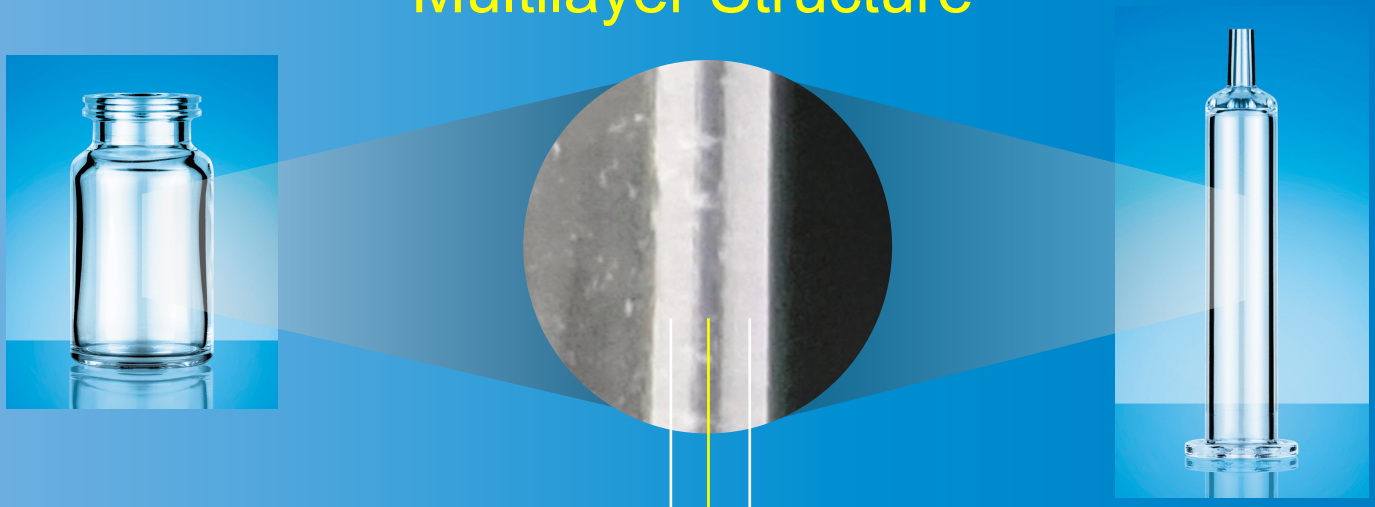
ON drugDELIVERY

2019/2020 EDITORIAL CALENDAR

Publication Month	Issue Topic	Materials Deadline
Apr 2019	Pulmonary & Nasal Delivery	Mar 7th 2019
May 2019	Injectable Drug Delivery	Apr 4th 2019
Jun 2019	Connecting Drug Delivery	May 2nd 2019
Jul 2019	Novel Oral Delivery Systems	Jun 6th 2019
Aug 2019	Industrialising Drug Delivery Systems	Jul 4th 2019
Sep 2019	Wearable Injectors	Aug 1st 2019
Oct 2019	Prefilled Syringes & Injection Devices	Sep 5th 2019
Nov 2019	Pulmonary & Nasal Drug Delivery	Oct 3rd 2019
Dec 2019	Connecting Drug Delivery	Nov 7th 2019
Jan 2020	Ophthalmic Drug Delivery	Dec 5th 2019
Feb 2020	Prefilled Syringes & Injection Devices	TBC

OXYCAPT™ Plastic Vial & Syringe

Multilayer Structure



Water Vapor Barrier Layer
(COP)

Oxygen Barrier Layer
(New Polymer)

Drug Contact & Water Vapor Barrier Layer
(COP)

- ✓Excellent Oxygen Barrier
- ✓High Water Vapor Barrier
- ✓Low Extractables & High pH Stability
- ✓High Break Resistance & Lightweight
- ✓Excellent UV Barrier
- ✓High Transparency
- ✓Silicone Oil Free Barrel
- ✓Low Protein Adsorption & Aggregation
- ✓Suitable for Biologics
- ✓Customizable

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