Piramal
Pharma Solutions

# SMALL-SCALE ADC DEVELOPMENT

A client requested > 2 mgs of an ADC to be manufactured using their new proprietary drug linker. The drug linker was only available in low quantity, its strength was unknown, and the drug was also hydrophobic. The client had requested quality targets to be met by the ADC: drug load, purity and residual free drug.

## PROBLEM

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## APPLICATION

For this type of project Piramal initially assesses at small scale the ability to conjugate the drug to the antibody based on one of its own generic conjugation protocols, generating at the same time conjugated material to allow suitability assessment and/or development of analytical methods.

In this particular case during the initial trial at < 1mg scale, one of our HIC analytical methods screened exhibited very good resolution for the conjugate, showing that the conjugation reaction was incomplete under our standard reaction time conditions and also that the reaction stalled. Addition of more drug linker in 2 successive aliquots allowed the conjugation reaction to go to completion. The reason for the incomplete conjugation was assigned to the unknown/low strength of the drug linker. The use of a suitable HIC in-process test allowed us to overcome successfully this unknown factor and enabled complete conjugation to take place.

The process was directly scale-up to a few mg's, using the HIC in-process test, to successfully conjugate fully the partially reduced antibody. Buffer exchange following conjugation led to the ADC meeting specification: DAR 3.5, aggregates < 5%, free drug < 2%.

# OUTCOME

Piramal successfully synthesised > 2mg's of the ADC and shipped it back within 2 weeks of the drug linker being receipted. All product quality targets were met.

Piramal Pharma Solutions is a contract development and manufacturing organization (CDMO), offering end-to-end development and manufacturing solutions across the drug life cycle. We serve our clients through a globally integrated network of facilities in North America, Europe and Asia. This enables us to offer a comprehensive range of services including Drug Discovery Solutions, Process & Pharmaceutical Development services, Clinical Trial Supplies and Commercial supply of APIs and Finished dosage forms. We also offer specialized services like development and manufacture of Highly Potent APIs, Antibody Drug Conjugation and are well versed in technologies such as Bio-catalysis, Route Scouting etc. Our capability as an integrated service provider & experience with various technologies enables us to serve Innovator and Generic companies worldwide.

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