

# Medicilon—CFDA GLP, FDA GLP, AAALAC

## ► Preclinical Services/临床前服务

Medicilon provides fully integrated pharmaceutical services to the global pharmaceutical community. The services across biology, chemistry and preclinical research are specially designed to help clients develop their research and discovery programs from the initial idea stage to the IND filing phase. Preclinical department in Medicilon has extensive and professional knowledge in drug metabolism/pharmacokinetics, pharmacology studies as well as toxicology. We offer the high-quality and cost-effective data with rapid turnaround time to support drug development, preclinical studies and clinical research. Our services cover various aspects of preclinical services, including protocol designing, in-life studies, sample analysis, professional data analysis, IACUC review, and preparation of documents for IND filing.

Medicilon is headquartered in Zhangjiang High-Tech Park, Shanghai, China, with wholly-owned research facilities in Chuansha Economic Park, Shanghai, China. We occupy over 250,000 SF lab space. Over 60% employees have MS and PhD degrees, and over 15% of our employees have significant foreign education and/or working experiences. Medicilon and MPI Research established a joint venture together during the period of 2008-2010 to set up a state-of-the-art 50,000 SF animal facility, which is fully accredited by AAALAC and in compliance with the US GLP. It is also being certified by CFDA for GLP compliance. Our comprehensive services facilitate the evaluation of the safety and marketing of life-changing compounds for our clients.

上海美迪西生物医药有限公司是一家提供集化学、生物学、药效学评价、药代动力学评价和毒理学评价为一体的一站式生物医药研发服务公司。我们的临床前部门在药物代谢/药代动力学，药效研究，以及毒理学方面有专业的知识，提供高质量的数据和快速的周转期以支持各项药物开发、临床前研究和临床研究。美迪西临床前研究服务，涵盖各个方面：方案设计，体内研究，样品分析，专业数据分析，IACUC审查，以及申报资料准备。

公司总部座落在上海张江高科技园区，并在上海川沙经济园区设有研发大楼。公司有超过60%的现有员工拥有博士学位或者硕士学位；超过15%的员工拥有很好的国外教育背景和/或工作经验。美迪西拥有25,000平方米实验室，其中5,000平方米动物实验室是美迪西曾与美国MPI Research公司（世界第三大毒理学研究公司）共同建立动物实验设施，并通过国际实验动物评估和认可（AAALAC），而且达到美国食品药品监督管理局（FDA）和中国食品药品监督管理局（CFDA）的GLP标准，其保障了我们的非临床安全评估实验有力的开展，加快了化合物市场化的进程。





Our pharmacokinetics department offers the clients a broad spectrum of high quality of services in the areas of *in vitro* ADME, *in vivo* pharmacokinetics and bioanalysis services, ranging from small molecules to large molecules, such as protein and antibody. The animal species involved in our services are non-human primate, canine, mice, rat, rabbit and hamster. Meanwhile, non-human primate experimental platform and isotope platform for protein/antibody are certified by the Shanghai government.

我们的药代部分为客户提供从所有小分子到大分子（蛋白质和抗体）的高质量药代动力学服务，包括体外ADME和体内药代以及生物分析。涉及的动物种类有非人灵长类、狗、小鼠、大鼠、兔、豚鼠等。其中非人灵长类平台及利用同位素蛋白质/抗体实验平台被上海市政府认定为重要实验室平台。

## ➤ Preclinical Pharmacokinetics

- Method development and validation (GLP&Non-GLP)
- Bioanalysis
- Pharmacokinetics (Tumor bearing rodents, Bioavailability, Crossover studies, Cassette (N in 1) dosing and analysis, Effects of gender on pharmacokinetics, BBB penetration)
- Stability in vehicles and plasma
- Drug interaction studies
- *In vitro* metabolic stability
- CYP 450 inhibition/induction
- Permeability studies
- Plasma protein binding studies
- Distribution studies
- Excretion studies
- Prediction and identification of major metabolites
- Toxicokinetics analysis

## ➤ 临床前药代动力学

- 方法开发和验证（GLP&Non-GLP）
- 生物样品分析
- 各项药代研究动物实验（肿瘤模型动物，性别差异，生物利用度，多周期交叉实验，盒式给药，血脑屏障穿透研究）
- 药物在血浆和溶媒稳定性研究
- 药物相互作用研究
- 体外代谢稳定性研究
- CYP450酶抑制研究
- 渗透性实验
- 血浆蛋白结合率
- 组织分布研究
- 排泄研究
- 代谢物推测及鉴定
- 毒代研究



➤ Pharmacokinetics with Radiolabelled Compounds

- Protein/antibody drug with <sup>125</sup>I labeled for PK
- Tissue distribution
- Mass balance

➤ 利用同位素标记的药代动力学研究

- 碘标记蛋白质/抗体药物的药代动力学研究
- 组织分布
- 质量平衡分析

➤ Pharmacokinetics Package for IND Filing

- DMPK package for CFDA and FDA IND filing
  - Chemical compounds
  - Traditional chinese medicine
  - Protein
  - Antibody

➤ 新药临床前药代动力学申报资料

- 符合FDA和CFDA新药注册要求的申报材料
  - 小分子化学药
  - 中药
  - 大分子蛋白药物
  - 单克隆抗体

**We have successfully helped many clients to prepare the DMPK package for CFDA and US FDA IND filing and have passed all audits smoothly.**

我们已经成功地帮助很多客户向CFDA和FDA递交符合新药注册要求的药代申报资料，并已接受多次核查，且顺利通过所有核查。

*Quick study initiation and scheduling flexibility will help you make your decisions faster and reduce your total research costs!*

实验的快速启动和安排的灵活性将帮助您做出更快的决定和减少总的研究费用!

➤ Neurological Disorders Models/中枢神经系统疾病模型

Disease 疾病	Model 模型	Species 动物
Antinociceptive Pain Tests 疼痛（中枢）	Hot-Plate 热板	Mouse/Rat 大小鼠
	Tail flick 热辐射	Mouse/Rat 大小鼠
	Formalin test (phase I & phase II) 福尔马林实验（I期和II期）	Mouse/Rat 大小鼠
	Acetic acid induced writhing 扭体	Mouse 小鼠
	LPS-induced thermal hyperalgesia 脂多糖诱导的热痛敏实验	Guinea pig 豚鼠
	STZ-induced diabetic neuropathy 糖尿病诱发的神经症状	Rat 大鼠
Sedation 镇静催眠	Potentiated pentobarbital-induced sleep 增强巴比妥类的睡眠时间	Mouse 小鼠
Antidepressant Tests 抑郁	Forced swimming test 强迫游泳实验	Mouse/Rat 大小鼠
	Tail suspension test 悬尾实验	Mouse 小鼠
	5-HTP-induced head twitches potentiation (5-HT) 5-羟色胺酸增强实验（5-HT）	Mouse 小鼠
	Reserpine-induced ptosis 利血平诱导眼睑下垂实验	Mouse 小鼠
	Yohimbine-induced lethality 育亨宾毒性增强实验	Mouse 小鼠
Anti-Parkinson Tests 帕金森病	Oxotremorine-induced tremors/salivation 氧化震颤素对抗实验	Mouse 小鼠
	Reserpine antagonism 利血平拮抗作用	Mouse 小鼠
	6-OHDA-induced rotation behavior 大鼠黑质纹状体损害后的旋转行为实验	Rat 大鼠
Antidementia Tests 抗痴呆实验	Morris water maze 水迷宫	Mouse/Rat 大小鼠
Antipsychotic Tests 精神病	Apomorphine-induced stereotype 大小鼠阿扑吗啡攀爬行为抑制实验	Mouse/Rat 大小鼠
	MK-801 induced hyperlocomotion 对MK-801引起小鼠运动和跌倒的拮抗作用	Mouse 小鼠
Anticonvulsant Tests 抗惊厥实验	Pentylene-tetrazol-induced clonic seizure 戊四唑惊厥	Mouse 小鼠
	Bicuculline-induced clonic seizure 荷包牡丹碱惊厥	Mouse 小鼠
	Picrotoxin-induced clonic seizure 印防己毒素惊厥	Mouse 小鼠
Miscellaneous 其他	Rotarod 旋转实验	Mouse 小鼠
	Spontaneous locomotor activity 自发活动	Mouse 小鼠

➤ Cancer Xenograft Models/肿瘤异种/同种移植动物模型

<b>Head and Neck Cancer</b>	KB, FaDu
<b>Nasopharyngeal Carcinoma Stem Cell</b>	S18, S26
<b>Lung Cancer</b>	DMS114, NCI-H69, NCI-H146, NCI-H209, NCI-H446, NCI-H526, NCI-H1688,95-D, A549, Calu-1, Calu-3, Calu-6, HCC827, NCI-H226, NCI-H292, NCI-H358, NCI-H441, NCI-H460, NCI-H520, NCI-H522, NCI-H1299, NCI-H1437, NCI-H1650, NCI-H1975, NCI-H1993, NCI-H2009, NCI-H2122, NCI-H2126, NCI-H2228, PC-10, QG-56, LLC
<b>Breast Cancer</b>	Bcap-37, BT-474, 2LMP, MCF7, MDA-MB-231, MDA-MB-435s, SUM159, MDA-MB-468, ZR-75-1, ZR-75-30
<b>Gastric Cancer</b>	BGC-823, HGC-27, MKN-28, MKN-45, NCI-N87, NUGC-3, SCH, SGC-7901, SNU-5, SNU-16, MGC-803
<b>Pancreatic Cancer</b>	AsPC-1, BxPC-3, Capan-1, Capan-2, CFPAC-1, HPAF-II, MIAPaCa-2, PANC-1, SU.86.86
<b>Renal Cancer</b>	ACHN, OS-RC-2, 786-O
<b>Hepatocellular Carcinoma</b>	Bel-7402, Hep-3B, Huh-7, PLC/PRF/5, QGY-7703, SK-HEP-1, SMMC-7721
<b>Glioblastoma</b>	U87-MG
<b>Colon and Cecum Cancer</b>	COLO 201, COLO 205, COLO 320 DM, CW-2, DLD-1, HCT-8, HCT-15, HCT116, HCT116 P53 K0(-/-), HT-29, LoVo, LS1034, LS174T, LS411N, NCI-H716, RKO, SW480, SW620, WiDr
<b>Prostate Cancer</b>	22Rv1, CL-1, DU145, LNCap Clone FGC, PC-3
<b>Urinary Bladder</b>	HT-1197, HT-1376, RT4, SCaBER, SW780, T24
<b>Ovary Cancer</b>	ES-2, HO-8910PM, PA-1, SK-OV-3, OVCAR-3
<b>Endometrium/Hystero carcinoma</b>	AN3 CA, HEC-1-A, ME-180, MFE-280
<b>Skin Cancer Cell</b>	A431
<b>Melanoma</b>	A375, B16, A2058, C32, HMCB, SK-MEL-30
<b>Osteosarcoma Cell</b>	MG-63, SJSA-1,
<b>Sarcoma</b>	S-180
<b>Muscle, Striated</b>	SJCRH30
<b>Myeloma</b>	KMS-11, KMS-26, RPMI-8226
<b>Leukemia / Lymphoma</b>	U937, THP-1, MV-4-11, HEL, TF-1a, ML-2, HL-60, L1210, K562, KARPAS-299, Daudi, Raji, Ramos, ARH-77, KMS-12-BM, KG-1,

\* Medicilon also offers primary tumor models.

美迪西也提供原代肿瘤模型用于药物筛选。

➤ Metabolic Disease Models/代谢性疾病

Disease 疾病	Model 模型	Species 动物
Diabetes 糖尿病	STZ-induced 链脲霉素糖尿病	Mouse/Rat 大小鼠
	Genetically engineered 自发性糖尿病	Db/db, ob/ob Mouse Db/db, ob/ob 小鼠
	High fat diet-induced obesity 高脂饮食诱导的肥胖小鼠	DIO Mouse DIO 小鼠
	Aged, diet-induced 老化, 饮食诱导	Rhesus Monkey 猴
Obesity 肥胖	Genetically engineered 遗传性	Db/db, ob/ob Mouse Db/db, ob/ob 小鼠
	High fat diet-induced obesity (growing/established) 高脂饮食诱导的肥胖小鼠	DIO mouse DIO 小鼠
Dyslipidemia 血脂异常	High-fat/cholesterol/fructose diet induced 高脂/胆固醇/果糖饮食诱导	Hamster 仓鼠

➤ Inflammation & Immunological Disease Models/炎症和免疫系统疾病

Disease 疾病	Model 模型	Species 动物
Acute Inflammation 急性炎症	Carrageenan-induced paw edema 足趾肿胀	Mouse/Rat 大小鼠
Arthritis 关节炎	Adjuvant-induced arthritis (AIA) 佐剂性关节炎 (AIA)	Rat 大鼠
	Collagen-induced arthritis (CIA) II型胶原诱导的关节炎 (CIA)	Mouse/Rat 大小鼠
	Air Pouch 气袋实验	Mouse/Rat 大小鼠
Sepsis 败血症	CLP-induced 盲肠结扎穿孔诱导法	Mouse 小鼠
Experimental Autoimmune Encephalomyelitis (EAE) 实验性过敏性脑脊髓炎	Antigen-induced 抗原诱导	Mouse 小鼠

➤ Others/其他

Disease 疾病	Model 模型	Species 动物
Cardiovascular 心血管	Spontaneously Hypertension Rat 自发性高血压	SHR Rat SHR 大鼠
	Myocardial Infarction 心肌梗死	Rat 大鼠
Renal Failure 肾衰	5/6 nephrectomy 肾切除 (5/6)	Rat 大鼠
Anemia 贫血	Renal failure induced 肾衰诱导	Rat 大鼠
Gastric ulcer 胃溃疡	Ethanol 乙醇诱导	Rat 大鼠
Hepatic injury 肝损伤	Carbon Tetrachloride 四氯化碳诱导	Mouse/Rat 大小鼠



Our toxicology department has professional teams with rich experience in toxicology studies. We offer high-quality data and rapid turnaround period to support drug discovery and development. Our toxicological study is conducted in various kinds of animal species. The toxicological evaluation from dose design, in-life studies to histology and pathology testing along with toxicokinetics studies are all complied with non-GLP or GLP standard. Our study platform is certified as one of Shanghai Public Service Research Platforms.

我们在毒理学方面有专业的团队和实战经验，可提供高质量的数据和快速的周转期以支持各项药物安全评价研究。毒理学研究在不同的动物种类中开展，从剂量设计，实验研究到组织学和病理学研究包括临床检测均可按照非GLP或者GLP标准执行。我们的研究平台已被评为上海研发公共服务平台。

➤ Drug Preclinical Safety Evaluations (CFDA, FDA GLP Compliance)

- Single dose toxicity study
- Repeated dose toxicity study
- Safety pharmacology study
- Genotoxicity study
- Reproductive toxicity study
- Immunogenicity study
- Toxicokinetic study
- Topical toxicity study

➤ 药物临床前安全评价

(符合CFDA, FDA GLP要求)

- 单次给药毒性试验
- 反复给药毒性试验
- 安全药理试验
- 遗传毒性试验
- 生殖毒性试验
- 免疫原性试验
- 毒代动力学试验
- 局部毒性试验

➤ Histopathology Capabilities

- Routine and special staining techniques
- Preparation of slides with high quality
- State-of-the-art automated equipment:
  - Slide and cassette printing (Leica)
  - Tissue processing (Leica)
  - Hematoxylin & eosin staining(Leica)
- Professional microscopic review by domestic and international pathologists

➤ 组织病理学

- 常规和特色染色技术
- 制备高质量病理切片
- 先进的自动化仪器:
  - 切片和包埋盒打号机
  - 全自动组织脱水机
  - 全自动染色机
- 由国内外专业病理学家进行病理读片



## ➤ Clinical Pathology Capabilities

- Hematology

Leukocyte count (total and 5 part differential), Erythrocyte count, Hemoglobin, Hematocrit, Mean corpuscular hemoglobin, Mean corpuscular volume, Mean corpuscular hemoglobin concentration, Absolute and percent reticulocytes, Platelet count, Blood cell morphology

- Urinalysis

Volume, Specific gravity, pH, Color and appearance, Protein, Glucose, Bilirubin, Ketones, Blood, Urobilinogen, Nitrite, Leukocyte, Microscopy of centrifuged sediment

- Clinical Chemistry

Alkaline phosphatase, Total bilirubin, Direct bilirubin, Indirect bilirubin, ALT, AST, Gamma glutamyl transferase, Urea nitrogen, Creatinine, Total protein, Albumin, Globulin, Glucose, Total cholesterol, Triglycerides, Electrolytes(sodium, potassium, chloride), Calcium, Phosphorus, Creatine kinase, High density lipoprotein cholesterol, Low density lipoprotein cholesterol, Bicarbonate

- Coagulation

Prothrombin time, Activated partial thromboplastin time, Thrombin time, Fibrinogen

## ➤ 临床检测项目

- 血液学

白细胞计数（白细胞总数和白细胞五分类计数）、红细胞计数、血红蛋白、红细胞压积、平均红细胞血红蛋白含量、平均红细胞体积、平均红细胞血红蛋白浓度、网织红细胞绝对值及百分比、血小板计数、血细胞形态学

- 尿液分析

体积、比重、pH、颜色和外观、蛋白、葡萄糖、胆红素、酮体、潜血、尿胆原、亚硝酸盐、白细胞、尿沉渣镜检

- 临床生化

碱性磷酸酶、总胆红素、直接胆红素、间接胆红素、丙氨酸氨基转移酶、天门冬氨酸氨基转移酶、 $\gamma$ -谷氨酰基转移酶、尿素氮、肌酐、总蛋白、白蛋白、球蛋白、葡萄糖、总胆固醇、甘油三酯、电解质（钾、钠、氯）、钙、磷、肌酸激酶、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、碳酸氢盐（二氧化碳）

- 凝血

凝血酶原、活化部分凝血活酶时间、凝血酶时间、纤维蛋白原





➤ Preparation of Toxicity Package Compliance with FDA and CFDA IND  
 Registration Requirements  
 符合FDA 和 CFDA新药注册要求的安全评价研究资料

**Animal Facilities and Capability**

- Totally 50,000 SF
- 12,500 SF of function area
- 12,500 SF of Canine housing: maximum capability for 350 animals
- 12,500 SF of NHP housing: maximum capability for 400 animals
- 12,500 SF of Barrier system for Rodent housing: Separate SPF and non-SPF area; maximum capability for 2400 animals of SPF area and 500 animals of non-SPF area
- Design and Operation of the facility is under international and Chinese regulations

**动物设施和能力**

- 总设施面积5,000平方米
- 功能区域1,250平方米
- 犬动物房1,250平方米：最多可容纳350只
- 非人类灵长动物房1,250平方米：  
最多可容纳400只
- 啮齿类屏障系统动物房1,250平方米：SPF和非SPF区域；SPF区域最多可容纳5000只；非SPF区域最多可容纳500只
- 设施的设计和运营均符合国际和国内的标准



Clean hallway in barrier system  
屏障系统洁净走廊



Non-clean hallway in barrier system  
屏障系统非洁净走廊



Specimen  
标本室



Wet tissue storage  
湿标本室



Rodent room  
大(小)鼠饲养室



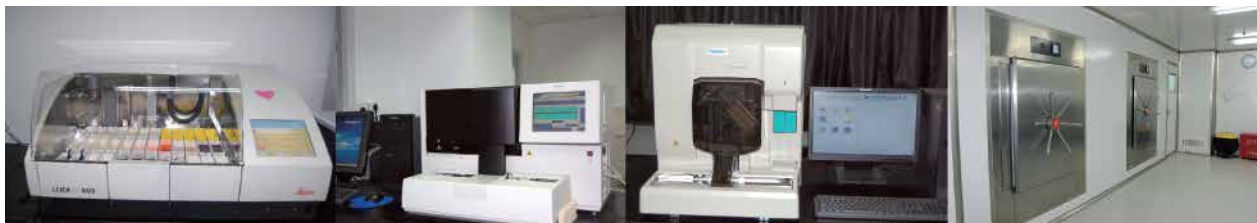
Dog room  
犬类饲养室



NHP room  
非人灵长类饲养室



Animal dissecting table  
解剖台



### Drug evaluation research completed from 2008 to 2012

More than 1000 per year preclinical researches have been completed, including single-dose toxicity studies, repeated-dose toxicity studies, topical toxicity studies, toxicokinetic studies and pharmacokinetic studies, now the company has been expanding the safety evaluation to safety pharmacology study, immunogenicity study, genotoxicity and reproductive toxicity study. At present, evaluation and research of four IND packages are being conducted and will be submitted to FDA soon.

### 2008到2012年期间完成的药物安全评价研究

每年完成超过1000项药物临床前安全评价研究，包括单次给药毒性试验、反复给药毒性试验、局部毒性试验、毒代动力学试验和药代动力学试验。公司现将药物安全评价能力扩展至安全药理试验、免疫原性试验、遗传毒性和生殖毒性试验。目前公司正开展4个新药全套临床前评价和研究的项目用于申报FDA。

Provantis and LIMS are used in data collection, analysis, storage and format reporting. All equipments and instruments used in GLP studies have been validated including software.

Provantis和LIMS软件用于数据采集、分析、储存和格式化报告,所有的设备和仪器已验证或正在验证包括跟数据生成有关的设备和仪器软件。

### From Sponsors Evaluations (selected)/选自客户的评估报告

“The results of an intensive three days audit onsite of GLP systems and procedures, as well as site and personnel, operating systems and procedures, and raw data and final report from one non-GLP study lead to the conclusion that Medicilon is qualified and capable of conducting non-clinical GLP studies in compliance with the US FDA GLP’s. The personnel who participated the audit were knowledgeable and professional.”

Please contact us for more information on how we can help move your drug along the development pathway.