



# Irganox 1076 Extraction

## Technical Report Series 2017-007

### Purpose

Testing was conducted to measure the effectiveness of the SiO<sub>2</sub> Medical Products, Inc. (SMP) coating system at blocking non-volatile extractables from the underlying plastic substrate from migrating into the liquid contained in the vial.

### Background

One of the downfalls of parenteral packages formed from plastic materials is the potential for extraction of components from the container by the liquid drug formulation contained within; the extracted compounds can contaminate the drug and ultimately find its way into the patient. Also, there are known cases of organic adhesives from labels on the container exterior migrating through the plastic and extracted into the drug formulation.

SMP addresses this problem with cyclic olefin polymer (COP) plastic containers through plasma application of amorphous silicate glass (SiO<sub>x</sub>) coating on the inside surface of the plastic container, offering an additional safeguard against potential extractables compromising the drug product.

Irganox 1076 is a low molecular weight stabilizer (Figure A) used in plastics processing as an antioxidant. It was chosen as an extraction candidate for its low molecular weight and high polarity, and thus high migratory rate to the surface of olefin plastics. If the SMP coatings could inhibit extraction of Irganox 1076, it was reasoned that higher molecular weight additives and degraded polymer oligomers, if present, would be at least as effectively inhibited.

### Method

Irganox 1076 was compounded with Zeonex 690r resin, and extruded into pellets comprising one percent weight/weight Irganox 1076.

These pellets were then extruded and injection-stretch molded into five milliliter vials.

To one set of vials, the SMP bilayer coating system was applied, of which one layer is the SiOx coating. This was to demonstrate that only the adhesive and barrier coatings are needed to provide an effective barrier to migration without the protective layer.

Both sets (uncoated and coated) of vials were charged with 15 percent volume/volume cyclohexane in isopropanol, sealed with aluminum foil, and heated to 65oC for 24 hours, followed by gas chromatography-mass spectrometry detection of the solvent extracted Irganox 1076 in the uncoated and coated vials, respectively. (Detection limit determined by external Irganox 1076 calibration was 0.1 microgram per milliliter).

## Results

Figure B indicates that under the conditions tested, almost 1.5 ppb of Irganox 1076 was extracted from the uncoated COP vial, while no detectable Irganox 1076 was detected from the bilayer coated vials.

## Conclusion

The bilayer coated vial provides an effective solute block to Irganox 1076, even at loadings 5-10x higher than normal, in COP plastic articles.

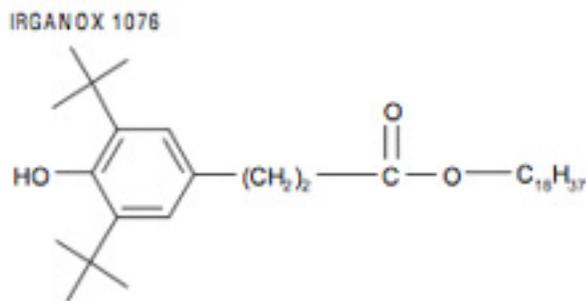


Figure A. Structure of Irganox 1076

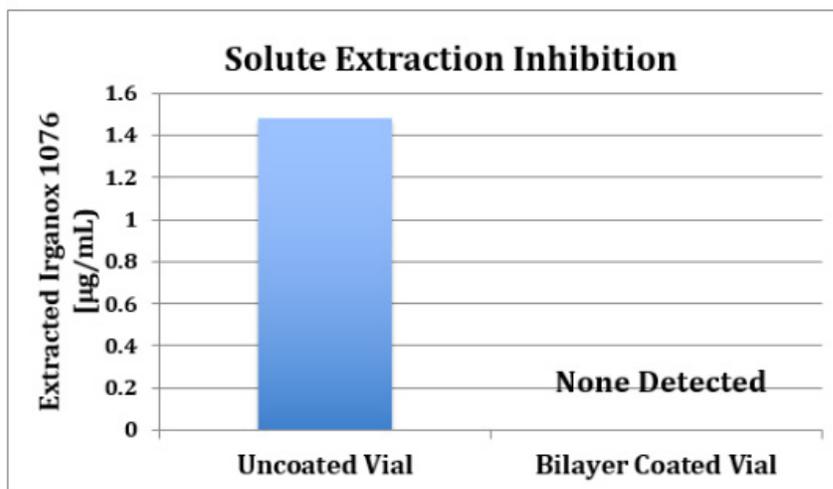


Figure B. SMP Bilayer Coating Solute Inhibition