Press Release
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Next level QbD: Processing glass containers

stress-free, contact-less transport a need, trend or just a new hype?

Describing the process steps

For years, glass has been both the most common and well established packaging material for liquid pharmaceutical products including drops, syrups and parenterals. Although using glass containers for application comes with many concerns, some of which include the fact that it can be brittle, there are also many undeniable advantages. An advantage of using glass is that it is absolutely gas tight, tasteless, most widely inert, and made of natural or natural-identical raw material. Glass however, is the most severe one regarding product safety and sterility. Authorities worldwide have focused on this issue for years claiming “0 defects on the market”. Still there are recurring recalls of pharmaceutical products because of defects on this packaging material with potential risks to patient’s safety like micro-cracks, glass particulates or even glass breakage. Replacing glass by another, more mechanical robust material does not work for all pharmaceuticals with some special product characteristics. Because of this there are many alternatives available on the market, none of which are as applicable as glass. Consequently, the most promising solution for solving this problem is to change or even modify processing glass (containers) both on production, and filling lines. As an indispensable basis a systematic risk analysis has to be performed regarding all production steps from glass molding to final packaging, to figure out what gives the risk of breakage.

Built from sand

Glass has been used by mankind for over 9000 years. Production of glass for the first time is unknown– but early archaeological traces lead us back to around 7000 B.C.. The production of glass jewelry items and small vessels became popular around 3000 B.C. in the Egyptian region. Since then, not a lot has changed in the manufacturing of glass. The raw material is made of quartz sand; chemically this is a silicate dioxide compound complemented with additives to e.g. colourate the glass or to gain extraordinary chemical resistance. The automated process of glass molding, typically using temperatures between 1200°C and 1300°C, still reminds us of the handmade glassblowing process. Starting with molten glass, tubes are shaped by a rotating pipe in a continuous drawing process. These raw tubes are segmented by scratching, followed by heating and cooling repeatedly to cause tensions within the glass body (“thermal shock”). Against common understanding glass is not a solid but rather an undercooled liquid, and any further process steps plays with viscosities. Heating and a form free shaping process generates e.g. the bottom of a bottle, the finger flange, or the edge of a syringe or vial. It is essential to reduce tensions in this production step. Although annealing is performed afterwards, remaining tensions and micro-cracks as well as inclusions or airlines from the molding process itself re-

duce the strength and quality of the glass product. Reliable quality control systems must be in place to reject these faulty products.

Little strokes fell big oaks (adage)

When the forming process is completed, the containers are further processed in order to, for instance, remove production residuals, to sterilize the containers or to add assemblies like needle shields etc.. Once this is complete, the final filling, closing and packaging can take place. The glass containers pass through different process steps. Traditionally they are turned and transferred from conveyor belts to star wheels to conveyor screws. They are heated and cooled again during sterilization and have numerous glass to glass contacts throughout all of these steps. Repeated glass-to-glass contacts and rough edges on the production line can eventually cause cosmetic defects like scratches, cracks, checks and even glass breakage. Processing glass containers always begins with a bulked handling step – even if the containers are delivered in a nested form afterwards. The process steps of a typical production line are shown in figure 1 below. There are only a few differences between the handling steps of bulked and nested material. Identification of the handling procedures causing stress and reducing or even eliminating them where possible is one of the measures to conform with authority regulations. This eventually results in new approaches for handling containers on a production line.

Figure 1: production steps for pharmaceutical containers (bulk handling + optional steps for nested configuration)

“The greatest of faults, I should say, is to be conscious of none.” (Thomas Carlyle)

As mentioned before, “0-defects” in manufacturing is a non-achievable claim – not only in the pharmaceutical industry. Keeping that in mind, a thorough risk analysis in order to identify sources of errors is essential. Some errors cannot be eliminated reliably, either because of given laws of physics or because alternative handling procedures have not yet been established. The objects have to be monitored according to the evaluated risks. As glass is a material that is hardly detected, finding contaminations with glass chips or powder resulting from glass breakage is very challenging (note: please do not mix delamination, a chemical attack by high pH-solutions with a force driven physical impact.) Additionally, some failures are covered by assembly material like crimping caps – which does not make them any less grave. Only few systems for automated failure detection are available, nearly all of which are camera-based systems. Although they are very fast, they are still struggling with their tight limitations. Recognizing this fact, especially in pharmaceutical industry “human control points” are still very

common and well established. But further improvement on that is necessary, keeping the latest recalls in mind:

- in Q1/2014 vials in Germany and in the US were objected to have cracks (afterwards 4 more of them were found on internal inspections),
- in Q4/2013 vials produced in the US were objected to have cracks right below the crimping cap accompanied with the risk of microbiological contaminations of the product itself– very hard to see and to detect.

Such recalls have to be absolutely avoided both for the protection of patients' health and safety and of the pharmaceutical company's reputation, which in turn can be of economical relevance.

"Don't find a fault, find a remedy." (Henry Ford)

Besides tight quality controls and monitoring programs, the source of glass stress and eventually glass breakage has to be eliminated. As this is a topic of the production line and not originating from the pharmaceutical product, machine building companies have developed different systems and concepts to address this problem. Our strategy pursued by groninger& co. gmbh is to avoid any stress on the glass during each single process step by eliminating any form of glass-to-glass contacts. In the particular areas where handling cannot be avoided e.g. a vacuum transport is applied. Any relative movement between glass and equipment has to be reduced to the absolute minimum. During the entire filling and closing steps, the objects are directly processed in the transporting segments (format parts) where they are safely mounted. They are placed in these segments right after cleaning (where cleaning is necessary) and only removed where required, which are firstly for IPC after filling and secondly for nesting at the end of the line. Another major benefit of this concept for nested objects is the so-called U-type version of the equipment: multi-container lines for syringes, cartridges and vials in combination with 100% IPC aren't fiction anymore. The modular construction allows a very quick changeover between different nested container types, and the filling module only depends on the chosen filling system. Solely the closing unit has to be adapted to the processed container type. Inline sampling points enable additional sampling during processing without stopping the machine. As an additional feature to support fault detection the machine offers position based error analysis.
Very similar is the concept of assembly lines for bulked objects like syringes and cartridges, where siliconizations as well as the following assembling steps are performed whilst the objects are located safely in the segments. Even during cleaning, the objects are kept separated by polymer-grippers. Additional optical monitoring and quality control units are integrated on the line without reducing the machine speed and its output.

Summary

Being a modern “machine builder” means the existing knowledge base has to reach far beyond the machine equipment itself. Today’s complex processes as well as interactions between containers, processes and equipment force a machine builder to know about all processes in detail. To achieve high safety and quality levels of our products, effects not triggered by the equipment itself, but anyhow influencing the design of it, have to be taken into account.

Our many years’ experience in building machines gained over the last decades allows the groniger&co.gmbh to weigh the pros and cons of different strategies. Taking a close look into existing strategies used to minimize the risk of glass damage which might influence the patient’s safety shows clearly two options.

1. Checking damages, cracks and breaks are important but will never succeed to the requested quality level.
2. Second, avoiding any damage as far we can influence the important process steps is far more effective.

Following the common rules of inspection will set us in a position to fulfill the formal needs of regulators, but never reduces the risk to avoid any recall. QbD (“Quality by Design”) means to design all processes in a way inspection is only needed to confirm quality; not to create quality. Inspection is an “add-on” to quality and should not be necessary to create it.

Therefore stress-less or even better contact-less design is an important step into better quality and more product safety to the patient. The best is yet to come: it is already available having no limitations on performance or container types. It is even open for integration of completely new processes and validations. Changeover is easy and can be done today.

Figure 2: stressless processing of vials – filling process
Figure 3: stressless processing of syringes
Figure 4: Essential process steps having influence to glass damage

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