

Altasciences is dedicated to helping you advance the development of ADCs to drive significant therapeutic advancements. We have specialized, cutting-edge equipment, and substantial expertise in ligand binding and mass spectrometry bioanalysis of ADCs to meet the unique needs of your project, whether for pharmacokinetic (PK) or pharmacodynamic (PD)-based endpoints in preclinical or clinical studies.

SELECTING THE RIGHT BIOANALYTICAL PLATFORM FOR ADC PK ASSAYS

Our bioanalytical laboratories are equipped with the two most common platforms for ligand binding assays (LBAs) and LC-MS/MS workflows for PK bioanalysis. With decades of expertise, we help you select the most suitable platforms for your project, considering the pros and cons specific to each study's requirements.

Ligand Binding Assays

In vivo biotransformation of ADCs can alter drug to antibody ratio (DAR) or modify the payload/linker. Several PK assays are required for the therapeutic drug. A total-antibody (TAb) assay is used to detect the antibody portion of the ADC, while the total conjugated ADC assay captures both the payload and the antibody. The difference between these profiles theoretically indicates the degree of drug deconjugation.

ADVANTAGES	DISADVANTAGES
<ul style="list-style-type: none"> • Used in pharmacokinetic assessments for approved ADCs • Excellent sensitivity • No purification needed 	<ul style="list-style-type: none"> • Can only measure total ADC or antibody alone • Limited multiplexing capability

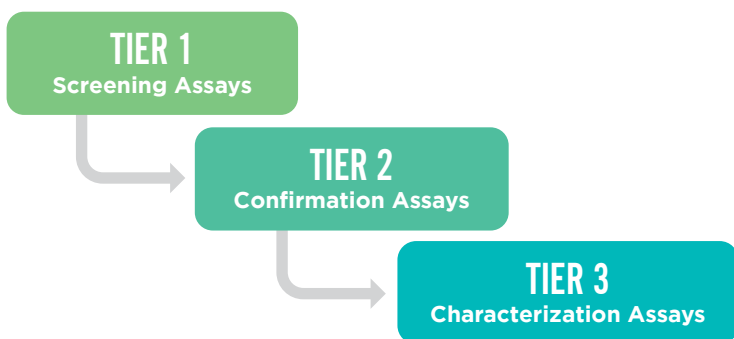
LC-MS/MS

LC-MS/MS is used for both qualitative and quantitative analysis of ADCs. Qualitative assessments include intact mass analysis, DAR ratio determination, and elucidation of biotransformation. LC-MS/MS is the primary platform for quantifying the free payload and hybrid LC-MS/MS workflows can be used to determine the Total Ab and ADC assays.

ADVANTAGES	DISADVANTAGES
<ul style="list-style-type: none"> • Single analytical platform for all three ADC assays: <ul style="list-style-type: none"> - Total Ab (hybrid LC-MS/MS) - Total ADC (hybrid LC-MS/MS) - Payload (LC-MS/MS) • Improved selectivity • Higher dynamic range • Multiplexing capability (payload and metabolite or linker-payload) 	<ul style="list-style-type: none"> • Intricate sample preparation workflows • Lower sensitivity and throughput

IMMUNOGENICITY TESTING FOR ADCs

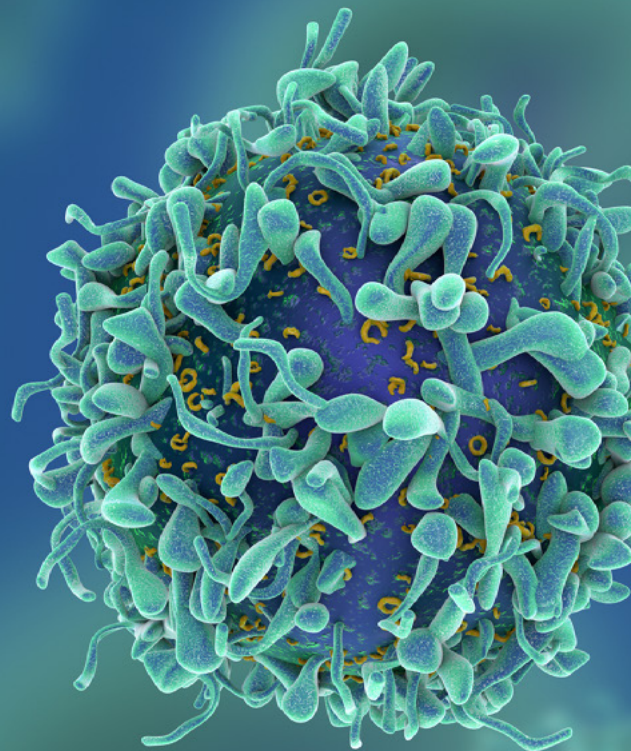
Anti-drug antibodies (ADAs) elicited by ADCs can include those specific to intact ADC, linker, payloads, and the unconjugated antibody. Altasciences' experts use the entire ADC molecule in an ADA assay to monitor the generation of antibodies to these components, employing a conventional tiered assay strategy to screen, confirm, and titrate ADA levels in your samples. Importantly for ADCs, **clinical samples confirmed positive may require additional characterization for domain specificity**. Our experts will provide you with the appropriate strategy required for this assessment.



In later phases of clinical development, a neutralizing antibody (NAb) assay may be used to further assess the impact of ADAs. Cell-based NAb assays are preferred by regulatory authorities for assessing ADA impact on ADCs due to their reflection of the drug's *in vivo* biological activity.

As other PD endpoints are also required for your preclinical and clinical studies, we also have **validated biomarkers**, including **cytokine and chemokine panels on the Mesoscale platform**, and **flow cytometry panels**.

Each bioanalytical assessment and platform presents unique challenges. Altasciences' years of experience conducting and evaluating ADC, PK, and PD studies gives us the breadth of knowledge required for assay development principles, experimental design, and stringent validation processes. This helps to ensure the **accuracy and reliability of immunogenicity testing, and pharmacokinetic analysis for ADCs**.



Scan the QR code to learn more about our bioanalytical capabilities:

