药明康德
WuXi AppTec

WIND,
WuXi AppTec IND, an Integrated
Services for your IND Package

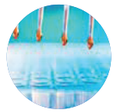
Let WIND Help You Sail through Your IND Journey

Laboratory Testing Division

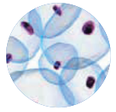
WuXi AppTec

WuXi AppTec is a leading pharmaceutical, biopharmaceutical, and medical device open-access capability and technology platform company with global operations. As an innovation-driven and customer-focused company, WuXi AppTec provides a broad and integrated portfolio of services to help our worldwide customers and partners shorten their discovery and development time and lower the cost of drug and medical device R&D through cost-effective and efficient solutions.

Small Molecule Drug R&D and Manufacturing



Biologics R&D and Manufacturing



Cell Therapy and Gene Therapy

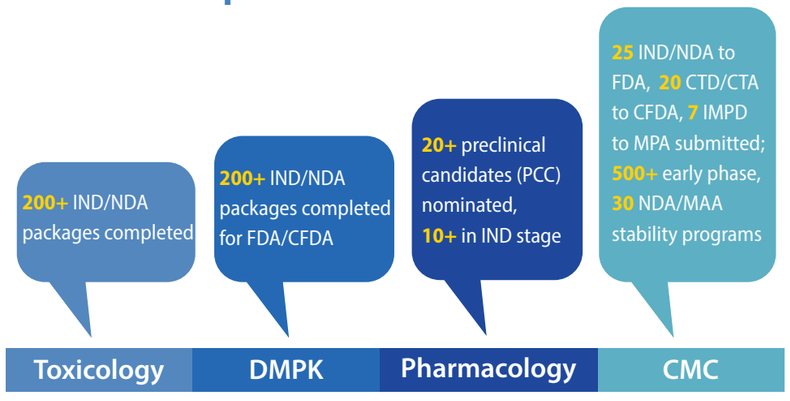
Genomics and Molecular Diagnostics

Medical Device Testing

Laboratory Testing Division

WuXi AppTec Laboratory Testing Division (LTD) provides a comprehensive range of services and an integrated testing platform for discovery and development of innovative drugs and medical devices. With operations in China and the U.S., LTD provides services and solutions in analytical chemistry, in vivo pharmacology, drug metabolism and pharmacokinetics, bioanalysis, toxicology, medical device testing and customized antibody and reagent preparation.

Extensive Experience



1st

CMC platform in China which passed FDA inspection for new chemical entities
cGMP biologics manufacturing facility in China compliant with U.S., European and Chinese regulatory standards
GLP preclinical laboratory in China double certified with an OECD country and NMPA (CFDA): passed FDA inspection
GLP/GCP bioanalytical lab in China which passed FDA, OECD, and NMPA inspections

Global Compliance

2009
- Analytical Laboratory Passed **MPA** Inspection
- Bioanalytical Laboratory Passed **FDA** Inspection
- New Jersey Site Passed **FDA** and **EPA** Inspection

2010
- Toxicological Animal Facility Received **AAALAC** Accreditation
- Toxicological Laboratory Received **GLP** Certificate from **NMPA**

2011
- Bioanalytical Laboratory Passed **NMPA** and **OECD** Inspection
- New Jersey Site Passed **FDA** Inspection

2012
- Analytical Laboratory Passed **NMPA** Inspection
- Toxicological Laboratory Received **GLP** Certificate from **OECD**
- Toxicological Laboratory Passed **NMPA** Inspection

2013
- Analytical Laboratory Passed **MPA** and **NMPA** Inspection
- Toxicological Animal Facility Received "Exemplary" Commendation from **AAALAC**
- New Jersey Site Passed **FDA** and **EPA** Inspection

2014
- Analytical Laboratory Passed **FDA** and **NMPA** Inspection
- Toxicological Laboratory Passed **FDA** and **OECD** Inspection
- Bioanalytical Laboratory Passed **EMA** Inspection
- New Jersey Site Passed **FDA** Inspection

2015
- Analytical Laboratory Passed **NMPA** Inspection
- Toxicological Animal Facility Passed **AAALAC** Inspection
- Bioanalytical Laboratory Passed **NMPA** and **OECD** Inspection
- New Jersey Site Passed **FDA** Inspection

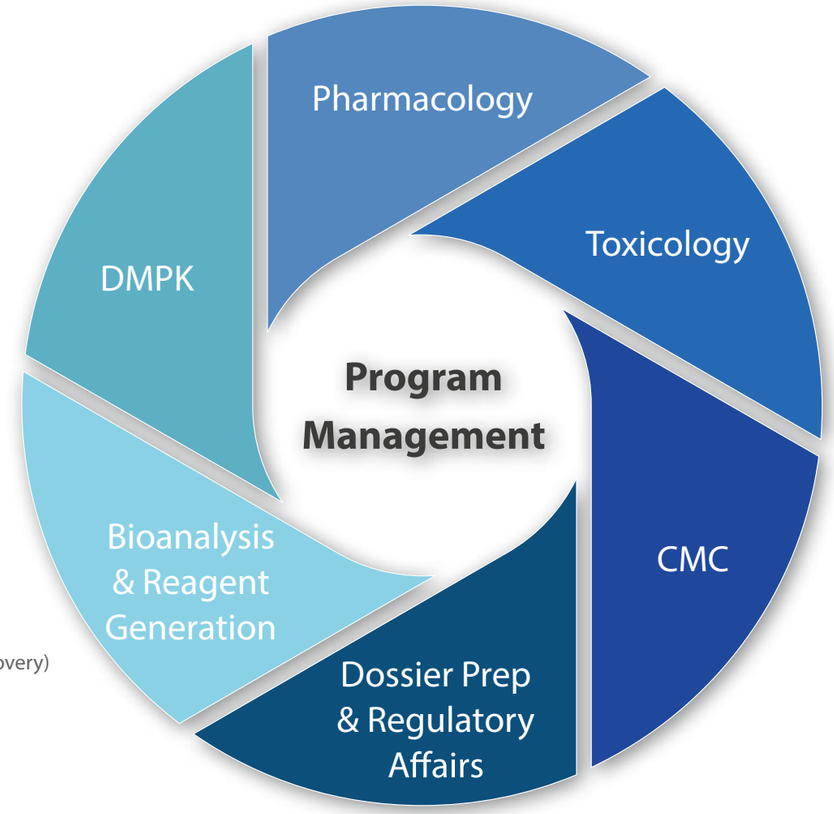
2016
- Analytical Laboratory Passed **FDA**, **MPA** and **NMPA** Inspection
- Toxicological Animal Facility Passed **OECD** Inspection
- Bioanalytical Laboratory Passed **NMPA** Inspection
- Central Lab Received **CAP** Certificate
- New Jersey Site Passed **EPA** Inspection

2017
- Analytical Laboratory Passed **NMPA** Inspection
- Bioanalytical Laboratory Passed **OECD** Inspection
- New Jersey Site Passed **FDA** Inspection

Comprehensive IND Enabling Service

- *In vitro* assays
- *In vivo* efficacy in disease models
- Mechanism of action & translational medicine

- Permeability
- Metabolic stability
- Plasma protein binding
- RBC partitioning
- DDIM/ HI/ PNT
- Transporter profiling
- PK/bioavailability
- Met ID (*in vitro*/*in vivo*)
- Mass balance & tissue distribution (QWBA)
- PBPK, PK/PD assessment
- Human PK projection



- General toxicology
- Safety pharmacology
- Genetic toxicology
- Immunogenicity
- Biomarker analysis
- Bioanalysis (GLP)
- Toxicokinetics assessment
- Developmental & reproductive toxicology (DART)
- Clinical pathology & anatomic pathology

- LC-MS/MS & Immunochemistry platform
- Method development, validation & transfer
- Pre-clinical sample analysis (TK, PK)
- High throughput sample analysis (ADME, *in-vitro*, discovery)
- Biomarker testing
- Customized antibody service

- Process development
- GMP API manufacturing
- Pre-formulation
- Formulation development
- Small scale manufacturing
- Method development & validation
- Compound characterization & batch release
- Stability study
- Regulatory CMC

WuXi AppTec IND™

- IND feasibility evaluation
- Gap analysis
- Contractual assistance
- Business units coordination
- Project updates and teleconferences

Accelerated Timeline
to expedite your molecule to IND

Dual Filing
in U.S. and China to increase asset value

Truly Integrated Platform
consolidating everything done within one organization

Flexible Collaboration
ranging from a la carte to IND package

High Quality
Scientific expertise and state-of-the-art facility to ensure standard with global regulatory compliance

Cross Functional Program Management

CMC

Inspected and approved by FDA, MPA and NMPA, WuXi AppTec analytical service laboratories provides full range of analytical services from early & late phase through clinical trial phase to commercial products.
Flexible analytical solutions include integrated CMC services and standalone studies covering method development and validation, stability study, analytical testing, reference standard, impurity control, microbial testing, physicochemical characterization, and regulatory CMC documentation.
State-of-the-art instruments, cutting-edge technologies, and experienced scientific staffs ensures efficient, high-quality and cost-effective services for small and large molecules.

Analytical Services

Method Development & Validation, Release Testing

- Potency & impurities
- Chiral
- Counter ion
- Mutagen/genetoxic impurity by LC-MS/GC-MS
- Residual solvents
- Heavy metal by ICP-OES/ICP-MS
- ID testing by IR/NMR
- Physical testing by XRPD/PSD/DSC/TGA
- Microbial limit test/sterility testing
- Endotoxin limit test
- Antimicrobial effectiveness/antibiotics assay/ preservative effectiveness
- Excipient release

Stability Program

- Development product stability programs
  - Accelerated and long term programs
  - Photo stability
  - Shipping studies and excursion evaluations
- Commercial product stability programs
  - Post approval commitment studies/annual studies
  - Process change studies
  - Forced degradation study/ASAP study

Integrated Impurity Research & Study

- Stability-indicating impurity method development and validation
- Impurity isolation and structure elucidation
- Impurity reference standard synthesis and characterization
- Impurity marker and metabolite synthesis and testing
- Impurity evaluation through software and toxic study
- Genotoxic impurity method development and validation
- Genotoxic impurity control testing

Pre-formulation

- API physicochemical properties
- Salt screening
- Polymorph screening
- Stability study at different temperature and pH
- Solubility, pH solubility
- Excipient compatibility
- Hygroscopicity

Analytical Services for Large Molecule

- Characterization
- Method development/ qualification/ validation/ transfer
- GMP/non-GMP release testing
- Stability testing

Drug Substance Development and Manufacturing

Process Synthetic Route Development

- Availability of raw materials
- Safety issues of synthetic route
- Cost efficiency of synthetic route
- Practical and scalable synthetic route

Process Development

- Scalable process development
- Reaction condition development
- Workup condition development
- Isolation condition development
- Drying condition development

API Manufacturing

- Raw material release
- R&D report
- Master batch record
- GMP manufacturing

Drug Product Development and Manufacturing

Formulation Development & Process Optimization

- Excipients and packaging materials screening
- Dissolution method development and validation
- Formulation development
- Process development
- Quality by Design (QbD)
- CPP and CQA
- Scale-up and optimization

Drug Product Manufacturing

- Prototype formulation
- Product lifecycle management
- Clinical product manufacturing

DMPK

During the IND development stage, DMPK studies, along with pharmacology and toxicology, play a very significant role in providing a thorough examination of the absorption, distribution, metabolism, and excretion properties of the experimental drug.
These studies are performed in animals of increasing size and similarity to humans as they are the most translatable models available to support the transition into human clinical trials.

Physicochemical Properties Analysis

- Solubility, pKa, log P / log D

In Vitro Permeability Assays

- PAMPA
- MDCK
- Caco2

In Vitro Drug-Drug Interaction Assays

- CYP inhibition (reversible and time dependent CYP inhibition)
- CYP induction
- CYP phenotyping
- Transporters (uptake and inhibition)

In Vitro Protein Binding & Partitioning Assays

- Plasma/serum protein binding
- Human serum albumin (HSA) and human alpha-1-acid glycoprotein(AGP) binding
- Tissue protein binding assays (microsomes, brain homogenate, liver homogenate and hepatocyte, etc.)
- Blood/Plasma partitioning

In Vitro Stability Assays

- Buffer, simulated intestinal fluid, and simulated gastric fluid stability
- Hepatic Phase I / II metabolic stability (hepatocyte, liver microsomes, liver S9 and cytosol, etc.)
- Ex-hepatic metabolic stability (intestinal microsomes, lung microsomes, plasma , and blood, etc.)

In Vivo Mass Balance

- Non-radiolabeled or radiolabeled mass balance study (rodent and non-rodent, including bile excretion)
- Human radiolabeled AME study (sample analysis)

In Vivo PK

- Screening single or cassette PK
- Routine single and repeated dose PK (multiple administration route)
- Dose escalation study
- Formulation / salt form evaluation
- Ocular PK
- Portal vein study, intestinal absorption study, P-gp KO mouse PK, etc.

In Vivo Tissue Distribution

- Rodent / non rodent tissue distribution (QTD or QWBA study)

Metabolite Identification

- Fast *in vitro* metabolite ID (plasma, S9, microsomes, and hepatocyte)
- Routine *in vitro* and *in vivo* metabolite ID (multi-matrix, multi animal species and human)
- *In vitro* and *in vivo* reactive metabolite trapping by GSH
- *In vivo* ^{14}C radiolabeled metabolite identification

Toxicology

The Toxicology Services unit located in Suzhou, China, is seamlessly integrated with the other centers of expertise offering comprehensive development services to our clients. Alternatively we provide stand alone toxicology studies when requested. We maintain one of the largest safety testing facilities in Asia at 580,000 ft^2 and an expert management team with over 150 years of international experience in Big Pharma and CROs

General Toxicity

- Acute toxicity study
- Repeat dose toxicity study
  - » 7-day, 14-day, 28-day, 13-week, 26-week and 39-week

  Species
  - » Mouse, rat, dog, monkey, rabbit, and mini-pig

  Administration route
  - » Oral, injection (iv, ip, sc), dermal, ocular etc.

Safety pharmacology

- Central nervous system (mouse and rat)
- Respiratory (mouse, rat, dog, and monkey)
- Cardiovascular (dog and monkey)
- hERG (*in vitro*)

Genetic Toxicity

- Ames (*in vitro*)
- Micronucleus (*in vitro* or *in vivo*)
- Chromosome abbreviation (*in vitro*)
- Mouse lymphoma assay (*in vitro*)

Special Toxicity

- Local irritation (skin, vessel, and eyes)
- Sensitization (ASA and PCA)
- Hemolysis (*in vitro*)
- *In vitro* phototoxicity study
- Ocular toxicity study

Developmental & Reproductive Toxicology (DART)

- Seg I fertility and early embryonic development to implantation (rat)
- Seg II embryo-fetal development (rat and rabbit)
- Seg III pre-and postnatal development (rat)
- Juvenile toxicity study (rat)

Pharmacology

WuXi AppTec's *in vivo* pharmacology platform has developed and validated disease models in multiple species with most efforts focusing on Oncology, CVMD, CNS and respiratory fields.
We offer robust drug efficacy data and high value interpretation to assist you in evaluating the potential of therapeutic compounds. Beyond our superior service, we attach great importance to animal welfare, customization and application of novel techniques.

Metabolic & Digestive System Disease

- Obesity
- Diabetes & complications
- Nonalcoholic fatty liver disease (NAFLD)
- Hyperlipidemia
- Hypertension
- Thrombosis
- Gastric ulcer
- Intestinal mobility
- Ulcerative colitis

Respiratory System Disease

- Allergic rhinitis
- Asthma
- Lung fibrosis
- Pulmonary hypertension (PH)
- Chronic obstructive pneumonia disease (COPD)

Infectious Disease

- HBV
- RSV
- Influenza virus
- HSV
- EV71
- Klebsiella pneumoniae
- Escherichia coli
- Clostridium difficile
- Mycobacterium tuberculosis
- Others

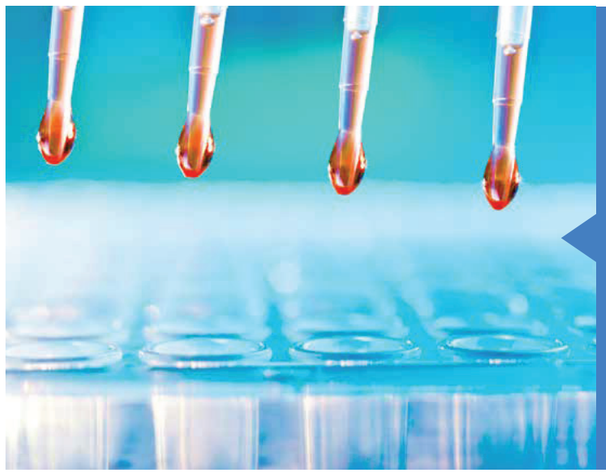
Oncology

- PDX: Comprehensive PDX model collection with genomic profile
- CDX: Subcutaneous and orthotopic CDX models with standard-of-care treatment data
- Syngeneic models validated with WX-mPD-1/mPD-L1 antibodies
- *In vitro* and *in vivo* capabilities for immuno-oncology drug discovery
- State-of-the-art flow cytometry and IHC platform

CNS & Pain

- Alzheimer disease (AD)
- Parkinson's disease (PD)
- Stroke
- Anxiety & depression
- Neuropathic pain
- Inflammatory pain
- Chronic pain
- Cancer pain

Bioanalytical Services (BAS)



Our Bioanalytical laboratory provides LC-MS/MS and ligand binding platforms in support of IND, NDA, BLA and ANDA packages. WuXi AppTec's bioanalytical lab has been developing methods and analyzing non-GLP / GLP bioanalytical samples since 2004 to support global preclinical and clinical studies.

With over 200,000 ft^2 of lab space and over 500 qualified scientists and expertise in both small and large molecule bioanalysis, we have become one of the largest bioanalytical laboratory in Asia and the first to pass inspections by the USFDA, NMPA, OECD, and EMA.

Bioanalytial Service at Glance

WuXi AppTec's experienced bioanalytical scientists support a full suite of services using state-of-the-art instrumentation

- Small molecule PK/TK
- Biologics PK/TK
- Immunogenicity (ADA, Neutralizing Antibody)
- Biomarker services
- Tissue sample analysis
- Assay development, transfer, and validation
- Clinical/Pre-clinical sample testing
- Immunophenotyping
- Receptor occupancy
- Protein LC-MS/MS quantitation

Technology Platform

LC-MS/MS

- Sciex API 6500+, 6500, 5500, 5000, 4000 MS
- Shimadzu, Agilent and Waters HPLC/UPLC
- Gilson, CTC/DLW and ADDA high throughput auto sampler

Immunochemistry platform

- Hamilton® Microlab Star workstation
- Tecan EVO automated ELISA workstation
- Janus workstation
- MSD Sector™ Imager 6000
- MSD QUICKPLEX™ SQ120
- Molecular device plate reader
- Perkin Elmer envision HTS microplate reader
- Bio-Tek microplate washer
- Luminex® BIO-PLEX PRO II microplate washer
- Gyrolab™ XP
- Perkin Elmer gamma counter
- Singulex Erenna detection system

Small Molecule Bioanalysis Services

Our bioanalytical team has over 70 LC-MS/MS instruments to support GLP analysis and over 40 instruments for non-GLP analysis, which are all available for methods development, validation and sample analysis.

We have capacity and expertise to meet high quality standard and study timelines.

- Stabilization of labile compounds and sample analysis
- Drug-drug interaction studies
- Protein binding studies

Biologics Bioanalysis Service

Our large molecule team supports a full range of biologics programs including peptides, proteins, monoclonal antibodies, bispecific antibodies, biosimilars, oligonucleotides, biomarkers, and antibody drug conjugates.

Critical reagent labeling

Biotin- and/or Sulfo-tag labeling for

- Anti-drug antibody assays
- Neutralizing antibody assays
- PK/TK assays

Customized Antibody Service

To provide end-to-end immunochemistry bioanalytical support, we provide customized monoclonal antibody and polyclonal antibody for PK, ADA and Nab testing.

Other service includes

Antibody labeling, isotyping, hybridoma sequencing, antibody pairing and IHC test

Biomarker Service

- Fit-for-purpose (FFP) and exploratory biomarkers
- Full method validation to support labelling claims, safety, efficacy
- Translational biomarkers

Biomarker assay platforms

- ELISA (single analyte)
- MSD (multi-plex)
- Luminex® (multi-plex)
- Singulex (ultrasensitivity)
- LC-MS/MS for small molecule and protein biomarkers
- QuantStudio™ 7 rtPCR
- Flow cytometry

Program Management

The program management team provides a full service for our global clients from IND program design, execution to dossier preparation and submission. The program management team provides information and consultation for clients during initial project discussion with Business Development team. A dedicated project manager will be assigned to each IND-enabling program once the project is finalized and the contracts are signed.

The program management team works with clients on program design based on global submission requirement and client's submission plan. The program management team works with WuXi AppTec's technical groups e.g. pharmacology, DMPK, toxicology and analytical services, to provide you with the best program design.

The program management team helps clients establishs project timelines for initiation and completion of required studies. The program management team helps clients track progress of their ongoing activities and coordinate efforts across technical groups to resolve any issues occurring during the conduct of their studies. The program management team work along side the regulatory affairs group to help prepare the dossier and submission plan.

Regulatory Affairs

Our regulatory team provides a complete package of services to support for global regulatory submission by incorporating internal expertise and partnering with external consultation networks.
Our one-stop service can make your global filling convenient, efficient and cost-effective.

Our services include Investigational New Drug (IND) Application, New Drug Application (NDA), Abbreviated New Drug Application (ANDA) to the National Medical Products Administration of China (NMPA); IND, NDA, ANDA and Drug Master File (DMF) application to U.S. Food and Drug Administration (FDA); Clinical Trial Application (CTA), Market Authorization Application (MAA), DMF and generic drug application to European Medicines Agency (EMA) etc.

We can assist you in the following aspects:

- Regulatory consultation, project feasibility assessment, product registration strategy and planning
- Gap analysis based on available dossier information
- Dossier composition
- Communication meetings with different regulatory agencies
- Electronic Common Techinical Document (eCTD) submission
- Coordination of on-site inspection
- National Institue for Food and Drug Control (NIFDC) testing progress follow-ups in China
- Annual reports and subsequent supplement submissions
- Other assistance in product registration

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LTD-DD-WN-BR-EX-02-20--PPS