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ALBA: AN OPTIMISED PLATFORM FOR HIGHLY SENSITIVE BIOLOGICS AND THE IDEAL SYRINGE SOLUTION FOR OPHTHALMIC DRUGS

Here, Alessio Bonati, EZ-Fill Product Development & CTS Manager, Ompi, discusses the problematic interactions between drugs and their primary containers. Mr Bonati goes on to introduce the Alba platform, Ompi's range of primary glass containers designed to address these issues and unify drug-container interactions over a product's lifecycle. The platform is particularly well suited to ophthalmic drugs.

The sensitivity of drugs to one or more elements of their primary packaging has always been a potential problem for the pharmaceutical industry. Biologics in particular are highly sensitive, leading to a higher risk of incompatibility between them and their containers (i.e. stability test failures). This potential incompatibility, and the consequent instability of formulations, may have multiple causes; it may be linked to the presence of silicone oil droplets, to an interaction between the drug and the surface of the primary container (leading to the protein aggregation phenomenon), or instead to the particles generated by the rubber in the closure system, such as plungers, stoppers, etc.

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Another well-known phenomenon representing a potential source of instability is delamination, especially in vials. This occurs because of the interaction between highly aggressive drugs and the internal glass surface of the container, appearing as visible flakes (lamellae).

In 2014, Ompi started the Alba project some market analysis suggested that anything from 5% to 15% of drug formulations had a high degree of sensitivity to one or more of the components of a primary container. On account of the increase of biological drugs, this figure is now in the region of 20-30%. Ompi decided three years ago to set up a project that could solve the problems associated with the interaction between drugs and their primary packaging.

The result has been the EZ-fill® Alba product range, a sterile glass container platform including vials, cartridges and syringes, with equivalent chemical and mechanical characteristics. The platform represents the ultimate primary packaging for biologics and for very sensitive and demanding drugs in general. All the Alba products have an internal layer, based on the standard silicone oil, Dow Corning 360 1000 cst, which is crosslinked with the surface of the glass.



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For syringes and cartridges, the Alba treatment replaces the standard siliconisation normally used to create a lubricant layer (silicone oil and baked-on silicone). This ensures that the number of particles present is normally one order of magnitude lower than standard oil siliconised syringes, simultaneously ensuring high performance in terms of glide and break-loose forces.

In addition, the Alba layer creates a barrier between the drug and the glass, thus reducing the amount of inorganic extractables significantly, compared with a standard bulk container, or even with the glass container before it was formed. The level of specific inorganic extractables (SiO_2 , AlO_3 , B_2O_3) is also a good indicator of the container's propensity to delaminate. The low concentration of inorganic extractables and the negligible surface corrosion indicate the low delamination propensity of Alba containers.

SOLUTION FOR BIOLOGICS AND OPHTHALMIC

The main technical improvement of the Alba layer is the strength of the chemical bond it forms with the glass surface of the container. This is considerably stronger than the one normally found with standard silicone oil or baked-on silicone. This characteristic is the main reason why there is an extremely low level of particles, together with a very good, stable and functional performance in terms of glide and break-loose forces.

The high performance of the Alba syringe was demonstrated by a comparison study with a syringe with standard silicone oil treatment, using a 1 mL long staked needle format. The syringes were filled with 1.3 mL of filtered ($0.22 \mu\text{m}$) distilled water and autoclaved for 1 hour at 121°C , which is definitely much more stressful than the standard method described in the US Pharmacopeia. The liquid was analysed by an MFI ProteinSimple 5200 series instrument.

As shown in Figure 1, the number of particles released from Alba syringes is normally one order of magnitude lower than from standard siliconised oil syringes.

The strong interaction of the Alba treatment with the glass surface limits the well-known effect of silicone migration that normally happens during the storage of filled containers. This characteristic leads to increased stability of the functional performances (glide and break-loose forces) of Alba containers.

OMPI ALBA SYRINGES

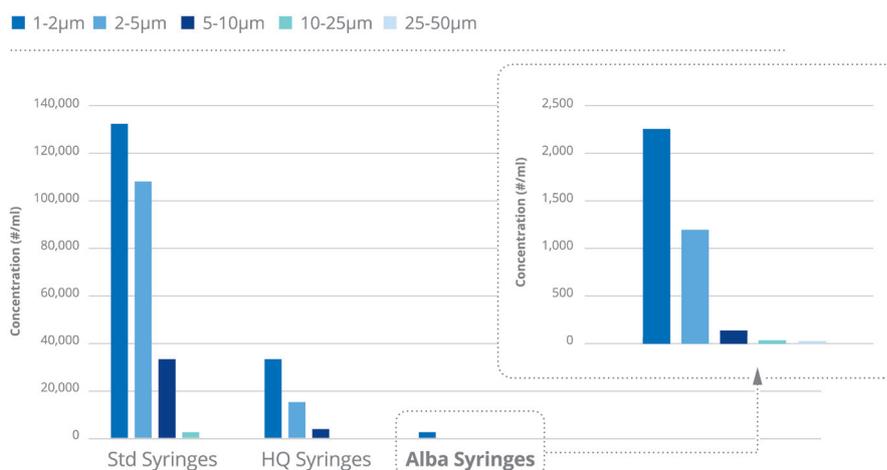


Figure 1: Alba syringe particle release performance in comparison with standard and high quality syringes.

“The number of particles present is normally one order of magnitude lower than standard oil siliconised syringes.”

With vials, for which the lubricant aspects are not relevant, the main added value of the Alba treatment is the barrier effect, preventing the occurrence of delamination after interactions with solutions of aggressive drugs and limiting the migration of inorganic extractables from the glass to the solution.

To demonstrate the barrier effect of the Alba treatment, a comparison study with a bulk vial was performed using a 2R ISO standard format. The vials were filled with 3.6 mL of distilled water and autoclaved for 1 hour at 121°C . The extracted solution

was analysed using an ICP-OES iCAP 7400 Thermo instrument.

Figure 2 shows the comparison between bulk vials, Alba syringes and Alba vials, demonstrating the lower inorganic oxides extraction from the Alba vials and the compatibility with Alba syringes.

FROM CONCEPTION TO INJECTION

The Alba platform has also been designed to support new drug development “from conception to injection”, with the aim of de-risking any switch from one container

OMPI ALBA VIALS

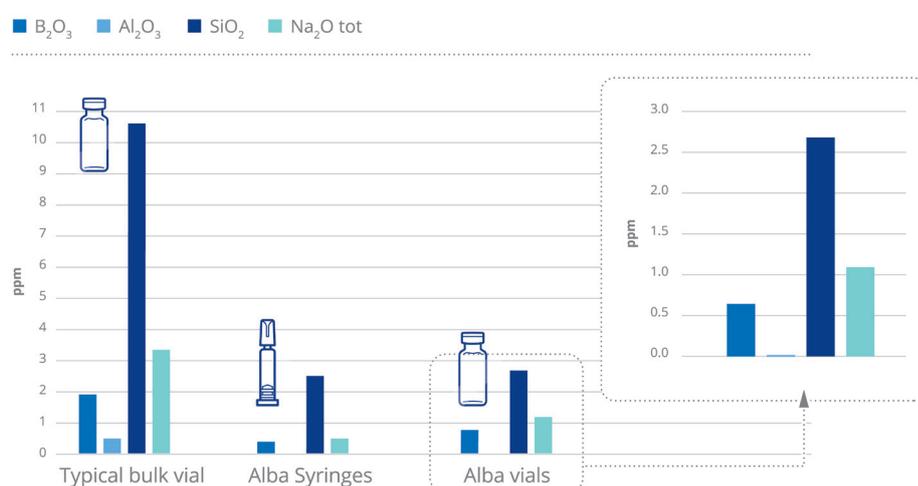


Figure 2: Alba vials inorganic extractables release performance in comparison with bulk vials and Alba syringes.

“The key benefit of the Alba platform is that all the containers, from vials to syringes and cartridges, show the drug the same contact surface.”

format to another. The final form of a drug is usually selected during clinical Phase II.

In fact, when the development process switches from the early phase container (normally a vial) to the final one (syringes or cartridges in many cases) the drug comes into contact with new materials (i.e. silicone oil and tungsten), not present in the relatively simple early phase container, that may compromise drug stability.

Even in the best case scenario – that is, if no problems occur – this switch of container will require a new stability study. In the worst case scenario, the drug would have to be reformulated, increasing both the time-to-market and the development costs.

This situation has been assessed by Ompi, conducting 30 interviews with pharmaceutical industry experts from different companies in 2014. The survey showed that there were different views about the recurrence of delays associated with failed stability tests in prefilled syringes due to drug instability. Nevertheless, all interviewed experts recognised that if a

problem occurs at that stage it has a significant impact on the drug development process, leading to additional costs and delays in the product launch.

The key benefit of the Alba platform is that all the containers, from vials to syringes and cartridges, show

the drug the same contact surface, thus removing the uncertainties associated with new packaging materials when moving from Phase II to Phase III, thereby de-risking the whole drug development process.

The same concept and the same benefits can also be applied to marketed drugs, when the pharmaceutical company decides to change the packaging, putting the drug in a different container format (e.g. from vial to syringe, or from syringe to wearable device cartridge). In this case, the Alba platform ensures that the switch can be made, drastically reducing the need for new characterisation and testing.

Because a relevant particle release contribution is normally generated by interaction between the rubber components and the drug, Ompi collaborated closely with rubber manufacturers during the Alba platform development, so as to screen the best off-the-shelf components that align with its key benefits. This screening was focused on different aspects: the best performance in terms of low particle

generation, lower inorganic and organic extractables, glide performance and the availability of the formulation for all the container formats included in the Alba platform (i.e. vial stoppers, syringe plungers and cartridge plungers). In this way, the value proposition related to the reduced variability of materials in contact with the drug applies to the rubber components as well as the glass barrel.

CONCLUSION

Alba represents a turning point in the development of parenteral primary packaging and is the best-in-class solution for biologics and ophthalmic drugs. The drastic reduction of silicone oil particles and the extremely low propensity to delaminate address some of the key requirements of protein-based drugs and help them to stay compliant with the latest guidelines coming from regulatory bodies.

Finally, the very limited variability of materials in contact with the drug throughout its lifecycle makes the Alba platform a perfect solution to de-risking the development process, saving on costs and securing a fast introduction to the market.

ABOUT THE COMPANY

As part of the Pharmaceutical Systems division of Stevanato Group, Ompi offers the widest range of glass primary packaging from the traditional, such as vials and ampoules, to the high-value, such as syringes and cartridges for autoinjectors and pen injectors. Vials, cartridges and syringes are available, sterile and ready-to-fill (Ompi EZ-fill®).

Ompi boasts a global footprint with high-quality production plants in Europe (Piombino Dese and Latina in Italy, Bratislava in Slovakia), Mexico (Monterrey), China (Zhangjiagang, near Shanghai) and a brand new plant in Sete Lagoas (Brazil).

ABOUT THE AUTHOR

Alessio Bonati holds a Master's degree in Electronic Engineering from the University of Ferrara and an MBA degree from Bologna Business School. Over the last 11 years, Mr Bonati has worked for international companies in several different businesses, but always with roles related to portfolio management and business development. He is currently EZ-Fill® Product Development & Customer Technical Support Manager for Ompi, the pharmaceutical glass primary packaging company, responsible of new product developments for all the business lines related to Ompi's portfolio, from vials to cartridges and syringes, all in a “ready to use” format.



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The simple way to streamline your drug development path



Using the same container lining throughout development improves life-cycle management and avoids validation failures. Alba platform maintains the advantages of siliconized containers, while guaranteeing ultra low particles quality.

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