www.asymchem.com

ASYMCHEM

Asymchem Labs.

ASYMCHEM

Sales Office

Asymchem Inc. (USA)
600 Airport Blvd, Suite 1000 Morrisville, NC, 27560, USA
Tel: +1 (919) 468-3884 Fax: +1 (919) 468-3916

Asymchem Shanghai Office
6-501, No. 338, Galileo Road, Pudong New Area, Shanghai, 201203, P.R. China

Beijing Branch of Asymchem Laboratories (Tianjin) Co., Ltd
Room 0918-20, 9th Floor, 129 Xuanwumen West St., Xicheng District, Beijing, 100031, P.R.China

Asymchem Limited
5th Floor, One New Change, London, England, UK

China R&D and Manufacturing sites

Asymchem Laboratories (Tianjin) Co., Ltd.
No. 6 Dongting 3rd Avenue, TEDA Tianjin, 300457, P.R. China
Tel：+86 22 5983 1988 Fax：+86 22 5983 1999

Asymchem Life Science (Tianjin) Co., Ltd.
No. 71, 7th Avenue, TEDA Tianjin, 300457, P.R. China
Tel：+86 22 6625 2888 Fax：+86 22 6625 2777

Tianjin Asymchem Pharmaceuticals Co., Ltd.
No. 71 Xinye 7th Avenue, TEDA WEST Tianjin, 300462, P.R. China
Tel：+86 22 66332009

Tianjin Asymchem Pharma Analytical Testing Service Co., Ltd.
No.71, 7th Avenue, TEDA Tianjin, 300457, P.R. China
Tel：+86 22 6625 2888 Fax：+86 22 6625 2777

Tianjin Asymchem Medical Science&Technology Co., Ltd.
Room 04-06, Floor 35th, No.39th Nanjing Road, Hexi District, Tianjin, 300202, P.R. China

Jilin Asymchem Laboratories Co., Ltd.
No. 99, Hongda Road, Economic Development Zone, Dunhua, Jilin, 133700, P.R. China
Tel：+86 0433 6341788 Fax：+86 0433 6361266

Asymchem Laboratories (Fuxin) Co., Ltd.
No. 90, Development Avenue, Fuxin High-tech Industrial Development Zone,
Fuxin, Liaoning 123000, P.R. China
Tel：+86 0418 2535888/2774999 Fax：+86 0418 2272558

Liaoning Asymchem Laboratories Co., Ltd.
Yimatu village, Yimatu town, Fu Mongolia county (Fluorine Industry Development Area),
Fuxin, Liaoning, 123129, P.R. China
Tel：+86 21 60870800

Green Chemistry
is the Future

Stock Code: 002821.SZ

2017EN03

ASYMCHEM

www.asymchem.com

CATALOG

ASYMCHEM OVERVIEW OF FACILITIES

Asymchem Laboratories Inc. (USA)
♦ Holding Company

Asymchem Laboratories (Tianjin) Co., Ltd. (TJ1)
USFDA inspected in 2014
♦ High Potency R&D and Manufacturing

Asymchem Life Science (Tianjin) Co., Ltd. (TJ2)
USFDA inspected in 2011 & 2014
QP inspected in 2013
♦ New Technology Development
♦ cGMP API & Drug Product Manufacturing
♦ Pharmaceutical Development and Manufacturing
♦ Analytical Research
♦ Stability Testing
♦ Process Engineering and Safety
♦ Biotransformation

Tianjin Asymchem Pharmaceuticals Co., Ltd. (TJ3)
♦ API and Drug Product Manufacturing


Asymchem Laboratories (Tianjin) Co., Ltd.


Tianjin Asymchem Pharmaceuticals Co., Ltd.

Asymchem Shanghai Office

Beijing Branch of Asymchem Laboratories (Tianjin) Co., Ltd

Tianjin Asymchem Medical Science&Technology Co., Ltd.

Asymchem Inc. (USA)

Tianjin Asymchem Pharma Analytical Testing Service Co., Ltd. (TJ4)
♦ Analytical Testing Service

Tianjin Asymchem Medical Science&Technology Co., Ltd. (TJ5)
♦ Clinical CRO

Jilin Asymchem Laboratories Co., Ltd. (DH1)
QP inspected in 2014
TGA inspected in 2015 & 2017
USFDA inspected in 2017
♦ Commercial cGMP Manufacturing

Jilin Asymchem Pharmaceuticals Co., Ltd. (DH2)
♦ Under construction

Asymchem Laboratories (Fuxin) Co., Ltd. (FX1)
USFDA inspected in 2011 & 2014
♦ Dedicated Carbapenem Manufacturing

Liaoning Asymchem Laboratories Co., Ltd. (FX2)
♦ Back Integration non-GMP Manufacturing

Asymchem Inc. (USA)
♦ Business Development and Technical Support

Beijing Branch of Asymchem Laboratories (Tianjin) Co., Ltd.
♦ Business Development

Asymchem Shanghai Office
♦ Business Development

Asymchem Limited
♦ Business Development


Asymchem Life Science (Tianjin) Co., Ltd.


Jilin Asymchem Pharmaceuticals Co., Ltd.


Asymchem Laboratories (Fuxin) Co., Ltd.


Liaoning Asymchem Laboratories Co.,Ltd.


Jilin Asymchem Laboratories Co., Ltd.

INTRODUCTION

Asymchem is a leading contract manufacturer serving the pharmaceutical and biotech industries at all stages of drug development and into commercialization. Asymchem's technical breadth of capabilities spans the development and manufacture of enzymes for use in bio-catalysis, to developing practical continuous flow technologies for commercialization, to beta lactam containment just to name a few. Since 1995, Investment and focus on technology driven innovation has enabled Asymchem to provide practical and sustainable long-term solutions to our partners in the global pharmaceutical industry, all the while maintaining a commitment to excellence, flexibility and customer-centric services.

Solution: Integrated Development

At the forefront of Asymchem's Technical Development Team is the senior management group, which can focus resources quickly to develop and implement solutions before obstacles can affect cycle times or cost. The R&D base of Asymchem's integrated Chemical Development team consists of over 1200 scientists experienced in the most challenging syntheses.

Asymchem's eight R&D and manufacturing sites offer innovative research and process development at every stage, from preclinical to commercial, running under either non-cGMP or cGMP conditions in labs, kilo labs, pilot plants, commercial scale cGMP production from Asymchem's facilities in P.R. China. Projects are handled at high standards of safety and environmental responsibility.

Benefits

An integrated solution from a CDMO is the most efficient way to bring more drug candidates to your R&D pipeline and commercialization through:

- Reduction of handoffs to multiple suppliers
- Eliminate time gaps in drug development
- Access to flexible resource when needed
- Reduce R&D cost through integrated pricing
- Effectively manage the risk of drug development

Since our beginning in 1995, Asymchem has built up a broad in-house technical expertise with a proven track record of on-time deliveries with high quality products. Solid fiscal growth since our beginning has gone hand in hand with the level of satisfied repeat customers year after year, including receiving supplier awards from Pfizer, Merck and Hutchison to name a few.

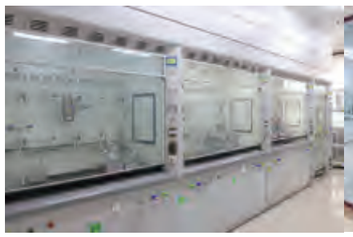
Merck awarded Asymchem with 2007 Supplier Tier One Award in 2008

Asymchem won Pfizer's 2008 Top intermediates CMO Award in 2009

Asymchem won Hutchison Medi Pharmas's Most Valuable Parner Award in 2016

INTERNATIONAL GREEN CHEMISTRY COLLABORATION LABORATORY

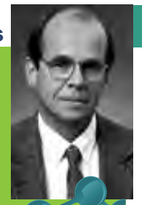
In 2014, Asymchem initiated external research collaborations with Professors Phil Baran, Barry Sharpless, and Jin-Quan Yu, all members of Asymchem's Board of Scientific Advisor, for the development of new process methodology that both improves on existing methods and is environmentally friendly, or "green". Several new laboratories at Asymchem's Tianjin2 site were fitted out for the work. In 2015, Asymchem is extending our commitment to green chemistry investment by joining a consortium of 4 US-based major pharma companies for the development of more sustainable alternatives to common metal-catalyzed cross coupling reactions.



- J. M. Smith, T. Qin, R. R. Merchant, J. T. Edwards, L. R. Malins, Z. Liu, G. Che, Z. Shen, S. A. Shaw, M. D. Eastgate, P. S. Baran*, Decarboxylative Alkynylation, Angew. Chem. Int. Ed., early view.
- E. Hansen*, C. Li, S. Yang, D. Pedro, D. Weix*, Coupling of Challenging Heteroaryl Halides with Alkyl Halides via Nickel-Catalyzed Cross-Electrophile Coupling, J. Org, Chem., 2017, 82, 7085-7694.
- Y. Kawamata, M. Yan, Z. Liu, D. Bao, J. Chen, J. T. Starr, P. S. Baran*, Scalable, Electrochemical Oxidation of Unactivated C−H Bonds, J. Am. Chem. Soc., 2017, 139, 7448–7451.
- J. T. Edwards, R. R. Merchant, K. S. McClymont, K. W. Knouse, T. Qin, L. R. Malins, B. Vokits, S. A. Shaw, D. Bao, F. Wei, T. Zhou, M. D. Eastgate, P. S. Baran*, Decarboxylative alkenylation, Nature, 2017, 545,213-218.
- E. Zhang*, J. Tang, S. Li, P. Wu, J. E. Moses, K. B. Sharpless*, Chemoselective Synthesis of Polysubstituted Pyridines from Heteroaryl Fluorosulfates, Chem. Eur. J. 2016, 22, 5692 – 5697.
- E. J. Horn, B. R. Rose, Y. Chen, J. Tang, K. Chen, M. D. Eastgate, P. S. Baran*, Sca lable and sustainable electrochemical allylic C-H oxidation, Nature, 2016,533, 78-81.

BOARD of SCIENTIFIC ADVISORS

Asymchem has assembled a Board of Scientific Advisors (BSA) of 10 distinguished academic and industrial scientists with expertise in areas including enzyme evolution, asymmetric catalysis, and green chemistry. The advisory board will provide advice on high level strategic issues faced by Asymchem, and to assist in identification of new business opportunities.



Professor K. Barry Sharpless

Professor at the Scripps Research Institute, the winner of the 2001 Nobel Prize in Chemistry

Professor Phil Baran

Professor at the Scripps Research Institute，USA MacArthur Award Winner, Member of the NAS

Dr. Stephane Caron

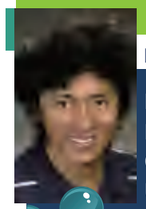
Senior Director of Chemical Process R&D at Pfizer

Professor Timothy Jamison

Professor at Massachusetts Institute of Technology (MIT), leading global expert for flow chemistry

Professor Stephen Buchwald

Associate Head of the Chemistry Department at the Massachusetts Institute of Technology (MIT), fellow of the American Academy of Arts and Sciences, memberof the NAS



Professor Jin-Quan Yu

Professor at the Scripps Research Institute, expert in C-H activation chemistry USA MacArthur Award Winner

Dr. Martin Eastgate

Director ,chemical and sythetic Development of BMS. over 11 years of experience in pharmaceutical industry

Dr. Tony Zhang

Senior Research Fellow of Eli Lilly, over 20 years experience in pharmaceutical industry

Professor Nicholas Turner

Professor at University of Manchester, one of the leading global experts for making better enzymes

Dr. Shuhong Zhang

Vice President of AbbVie, has over 20 years experience in pharmaceutical industry

ASYMCHEM OVERVIEW OF MANUFACTURING CAPABILITIES

	Asymchem Laboratories (Tianjin) Co.,Ltd TJ1	Asymchem Life Science (Tianjin) Co.,Ltd TJ2	Tianjin Asymchem Pharmaceuticals Co., Ltd TJ3	Jilin Asymchem Laboratories Co.,Ltd DH	Asymchem Laboratories (Fuxin) Co.,Ltd FX1	Liaoning Asymchem Laboratories Co.,Ltd FX2	Total
High Potency Plant <0.1μg/m³	Kilo plant 5-80L, glass reactor, 0.3m³ Pilot plant 500-1,000L,GL/SS, 5m³						**HiPo plant 5-80L,500-1,000L, Glass reactor/GL/SS, 5.3m³**
API Plant		Kilo lab 20-50L, GL, 0.2m³ Pilot plant 500-3,500L, GL/Hastelloy, 10.5m³	Bulk plant First stage: 500-8,000L, 6Hss/Ti/Hastelly, 103.5m³ Second stage: 500-8,000L, GL/SS/Ti/Hastelly				**API plant 20-50L,500-8,000L, GL/SS/Ti/Hastelloy 114.2m³**
cGMP Plant		Pilot/bulk plant 200-8,000L, GL/SS/Ti, 213.7m³		Catalytical Hydrogenation Plant 1,000-5,000L, Autoclave/GL, 24m³ Pilot/Bulk plant 1,000-20,000L, GL/SS/Ti, 451.5m³ 3,000-5,000L GL/SS,400m³	Bulk plant 200-12,500, GL/SS, 352m³ Dedicate for carbapenem		**cGMP plant 200-20,000L, GL/SS/Ti/Autoclave, 1041.2m³ *3,000-5,000L GL/SS,400m³***
cGMP-like Plant				Bulk plant 3,000-20,000L, GL/SS, 213m³	Bulk plant 100-8,000L, GL/SS, 265.6m³ Autoclave 500-3,000L, 5.5m³,-20~300℃	Bulk plant First stage: 500-12,500L GL/SS, 191.5m³ Second stage: 500-12,500L GL/SS	**cGMP-like plant 100-20,000L, GL/SS/Auto clave 675.6m³**
Flow Chemistry Plant		Two continuous Diazomethane reactors, three continuous Ozonation reactors, two continuous Low Temperature reactors, one CSTR, four continuous coil reactors 500-1,000L, GL					
Fermentation Plant		50Lx4, 500Lx4, 5000Lx2 Fermenters					
Formulation Plant		Pilot plant Oral solid dosage Drug product manufacturing center	Oral solid dosage, Lyophilized powder injection, injection: 100-300MM units/year				

Notes

Production capacity that has been put into use

Expansion plan or under construction

ASYMCHEM OVERVIEW of MANUFACTURING CAPABILITIES

ASYMCHEM OVERVIEW OF R&D CAPABILITIES

R&D Capabilities

Discovery Chemistry

- Discovery chemistry synthesis

Chemical Engineering

- Flow chemistry
- Process safety asssessment
- Data trending
- Data-driven process improvement

High Potency

- HiPo API development
- Peptide hormones
- Synthesis, characterization, and handling of antibody drug conjugates

Process Research

- Chemical process research
- New process research

Biotransformations

- Use of enzymes as catalysts
- Enzyme screening
- Development of improved "engineered" enzymes
- Seamless integration of biotransformation step into process

Formulation

- Preformulation and formulation development
- Stability testing

Process Development

- Process development for validation and commercialization
- Process development and optimization

New Technology Development

- Electrochemistry
- Non-precious metal catalysis

Analytical

- Analytical research
- Analytical development
- Microbiology test

Core Technology

Biotechnology	In-house enzymatic transformations for process chemistry In-house enzyme screening, optimization and production
Flow Chemistry	Catalytic hydrogenation Low temperature Curtius rearrangement Ozonolysis/ozonation Diazomethane Nitration High temperature
Low Temperature Chemistry	-90℃
High Temperature Chemistry	Over 200℃
High Pressure Chemistry	20~30 atm
Asymmetric Synthesis	Large tool kit of enzymatic and chemical catalysts
Heterocyclic Chemistry	Handle all shapes and sizes
Transition Metal Chemistry	Immobilized metal catalyst
Eletrochemistry	Optimization of classical electrochemical reactions for new application Develop and apply electrochemical technology in chemicals production
Non-precious metal catalysis	Optimization and scope definition in non-precious metal catalyzed reactions Develop and apply the non-precious metal catalytic technology in industry

Key Services

- Synthetic route design and evaluation
- Optimization of reaction conditions and process development
  - Key process parameters
  - Cost of goods
  - Process safety assessment
  - Catalyst screening and optimization
  - Impurity profile assessment
- Development of robust and scalable processes
- Crystallization procedures
- Reference standard preparation

DISCOVERY CHEMISTRY

Asymchem offers Discovery chemistry capabilities from Hit identification to lead optimization. These new capabilities at Asymchem has been initiated and grown by proven industry leadership with over 15 years of experience. Asymchem discovery chemists are highly skilled and efficient synthetic and medicinal chemists. Utilizing the principles of medicinal chemistry, our goal is your goal: the identification of novel, targeted compounds suitable for scale up and further development. With strong IP Protection, we ensure that every request from the client is achieved and that the data produced is confidential. Our international chemical shipping & handling expertise is a big plus to shorten the delivery time.

Capability

- Rapid and cost-effective execution of collaboration tasks
- Medicinal chemistry expertise in major target classes and disease areas
- Integrated drug discovery services through our strategic alliances and partners
- Experience in all type of chemistry and synthesis
  - Low temperature chemistry
  - High temperature and high pressure chemistry
  - Asymmetric synthesis
  - Transition metal catalyzed reactions
  - Continuous flow chemistry
  - Biotransformation
- Synthesis of high potency API
- Chiral separation (SFC)

Discovery Medicinal Chemistry Services

- Design synthetic route and synthesize target compounds
- Co-pilot drive project to develop SAR
  - Hit assessment
  - Hit to lead
  - Lead optimization
- Library generation

Discovery Chemistry Synthesis Services

Customer synthesis from milligrams to kilograms
Provide scale up support for discovery medicinal chemistry at various stages

- Any target compound
- Advanced intermediates and building blocks
- API
- Reference compounds
- Stable isotope-labeled compounds
- Light sensitive compounds

State of The Art Modern Medicinal Chemistry Facility

- 22,000 sq. ft. labs and offices space
- 107 fume hoods with house vacuum, house nitrogen and house waste disposal

State of The Art kilo Lab Facility

- 20,000 sq. ft. kilo lab facility
- 50 walk-in hoods
- 10-72L reactors
- Access to current facilities such as autoclaves and pilot plant

Advantage

- >15 years of service with a proven track record of success
- Exceptional management team supported by skilled scientists
  - Medicinal chemistry leaders with global pharma/biotech and CRO/CMO experience
  - Routine employee training programs so that each FTE members can meet or exceed our stringent performance/productivity requirement
- International chemical shipping & handling expertise
- Strict IP controls

CMC SOLUTION

Custom Manufacturing

With a solid foundation of an innovative process R&D culture, Asymchem able to seamlessly transfer from laboratory into production processes which are cost and environmentally feasible for long-term supply. Asymchem has tremendous back integration capacities together with a wide range of capabilities for assurance of supply. We are USFDA inspected at 4 of our 8 sites to date, with the availability of both dedicated and multipurpose production modules to suit your needs.

Raw Material Back Integration

Asymchem recognizes that having the ability to guarantee RM supply for quality and timeliness is key in controlling not only downstream impurity profiles, but also cost and lead-times. Since operations began in 2003 for custom and bulk production of RM and RSM's, Asymchem has consistently maintained a track record of on-time delivery by being able to guarantee raw material supply through our own in-house production.

Due to stricter enforcement of environmental regulations over the years, many suppliers of raw materials have since been closed down by the government. As a result, some raw material supply shortages are being observed. In order to continue protecting our supply chain, Asymchem is constructed a new facility in Liaoning ("Fuxin2") which will be dedicated to the production of non-cGMP material.

Since we have a history of the synthesis and development of building blocks, should the starting material needed for your synthesis not be commercially available in China, chances are that we can make it efficiently ourselves. Asymchem has an excellent environmental protection track record and are fully committed to retaining our leading position in this area.

Manufacturing Campaign

- Raw Material sourcing, quality control, and release
- Site visits by our clients are encouraged and welcomed
- Campaign updates on a regular basis, agreed upon in advance
- Delivery of final product with CofA and supporting analytical data
- Support of internal compliance and controls such as BSE/TSE, TSCA, etc.
- Final production campaign summary

API Manufacturing

- cGMP kilo lab and Pilot Plant facilities built to western standards
- Rapid scale up of existing route with aggressive timeline
- API manufacturing to support drug candidate selections
- API manufacturing for GLP toxicology studies
- cGMP API manufacturing for clinical studies
- Internal expertise in asymmetric synthesis, transition metal catalyzed reactions, low temperature and high pressure reactions and heterocycle chemistry

Client Technology Transfer (TT) Approach

For those projects that have been more developed, the technical transfer of our Clients' methodology and the subsequent development and validation of those processes for development and scaleup is necessary:

- Review of technical packages
- Client teleconferences and face to face meetings for smooth technical gathering
- Coordination and development of analytical methods with both QC departments (internal and Client)
- Direct manufacturing support by TT team

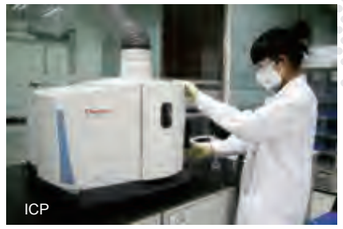
ANALYTICAL SERVICES

Analytical in House Capabilities and Services

Asymchem provides analytical research and development services for a wide range of chemical and pharmaceutical programs, incorporating full quality control and quality assurance support for all cGMP and non-cGMP manufacturing.

The expansion of Asymchem's Analytical Center (AC) went hand in hand with the increase of the R&D and manufacturing capacity.


SFC


ICP


500MHz NMR

Analytical Services

- Analytical Method Development and Validation
- Stability Testing
  - Force degradation studies
  - Stability testing to support clinical studies
  - Stability testing under ICH guidelines
- API Reference Standard Qualification and Maintenance
- Spectroscopic Structure Confirmation
- Release testing
- Identification product and pathway
- Cleaning validation
- Physical property characterization

Major Analytical Equipment

- HPLC, GC, ICS-1500/5000, UPLC,SFC
- LC-MS, LC-MS/MS, LC-TOF, ICP-MS
- GC-MS, HS GC-MS
- NMR(300, 400,500MHz), ICP-OES, XRD, FTIR, UV-vis, OR
- pKa logP/D test, HS KF-V20, KF-C20, TOC, Melting point detector
- TGA, DSC, DVS, PSA, Potentiometric titrator
- Stability chambers

Microbiology Test Capability

Asymchem microbial lab was mainly designed to perform microbiology testing related to purified water system, environment monitoring, raw material, intermediate and drug product. The lab function includes endotoxin testing, aseptic micro testing, routine micro testing, and potency testing and related positive bacteria testing.

Major Equipment include thermo ultra-clean workbenches, biosafety cabinets, moist heat sterilizers with pulse vacuum, dry heat sterilizer, microbiological incubators, and microbiological air monitoring system.

PROCESS RESEARCH AND DEVELOPMENT

World class process R&D is fundamental to robust, reliable drug development and commercial processes. Asymchem has invested heavily and wisely in this expertise, through areas such as:

- Process characterization and validation
- Reaction optimization to reduce costs and maximize output
- Catalysts screening and optimization
- Statistical Design of Experiments (DOE) utilizing Quality by Design (QBD) and Multivariate Data Analysis principles
- Crystallization studies
- Salt selection and polymorph screening
- Cryogenic (-90° C), high temperature, and high pressure (40 atm, 587 psi) capacities
- API synthesis to support from GLP toxicology to clinical studies
- Capable of handling highly potent compounds with OEL < 0.1 ug/m3
- Critical process parameter assessment
- Impurity profiling and isolation
- FTE Services for utilizing Lab, Kilo and/or Pilot Plant facilities

Process Safety Assessment

Asymchem's Process Safety Control Group evaluates potential hazards of each stage of synthesis, and all unit operations, then defines critical parameters for inclusion as part of a final campaign summary, or as a process FTE service.

- Measure the reaction heat, rate of heat liberation, heat accumulation ratio of unreacted material, system heat capacity rapidly and accurately;
- Evaluate the system temperature rise under the worst case;
- Evaluate the rate of heat liberation and the rate of heat removal when the process is scaled up to production batch sizes;
- Evaluate the feeding speed when the process is scaled up to production batch sizes;
- Measure the thermal stability of samples;
- Evaluate heat evolution in bulk material and the critical size of self-heating;
- Measure gas evolution of samples and evaluate thermal stabilities.

BIOTECHNOLOGY

Biotechnology at Asymchem focuses on the seamless development, application, and scale-up of advanced enzymes with direct incorporation on site into the process of interest. By combining molecular biology, fermentation, and chemical development skills in a single organization, Asymchem can help you realize the full potential of biotransformation while reducing cost and environmental impact.

Our Concept of Service

Asymchem designs enzymes with the whole chemical process in mind. We understand your need to move away from proprietary enzymes offered by a single enzyme supplier. Instead of merely screening a panel of enzymes, we also optimize and produce the catalyst on site for use in the process. We will immobilize the enzyme or modify its properties for maximal efficiency in a manufacturing environment. Manufacture and use in a single location avoids loss of enzyme activity and opens the door for application of other advanced technologies. Many companies offer to develop an enzymatic step, but Asymchem builds this step into a full multistep chemical process.

Enzymes made real-six functions

R&D and Manufacturing Capability

Enzyme Engineering

- Enzyme discovery and development for chemical synthesis.
- Collect enzymes in the public domain, produce proprietary enzymes, build in-house enzyme toolbox.
- Enzyme evolution technology to fulfill specific enzyme upgrading needs, for example, enhancing conversion, stereoselectivity or diastereoselectivity.

Bioorganic Chemistry

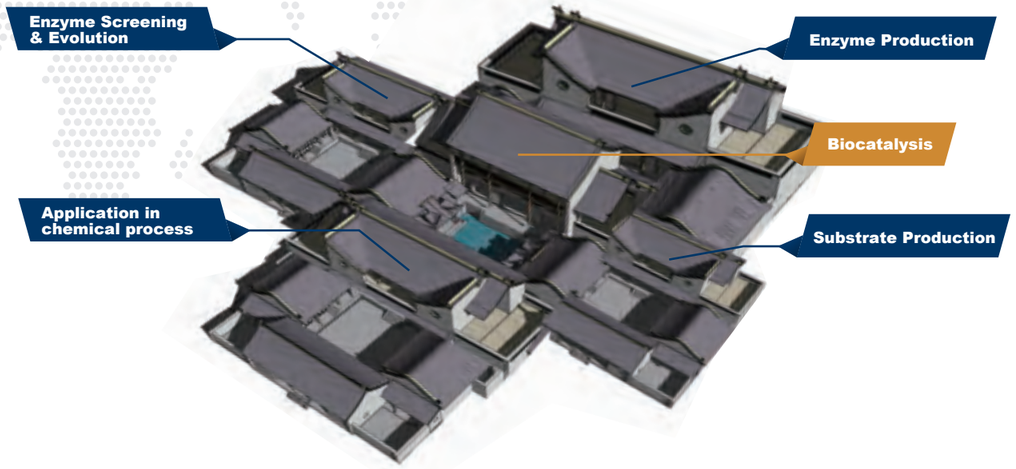
- The high throughput screening of enzyme libraries for organic reactions.
- The development of scalable biotransformation processes for the production of pharmaceutical intermediates and ingredients, and fine chemicals.
- The development of new technologies, including enzyme immobilization.

Enzyme Production

- Asymchem conducts fermentation at scales up to 5,000L and utilizes advanced tools to prepare purified enzyme solutions suitable for direct use.

Core Synthetic Technologies: Biotransformation

All enzymatic functions performed in-house:



Available Services

Enzyme Screening

Asymchem provides multiple enzyme screening kits that target a broad range of biotransformation. We provides standalone enzyme screening against your processes.

Enzyme Production

With great experience, technology and facility in fermentation, Asymchem is well positioned to supply client enzymes from gram to ton scale.

Biotransformations in Chemical Production

By producing purified enzyme solutions at the same site that the rest of a chemical process will run, Asymchem delivers extra value by avoiding unnecessary steps making the enzyme suitable for shipment. Asymchem can also seamlessly combine the biotransformation with other technologies for the best overall process

Biotransformation Process Optimization

Asymchem has a wealth of experience in enzyme catalyzed biotransformation chemistry and process optimization. Asymchem can be your partner in developing an efficient, scalable process, including the immobilization of enzymes where warranted.

Enzyme Evolution

Develop custom enzymes for improved characteristics or IP/freedom to operate considerations. The technology platforms include DNA shuffling, directed evolution, rational design etc.

Integrated Service Project

Asymchem provides an integrated service for a biotransformation process development. This type of service can be project-based or FTE based service according to client's need.

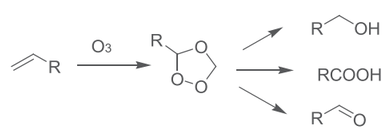
FLOW CHEMISTRY

Asymchem's Chemical Engineering Lab was set up in 2009, mainly for flow chemistry research. Our services include assessment of flow reaction feasibility, design of prototypes, process definition and optimization, equipment design and validation, and technology transfer to production. We have developed different types of equipment to support a wide range of reaction types and implemented processes on a wide range of scales, leading to many happy customers. We also have applied for a number of patented technologies home and abroad.

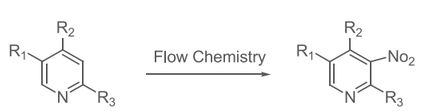
Advantages

- Inherent engineering advantages such as high-speed mixing, highly efficient heat transfer, controllable reaction residence time, repeatability, and lack of amplification effect often lead to improved process performance.
- Often needs fewer chemicals, and can sometimes be applied to reactions that cannot be run safely in batch mode.
- For multi-ton processes, smaller floor coverage and less up-front investment than intermittent batch reaction, and can easily be automated control. This is of great significance for large-scale production.

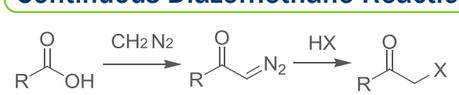
Continuous Ozonolysis/Ozonation Reaction



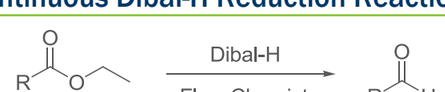
Continuous Nitration Reaction



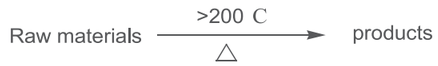
Continuous Diazomethane Reaction



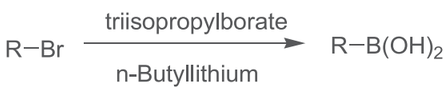
Continuous Dibal-H Reduction Reaction



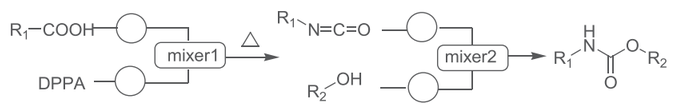
Continuous High Temperature Reaction



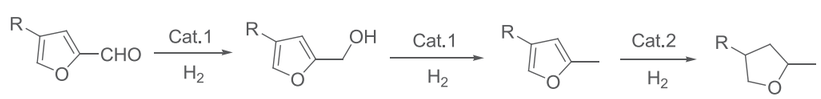
Continuous Low Temperature Reaction



Continuous Curtius Rearrangement Reaction



Continuous Catalytic Hydrogenation Reaction



HIGH POTENCY CAPACITY

High Potency API Manufacturing

Asymchem operates dedicated potent compound production facilities in both cGMP and non-GMP configurations. We have specialized facilities for common potent compounds classes (cytotoxics, b-lactams) and offer the following scales:

Asymchem has the facility to handle compounds with an occupational exposure limit (OEL) of less than 0.1 ug/m^3. Equipment trains are designed for maximum flexibility – after dispensing solids in a controlled area, solutions are transferred to glass reactors fitted to the process, then Nutsche is used for filtration/drying.

Elements of Asymchem's High Potency Program:

- Medicinal chemistry
- API manufacturing
- Drug product manufacturing
- Analytical development
- Environmental health and safety

Overview of HP Capabilities

Site	Function	Equipment/Capability	OEL Rating
Asymchem Laboratories (Tianjin) Co., Ltd (TJ1)	HiPo R&D Labs	2 labs; < 2L Glass reactors 1 QC Lab	
	HiPo Kilo Labs *	3 labs:< 2-20L Glass reactors	
	HiPo API Mfg	Module 1: 5-80L Glass reactors	< 0.1 μg/m^3 Certified in the ISS testing
		Module 2: 500-1,000L GL/SS reactors	
	HiPo DP * (Depending on individual project requirements, the plant can be ready from anywhere between 3~6 months)	Encapsulation, Compression, Blending, Granulation for oral dosage	< 1.0 μg/m^3

* Under construction

Prominent Features of Asymchem's Potent Compound Program :

- A well-developed program to eliminate contamination vectors, such as pressurization, primary decontamination stations within suites, and qualification of facilities and processing equipment
- Ongoing facilities performance monitoring, including dust testing of isolators and air monitoring
- Rigorous worker training for potent compounds specific practices relating to PPE, decontamination, and incident response

ADC (Antibody Drug Conjugate) Development

Asymchem's ADC capabilities include warhead synthesis, linker synthesis, conjugation of the warhead/linker with the antibody, and analytical characterization of the resulting ADC. The development work is performed in Asymchem's High Potency labs in Asymchem Laboratories (Tianjin) Co. Ltd., with validated PPE monitoring by a dedicated quality control group.

Peptide Hormones Development

Asymchem has a research group dedicated to the process optimization, pilot manufacturing and DMF filing of peptides and peptide containing drugs. Asymchem produces a variety of peptides that contain sequences specified by our customers, as well as back integrating the manufacture of raw materials used in the production of various peptide drugs. The production environment is performed strictly in accordance with FDA 21 CFR Part 210 and 211, and supported and monitored by a dedicated QA/QC group.

Production Capability

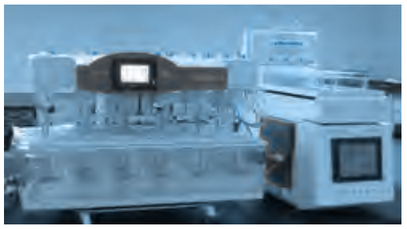
- Two independent production lines;
- The highest yield is 10 kg per batch;
- Synthesis reactors with different specifications: 10L, 50L, 200L;
- Different levels of the production area with air purification system.

PHARMACEUTICAL SERVICES

Asymchem provides customers with fully integrated services in pre-formulation development, formulation development and drug product manufacturing. For early stage molecules, we work with our clients to develop a practical, cost-effective and fastest route to bring your molecule to the clinical studies. If there is a need to optimize the formulation and process for later clinical trials, we take into account molecule's biopharmaceutical, physicochemical and mechanical properties to identify potential formulation and manufacturing process options that has the best chance to achieve optimal in vivo performance and process scalability.

Dynamic vapor sorption

Surface area and porosity tester



Preformulation Development

Equipped with advanced analytical instruments and technical expertise, Asymchem can fully characterize the physicochemical properties of drug molecules to guide drug product development. The following services are offered by Asymchem:

- Salt selection
- Polymorph screen
- Solubility screen
- Solution and solid state stability testing
- Characterization of physicochemical properties: dissociation constant and partition coefficient(pKa and LogP tester), hygroscopicity(DVS),particle size(PSA), surface area(BET) and IDR (Intrinsic Dissolution Rate)

Prototype Formulation Development

- Wide array of formulation platform technologies
- Tablets, capsules, solution and suspension
- Customized release profile - immediate release and modified release dosage forms
- Mechanical property characterization
- Assessment of processibility
- Particle size control and characterization (Jet mill, Dyno-mill, Co-mill and Granumill)
- Stability assessment
- Drug excipient compatibility testing
- Stability of prototype formulation
- Functionality testing: dissolution, disintegration, hardness, friability, content uniformity etc.
- Solid dispersion preparation (Mini Spray Dryer)

Asymchem's Integrated Approach to Formulation Design

Our scientists approach each formulation project with unique characteristics of your compound in mind. We take into account multiple factors such as quality, speed, cost constraints and availability of API during formulation development. With a full range of preformulation, formulation and analytical development capabilities, along with a SFDA approved pilot scale cGMP facility, we can accelerate your molecule through development to market.

Drug Product Manufacturing

Asymchem's goal is to develop and manufacture quality products with competitive pricing and rapid turnaround time. The drug product facility has received the manufacturing certificates from SFDA.

Processing Capabilities

- Blending
- Encapsulation – powder/pellet/liquid fill
- Granulation – wet granulation, roller compaction and fluid bed granulation
- Fluid bed drying
- Particle coating
- Tablet compression
- Tablet film coating – immediate and modified released film coat

Oral Solid Dosage cGMP Batch Manufacturing

- Clinical Supply: 500~150,000 units/batch
- Large scale and Commercial Manufacturing: 15~300kg/batch and 50MM~500MM units/year (Expansion Plan)
- Obtained sFDA manufacturing certificate for oral formulations
- Able to handle potent and cytotoxic compounds

Stability Study Services

Asymchem provides many types of Stability Studies Services to support all phases of Drug Development. We have expertise and experience in managing International Stability Studies. We have the infrastructure to carry out these studies efficiently and in full compliance with current regulations meeting the cGMP.

Chambers Capabilities

Stability chambers are computer controlled to maintain humidity and temperature with a 100% backup system and redundancies for each critical system to ensure uninterrupted maintaining of conditions throughout the study.

Asymchem can generate the stability indicating method development and validation, provide the study protocol, and produce the report and support documentation at wrap-up for your filing (IND, NDA, ANDA, etc.) needs.

Stability conditions	Total volume
25℃/60% RH	>40,000 L
30℃/65% RH	>40,000 L
40℃/75% RH	>40,000 L
5±3℃	>42,000 L
6±2℃ (For SFDA)	>40,000 L
-20±5℃	400 L
Back-up chamber	>42,000 L

Reach-in stability chamber

Walk-in stability chamber

CLINICAL RESEARCH SERVICE

Tianjin Asymchem
Medical Science&Technology Co., Ltd.

Clinical research service

Clinical research services rang from exploratory clinical research to confirmatory clinical research, from registration oriented research to phase IV research after drug launching, with clinical research through the complete life cycle of drugs. High quality and efficient clinical research is the prerequisite of the drug's value.

Phase I → Phase II → Phase III → Phase IV

Purpose	Safety	Dosage Exploration	Efficacy Authentication	Post-marketing Study
Sample Size	20-100	90-300	300-3000	1000+
Research Cycle	1 month+	6-36 months	12-48 months	12 month+
Yield Rate	0%	33%	25-30%	70%

Tianjin Asymchem Medical Science&Technology Co., Ltd. boasts a dedicated clinical research team with rich clinical research experience and professional expertise, focusing on phase I-IV clinical research including pharmacokinetics research, BE research, exploratory research on dosage safety, interaction of food and drugs, clinical efficacy, safety research, quality management and medical writing, as well as service of import registration of drugs. Building and execution of quality management system are especially emphasized to ensure the authenticity and standardization of clinical research conforming to CFDA demands.

- Complete SOP system (includes clinical operation, medical writing, quality control, quality assurance)
- Rich experience in clinical operation
(for large-scale central companies, listed companies, multinational pharmaceutical companies,/CRO clinical research)
- Multi-field project experience (internal secretion, oncology, respiration, cardiovascular etc.)

QMS (Quality Management System) is the basis of quality guarantee for all clinical researches. QMS includes but not limited to QA. QA is more than audit. QMS is a system to ensure clear division and integration of work. The separate and compliant QMS lays a solid foundation for quality assurance for applicants.

Quality guarantee-quality compliance

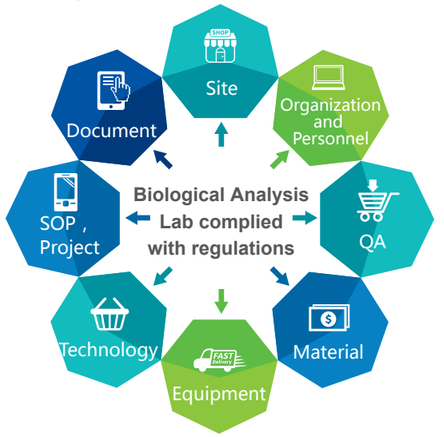
-Quality Assurance(QA)
-Quality Control(QC)
-Quality System (QS/QMS)
-Risk Management
-Compliance
-Audit
-QC Check/Quality Evaluation
-Regulatory Inspection

Quality Assurance (QA)	Ensure the Right persons do the Right thing in accordance with Right process and requirement.
Quality Control (QC)	Coordinate/ensure products/services delivered within elivery timeliness stipulated in the contract, namely compliance which means conforming to legal regulations, guidances, industry standards and company/client's standardized procedure and project demands.

BIOANALYTICAL SERVICE

FDA / OECD / EMA / CFDA complied GLP labs equipped with Triple Quad LC-MS/MS systems and validated lab information management system (Watson LIM 7.4) . Especially, the pg level detection limit can be achieved by the Triple Quad 6500+ LC-MS/MS system. Quantitative analytical service are available to global clients due to the great capacity of receiving and operating samples with global logistics and reagent purchasing system.


LC-MSMS



Compliance of biological analysis test are guaranteed by experienced dedicated team, sound lab system and life cycle management to ensure the right persons do the right thing in accordance with right SOPs.

- Life cycle of data
- Life cycle of personnel
- Life cycle of SOPs
- Life cycle of instruments
- Life cycle of projects
- Life cycle of documents
- Life cycle of samples

Regulatory Compliance

- FDA Guidance for Industry, Bioanalytical Method Validation, 2001
- EMA Guidance on Bioanalytical Method Validation, 2012
- FDA: Code of Federal Regulations, Title 21 part 11, ER/ES. 2003
- FDA: Guidance for Industry: Computerized Systems Used in Clinical Investigation. 2007
- 中国药典： guidance on the Quantitative Analysis of Biological Samples (method validation and sample analysis) ,Part 9012 of Chinese Pharmacopoeia 2015
- May 4th 2016 Document Demand on Chemical Drug New Registrations. (report form)
- CFDA Guidance on Technology of Electronic Data Collection from Clinical Experiments 2016

ENVIRONMENTAL HEALTH & SAFETY (EHS)

Safety

- Facility and major process HAZOP
- Process hazards assessment (PHA) and safety training prior to production
- Hazardous material storage and handling
- Emergency Response Plan in place for fire fighting, first aid, chemical spills, accidents, etc.
- Annual fire fighting and evacuation drills conducted at all Asymchem sites
- Back up systems for power, water and nitrogen are available in all production sites
- Smoke detector, fire alarm, fire hydrant, extinguishers and sprinkler system present in all buildings
- Fixed combustible gas monitoring system present in all chemical related work places
- Security monitoring system installed throughout site

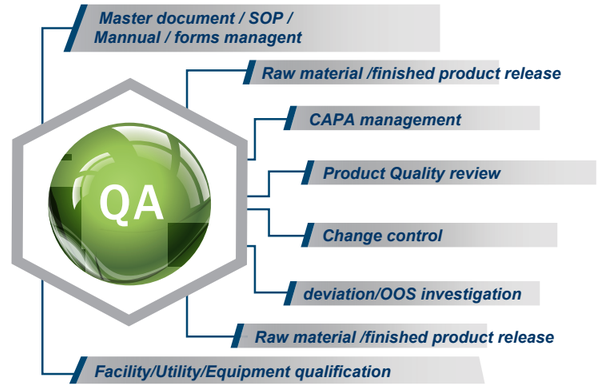
Waste Treatment

- Devloping green chemistry technologies for cleaner and safer production
- Source control and end-of-pipe control
- On-site incierators at each manufacturing site
- On-site solvent recovery at each manufacturing site
- Production Monitoring

QUALITY ASSURANCE& IP PROTECTION

Quality Assurance

The Quality Policy of Asymchem is for all operations as an approved manufacturing site to develop and produce active pharmaceutical ingredients in compliance to high quality standards fit for human consumption as defined in current Good Manufacturing Practices, and the International Convention for Harmonization (ICH) Q7/Q8/Q9/Q10/Q11 guidelines to meet EU and US FDA regulatory requirements.



IP Protection

At Asymchem we value our customer's trust and understand the practical concerns in outsourcing work involving IP to suppliers in China.

At the heart of Asymchem's core values and standards policies is the approach that the property of our clients starts and remains secure in our hands.

Security starts with our employees

- All IP developed as a service by Asymchem's chemists, under a client CDA or MSA, is the property of the Client.
- Duty of confidentiality carries forward outside of employment contract.
- Client and Asymchem's IP are protected by both national law and company agreements.

Electronic security access and information dissemination are strictly controlled.

- Secure VPN tunnels for email transfer of confidential info to Clients
- Asymchem Central Document Server (CDS) with assigned security access controlling access of project specific information
- Notebooks, MOR's and others are locked in archived room under strict access.
- Project details are shared on a need to know basis only

SYMPOSIUM

Since 2009, Asymchem has been held seven Symposia in TEDA Tianjin. The symposium served as a forum for the exchange of ideas among scholars and industry experts in the pharmaceutical CMC area. Asymchem invited a diverse group of participants from academia and the pharmaceutical industry, who are well placed to shape and promote the future of Green Chemistry.

3rd Asymchem Pharmaceutical CMC 2012,Tianjin

4th Asymchem Green Chemistry Symposium 2013, Tianjin

6th Asymchem Green Chemistry Symposium 2016, Tianjin

Members of Asymchem Scientific Advisory Board visited Asymchem plants

Nankai University-Asymchem Lecture