Formation and Quantitation of an Elusive Anhydrate

CASE STUDY

The challenge

Production batches of an API, which was a variable hydrate, revealed traces of an anhydrous polymorph. Elucidating the anhydrate formation mechanism and establishing a reproducible method for its preparation and quantification were imperative.

How?

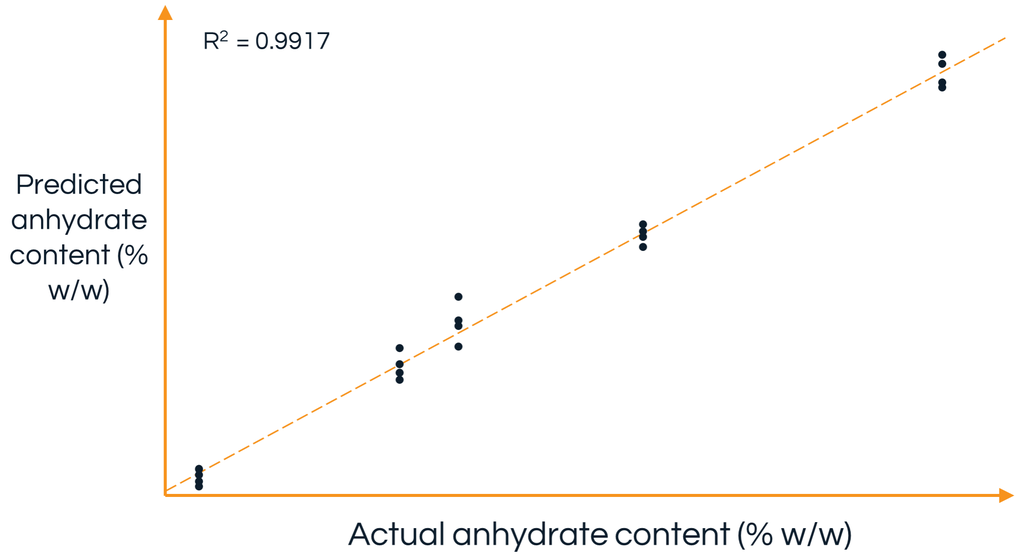
The CatSci team investigated the cause of the contamination through studying the inter-relationship between the two forms and replicating process conditions as closely as possible. Quantitative XRPD and FT-IR models using multivariate analysis were developed to quantify the level of anhydrate in the hydrate. Additionally, the anhydrate was synthesised on 2 g scale to determine the critical water activity for hydrate dehydration.

The achievement

Through CatSci's comprehensive investigation into our customer's process:

- The mechanism of anhydrate formation was elucidated.
- A reproducible method for preparing the anhydrate was defined.
- A calibration curve was constructed using XRPD and FTIR deploying multivariate methods.
- Models were validated giving a predicted accuracy of ± ~1.6% w/w anhydrate.
- Advised customer on achieving a successful regulatory submission.

Predictive accuracy of XRPD model

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