SiO2 MATERIALS SCIENCE℠

pH Shift Resistant Coated Vials Filled with Water for Injection

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INTRODUCTION

Type I borosilicate glass is not ideal for long-term storage of small volume water for injection (WFI). Ion exchange between the glass and WFI can alter its pH. Metal ions in the glass, such as Ca+2 and Na+, are exchanged with H3O+ ions, which increases OH- ion concentrations in WFI. This results in an upward pH shift resulting in a more alkaline WFI. The US pharmacopeia specification for WFI pH is 5-7. A shift in pH can increase the risk of delamination and non-compliance with pharmacopeia specifications.

This study evaluated the pH of WFI stored in barrier system coated COP versus standard Type I borosilicate glass vials at 40°C. The barrier system is three layer stack of silica-based coating whereby the first and last layers are organosilica and the middle layer is pure amorphous silicon dioxide. The hypothesis was that the absence of metal ions coated COP vials would suppress a shift in WFI pH as compared to borosilicate vials.

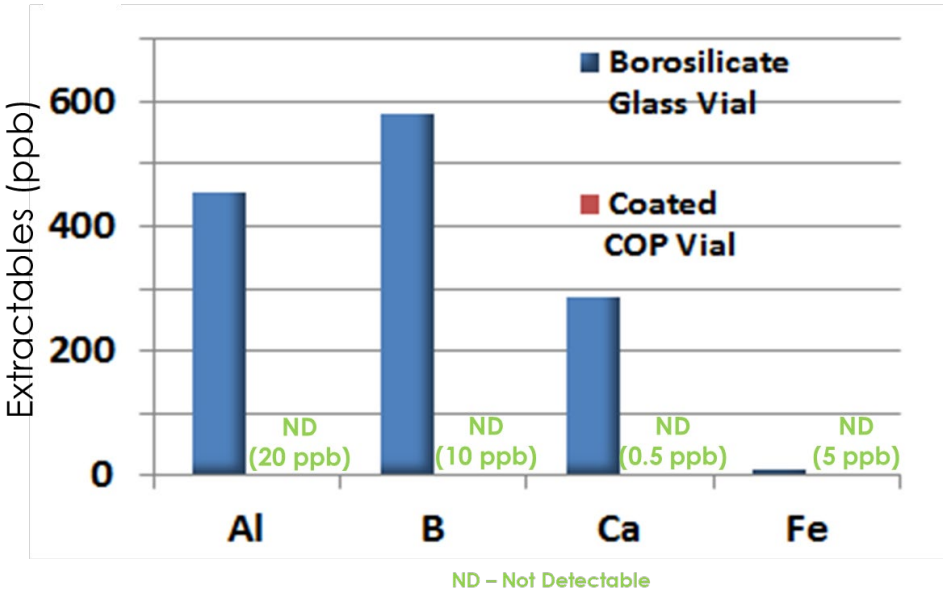
Methods & Materials

Borosilicate glass vials, coated COP and COP vials were filled with 5ml of the same batch of WFI with a pH of 5.0. Saturated KCl solution was added to the vials just prior to measuring the pH at the concentration of 0.3 mL per 100 mL of solution to provide enough ionic strength to help stabilize the pH readings. Filling was conducted in a laminar flow hood using aseptic technique. The filled containers were stored at 40 °C over 3 months. Several of each vial type were pulled and the pH of the WFI was measured.

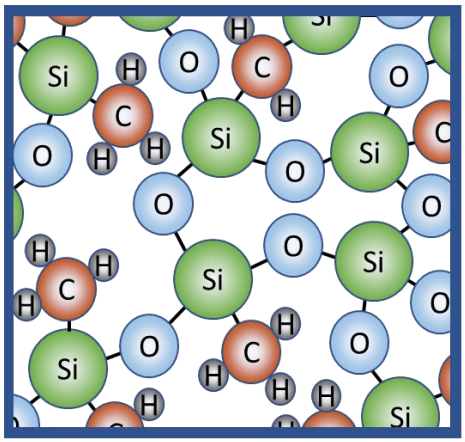
All coated vials were gamma sterilized. Glass vials were rinsed with WFI and depyrogenated by heating to 250°C for 2 hours to expose the glass to conditions that it would experience during pharmaceutical processing before sterile filling.

Results & Discussion

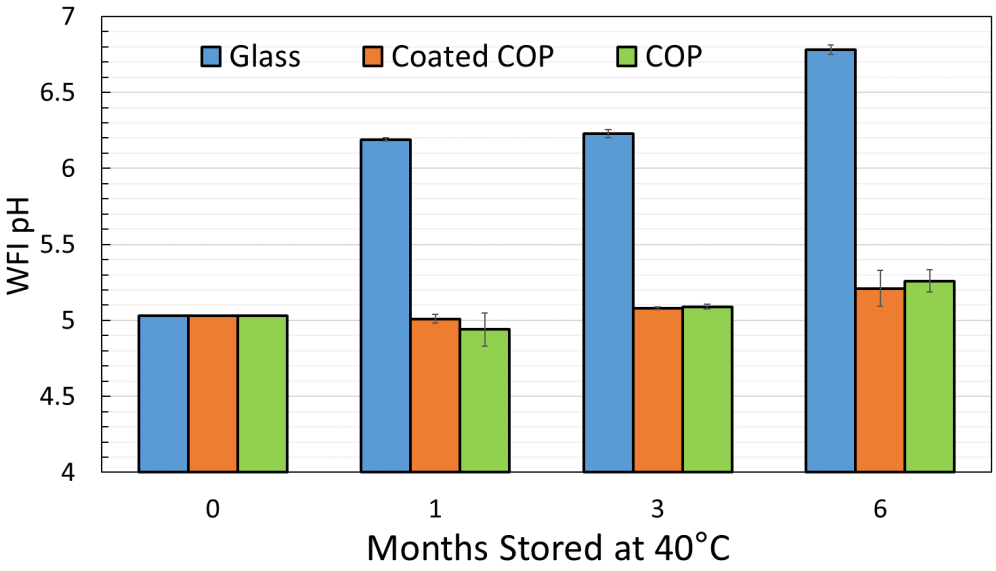
A comparison of the metal ion extractables was conducted between Type I borosilicate glass and coated COP vials. Vials were filled aqueous solution buffered to pH 2.5 and stored for 72 hrs at 50 °C. Inductively coupled plasma – optical emission spectroscopy (ICP-OES) was used to measure the concentration of metal ions in solution and plotted in the bar graph below. Borosilicate glass exhibits 200-600 parts per billion (ppb) of aluminum (Al), boron (B) and Calcium (Ca). A lower concentration of iron (Fe) was also detected above the lower detection limit of 5 ppb.



The coated COP vials did not exhibit any metal ion extractables above the detection limits of the ICP-OES. This may not be surprising considering the chemistry and composition of the coating surface in contact with the pH 2.5 buffered aqueous solution. The picture below illustrates a model molecular structure of the coating surface, which contains only silicon, carbon, oxygen and hydrogen atoms. This coating chemistry not only eliminates ion migration at low pH, but also has extremely high hydrolytic resistance to dissolution at high pH compared to borosilicate glass.



The pH shift results in the bar graph below are shown for both borosilicate glass and coated COP vials filled with WFI for 6 months at 40 °C. Borosilicate glass show a pH shift of 5 to over 6 in the first month and continues to increase over the next 5 months. Coated COP vials, by comparison, exhibit virtually no change in pH over 3 months and a marginal change of pH 5.4 at 6 months. The marginal pH shift of coated vials was similar to ordinary COP vials.



CONCLUSIONS

pH shift of WFI did not change significantly when packaged in barrier coated COP. There was at least 2 pH units of change in WFI packaged in borosilicate glass. This is indicative of metal ions leaching from glass into WFI. This could lead to delamination and could cause drug products to be out of compliance with pharmacopeial monographs or product specifications. By using COP vials the leaching of packaging components and delamination of glass flakes into the drug product can be mitigated.