

446e Trouble-Shooting of High Residual Solvent during Drying of Biological Derived Api

Yubo Yang, Stephen Tyler, and Kenneth Wilson

The final wet cake of this biological derived API, from a mixture of acetone (anti-solvent) and water, is dried with a tray dryer under vacuum and heat. The residual solvent specification (acetone) for the API is NMT 2.0%. There had been some difficulties to meet this specification in the plant in 2003-2004. Few lots failed the residual solvent specification and they had to be reprocessed.

The purpose of this investigation was to examine what parameters affect the residual solvent and to develop a proper procedure to minimize the residual solvent in API production. The parameters that affect the residual solvent in API drying were examined first by carefully and critically reviewing the historical plant data for the previous 3 years, and a “think-out-box” hypothesis and model were developed. Many well-designed lab experiments were conducted to confirm the process model and hypothesis. It was concluded that too high vacuum during the first phase of drying at 25°C, relatively low wetness of the wet cake and smaller batch were the root causes for the lots that failed the residual solvent specification. This caused water in the wet cake to escape more easily and the formation of hard shell earlier than that in a typical drying operation, resulting in trapping more solvent into the product. It was recommended to reduce the vacuum to about 100mmHg, instead of typical less than 20 mmHg vacuum, during the first phase of drying, which effectively reduces the residual solvent to meet the specification in the final API.