



PPD® LABORATORIES

PPD®

## Applying LC-MS/MS techniques to the development of biologics

### PPD® Laboratories' Unique Approach to Biologics

For three decades, PPD Laboratories has been developing and validating bioanalytical assays for all phases of pharmaceutical development across a wide variety of disciplines including chromatography, immunochemistry, cell-based and molecular platforms.

#### UNSURPASSED DEPTH AND BREADTH OF BIOANALYTICAL EXPERTISE

Over time, PPD has accumulated a significant breadth and depth of expertise in small molecule and biologics analysis and vaccine and biomarker development. Over the past several years, PPD has been applying this expertise to leverage traditional small molecule LC-MS/MS analytical methods to the analysis of biologics (a.k.a. large molecules).<sup>1</sup>

The PPD Laboratories biologics development team has experience with a range of sample preparation approaches from simple protein denaturation and digestion to complex affinity capture enrichment techniques. While the majority of applications will utilize LC-MS/MS to indirectly measure one or more surrogate peptides produced by proteolytic digestion, our team also has experience with the semi-quantitative analysis of intact proteins and antibody-drug conjugate (ADC) characterization using high resolution mass spectrometry (HRMS).

#### APPLYING LC-MS/MS TO BIOLOGICS DEVELOPMENT

The PPD Laboratories development team understands that the development and validation of LC-MS/MS methods for protein bioanalysis is different than for small molecules. Our team will work with you to understand the intended use of the assay, the unique characteristics of your protein biotherapeutics, potential interferences and the availability of reference materials and standards. With this knowledge our team can design and validate custom assays, or adapt existing assays, and quickly generate meaningful data to help inform project decisions.

#### OUR BIOLOGICS CAPABILITIES INCLUDE:

- + LC-MS/MS of macromolecules (peptides, conjugated toxins, lipids, polysaccharides, etc.)
- + Atypical peptides, monoclonal antibodies, ADCs, Fab fragments and fusion products
- + Unusual matrices (variety of tissues)
- + Difficult compounds (reactive, endogenous)

#### INSTRUMENTATION AVAILABLE FOR BIOLOGICS DEVELOPMENT INCLUDES:

- + More than 100 LC/MS systems
  - 92 Waters and Sciex triple quadrupoles, including 16 Sciex Triple Quad™ 6500 instruments
  - Nine Waters Xevo® TQ-S systems
  - Four Sciex Q-Traps
  - One Waters Xevo® G2 QTof (HRMS)
  - One Thermo Scientific™ Q Exactive™ Plus (HRMS)
- + 10 Thermo Scientific™ Aria® multiplexing systems
- + 29 UHPLC systems
  - 23 Waters Acquity UHPLC systems, Four of which have 2-D capabilities
  - Six Shimadzu Nexera UHPLC systems with 2-D capabilities
- + Hamilton® MICROLAB® STARlet automatic pipetting workstation

# Applying LC-MS/MS techniques to the development of biologics

## OUR BIOLOGICS EXPERIENCE INCLUDES:

PROTEINS	
METHODS	Extracted by protein precipitation, SPE or affinity-based methods
	Smaller proteins (<10KDa) analyzed intact
	Larger proteins (>10KDa) analyzed following denaturation, reduction, alkylation and digestion
EXPERIENCE	Human IGF-1
	Somatropin (recombinant hGH)
	mAbs + Various IgG and IgM including ADCs + Universal preclinical and specific (anti-ID, target capture) approaches + 63+ assays, including multiplexed mAb assay
	Antibody-drug conjugates + 51+ antibody conjugated assays + 29+ unconjugated toxin assays from five toxin families: auristatins, pyrrolobenzodiazepines (PBD), maytansines, tubulysins, and calicheamicins

PEPTIDES	
METHODS	Extracted by selective PPT or $\mu$ Elution SPE
	Analyzed by 2D-UHPLC-MS/MS
EXPERIENCE	Salmon calcitonin (MW-3400; 5.00 to 500 pg/mL; 0.3 mL aliquot)
	Somatropin (recombinant hGH)
	Exenatide (MW-4200; 10.0 to 1000 pg/mL; 0.3 mL aliquot)
	Liraglutide
	PEGylated peptide
	Phosphopeptide
	Amyloid- $\beta$ biomarker peptides
	Peptidyl-Gd <sup>3+</sup> -DOTA imaging agent
	Teriparatide (PTH [1-34])
	40+ sponsor proprietary assays

## ABOUT PPD LABORATORIES

PPD Laboratories provides world-class scientific expertise with state-of-the-art technologies supported by a commitment to exceptional quality. From pharmaceutical discovery through late stage research, our clients benefit from comprehensive lab services spanning bioanalytical, vaccine sciences, GMP, central lab testing and biomarkers. Our laboratory services accelerate pharmaceutical discovery and development for small molecules and biologics, allowing clients to make faster decisions about their compounds.

<sup>1</sup> Jenkins et. al. Recommendations for Validation of LC-MS/MS Bioanalytical Methods for Protein Biologics. The AAPS Journal, Vol. 17, No.1, Jan 2015.