Fact Sheet

IQVIA Laboratories Biosciences for Oligonucleotide Drug Development

As the field of oligonucleotide therapeutics continues to expand rapidly, challenges related to specificity, sensitivity, and bioanalytical characterization remain at the forefront of drug development. At IQVIA Laboratories Biosciences, we apply a science-driven approach backed by deep expertise and advanced methodologies that support the rigorous demands of both preclinical and clinical development, enabling the advancement of oligonucleotide-based therapies with precision and confidence.

Our extensive experience and methods:

We have vast experience with the following specific types of oligonucleotides:

- Antisense Oligonucleotides (ASOs)
- Small Interfering RNAs (siRNAs)
- Locked Nucleic Acid olilgonucleotides (LNA)
- MicroRNAs (miRNAs)
- Aptamers
- Antibody RNA Conjugates (ARCs)

“Fit-for-purpose” non-GLP discovery/ development/qualification and investigative tox samples testing

ADME (Absorption, Distribution, Metabolism, and Excretion) analysis is crucial for understanding the Pharmacokinetics (PK) and Pharmacodynamics (PD) of oligonucleotide modalities.

Expertise and capabilities:

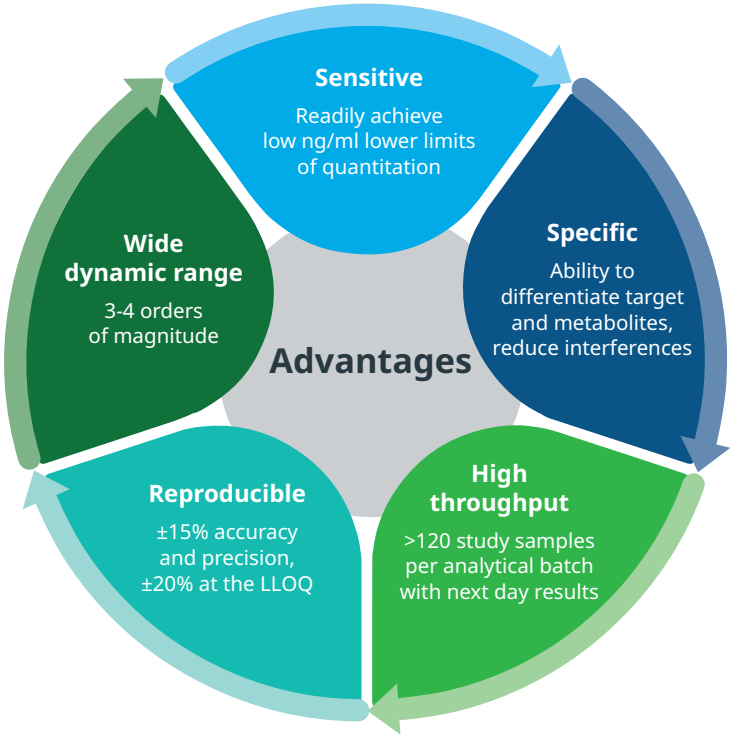
- Discovery/development/establishment and qualification of bioanalytical methods for oligonucleotides (e.g., various siRNA modalities).
- Oligonucleotide in-vitro stability evaluations in biological matrices (plasma and various tissue homogenates) that employs incubation, Solid-Phase Extraction (SPE) and Ion Pair Reverse-Phase (IPRP)-Liquid Chromatography Mass Spectrometry (LC-MS).
- Oligonucleotide in-vivo bio-analysis (investigative toxicology studies) in plasma and various tissues using SPE and IPRP-LC-MS.
- Metabolism Identification (MetID) of oligonucleotides using relative intensities of potential truncations or other observable degradants using LC-MS.
- Protein binding assays of oligonucleotides (e.g., various siRNA modalities) that employs e.g., various equilibrium dialysis, SPE and IPRP-LC-MS.

Pre-clinical and clinical

With our wealth of experience in pre-clinical and clinical siRNA/oligonucleotide bioanalysis, we are well-equipped to support your projects by ligand binding assay or liquid chromatography mass spectrometry (LC-MS) that can offer enhanced sensitivity, providing you with more detailed and insightful data.

LC-MS approaches:

- Perform analysis without a capture probe or without using mixed mode SPE or LLE. These critical reagent free approaches deliver flexible and sensitive quantitation of oligonucleotides.
- Utilization of triple-quadrupole mass spectrometry (QqQ) MS/MS and High-Resolution Mass Spectrometry (HRMS) using full scan analysis can differentiate between metabolites.
- Low ng/mL Lower Limits of Quantitation (LLOQ) are readily achievable (<10ng/ml) and we have the ability to quantify the parent and major metabolites in one analysis.
- Suitable for high-throughput needs using 96-well platforms and cycle times typically 2-6 minutes.
- Development of methods to quantitate conjugates including peptide and antibody modalities.



Advantages of using LC-MS for oligonucleotide analysis

Sample preparation

- Experience and support with pre-clinical tissues studies and Cerebrospinal Fluid (CSF) analysis, supporting full preclinical toxicology and PK. We can provide a full offering for plasma, tissue, and CSF analysis.
- Experience with antibody RNA conjugates, quantitation of the antibody with the oligonucleotide payload.

We provide full support of bioanalytical method validation criteria set forth by the ICH M10 Bioanalytical Method Validation and Study Sample Analysis guidance document.

Development of **50+** oligonucleotide methods and processing **1,000s** of samples per year

Ligand binding approach

Ligand binding immunoassays are an effective tool for the quantitation of oligonucleotides. In addition to our LC-MS experience and expertise outlined, our ligand binding team is ready to help support your oligonucleotide PK and immunogenicity analysis via traditional or hybridization ELISA methods.

We have experience providing support in the following areas:

- ASO and aptamer-based oligonucleotide method transfers, validations, and clinical trial support to advance gene therapy programs, performed as conventional Horseradish Peroxidase (HRP) driven formats or on the Meso Scale Discovery (MSD) platform for increased sensitivity and dynamic range. Hybridization LBA with picogram sensitivities achieved in plasma and CSF.
- Our expert team have the capabilities to design and prepare the necessary primer to streamline method development and optimization phase ensuring a sensitive and specific assay as quickly as possible.
- Necessary immunogenicity testing required to complete the portfolio of assays required for oligonucleotide therapies.
- Support and delivery of development/validation/ and sample analysis towards quantitation of biomarker, product, and cargo or the evaluation of the immunogenicity of any product or cargo as needed.

Working with us

IQVIA Laboratories Biosciences leads with science and is an industry leader with experienced bioanalysts who are driving innovation forward with their successful methodologies for a full range of oligonucleotide and siRNA drug modalities. While complying with regulatory guidelines, we offer higher confidence in your results for key decision making that will help deliver your project to plan.

IQVIA LABORATORIES

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