

# The Effects of Ozone and Various Sterilization Techniques on Elastomeric Rubber Needle Shields and Tip Caps

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**Sample A**  
Natural rubber formulation  
3-minute ozone exposure

**Sample B**  
Synthetic isoprene-  
bromobutyl blend  
4-minute ozone exposure

**Sample C**  
Synthetic isoprene  
2-hour ozone exposure

## ABSTRACT

Cracking of elastomeric needle shields and tip caps is a costly problem for pharmaceutical manufacturers. Cracked components can cause leaks that can result in loss of drug potency and sterility and may lead to a safety risk for the person administering the drug and the patient. This cracking has been attributed to ozone degradation of the elastomer formulations. In this study, several elastomeric needle shields and tip caps were exposed to ozone for various time periods and analyzed to determine the effects the ozone had on the elastomers.

In addition to being resistant to ozone degradation, elastomeric needle shields must be compatible with various forms of sterilization. In this study, the elastomeric needle shields and tip caps were also exposed to several types of sterilization and evaluated to determine the effects this exposure has on the elastomers.

## PREPARATION

### Methodology

In this evaluation, three (3) different elastomer formulations that are used to manufacture needle shields and tip caps were tested. The needle shields included in the study were based on natural rubber, a synthetic isoprene and bromobutyl blend, and a synthetic isoprene. The first two are representative of current industry elastomer formulations for needle shield and tip cap applications. The synthetic isoprene needle shield used in the study is representative of a more recently developed elastomer formulation.

The Ozone Exposure study consisted of exposing the needle shield samples to an exaggerated ozone concentration of  $7\text{g/m}^3\text{O}_3$  to determine the robustness of each rubber formulation. Once exposed to the ozone, the needle shields were examined every minute for up to 2 hours. The needle shields were then examined visually for any cracking or splitting. After examination, if cracking or splitting was observed on a needle shield, a photo was taken to document the phenomenon and the sample was no longer exposed to the ozone.

The Sterilization study consisted of exposing the needle shields to both steam and gamma irradiation sterilization. For steam sterilization, the needle shields were sterilized at  $121^\circ\text{C}$  for 30 minutes. The doses of the gamma irradiation sterilization of the needle shields were 25 kGy and 50 kGy. The needle shields were exposed to Bierer Davis Aging according to DIN 53.508 part 6.2.2 in which the conditions are 3 and 5 Days/21 Bar  $\text{O}_2/70^\circ\text{C}$ . The testing of the samples included Ph. Eur. 5th Edition Section 3.2.9 Chemical Test Series.

**Figure 1: Sample Reference Table**

Sample	West Reference
A	West Natural Rubber Needle Shield
B	West Synthetic Isoprene - Bromobutyl Blend Needle Shield
C	West Synthetic Isoprene Needle Shield

**Figure 2: Sterilization Study Matrix**

Sterilization	West Natural Rubber Formulation	West Synthetic Isoprene - Bromobutyl Blend Formulation	West Synthetic Isoprene Formulation
Unprocessed	X	X	X
Sterilized at 121°C for 30 minutes		X	X
Gamma Irradiation at 25 kGy	X	X	X
Gamma Irradiation at 50 kGy	X	X	X

**Results: Ozone Exposure Study**

Sample	Splitting/ Cracking Observed	Time Observed
A	Yes	3 minutes
B	Yes	4 minutes
C	No	120 minutes (2 hours)

Steam Sterilization Study Results - *Ph. Eur. 5th Edition Section 3.2.9 Chemical Test Series										
	Sterilization	Reducing Substances (mL of 0.01 KMNO <sub>4</sub> /20 mL of Sol S)	Absorbance (Sol S Abs. 220-360 nm)	Residue on Evaporation (mg/50 mL of Sol S)	Appearance of Solution (Opalescence - NTU)	Extractable Heavy Metals (ppm)	Extractable Zinc (ppm)	Ammonium (ppm)	Acidity or Alkalinity (mL of NaOH or HCL)	Volatile Sulphide (mg Na <sub>2</sub> S/ 20 cm <sup>2</sup> )
Sample A	Unprocessed	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Processed	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sample B	Unprocessed	0.4	Complies Type I	0	Complies Type I	Complies Type I	0.6	Complies Type I	0.04 NaOH	0
	Processed	0.3	Complies Type I	0	Complies Type I	Complies Type I	0.6	Complies Type I	0.04 NaOH	0
Sample C	Unprocessed	0.8	Complies Type I	0.9	Complies Type I	Complies Type I	0.5	Complies Type I	0.1 NaOH	0
	Processed	1.2	Complies Type I	1.9	Complies Type I	Complies Type I	0.3	Complies Type I	0.1 NaOH	0

25 kGy Gamma Irradiation Study Results - *Ph. Eur. 5th Edition Section 3.2.9 Chemical Test Series										
	Gamma Sterilization	Reducing Substances (mL of 0.01 KMNO <sub>4</sub> /20 mL of Sol S)	Absorbance (Sol S Abs. 220-360 nm)	Residue on Evaporation (mg/50 mL of Sol S)	Appearance of Solution (Opalescence - NTU)	Extractable Heavy Metals (ppm)	Extractable Zinc (ppm)	Ammonium (ppm)	Acidity or Alkalinity (mL of NaOH or HCL)	Volatile Sulphide (mg Na <sub>2</sub> S/ 20 cm <sup>2</sup> )
Sample A	Unprocessed	2.0	Complies Type II	<0.5	Complies Type I	Complies Type I	0	Complies Type I	0.01 NaOH	<0.15
	Processed	3.7	Complies Type II	0.5	Complies Type II	Complies Type I	0	Complies Type I	0.01 NaOH	<0.15
Sample B	Unprocessed	0.4	Complies Type I	0	Complies Type I	Complies Type I	0.6	Complies Type I	0.04 NaOH	0
	Processed	0.7	Complies Type I	0	Complies Type I	Complies Type I	1.1	Complies Type I	0.04 NaOH	0
Sample C	Unprocessed	0.8	Complies Type I	0.9	Complies Type I	Complies Type I	0.5	Complies Type I	0.1 NaOH	0
	Processed	1.9	Complies Type I	0.5	Complies Type I	Complies Type I	0.8	Complies Type I	0.1 NaOH	0

50 kGy Gamma Irradiation Study Results - *Ph. Eur. 5th Edition Section 3.2.9 Chemical Test Series										
	Gamma Sterilization	Reducing Substances (mL of 0.01 KMNO <sub>4</sub> /20 mL of Sol S)	Absorbance (Sol S Abs. 220-360 nm)	Residue on Evaporation (mg/50 mL of Sol S)	Appearance of Solution (Opalescence - NTU)	Extractable Heavy Metals (ppm)	Extractable Zinc (ppm)	Ammonium (ppm)	Acidity or Alkalinity (mL of NaOH or HCL)	Volatile Sulphide (mg Na <sub>2</sub> S/ 20 cm <sup>2</sup> )
Sample A	Unprocessed	2.0	Complies Type II	<0.5	Complies Type I	Complies Type I	0	Complies Type I	0.01 NaOH	<0.15
	Processed	4.8	Complies Type II	0.5	Complies Type II	Complies Type I	0	Complies Type I	0.04 NaOH	<0.15
Sample B	Unprocessed	0.4	Complies Type I	0	Complies Type I	Complies Type I	0.6	Complies Type I	0.04 NaOH	0
	Processed	0.8	Complies Type I	0	Complies Type I	Complies Type I	1.1	Complies Type I	0.04 NaOH	0
Sample C	Unprocessed	0.8	Complies Type I	0.9	Complies Type I	Complies Type I	0.5	Complies Type I	0.1 NaOH	0
	Processed	2.1	Complies Type I	0	Complies Type I	Complies Type I	0.9	Complies Type I	0.1 NaOH	0

## CONCLUSION

The effects of the exaggerated ozone exposure study are dependent on the rubber formulation. As was observed in the study, some rubber formulations are more resistant to ozone exposure. The synthetic isoprene rubber formulation (Sample C) was superior to the other formulations as it related to cracking/splitting when exposed to the ozone concentration.

The data collected demonstrates that steam and gamma irradiation-processed samples had no significant differences compared to the unprocessed samples of the synthetic isoprene and bromobutyl blend formulation and the synthetic isoprene formulation. However, the gamma irradiation of the natural rubber formulation appears to have affected the chemical characteristics of the rubber formulation.

<b>* Ph. Eur. 5th Edition Section 3.2.9 Chemical Test Series Requirements</b>		
<b>Test</b>	<b>Type I Requirements</b>	<b>Type II Requirements</b>
Reducing Substances	Max. 3.0 mL 0.01M KMNO <sub>4</sub> /20 mL of Sol S	Max. 7.0 mL 0.01M KMNO <sub>4</sub> /20 mL of Sol S
Absorbance	≤ 0.2 absorbance 220-360 nm	≤ 4.0 absorbance 220-360 nm
Residue on Evaporation	Max. 2.0 mg/50 mL Solution S	Max. 4.0 mg/50 mL Solution S
Appearance of Solution	Opalescence not greater than reference; Suspension II (2.2.1); Color not greater than reference solution GY <sub>5</sub> (2.2.2, method II)	Opalescence not greater than reference; Suspension III (2.2.1); Color not greater than reference solution GY <sub>5</sub> (2.2.2, method II)
Extractable Heavy Metals	Max. 2 ppm Pb <sup>2+</sup>	Max. 2 ppm Pb <sup>2+</sup>
Extractable Zinc	Max. 5µg Zn <sup>2+</sup> /mL Solution S (= 5ppm)	Max. 5µg Zn <sup>2+</sup> /mL Solution S (= 5ppm)
Ammonium	Max 2 ppm in Solution S	Max 2 ppm in Solution S
Acidity or Alkalinity	Titration of 20 mL of Solution S; Max. 0.3 mL 0.01M NaOH Max. 0.8 mL 0.01M HCl	Titration of 20 mL of Solution S; Max. 0.3 mL 0.01M NaOH Max. 0.8 mL 0.01M HCl
Volatile Sulphides	Black stain on acetate paper is not greater than a reference of 0.154 mg Na <sub>2</sub> S and 50 mL 20 g/l citric acid using 20 cm <sup>2</sup> stopper surface area	Black stain on acetate paper is not greater than a reference of 0.154 mg Na <sub>2</sub> S and 50 mL 20 g/l citric acid using 20 cm <sup>2</sup> stopper surface area

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