Parenteral Packaging: Raw Material Substitution and Procurement Impact

1. Introduction: The industry of glass packaging is seeing a rapid shift towards usage of plastic substitutes for specific end uses such as biotech drug packaging, prefilled syringes etc. The main reason for the shift is the characteristic of glass as a raw material (flaking and delamination) and its failure to safeguard the product formulations inside, leading to recalls.

2. Main: This white paper deals with the underlying facts related to the issue of glass substitution. The seriousness of the issue at hand is discussed with apt industry examples and facts. The main substitute (COC/COP) has been discussed with industry examples such as that of Schott’s (a glass packaging supplier) TOPPAC plastic vials. Global insights pertaining to this trend, and a comparison of glass over plastic to find out qualitatively which is the better suited material in the future is provided in the paper. Going further, the white paper provides explanation of the reason for the shift to plastic from glass, taking into consideration the cost of recalls and total cost of ownership. And finally, the impact substitution has over procurement factors such as raw material sourcing, industry integration, and manufacturing of packaging.

3. Recommendation: For a company which has invested time and money in the research and development of an innovator drug, the decision concerning the right kind of material for the package and the right volume of dosage is of paramount importance. As the company has already invested millions, maybe billions, to reach this stage, a wrong decision will lead to recalls, which is a costly affair.

It is for this reason that pharmaceutical packaging buyers spare no effort and money to source the right kind of packaging material best suited for their drugs.

To avoid the issues with glass and its characteristics, companies must follow a two-pronged approach:

The glass to plastic shift decision: The company, while deciding upon the best raw material for this drug packaging, needs to take into consideration the time period of storage of the drug, the complexity of the delivery format and the risk associated while choosing plastic over glass.

Increase collaborations during raw material sourcing and final packaging: The buyers, who, after R&D, opt for COC/COP as their packaging material need to initiate collaborations with the COC/COP resin manufacturers so that they can work together to form the best packaging raw material for their product. From a supplier point of view, the supplier who has decided to provide COC/COP packaging as a part of their product portfolio needs to source special machinery which is aimed to use COC/COP as its feed stock.

Is it Really that Serious?

The essential purpose of a packaging material is to ensure the security of its contents. But when the package itself reacts with the contents, creating detrimental effects and costly recall issues, the purpose of using that material is defeated. For centuries, glass has been the primary packaging raw material for the pharmaceutical packaging and parenteral packaging industry, however, this dominant primary packaging raw material is being replaced by plastic, slowly but surely.

This substitution shift, though costly, is being driven by the high demands from biotech drugs which require advanced technologies in package forming. Another important reason for the substitution of glass is the need for alternative packaging materials due to the problems that glass has, such as delamination and tungsten residues.

Traditionally, Type I glass is the established packaging raw material for the parenteral industry. However in the context of new biotechnological drugs, borosilicate glass or Type I glass has a high interacting possibility dependent upon the acidity of the product packaged inside. Added to this pitfall for glass packaging, is the fact that glass flakes may peel off over a period of time, causing the composition of the product packaging inside to react with the package walls, thereby leading to massive drug recalls. Some of the recalls that have happened due to delamination are Baxter’s recall of Hylenex, Sandzol’s recall of Methotrexate, Amgen’s recall of Epogen and Procrit etc. – and the list keeps on growing.

Prefillable packaging formats, with a growth rate of 11% till 2014, will be the area where most of the substitution will take place. Proof of this substitution trend is the fact that out of the total number of prefilled syringes manufactured, 20-30% of them are made out of plastic raw material substitutes.

COC/COP - The Strongest Competitors to Glass as Raw Material Substitutes

The high cost of transition to plastic from established glass processes and lack of incentive in terms of drug formulation innovation discouraged the majority of producers of parenteral products from initiating the shift until now. But with the industry evolving with new and demanding types of protein formulations, innovative materials such as cyclic olefin copolymers (COC) and cyclic olefin polymers (COP) are being utilised more often.

One of the pioneers in the utilisation of COC and COP materials for glass primary packaging is Schott glass, which is the world’s largest pharmaceutical primary packaging provider, with a clear 30% market share of the glass primary packaging industry, and is third in line for prefilled syringes after Becton Dickinson and Gerresheimer.

Let us delve deeper into this industry example, for better understanding of the substitution trend.

The TOPPAC COC vials (2ml to 200ml) manufactured by Schott as one of their product portfolio have found increasing acceptance in the industry for pharmaceutical primary packaging. Schott claims that its new COC vials are suitable for liquid filling and lyophilisation.
and lower interaction rates, which in turn improve the shelf-life of the product packaged.

“COC polymer offers a few important advantages. Glass has been a well-tried and accepted material for parenteral packaging by the pharmaceutical industry for decades, but depending on the drug and its application, it has also certain limitations. In these cases COC polymer can offer a very good alternative,” says Schott product manager Wolfgang Streu. Some of the areas where Schott uses their COC vials are ophthalmic medicine, oncology and veterinary medicine.

Still Not Convinced? Well, Let’s Go Global.

COC has become very well accepted as a substitute to glass and normal plastics due to two main factors, viz. the innovation opportunities it provides in terms of design during the forming process for prefilled syringes, and the lightweight savings it provides as compared to its glass counterparts.

Some of the companies which have started using COC as a raw material are Gerresheimer, Alcan packaging and Schering. Even the global packaging giant Amcor has warmed up to COC as a substitute to glass and traditional plastic by using this material in its chlorine-free thermoformable coextruded COC/PP blister packs.

The largest substitution in primary containers has been in Asia, especially Japan. Japan has always had a good spending trend in terms of R&D, and until now remains the only country in Asia to have produced innovator drugs, with the rest of Asia focusing on generics. Along with this, the capability and capacity to accept disruptive technologies ensure that Japan as a country is at the forefront of all futuristic technology applications. Almost 60-70% of the prefilled syringes used in Japan are made out of plastic, especially, COC/COP. The Daikyo Crystal Zenith with its improved thermo mechanical properties, ease of precision moulding, sterilisation and improved moisture barriers, is a COP that has seen good acceptance in Japan.

Let us Understand why Plastic is being Considered Over Glass

For a layman, the first property of plastic when pitted against glass is the fact that packaging made out of plastic will be highly break-resistant. But it doesn’t end there. pH resistance of COC/COP plastic has higher values, and plastic doesn’t leach, i.e. there is no flaking of plastic over a period of time as there is in glass. One more important factor that is characteristic to plastic is its drainability i.e. the product doesn’t stick to the walls when coming out.

However plastic does have its own share of cons, a major one being the permeability of the COC/COP material towards gas and vapour. Coatings and additives which decrease the gaseous permeability of the COC/COP package are some of the areas where companies using substitute materials are trying to innovate. Some comparisons are as follows

Let us look at this issue objectively.

For a company which has a major stake in manufacturing and sale of a biotech drug, a significant amount of capital is invested right from the start of the project. For instance, for a biotech drug without RNA Interference technology (a costly technology to accelerate the pace of discovery biology) takes about 14 years to reach its preclinical phase. It is during this 14-year time period the effective method of drug delivery is optimised and decided. For a biotech drug with small volumes, the most common delivery format would be a prefilled syringe. A decision concerning the right kind of material for the package and the right volume of dosage is of paramount importance at this stage. As the company has already invested millions, maybe billions, to reach this stage, a wrong decision will lead to recalls, which is not only inconvenient but may cause complete bankruptcy. It is for this reason that pharmaceutical packaging buyers spare no effort and money to source the right kind of packaging material best suited for their drugs. Traditionally, PFS made out of COC/COP polymers cost around 20-25%
more than the normal package material that is glass. However from a total cost of ownership view, the prefilled syringes made out of COC will have better cost savings on the basis of reduced costs of recalls and increased throughput and cost saving from design flexibility. Along with this there are added benefits, such as those accrued by using plastic as a raw material, e.g. reduced delamination, light weighting, etc. With the improvement in technology, new and cost efficient COC/COP are being developed which will not only provide all the best properties of glass but also that of polypropylene. A very good example of such a product would be the Zeonex(r)/ZEONOR(r)

• Costs 1/4 to 1/10 of the price of glass syringes with luer lock assemblies
• Highly shatter-resistant
• Less than 50% weight than that of the glass counterparts, thereby improving freight and shipping costs
• Improved design opportunities through injection moulding technologies

This not only proves that plastic as a substitute is not just a trend being noticed in some instances, but also is here to stay and provide benefits to the pharmaceutical and healthcare companies, as well as packaging suppliers.

A Raw Material Substitution Will Lead to Industry Movement, Won’t It?

Improving opportunities of sourcing plastic for parenteral packaging and level of innovations in the industry provide pharmaceutical companies with ample opportunities to source the best packaging material for their parenteral product. The current industry norm is to develop long-term supplier contracts and involve the supplier in the overall R&D of the product developed, so that the optimised drug delivery format and the dosage is decided in consensus. This way the pharmaceutical companies can not only mitigate the risk of recalls due to wrong package, but also can capitalise upon the combined R&D capabilities of both partners. The following representation provides insights to the impact of the substitution on the procurement of packaging for parenteral products.

To Conclude:
The shift from glass to plastic may be slow, but is going to happen, and that is evident through the industry movements in the parenteral packaging sector. For normal or standard drugs a complete shift to plastic is not feasible, especially if the drug has become generic and mature. However, with sophisticated drugs and delivery technologies being developed, the packaging formats need to evolve. “Glass has been around for many years and will continue to be a suitable material for drug containment for many years to come. However, as newer and more sophisticated drug products and delivery technologies are developed, containment systems must evolve,” says Graham Reynolds, Vice-President of Marketing and Innovation of Pharmaceutical Delivery Systems at West. COC/COP are now finding an increased usage as substitutes for glass in special conditions where the issues with glass, such as delamination and tungsten residues, can lead to costly recalls. Pharmaceutical companies need to understand their product formulation and decide upon the best package material to improve shelf-life of the product. To do this, the companies have to involve suppliers in their sourcing strategies, especially at the product development stage. Currently, it can be said that glass and plastic are moving parallel to each other, and major companies are trying to improve the properties of these materials through surface coating and barrier technologies; however the industry cannot ignore the immediate delamination threat that glass has as a packaging material, and hence must move towards plastic, especially for demands from large molecule biotech drugs.

References
• Plastic Shows Benefits in Parenteral Packaging by Jennifer Markarian
• Trending Towards Plastic by Graham Reynolds
• Glass breakage, delamination and compatibility with biologics have boosted interest in novel materials in pharma packaging By Fran DeGrazio and Diane Paskiet
• TRENDS IN PHARMACEUTICAL PRIMARY PACKAGING FOR INJECTABLES by Claudia Petersen, Director of Business Development at Gerresheimer Bünde
• Cyclo olefinic copolymers make medical progress by By David Vink
• NEW CYCLIC OLEFINS By Jan H. Schut
• http://lifesciencleadermag.epubx.com/i/140470/13(Life Science Leader)

M. Abhiraj, is a Domain Lead working with Beroe Inc. a global provider of customized procurement services specializing in sourcing, supply chain visibility, financial risk analysis and environmental impact to Fortune 500 organizations.

M. Abhiraj specializes in tracking the pharmaceutical Primary packaging (Rigid) industry. He has worked on multiple projects for many Fortune 500 clients involving categories such as Rigid and flexible packaging in the end use markets such as pharmaceuticals and Consumer packaged goods.

M. Abhiraj has earned his degree B-Tech Biotech (IASE University) with MBA in Marketing (Christ University).

Email: info@beroe-inc.com