

Root Cause Analysis of Color Change in Aqueous Drug Product



Summary

CPG utilizes a range of analytical techniques and applies fundamental materials science, engineering, and chemistry knowledge to identify the root cause of manufacturing or performance failures. In this case study, CPG employed microscopy and elemental analysis to inspect and analyze a discolored drug product.

Description

An aqueous drug product failed inspection due to a purple hue in the normally colorless solution. The drug solution was contained in a glass vial with a rubber septum, and in addition to the purple hue, a discolored region on the vial wall was identified. CPG performed root cause analysis to determine the cause of both discolorations.

Analysis

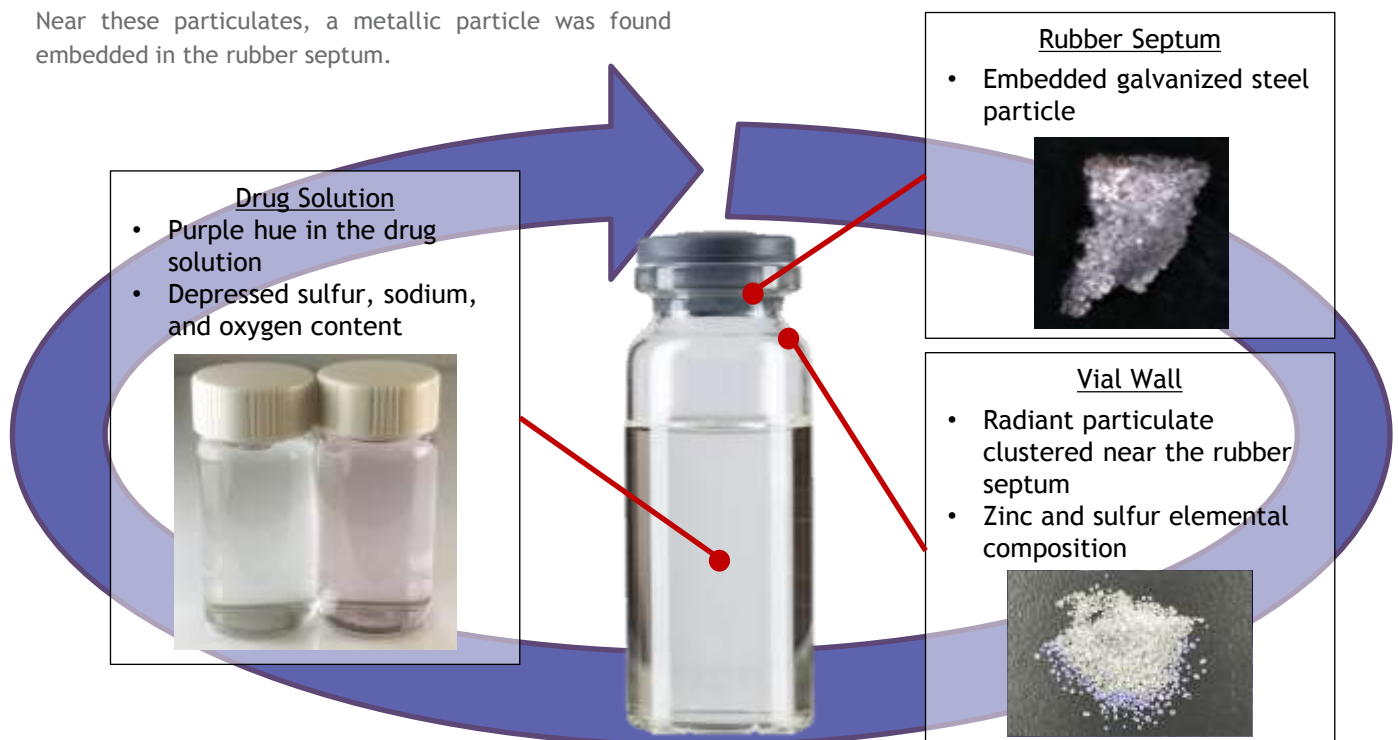
Using optical microscopy, the “discoloration” on the vial wall was identified as a cluster of radiant particulates. Near these particulates, a metallic particle was found embedded in the rubber septum.

Scanning electron microscopy with energy dispersive spectroscopy (SEM-EDS) identified the embedded metallic particle as galvanized steel, and the particulates were identified as zinc sulfide.

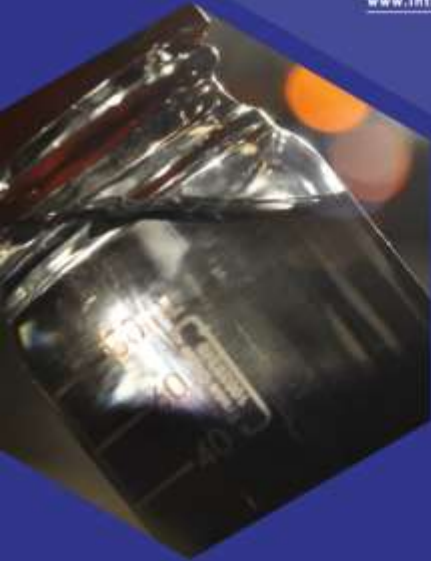
Conclusions

A galvanized steel particle was incorporated into the vial’s septum during molding. The zinc coating on the particle corroded and reacted with a sulfur-containing antioxidant in the drug solution, producing zinc sulfide, a water-insoluble, phosphorescent compound. The purple color change in the drug solution was attributed to solubilized chromium ions from the steel particle.

The root cause analysis performed by CPG identified the cause of the discolorations, enabling release of a production hold placed on the drug product.



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