General European OMCL Network
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# Official Medicines Control Laboratories (OMCL)

# Market Surveillance Study (MSS)

# MSS061 Breaking of glass ampoules

# Summary report

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## BACKGROUND

Following the outcome of a national study carried out to investigate reported quality issues, the Hungarian Official Medicines Control Laboratory[1] responsible for human medicines proposed in 2021 to organise a Market Surveillance Study within the OMCL Network on the breaking of glass ampoules (MSS061).

## SCOPE OF MSS061

- Medicinal products for parenteral/oral/inhalation use, packaged into glass ampoules with different breaking systems.
- Type of glass ampoules:
  - One point cut (OPC) systems (= ampoules with break points).
  - Ampoules with break rings (rupture disc, VIBRAC system).
  - Ampoules with double tip systems.
  - Ampoules with other types of breaking systems.
- Volume of the ampoules: from 0.2 mL to 100 mL.

## PARAMETERS CHECKED

- Before opening the ampoules:
  - Appearance.
  - Presence of visible particles.
  - Glass delamination.
- After breaking the ampoules by hand:
  - Formation of glass particles when opening the ampoules.
  - Investigation and assessment of the fluid extracted from the ampoules.

[1] Pharmaceutical Chemistry and Technology Laboratory of the National Centre for Public Health and Pharmacy

## RESULTS

Nine OMCLs from 9 countries (Austria, Bosnia & Herzegovina, Bulgaria, Denmark, France, Germany, Greece, Hungary, and Portugal) participated in the study.

A total of 2190 ampoules from 138 samples were analysed, over a testing period running from November 2021 to August 2023.

Before opening the ampoules:

1) **Appearance**: The packaging was intact and within specification for 99.7% of the ampoules.

2) **Presence of visible particles**: 99.5% of the unopened ampoules were free from particles.

3) **Glass delamination**: 0.5% of the ampoules, all with OPC breaking systems, showed glass delamination.

After breaking the ampoules by hand:

**4) Formation of glass particles when opening by hand**

**4.1 Ampoule shattering:** Considering all types of breaking systems, 12% (256/2190) of the ampoules tested shattered.

Ampoules with breaking systems other than OPC and break rings did not shatter.

**4.2 Formation of glass particles**: Considering all types of breaking systems, glass particles were formed in 31% (673/2190) of the ampoules opened.

Ampoules with OPC breaking systems seemed to be less prone to the formation of glass particles when opened by hand than other systems.

The formation of glass particles seemed to increase in proportion to the volume of the ampoules.

**4.3 Formation of harmful breaking surfaces**: Considering all types of breaking systems, harmful surfaces were formed in 32% (699/2190) of the opened ampoules tested.

Ampoules with break ring systems showed less formation of harmful surfaces when opened than ampoules with OPC and double tip systems.

**5) Investigation and assessment of the fluid extracted from the ampoules**

**5.1 Fluid free of foreign particles**: Considering all types of breaking systems, the fluid extracted from 76% of the ampoules was free from foreign particles.

**5.2 Presence of glass particles in the fluid:** Considering all types of breaking systems, glass particles were found in the fluid from 23% of the ampoules.

Figure 1 shows the histograms of the results obtained in relation to the volume of the ampoules and Figure 2 shows the histograms of the results in relation to the type of ampoule breaking system.

## CONCLUSIONS

Based on the statistical evaluation of the results, it can be concluded that the appearance (freedom from visible particles) and lack of glass delamination of unopened ampoules were adequate but not 100%: 0.3-0.5% of defective units means 3000-5000 defective units per million ampoules manufactured, which would represent a significant production loss if they were rejected.

The focus of this Market Surveillance Study was the question of the formation of glass particles when opening the ampoules by hand. The **formation of glass particles was observed in 31% of the ampoules**. The study confirmed that OPC breaking systems (glass particles formed in 22% of the ampoules) are better than other types of breaking systems (57-62%), but 22% is still a large amount.

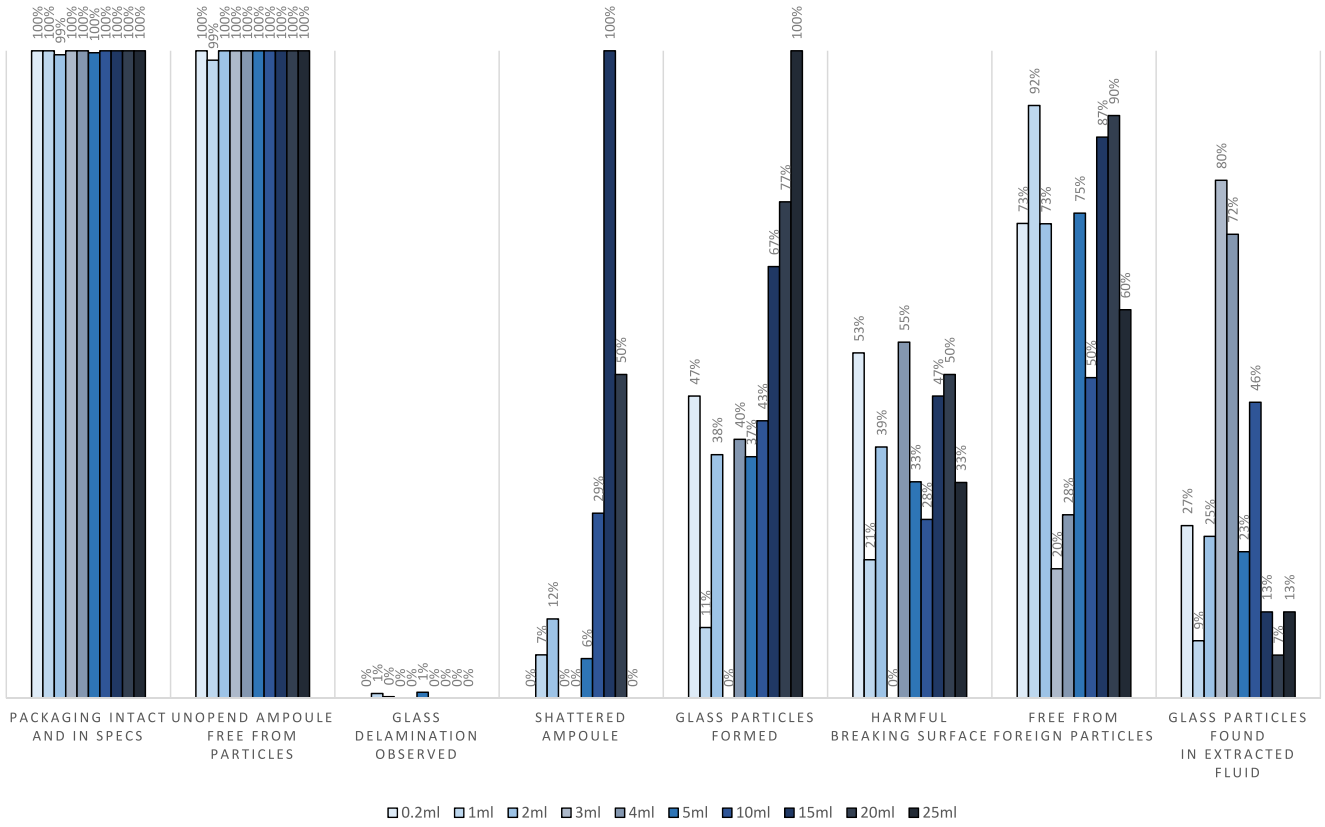
**The fluid extracted from 24% of dosage units (ampoules) contained foreign particles**, 94% of which were glass particles formed during opening of the ampoule. The other type of contamination (e.g. coloured material from the break ring) discovered during the study is an additional outcome of the market surveillance. Particles with a diameter below 0.8 mm can pass through an 18G needle, and particles with a diameter below 0.5 mm can also pass through a 21G needle, posing a serious risk to patients' health.

Ampoules with the most frequently used types of breaking systems (OPC and break rings) shattered more often. Opposite trends were observed for shattering and the formation of glass particles: OPC ampoules shattered more often (15%) than break ring ampoules (5%), while formation of glass particles was more common with break ring ampoules (OPC 22% and break ring 52%).

Harmful (sharp) breaking surfaces were also formed in an unacceptable proportion of ampoules (32% in total). This phenomenon can cause cut/puncture injuries to both those administering the medicinal product and patients, and bleeding, particularly in a hospital setting, also carries serious risks (e.g. transmission of life-threatening infections).

The available information on the composition of the glass used for the manufacture of ampoules and the details of the manufacturing processes are very limited in the technical documentation (CTD) of this type of medicinal product. The participating OMCLs tested a wide range of products with a wide range of ampoule types and manufacturers. The results confirm the conclusion of the national market surveillance in Hungary: **the problem is not related to the batch, the product, or the manufacturer, but only to the glass** (primary packaging material) of the ampoules.

## FIGURE 1 - RESULTS BY VOLUME OF AMPOULES




## FIGURE 2 - RESULTS BY TYPE OF AMPOULE BREAKING SYSTEMS