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A newly identified impurity in Polysorbate 80, the long-chain ketone 12-tricosanone, forms visible particles in a biopharmaceutical drug product

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Title

A newly identified impurity in Polysorbate 80, the long-chain ketone 12-tricosanone, forms visible particles in a biopharmaceutical drug product

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Abstract

Visible particles linked to polysorbates used in biopharmaceutical drug products have been observed repeatedly in recent years as an industry-wide issue, with polysorbate degradation and insoluble degradation products, especially fatty acids and fatty acid esters, being suspected as root-cause. We have shown that the visible particles observed in a monoclonal antibody (mAB) drug product solution in vials after 18 months of long-term storage at $5 \pm 3^\circ\text{C}$ were neither linked to reduction in polysorbate (PS80) concentration nor to any known polysorbate degradation product, but consist of 12-tricosanone, an impurity present in the raw material PS80, not a degradation product. The occurrence of visible 12-tricosanone particles in drug product correlated with the usage of specific PS80 raw material lots, where 12-tricosanone was found as impurity at elevated levels. The quantities detected in these PS80 lots directly translate into the amount found in the respective mAB drug product batches. This is the first time that a clear correlation between the occurrence of the impurity 12-tricosanone in PS80 and the occurrence of visible particles in drug product batches is reported. The observation and techniques described enable the control of this ketone in polysorbate raw materials, providing means to prevent respective visible particle formation in drug products.

Keywords

Biopharmaceutical characterization, particle sizing, formulation, surfactants, protein formulation, monoclonal antibody

Abbreviations

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