

Comparison of shatterproof safety packaging devices for cytotoxic drugs

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Four safety packaging devices for 100 mL glass vials were drop-tested from a height of 180 cm. Each container protects the vial for a single downfall. No glass breakage occurred. There are three containers with a thread cover cup and one container with a snap cover cup and additional bottle locker. For the withdrawal closed systems can be used with all containers.

Introduction

The carcinogenic, mutagenic and teratogenic potential of cytotoxic or cytostatic substances presents a serious risk to the health of persons involved in their production, preparation, administration and waste management. The drugs or metabolites were detected in the urine of pharmacy personnel [1-3] and the consequences in the case of pregnancy were discussed [4, 5, 6]. The substances may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukaemia and other neoplastic diseases. It was shown [7, 8, 9, 10] that industrially produced vials containing cytostatics are contaminated on the outside with these substances in an amount that can be responsible for the uptake into the bodies of the workers.

All cytotoxic drugs should be packaged to prevent direct contact to the glass surface and should be stored and transported in such a way as to prevent damage to the vials and subsequent contamination of the environment: the work materials, rooms, storage shelves, transport equipment and the personnel. Suppliers of cytotoxic drugs have designed different protectors to minimise the risk of breakage by using outer containers made of plastic break-resistant materials.

The aim of this article is to compare the containers which are actually on the market (or are soon to be launched; information as of July 2009).

- Onco-Safe®/NeoSafe®
- Onko-Guard®
- Onkoprotektor®
- TopLoad®.

All of these containers are registered either by trade mark™ or copyright®. In this article the term “®” is used only for simplification.

The comparison was done with regards to shatterproof and handling. The four safety packaging devices for 100 mL glass vials were drop-tested from a height of 180 cm. (DIN EN 22 248). The results show that each container protects the glass vial sufficiently for a single downfall. No glass breakage occurred. The handling of the devices differs. Containers with the thread on the outside of the bottom part have to be disinfected in two steps. It is possible to remove the vial from the container and a potential contamination could be touched by the personnel. The container with a snap cover cup is disinfected in one step. This container has a bottle locker which prevents the removal of the glass vial. The protection against contamination is thereby safeguarded. For the withdrawal of the drug solutions the use of commercially available closed systems is possible with all containers.

Teichmann and colleagues published data from different vertical fall tests according to DIN EN 22 248 (Packaging, complete, filled transport packages, vertical impact test by dropping) [11]. In the year 2008, only the Onco-Safe®/NeoSafe® container was commercially available. Teichmann compared:

- unprotected glass vials,
- plastic foil protected glass vials,
- plastic foil protected glass vials with reinforced bottom, and
- glass vials protected in an outer second container Onco-Safe®/NeoSafe®.

Vials with 10 mL and 100 mL volume were tested.

Relevant for the situation in the pharmacies was the test of break protection regarding the handling and shelf storage practices. The usual storage in shelves is not higher than 180 cm (eye level). The test found that glass vials protected in the Onco-Safe®/NeoSafe® are resistant against breaking. At 180 cm falling height, no vials protected in the Onco-Safe®/NeoSafe® broke. See Figure 1.

For 100 mL vials, the containers Onko-Guard®, Onkoprotektor® and TopLoad® are now available (or are soon to be launched; information as of July 2009) in addition to Onco-Safe®/NeoSafe®.

Vertical shock tests

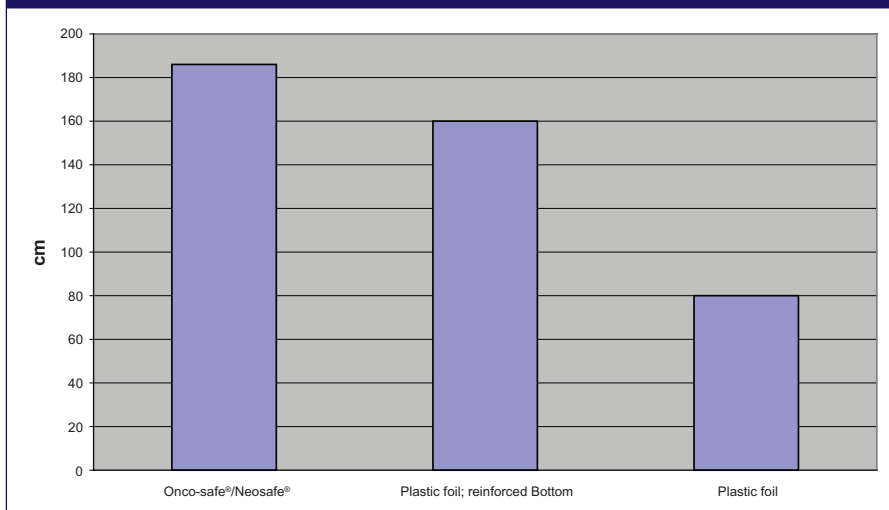
The containers were stuffed with 100 mL glass vials containing 0.9% NaCl solution; (Fresenius Kabi; lot 14CD33/072; expiry 04 2014). They were tested analogue Teichmann by dropping on a steel block, covered with a PVC floor tile, with a falling height of 180 cm according DIN EN 22 248 [11]. Onco-Safe®/NeoSafe®, Onko-Guard®, Onkoprotektor®, TopLoad®: ten containers of each specimen were tested by a single drop and collision with a steel block covered with a vinyl floor tile.

Description of the containers

Onco-Safe®/NeoSafe®

Onco-Safe®/NeoSafe® are two names for an identical construction. It consists

Figure 1: Average fracture drop height in cm; 100 mL glass vials [11]



of two parts. The bottom part is a cup made out of polypropylene. The screw cup cover is made out of polyethylene. The complete can is round, smooth, and nearly cylindrical. The four-start coarse thread is located on the outside of the bottom cup and is made visible by unscrewing. The internal bottom curvature has bars acting as bearers which clamp the vial and keep it at a certain distance from the wall. Thereby the vial is safely gripped and cannot fall out even in the case of withdrawing the cytostatic solution in overhead position. The cup is also cylindrical and smooth with the thread on the inner surface. The seal between the bottom and cover is achieved by an integrated circumferential lip seal, which caulks the parts together by screwing. The internal cover cup shows three bearings. Thereby, the flip off cap of the vial is fixed and the vial cannot get jammed to the side in case of dropping. The vial is positioned within the can so that there is 2–3 mm space on

all sides. The flip off cap of the vial is the only exception, having direct contact to the screw cover.

The Onco-Safe®/NeoSafe® is sufficiently transparent and the label can be read acceptably. The Onco-Safe®/NeoSafe® is constructed to be space-saving, and cover and bottom have outer smooth surface.

Handling

The Onco-Safe®/NeoSafe® is completely disinfected on the outside surface by wiping with a disinfectant-soaked non-woven tissue. It is transferred in the laminar air flow (LAF) clean bench and the cover is unscrewed by an approximately 120 degree gyration. After the thread area of the bottom cup is presented it should be disinfected in the same way. In every case the glass vial stays in the bottom cup. If the vial is not left in the protective container, the possible contamination on

the outside of the glass may be touched by the personnel. The rubber stopper is disinfected by wiping after removal of the flip-off cap. The withdrawal of the cytostatic drug should be done in the usual way by using a canula or a spike, which are clearly visible through the glass. It is possible to work with commercially available closed systems like Teva Adaptor® or PhaSeal®.

Onko-Guard®

The Onko-Guard® is a construct consisting of two parts. The bottom part is a cup made out of polypropylene. The screw cup cover is made out of orange pigmented polyethylene. The complete smooth can is octagon-shaped; only the area of the thread is cylindrical. The four-start coarse thread is located on the outside of the bottom cup and become visible by unscrewing. The internal bottom curvature has bars acting as bearers which clamp the vial and keep it in distance to the wall. Therefore the vial is safely gripped and cannot fall out even in the case of withdrawing the cytostatic solution in overhead position. The bottom cup is considerably cone-shaped. The screw cup is also octagonal with the thread on the inner surface. The seal between bottom and cover is achieved by an integrated circumferential lip seal, which caulks the parts by screwing. The internal cover cup shows no bearings. The vial is positioned with a distance to all sides of the can of 3–4 mm. Only the flip-off cap has direct contact to the screw cover. There is no bearing device for the vial in the screw cap. The Onko-Guard® is sufficiently transparent and the label can be read acceptably. The cover and bottom of





Onko-Guard® opened



Onkoprotektor® closed



Onkoprotektor® opened

the Onko-Guard® have smooth surfaces on the outside.

Handling

The Onko-Guard® is completely disinfected on the outside surface by wiping with a disinfectant-soaked non-woven tissue. It is transferred in the LAF clean bench and the cover is unscrewed by a 120 degree gyration. After the thread area of the bottom cup is presented it should be disinfected in the same way. In every case the glass vial stays in the bottom cup. If the vial is not left in the protective container the possible contamination on the outside of the glass may be touched by the personnel. The rubber stopper is disinfected by wiping after removal of the flip-off cap. The withdrawal of the cytostatic drug should be done in the usual way by using a canula or spike, which are clearly visible through the glass. It is possible to work with commercially available closed systems like Teva Adaptor® or PhaSeal®.

Onkoprotektor®

The Onkoprotektor® is a construct consisting of two parts. The bottom part is a cup made out of polypropylene. The screw cup cover is made out of dark red pigmented polyethylene. The complete can is round, smooth, and nearly cylindrical. The four-start coarse thread is located on the outside of the bottom cup and is made visible by unscrewing. The internal bottom curvature has bars acting as bearers which clamp the vial and keep it in distance to the wall. Therefore the vial is safely gripped and cannot fall out even in the case of withdrawing the cytostatic solution in overhead position. The cup is also cylindrical and smooth with the thread on the inner

surface. The cup is corrugated on the upper cylindrical part which gives a better grip. The seal between bottom and cover is achieved by an integrated circumferential lip seal, which caulks the parts by screwing. The internal side of the cover cup is reinforced in the centre to give extra protection for the flip-off cap. The vial is positioned within the can so that there is a 2–3 mm space on all sides. The flip-off cap of the vial is the only exception, having direct contact to the screw cover. The Onkoprotektor® is sufficiently transparent and the label can be read acceptably. The Onkoprotektor® is constructed to be space-saving and the cover and bottom have smooth surfaces on the outside.

Handling

The Onkoprotektor® is disinfected on the complete outside surface by wiping with a disinfectant-soaked non-woven tissue. It is transferred in the LAF clean bench and the cover is unscrewed by a 180 degree gyration. After the thread area of the bottom cup is presented it should be disinfected in the same way. In every case the glass vial stays in the bottom cup. If the vial is not left in the protective container the possible contamination on the outside of the glass may be touched by the personnel. The rubber stopper is disinfected by wiping after removal of the flip-off cap. The withdrawal of the cytostatic drug should be done in the usual way by using a canula or spike, which are clearly visible through the glass. It is possible to work with commercially available closed systems like Teva Adaptor® or PhaSeal®.

TopLoad®

The TopLoad® is a construct consisting of three parts: the bottom cup, the bottle

locker ring and the cover cup made out of very transparent elastic smooth polypropylene. There is no thread; the parts are simply snapped together. The horizontal areas of bottom and cover are moulded concavely and are reinforced with cross shaped bars.

The bottom cup is slightly cone-shaped; the bottle locker and the cover cup are mounted very tightly on the inside of the bottom cup. The cylindrical area of the bottom is profiled with eight broad grooves. On one hand these grooves fix the glass vial inwardly and on the other hand create distance space for shock absorption and break protection. The bottle locker ring shows five fins pointing inwardly which fix the glass vial irreversibly in the container. There is a flap for easy opening on the side of the cover cup. The packaging process is guided in three steps. The glass vial is set from above down in the bottom cup. The bottle locker is pressed in position fixing the vial at the lower curvature of the bottle neck. The cover cup is pressed in the circular sealing rill of the bottom part. The polypropylene



TopLoad® closed



material of the TopLoad® is very transparent and the label can be read well. The TopLoad® is constructed space-saving; all parts have smooth surface on the outside. The grooves also give a very good grip.

Handling

The TopLoad® is disinfected on the complete outside surface by wiping with a disinfectant-soaked non-woven tissue. It is transferred in the LAF clean bench and the cover is flipped off. The vial cannot be removed from the protective container—the possible contamination on the outside of the glass cannot be touched by the personnel. The rubber stopper is disinfected after removal of the flip-off cap by wiping. The withdrawal of the cytostatic drug should be done in the usual way by using a canula or spike, which are clearly visible through the container and the glass. It is possible to work with commercially available closed systems like Teva Adaptor® or PhaSeal®.

Weight and volume

It is obvious that an additional second package is associated with additional material and additional volume. Due to this additional volume and additional circumference the handling may be more difficult especially for workers with small sized hands as well as for the storage since more place is needed and more material must be disposed. A very space-saving and material-saving construction should be aspired as well as a good grip even for small sized hands. These requirements are fulfilled quite enough by each container.

To determine the used amount of plastic material the empty containers with all components were weighed.

The total gross volume was determined by submersing the containers in water. The displaced volume was measured (mean value of ten measurements). Due to variations in closure tightness of the caps the gross volume may vary. See Figure 2.

Discussion — Pros and cons

In no case did a glass vial break. If the cytostatics as recommended are stored below eye level the protection of personnel and storage equipment and rooms is sufficient.

Each container performed well and provided sufficient break protection if a single fall occurred. Due to the similar construction principle of the Onco-Safe®/NeoSafe®, Onko-Guard®, and Onkoprotektor® with bars acting as bearers which clamp the vials in the bottom cup the force of the impact on the steel block result in more or less damage of these bars. After the drop test little damage on the Onco-Safe®/NeoSafe®, considerable damage on the Onko-Guard® and extensive damage on the Onkoprotektor® could be seen. If the bearers are damaged or broken the vials are not clamped and securely fixed in the bottom cup. There is the danger that the vial may fall out during the preparation of the cytostatics. The TopLoad® is constructed without bearers and resists the force of the impact without observable damage. Therefore the TopLoad® protects the vial also in the case of multiple drops. But it is not a realistic situation that

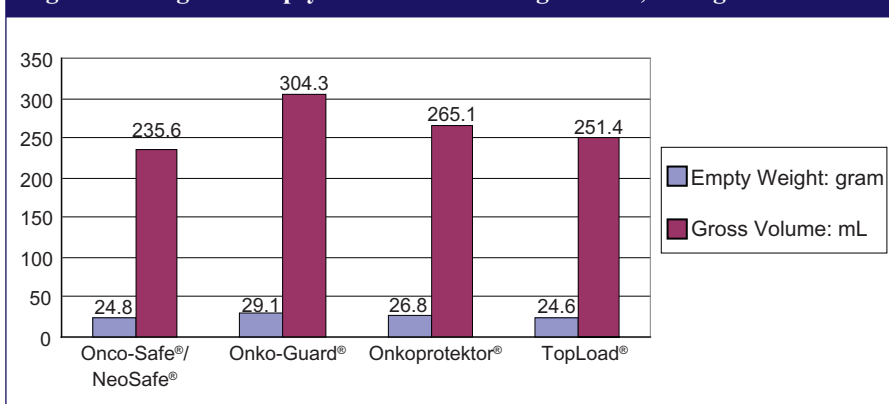
cytostatic medicaments undergo multiple drops in a pharmacy.

The Onco-Safe®/NeoSafe® are relatively space-saving and produce little extra volume. They are unscrewed with a 120 degree gyration. They provide effective break protection. The vial can be removed—the protection may be sabotaged. Due to the non profiled smooth surface the Onco-Safe®/NeoSafe® must be strongly gripped. The thread on the outside has to be extra disinfected. The Onco-Safe®/NeoSafe® are good and stable protective containers with effective prevention of breakage. If used in the designed way the Onco-Safe®/NeoSafe® are effective to prevent contamination.

The Onko-Guard® is relatively voluminous. It is unscrewed with a 120 degree gyration. It provides effective break protection. The vial can be removed—the protection may be sabotaged. Due to the octagonal shape the smooth surface has a good grip. The thread on the outside has to be extra disinfected. The Onko-Guard® is a protective container with effective prevention of breakage. If used in the designed way the Onko-Guard® is effective to prevent contamination.

The Onkoprotektor® is relatively space-saving and produces little extra volume. It is unscrewed with a 180 degree gyration. It provides effective break protection. The vial can be removed—the protection may be sabotaged. The screw cup has a very good grip. The thread on the outside has to be extra disinfected. The Onkoprotektor® is a protective container with effective prevention

Figure 2: Weight of empty container without glass vial; total gross volume



of breakage. If used in the designed way the Onkoprotektor® is effective to prevent contamination.

The TopLoad® is relatively space-saving and produces little extra volume. Due to the grooves on the bottom part, the TopLoad® has a very good grip and is transparent. The snap-off cover cup allows easy and fast opening. The glass vial is locked and cannot be removed; the protection is safeguarded.

The TopLoad® is disinfected in one step and there is no thread. The TopLoad® is a protective container with the most effective prevention of breakage and contamination.

Onco-Safe®/NeoSafe®: EBEWE

Pharma, a Sandoz company

Onko-Guard®: Actavis Deutschland

Onkoprotektor®: Cell Pharm / STADA

TopLoad®: LOGENEX Pharm

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