

CASE STUDY

Magnetic Bead-Enabled Hybrid LC-MS Workflows: Advancing Bioanalysis at a Leading Contract Research Organization (CRO)

Magnetic Beads, such as Biozen Streptavidin Magbeads, are integral to a hybrid LC-MS approach for modern bioanalysis.

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"Usage of magnetic beads is a smarter approach to modern bioanalytical workflows," says Dr. Rathna Veeramachaneni, Director of Mass Spec Bioanalysis – Development at KCAS Bio. "They provide flexibility, scalability, and multiplexing."

This statement reflects a broader transformation occurring across the field of bioanalysis. As the demand for increasingly precise, sensitive, and scalable therapeutic analyte quantitation continues to grow, KCAS Bio, a global Contract Research Organization (CRO), has strategically positioned itself at the forefront of modern approaches to bioanalytical and biomarker services. Magnetic bead-based affinity capture selectively enriches target analytes from complex biological samples, providing the first layer of selectivity. LC-MS adds a second layer through chromatographic separation and mass spectrometric identification. Holistically, a hybrid LC-MS platform approach produces cleaner samples and enables precise differentiation of target molecules from background interference. By standardizing magnetic bead-based workflows, KCAS Bio delivers reliable bioanalytical data that underpins the success of therapeutic programs, particularly as new biologic modalities introduce unprecedented levels of complexity.

With over 45 years of experience, KCAS Bio has established itself as a trusted partner to provide the ultimate strategic values - helping customers navigate complex modalities, generate richer datasets, and make faster, more confident development decisions. Dr. Veeramachaneni adds: *"[Our] customers need reliable data to make decisions on whether this molecule has a future or not. In order to get to that answer, we are utilizing magnetic beads with Hybrid LC-MS; it gives you an absolute decision-making capability - an answer with confidence."*



KCAS Bio Headquarters in Olathe, Kansas

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From a regulatory perspective, magnetic beads enhance analytical confidence and mechanistic understanding through affinity-based capture, reducing matrix interference and variability that results in more reproducible data. Recent regulatory expectations are encouraging more translational relevance data with deeper molecular insight as part of the movement away from traditional animal models toward human-relevant systems like organoids and cell-based platforms. This impending paradigm shift increases the need for analytical methods that can distinguish closely related species, minimize ambiguity, and provide orthogonal confirmation.

“There is not much transferability from the data in a preclinical model to when that molecule shifts to clinical trials; human versus preclinical species behave very differently. They are encouraging more systems [that are] representative of humans.”

- Dr. Amrit Chakravarty, Scientist II, PI.

KCAS Bio is increasingly using this type of hybrid LC-MS approach to support a diverse array of biotherapeutic modalities such as monoclonal antibodies (mAbs), antibody-drug conjugates (ADCs), fusion proteins, multi-specific antibodies, antibody fragments (Fab, scFc), and more recently, antibody-oligonucleotide conjugates (AOCs). In many of these applications, the hybrid LC-MS approach has proven not just complementary but sometimes preferred to traditional Ligand Binding Assays (LBAs). For example, in cases where LBA methods encounter interferences, cross-reactivity, or selectivity limitations, a hybrid LC-MS can often provide a clearer and more reliable path forward. This is particularly true for ADCs and AOCs, where multiple analytes – such as total antibody, conjugated drug, and free payload – must be quantified simultaneously due to stability or sample limitations.

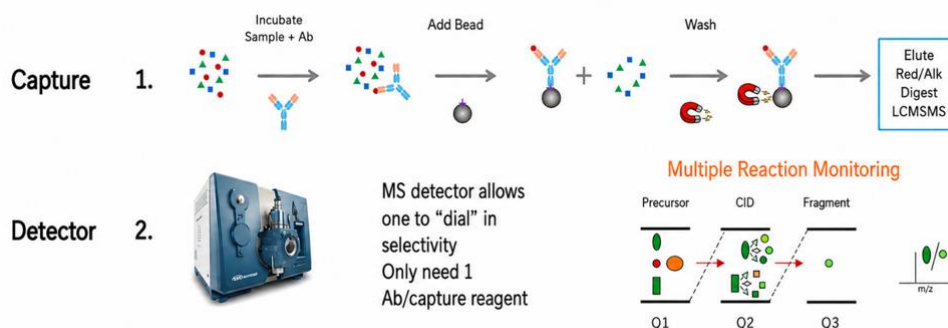


Scientist in the laboratory

Magnetic Beads and its Role in Hybrid LC-MS workflow

Magnetic beads serve as the first layer of selectivity by initially binding and enriching the target analyte from biological matrices via affinity capture. Isolating the analyte prior to optional digestion into surrogate peptides allows for accurate quantitation due to minimized interferences. As a result, highly specific detection by liquid chromatography tandem mass spectrometry (LC-MS), the second layer of selectivity, can be achieved.

- Definition: Hybrid LCMS is a technique which combines an enrichment step (typically an antibody enrichment on beads or columns) with the selectivity and sensitivity provided by LC-MS/MS
- Various surrogate peptides can be chosen for detection depending on needs



Hybrid LC/MS Workflow at KCAS Bio

Practical Considerations

A key distinction of a hybrid LC-MS bioanalysis approach is the presence of an enrichment step, but the advantages are context-dependent.

Traditional LC-MS workflows typically involve direct digestion, followed by cleanup techniques such as solid-phase extraction (SPE). This approach is advantageous when specific capture reagents are unavailable or when a broader, non-selective analysis is desired. SPE remains a widely used analyte extraction because it does not rely on specific capture reagents, is less impacted by endogenous IgG interferences, and supports broad analyte coverage that can include metabolites and related species. It is also easier to deploy, making it a practical default in early-stage workflows or when reagent availability is limited. Additionally, SPE often serves as a complementary or fallback approach when magnetic bead-based methods are unsuitable due to reagent gaps, saturation effects, or the need for broader analyte profiling.

However, when higher specificity and selective enrichments are required, especially where endogenous proteins are abundant, *“that’s when we use [Biozen Magbeads], streptavidin encoded beads purchased from Phenomenex,”* comments Dr. Rathna Veeramachaneni. It should be noted there can be times when custom antibodies or specialized capture strategies are required to isolate the target from high background, capture reagents are unavailable, or when binding capacity is constrained at high analyte levels.

In essence, magnetic beads have not replaced sorbent extraction because they are not designed to; they are a precision tool rather than a universal one. Sorbents remain dominant for broad capture, while magnetic beads excel in specificity, sensitivity, and mechanistic insight.

Analytical Performance Gains

Magnetic beads have demonstrated clear advantages for hybrid LC-MS bioanalysis:

- Enhanced selectivity and sensitivity, enabling lower limits of quantitation, broader dynamic range, and more reliable detection of low-abundance species.

- Compatibility with Automated Sample Preparation, enabling controlled processing that reduces variability, improves reproducibility, and increases throughput.
- Flexible, adaptable capture strategy, enabling rapid method adaptation across targets and studies with scalable, consistent performance, without full assay re-development.

“The ability to just change one aspect and the protocol stays the same is huge for day-to-day bioanalysis.”

- Ryan Darling, Associate Director, Mass Spectrometry Bioanalysis

- Multiplexing, analyzing multiple analytes within a sample to reduce the number of assays, setup steps, and sample volume.

“We can do [simultaneous] assays; one capture gives multiple readouts, saving time and resources.”

- Dr. Nitish Mishra, Scientist II, PI

- Large & small molecule analysis support, enabling efficient use of one extraction platform across modalities.

The Future of Magnetic Beads in Bioanalysis

Magnetic beads are emerging as core analytical tools in bioanalysis, bridging scientific complexity and regulatory expectations, driven by the increasing structural complexity of modern biotherapeutics and more stringent regulatory requirements. Bioanalytical workflows are shifting to be mechanism-centric, where structural integrity, heterogeneity, functional activity, and molecular transformations are evaluated alongside concentration. Magnetic beads address these demands through target-specific capture strategies that enable adaptability while preserving workflow consistency.

As therapies become more targeted and regulatory expectations for human-relevant data increase, KCAS Bio anticipates continued development of improved capture chemistries and reagents, including probes, oligonucleotide-based approaches, and aptamers. Magnetic beads are viewed as a stable, adaptable platform that will evolve in parallel with advances in bioanalytical methods and therapeutic complexity.

"You don't always need an antibody. You can biotinylate a DNA or RNA probe that can capture via an aptamer or by the sense strand to an antisense strand," says Andrew Bergdorf, Sr. Scientist – PI.



KCAS Bio Team and Phenomenex (PHX)

Back row – Andrew Bergdorf, Dr. Nitish Mishra, Dr. Amrit Chakravarty, Ryan Darling

Front row – Tran N. Pham (PHX), Dr. Rathna Veeramachaneni, Gerald Nagatani (PHX), Bryan Dockery (PHX)

At KCAS Bio, bioanalysis is approached with flexible, development-focused strategies, optimizing selectivity in complex matrices and resolving limitations like capacity saturation by re-optimizing or shifting between orthogonal methods. Both hybrid LC-MS and ligand binding platforms are leveraged for method switching or parallel feasibility studies to generate actionable data.

References

1. For additional information about KCAS Bio, please visit www.kcasbio.com
2. For additional information on Phenomenex Biozen Magbeads, please click [here](#).

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