

BIOANALYTICAL



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➤➤ TRANSFORMING PROMISING IDEAS INTO COMMERCIAL REALITY

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»» Overview

SCIENTIFIC EXPERTISE. COMMITMENT TO QUALITY.

inVentiv Health Clinical provides high quality bioanalytical services across the entire continuum of drug development. Our significant experience with small and large molecules, peptides, immunochemistry, LC/MS/MS, HRMS, GC/MS/MS and ICP-MS, combined with having one of the largest capacities in the industry, allows us to blend innovative science with effective, validated processes to deliver quality data on time, every time.



Our approach to bioanalytical study management includes a project management team of knowledgeable scientists, regulatory resources and support staff that can rapidly respond to changing project needs and deliver results. Through our two GLP-compliant laboratories, we offer more than 1,000 validated assays, extensive method development and rapid data handling capabilities.

INVENTIV HEALTH CLINICAL'S LABORATORIES OFFER COMPLETE ANALYTICAL SUPPORT FOR PROGRAMS, INCLUDING:

- Preclinical
- Bioavailability and drug metabolism studies
- Bioequivalence studies
- Clinical study compliance samples
- Drug interaction studies

>> At A Glance

Bioanalytical Laboratories at a Glance

- Two GLP-compliant laboratories with robotics and LIMS
- Bioanalytical services from discovery to development
- Rapid turnaround times
- 1,000+ validated assays
- More than 850,000 samples analyzed successfully per year
- Excellent regulatory track record
- 60 LC/MS/MS
- 13 GC/MS/MS
- 20 robotic systems

BIOANALYTICAL AND CLINICAL LAB

2500, rue Einstein
Québec, QC G1P 0A2

+1 418 527 4000 Phone
+1 800 831 4001 Toll Free
+1 418 527 3456 Fax

- 16,000 sq. ft.
- 140+ dedicated professionals
- Operates 24 hours per day, 7 days per week
- 15+ years experience
- Regulated bioanalysis, annually
 - 700,000+ samples
 - 500+ projects
- Successfully audited by the ROA, EMA, ANVISA, HPFB and other agencies

MASS SPECTROMETERS

API 3000™
API 4000™
API 5000™
Agilent 7500ce ICP-MS

LIQUID CHROMATOGRAPHY SYSTEMS

Agilent 1100 Series
Cohesive systems
Waters Acquity UPLC®

SAMPLE STORAGE

Walk-in rooms -20°C
Freezers -80°C

ROBOTIC SYSTEMS

PerkinElmer Janus® MultiPROBE® II EX HT
PerkinElmer Janus® Automated Workstation

OTHER INSTRUMENTATION

Gamma counter (RIA)

CLINICAL CHEMISTRY LABORATORY

Roche Integra 800
Roche Hitachi 911 Analyzers
Bayer Advia 2010
Bayer Atlas
Abbott Cell-Dyn Hematology Analyzers
Beckman-Coulter Coagulation Analyzer
Chronolog Platelet Aggregometers (4)
Abbott AxSym Analyzer
LDS Gamma Dynacare Montréal
Immulite 2000 Chemiluminescence Immunoanalyser
Centaur XP (2010)

>> At A Glance

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BIOANALYTICAL AND CLINICAL LAB

301D College Road East
Princeton, NJ 08540
USA

+1 609 951 0005 Phone
+1 609 951 0080 Fax

- 24,000 sq. ft.
- 60+ dedicated professionals
- 18+ years bioanalytical experience
- Regulated bioanalysis, annually
 - 200,000+ samples
 - 180+ projects
- Discovery bioanalysis, annually
 - 20,000+ samples
 - 350+ projects

MASS SPECTROMETERS

API 3000™
API 4000™
API 5000™
Finnigan TSQ™
7000 GC/MS/MS
Thermo TSQ Quantum™
Thermo TSQ Vantage™
Thermo Exactive™ LC-HRMS

LIQUID CHROMATOGRAPHY SYSTEMS

Agilent 1100/1200
Waters Acquity UPLC®
Shimadzu 20 Series
PerkinElmer® Series 200 HPLC System
CTC PAL AutosamplersROBOTIC

ROBOTIC SYSTEMS

Tomtec Quadra4™
Tomtec Quadra96®
Hamilton MICROLAB® STAR

OTHER INSTRUMENTATION

Meso Scale Discovery SECTOR®
Imager 6000
SpectraMax® M5 multi-mode microplate reader
SpectraMax® Plus384
Gel electrophoresis

»» Services

GLP METHOD DEVELOPMENT, VALIDATION AND ANALYSIS

inVentiv Health Clinical offers method development, assay validation and sample analysis using state-of-the-art LC/MS/MS and immunochemistry assays. Innovative LC/MS/MS methods allow us to routinely quantify levels below one pg/ml, and we have proven methods for multiple analytes, metabolites, pro-drugs, and light- and temperature-sensitive compounds. inVentiv Health Clinical scientists also have considerable expertise in developing methods for ligand binding assays and cell-based assays.

Because we recognize your need for fast turnaround, method development and proof-of-concept can typically be performed within a few days, enabling quick go/no-go decisions. We then work closely with your scientific staff to validate methods and ensure that assays have demonstrated linearity, recovery, reproducibility, specificity, accuracy and stability under all conditions. inVentiv Health Clinical method validations are performed according to GLP and FDA, EMA, ANVISA and HPFB guidance, and will comply with your company's SOPs.

Biomarker Support

inVentiv Health Clinical provides high-quality, mass spectrometry-based and immunochemical analyses for the development, validation and measurement of biomarkers to improve the effectiveness of drug development. This includes targeted and non-targeted biochemical and protein profiling. We have developed and validated methods for small-molecule biomarkers for a variety of disease states and therapeutic areas.

Large Molecule

Significant experience in the development and validation of immunoassays for large molecules and biomarkers gives inVentiv Health Clinical scientists special insight into biotechnology product development. Work performed in our GLP-compliant ligand binding group includes proprietary and non-proprietary pharmacokinetic and immunogenicity assays, as well as a wide range of cell-based and enzymatic assays. By rapidly providing specialized immunogenicity testing for the presence of antibodies to biologic and biosimilar products, inVentiv Health Clinical can help move your large molecule development programs



forward quickly and smoothly. inVentiv Health Clinical scientists have an understanding of what is necessary to gain approval for neutralizing assays to determine whether antibodies are blocking a drug's mechanism of action.

Antibody Drug Conjugates

inVentiv Health Clinical is ideally equipped to assist clients with their antibody drug conjugates. Our small and large molecule teams co-located at our Princeton, New Jersey, laboratory are skilled in the variety of assays (PK, immunogenicity) required to interrogate products. In addition, our scientists are cross-trained on the analysis of antibodies and molecules.

>> Services

Our technology and experience allow application of a variety of immunoassay platforms, including:

- Electrochemiluminescence (ECL)
- ELISA
 - Chromogenic
 - Fluorescence
 - Luminescence
- Radioimmunoassays

Ligand Binding Assays

inVentiv Health Clinical has an ever-expanding menu of standard and custom assays optimized for the quantitation of multiple analytes (proteins) in serum, EDTA and heparin, as well as sodium citrate plasma, culture supernatants and other sample types. Our immunoassay capabilities include single analytes and multiplexing.

Services include:

- Development, optimization and validation of proprietary assays
- Transfer and validation of existing assays
- Validation of commercially available kits
- Adaptation and validation of commercially available kits



Services

EXPLORATORY BIOANALYSIS

To meet your needs for fast turnaround and accurate results, inVentiv Health Clinical offers approximately 60 dedicated professionals and 24,000 square feet of laboratory space, housing more than 60 LC/MS/MS systems. Even when the starting point is no more than reference material and the empirical formula of the compound, complete turnaround time is targeted at five days or less using robotic liquid handlers and well-characterized LC/MS/MS methods. *In vitro* or *in vivo* samples generated through our laboratories, a third party or your own facility are handled with equal care.

Lead Optimization for Small and Large Molecules

inVentiv Health Clinical has a long history of partnering with pharmaceutical companies for *in vivo*, non-regulated preclinical bioanalysis of plasma and tissue samples. inVentiv Health Clinical offers experience, in-house expertise and access to a sophisticated array of modern instrumentation that enables rapid turnaround times.

Clients look to us to develop bioanalytical methods and assay samples generated in a non-GLP, high-throughput environment and to report sample concentrations with preliminary pharmacokinetics (PK) using WinNonlin® or Watson LIMS.

We offer HRMS-based methods, as well as traditional multiple reaction monitoring (MRM) assays using ultra-performance liquid-chromatography (UPLC) triple quadrupole LC/MS/MS analysis for PK work. We also offer specialized expertise in tissue analysis to support drug distribution studies.

Our process is standardized around a robotics platform, which allows for improved precision, better reproducibility and fewer errors. We offer protein binding, bioavailability, early toxicology and method qualification services for the target compound, as well as its metabolites.

OUR BIOANALYTICAL TEAM ROUTINELY PERFORMS THESE DISCOVERY STUDIES:

- Animal health non-GLP bioanalysis of plasma and tissue
- Bioavailability
- Early toxicology
- Fast PK
- Peptide bioanalysis
- Protein binding
- Semi-quantitative metabolite analysis during Fast PK analysis
- Tissue distribution

>> Services

EXPLORATORY BIOANALYSIS (CONT.)

Semi-Quantitative and Quantitative Metabolite Analysis for Small Molecule

inVentiv Health Clinical offers simultaneous, semi-quantitative and quantitative metabolite analysis based on the calibration curve of the parent compound during fast PK bioanalysis. The most abundant metabolites are first identified using accurate mass measurements and mass-defect filtering (MDF).

High-Quality Tissue Analysis

We understand the nuances of working with drug distribution studies involving a wide variety of tissues. Our experience includes analyzing brain, lung, adipose, muscle, liver, skin, kidney, intestine, trachea, spleen, pancreas and eye tissues. Our method development uses FastPrep™ bead-based homogenizer technology to efficiently lyse tissue samples, followed by a protein precipitation-based sample cleanup, which offers high-quality results in less time.

Protein Mass Spec and Antibody Dry Conjugates

The advent of novel drug therapeutics (e.g., ADCs) has spurred the development of new mass spec techniques for their analysis. inVentiv Health Clinical's experienced scientists are collaborating to develop immuno-affinity mass spec techniques for the analysis of peptides, proteins, antibodies and antibody dry conjugates.



Services

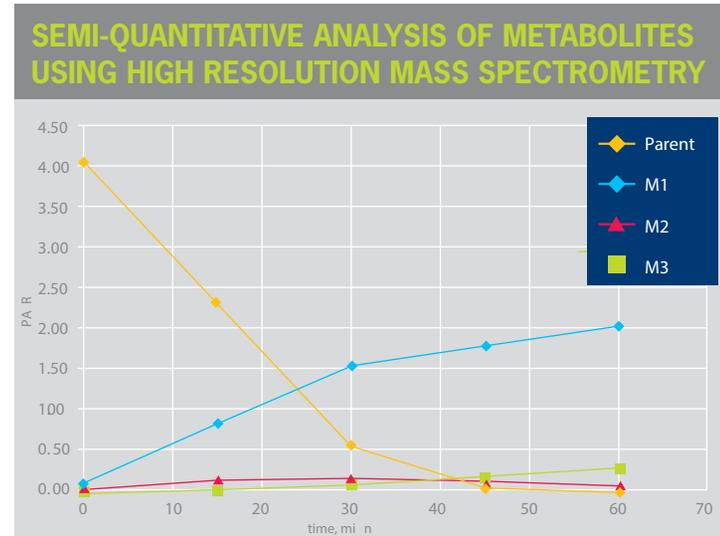
EXPLORATORY BIOANALYSIS (CONT.)

Fast PK

In the competitive world of pharmaceutical development, it's essential to eliminate poor candidates as early as possible in the process. Because new chemical entities often fail based on unfavorable pharmacokinetic (PK) properties, inVentiv Health Clinical's bioanalytical experts have developed a fast PK process, which can extend your lead optimization capabilities by eliminating candidates in as little as five days.

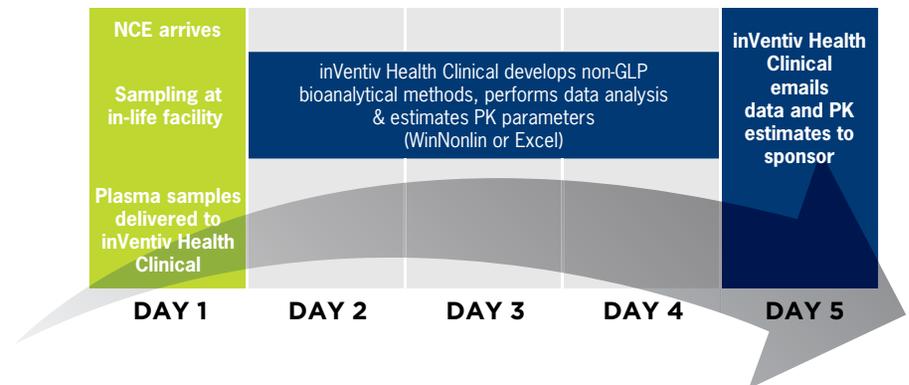
inVentiv Health Clinical's basic fast PK rodent package offers formulation, dosing and bioanalysis at seven time points (5 min, 15 min, 30 min, 1h, 2h, 4h and 6h) in six animals (three IV and three PO) in less than five days. We also offer fast biotransformation data using mass defect filtering (MDF) at the 2h and 6h time points. All quality control procedures are observed, and front and back standard curves are provided.

inVentiv Health Clinical can also conduct Fast PK studies on large molecules. Provide inVentiv Health Clinical with the raw materials and assay reagents, and our experienced team will coordinate the implementation of the dosing, develop a basic bioanalytical methodology and provide rapid results, allowing you to move the decisions on your large molecule therapeutic forward.



Unique Fast PK

The figure shows the bioanalysis of chlorpromazine and the semi-quantitative analysis of its metabolites using the Exactive™ (Orbitrap™). The metabolites were analyzed relative to the chlorpromazine calibration curve and initially identified using mass defect filtering (MDF). Data are from a 60-minute microsomal incubation study.



Services

EXPLORATORY BIOANALYSIS (CONT.)

Dried Blood Spot (DBS) Analysis

Traditionally, PK animal studies require large volumes of blood from one or more test animals to provide sufficient plasma volume for analysis over several time points. Additionally, the plasma must be isolated from whole blood, separated and prepared for bioanalysis.

DBS analysis, such as that offered by inVentiv Health Clinical's bioanalytical team, presents numerous benefits, including improved efficiency and reduced cost. With DBS, a single, small animal can be used for multiple draws, thus improving data quality from serial PK profiles and TK analysis. In human studies, smaller volume samples can be drawn using a finger prick rather than a venous blood draw, making DBS convenient for a variety of clinical trials, such as pediatrics, geriatrics and ischemia-compromised patient populations.

inVentiv Health Clinical's DBS analysis reduces overall costs because samples can be shipped and stored under ambient conditions, significantly simplifying the sample-handling process. DBS cards are also considered non-hazardous, eliminating the need for sub-aliquoting prior to bioanalysis.

ASSAYS AND BIOMARKERS LIST

inVentiv Health Clinical offers more than 1,000 validated bioanalytical methods for one or more analytes from human or animal matrices. In addition, our laboratories can develop and validate custom (or project-specific) ELISAs, ligand binding or cell-based assays.

We are actively working on developing new proprietary methods. A complete and up-to-date list of validated assays and biomarkers is always available on our website at www.inventivhealthclinical.com.

inVentiv Health Clinical also has a bioanalytical mobile application for your iPhone®, iPad® or Android™ device, putting more than, 1000 validated methods at your fingertips – for all your PK needs.

iPhone® and iPad® are registered trademarks of Apple, Inc. Android is a trademark of Google Inc.

TECHNOLOGY PLATFORMS

MS/MS

We also perform traditional GC/MS/MS and LC/MS/MS analyses of small and large molecule analytes. With one of the most extensive lists of validated methods in the industry, our capacity includes more than 60 LC/MS/MS, including API 5000™ and 4000™, and 13 GC/MS/MS.

Meso Scale Discovery® (MSD)

Array kits are based on MULTIARRAY® technology, a proprietary combination of electrochemiluminescence (ECL) detection and patterned arrays. ECL detection uses labels that emit light when electrochemically stimulated. Background signals are minimized because the stimulation mechanism (electricity) is de-coupled from the signal (light). The MSD SECTOR® Imager 2400 applies a voltage that causes electrode-bound labels to emit light at an intensity that is proportional to the amount of the analyte present. The raw data file acquired is imported into the Discovery Workbench Data Reduction Software 3.0, which generates a four-parameter logistic (4PL) curve by plotting the mean MSD® count for each standard against the nominal concentration. Final concentrations are interpolated from the standard curve and adjusted based on sample dilution.

Enzyme-Linked Immunosorbent Assay (ELISA)

inVentiv Health Clinical offers a long and growing list of fully validated kits—both commercial kits and kits developed in-house for the quantitative measurement of human chemokines, cytokines and biomarkers present in various matrices.

Immulite®

In addition to manual ELISAs, we also offer the Immulite platform for automating immunoassays. With this technology, patient serum and a ligand-labeled tracer are added to a test unit containing a polystyrene bead coated with an antibody specific to the analyte to be measured. After an incubation step, the test units undergo a centrifugal wash, removing the residual sample and unbound analyte from the bead. An anti-ligand enzyme is then introduced and the test unit undergoes a second incubation, after which unbound enzyme is removed. A substrate is added, which produces the emission of photons in the presence of the enzyme. These are measured by the Immulite instrument and converted into digital concentrations.

Radioimmunoassay (RIA)

inVentiv Health Clinical provides a full array of testing services for biomarker detection, including RIA methodologies using a gamma-counter for raw data acquisition for each standard, control and sample.





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