







Welcome to Hengdian!



2016



Contents

-  Apeloia
-  R&D Center
-  EHS System
-  Quality System



Location



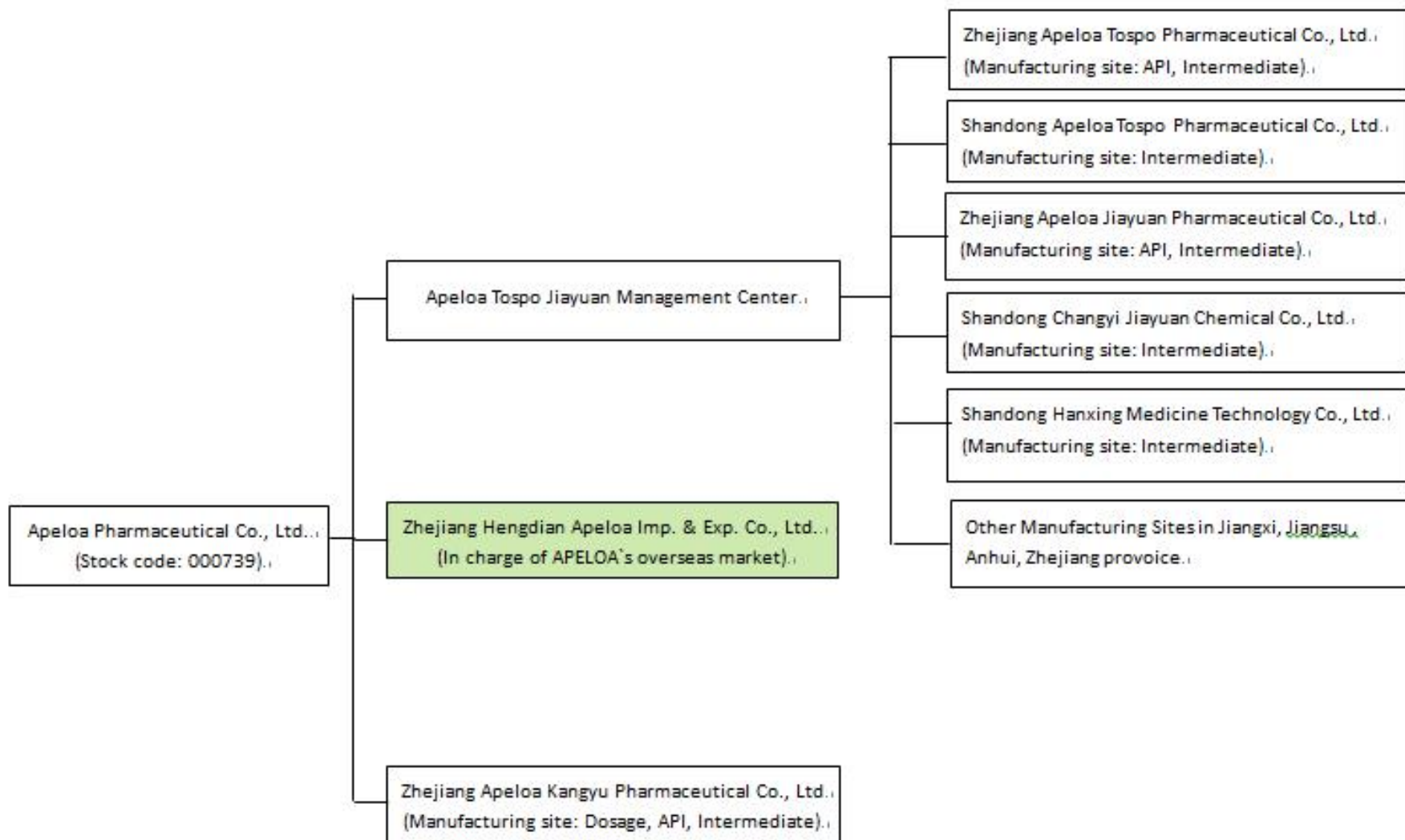
Headquarter

- 180 km away from Hangzhou City
- 380 km away from Shanghai City





Apeloa Organization





Apeloa Tospo Jiayuan

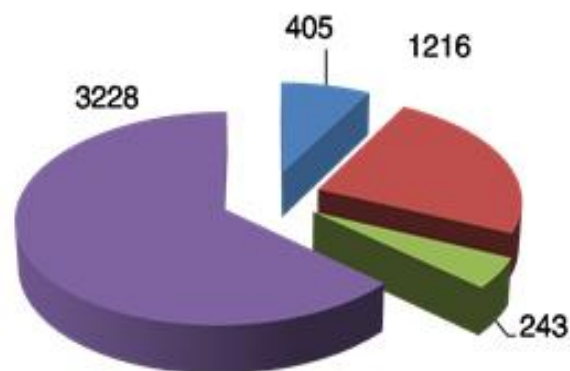
- 5 manufacturing site approved by cGMP
- 2 API site approved by USFDA site inspection
- Some products approved by USFDA, KFDA and PMDA
- ISO9001, ISO14001, OSHAS18001 certified
- Passed several top US, European Pharmaceutical companies' EHS audits





Human Resources

- 300 R&D, 32 Ph.D
- The Recruitment Program of Global Experts: Dr. Tang Xiaoping and Dr. Wang Xiaojun
- 30 people with overseas working experience



- Senior professional titles
- Intermediate title and technician
- licensed pharmacist
- Others



Advantages

- Integrated product chain
 - Intermediate — API — Finished Dosage — Sale (home and abroad)
- Various drug forms
 - API (β -Lactam ,tumor, and others)
 - Oral preparation (tablet, capsule , particle and etc.)
 - Injection (liquid, powder)
 - Sustained/Controlled release drugs
- Wide treatment area
 - Anti-infection
 - Cardio-cerebrovascular
 - Anti-tumor
 - Digestion

Capacity

✓ **Total Capacity in Multi-purpose Workshop**

Apeloa Jiayuan: 367 m³

Apeloa Tospo: 534 m³

Apeloa Jiayuan		Apeloa Tospo	
Vessel Size	Amount	Vessel Size	Amount
100 L & 200 L	5	100 L	20
500 L	16	500 L	25
1000-1500 L	30	1000 L	40
2000-3000 L	94	3000 L	50
5000 L	2	5000 L	55
8000 L	7	8000 L	3
10000 L	2	10000 L	3

Analytical Capabilities

R&D centers

HPLC (Waters & Agilent)

LC-MS

GC (Shimadzu & Agilent)

GC-MS

NMR (300 MHz)

DSC/TGA Others

QC Lab

HPLC

UV-Vis

LOD

Laser Particle

GC

Polarimeter

Sulfated Ash

Size Analyzer

IR

KF titrator

Stability Chamber

(Malvern)

TOC

Microscope

Incubator

Others

Contract Lab

XRD NMR (500 MHz)



Our Star Finished Dosage

- Cefixime (capsule, dispersible tablet)
- Cefdinir capsule
- Amoxicillin and Clavulanate Potassium Capsules
- Cilnidipine Tablets
- Flucloxacillin sodium for injection
- Diisopropylamine ascorbate



Our Star Product

■ API

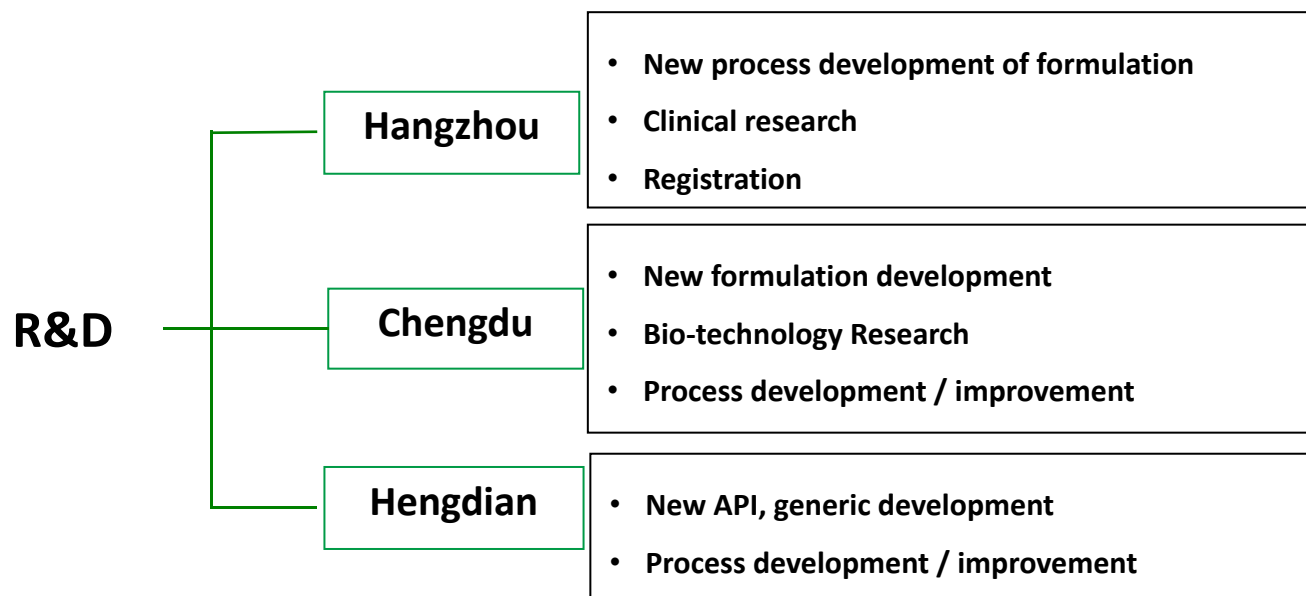
- Bupropion HCl
- Cefixime
- Cefprozil
- Cefdinir
- Florfenicol

■ Intermediate

- PHPG Dane Salt, PG Dane Salt, D-PG
- OTBN



R&D Center



Associated partner: PKU, ZJU, ZJUT, etc.



Hengdian R&D

- National-recognized Enterprises Technology Center
- National Post-Doctoral Work Station
- Academician Workstation
- Develop over 30 products annually
- Own more than 20 product with independent intellectual property rights
- Own 40 invent patents

Expertise

Reaction Type:

★ Chiral synthesis and resolution

Grignard

High vacuum Distillation

Oxidation

★ Fermentation and Enzyme Catalyzed Reactions

★ Fluorination/Halogenation

Cyanogenation

Alkylation

Impurity Study

Polymorphism Study

Temp. range:

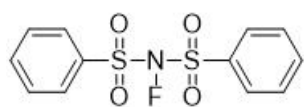
-80~250°C

Pressure range:

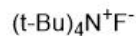
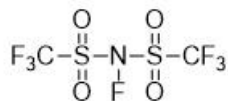
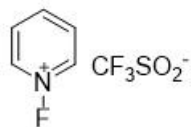
-0.1~5×10⁶ pa



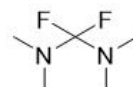
Fluorination



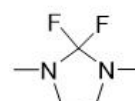
NFSI: 50t/a



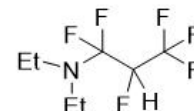
TBAF



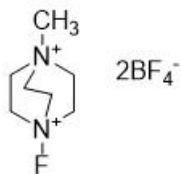
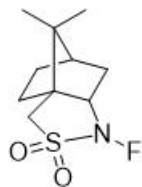
F-urea



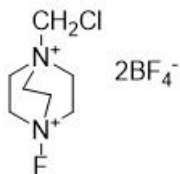
DFI



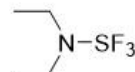
Ishikawa's Reagent



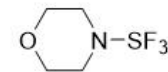
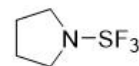
Selectfluor II



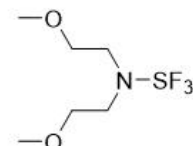
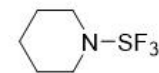
Selectfluor I



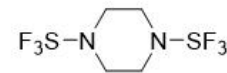
DAST



Morpho-DAST



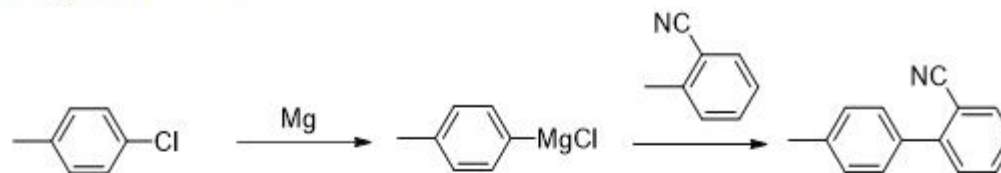
Deoxofluor



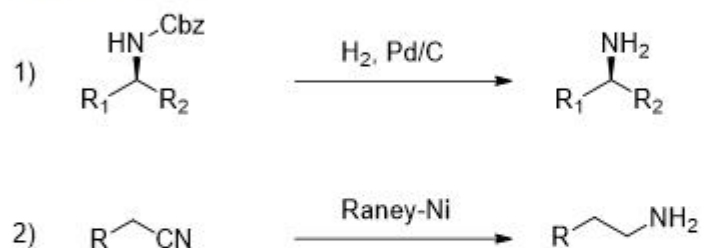


Other technologies

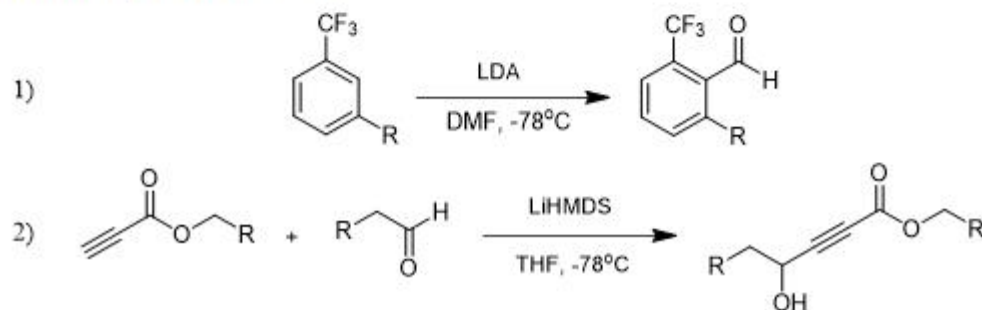
*Grignard Reaction



*Hydrogenation

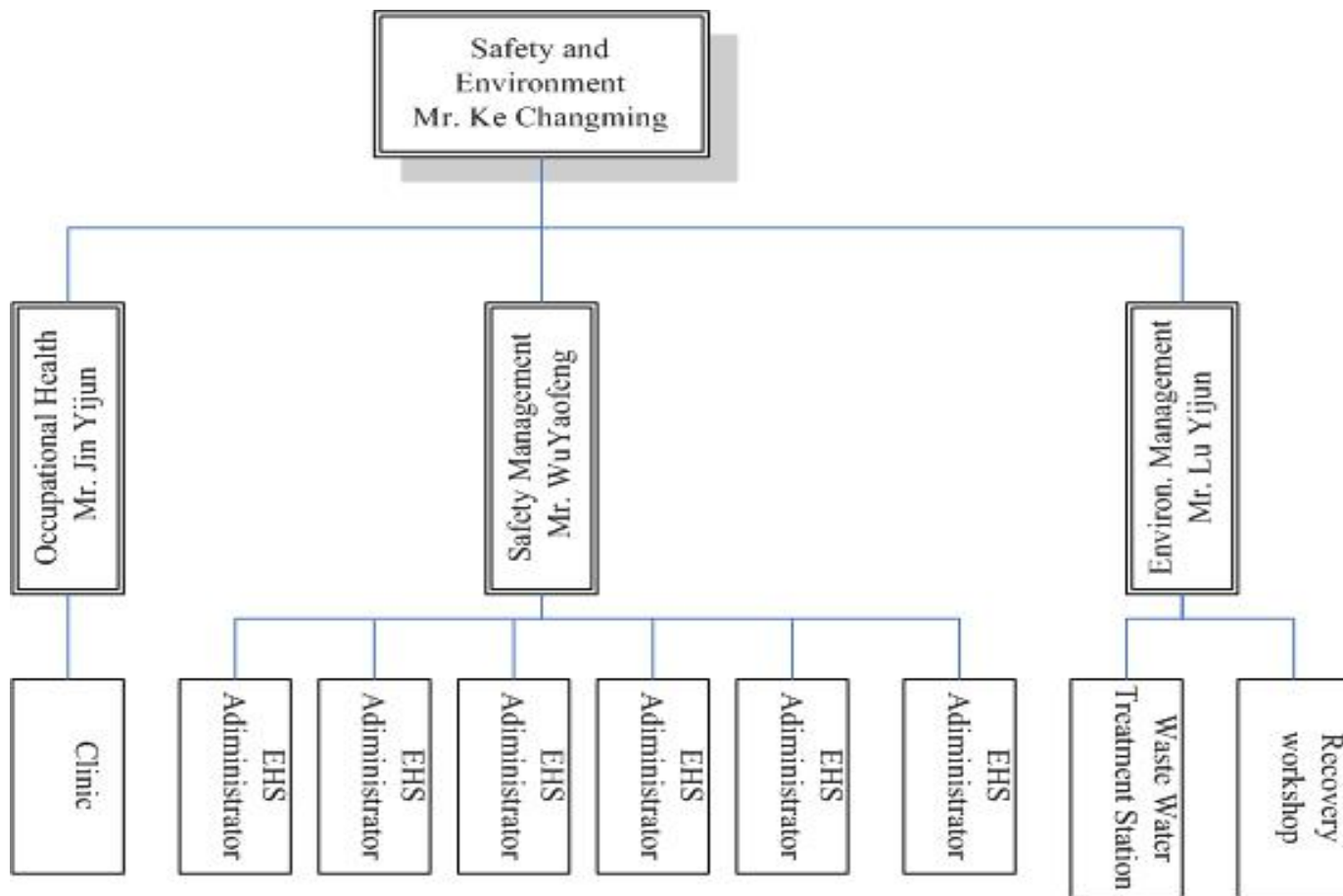


*Low temperature Reaction



EHS System

EHS Organization Chart





EHS Targets

- **No Severe Injury ;**
- **No Major fire and explosion accidents;**
- **No Occupational disease;**
- **Year Rate of slightly wounded cost working day $\leq 0.3\%$;**
- **No Major Environmental Pollution Accident and No Government Warning;**
- **Discharge Waste Gas and Water after Meeting the Standard;**

EHS Management System

- ◆ Spillover control
 - ◆ Chemical management
 - ◆ Special work permit
 - ◆ VOC
 - ◆ LOTO
 - ◆ Accident
 - ◆ PPE
 - ◆ Emergency issue
- ◆ New product
 - ◆ Contractor
 - ◆ Staff training
 - ◆ ...



Environmental Management

The waste water treatment daily capacity: 3000mt

Daily incoming waste water: 2100mt

Releasing standards: COD≤800ppm

Ammonia Nitrogen ≤35ppm



Waste water treatment station





Environmental Management



Incinerator capacity:
300kg/h(solid), 200kg/h(liquid)



**More than 10 suits of waste Gas
treatment facilities at present.**

Safety Management



Cover the sewage tank

当心
CAUTION

维修前，
请断开电源并上锁
DISCONNECT POWER
AND LOCK OUT
BEFORE SERVICING



危险

不准操作

此吊牌及锁具
只准以下人员移除：
姓名 _____
部门 _____
预计完成时间 _____

Lock out

Safety Management



PPE training



Emergency drill

Safety Management



Emergency material

Safety Management

Training



Newcomers: safety education of three-degree level

Staffs: periodically safety training

EHS staff: technical examination



Safety Management

Special Work Permit

Hot Work

Work in high place

Work in Confined Spaces

Excavation Work

Hoisting Work

Circuit Work

Work of Blocking Blind Board

When everything is considered and approved, the operation can be permitted

Occupational Health



职业健康检查表

姓名	性别	年龄	职业	检查项目	检查结果	备注
张三	男	35	司机	血常规	正常	
李四	女	28	文员	血常规	正常	
王五	男	42	工人	血常规	正常	
赵六	女	31	护士	血常规	正常	
孙七	男	25	学生	血常规	正常	
周八	女	38	教师	血常规	正常	
吴九	男	45	农民	血常规	正常	
郑十	女	22	白领	血常规	正常	
冯十一	男	33	工人	血常规	正常	
陈十二	女	27	文员	血常规	正常	
林十三	男	39	司机	血常规	正常	
周十四	女	30	护士	血常规	正常	
吴十五	男	41	工人	血常规	正常	
郑十六	女	24	学生	血常规	正常	
冯十七	男	36	白领	血常规	正常	
陈十八	女	29	工人	血常规	正常	
林十九	男	43	文员	血常规	正常	
周二十	女	26	司机	血常规	正常	
吴二十一	男	37	护士	血常规	正常	
郑二十二	女	40	工人	血常规	正常	
冯二十三	男	23	白领	血常规	正常	
陈二十四	女	32	工人	血常规	正常	
林二十五	男	44	文员	血常规	正常	
周二十六	女	21	司机	血常规	正常	
吴二十七	男	34	护士	血常规	正常	
郑二十八	女	46	工人	血常规	正常	
冯二十九	男	20	白领	血常规	正常	
陈三十	女	35	工人	血常规	正常	

中华人民共和国卫生部制

- Periodically arrange physical examination in Dongyang People`s Hospital and Jinhua centers for diseases control and prevention
- Establish the health records.

Quality System

Health Authority Audits

✓ TOSPO site:

Time	Audit organization	Audit content	
2008.08	SFDA	GMP Audit	APIs
2011.11	Ministry of Agriculture	GMP Audit	APIs for veterinary use
2012.06	SFDA	GMP Audit	APIs (New version GMP)
2012.08	PMDA	GMP Audit	Advanced Intermediates
2013.04	SFDA	GMP Audit	APIs
2014.03	FDA	GMP Audit	API starting material, intermediate and veterinary API

Health Authority Audits

✓ Jiayuan site:

Time	Audit organization	Audit content	
2007.05	FDA	GMP Audit	APIs
2009.01	FDA	GMP Audit	Advanced Intermediates
2009.12	SFDA	GMP Audit	APIs
2012.01	SFDA	GMP Audit	APIs (New version GMP)
2012.05	FDA	GMP Audit	APIs
2012.08	SFDA	GMP Audit	APIs
2014.03	Korean FDA	GMP Audit	APIs
2014.05	FDA	GMP Audit	APIs

All of the audits passed without 483.

Quality Assurance

Main Responsibilities

- Material Release and Rejection
- Documentation Management
- GMP Training
- Supplier Management
- Change Control Management
- Deviation Management



- Validation Management
- Customer Complaint Management
- Stability Management
- Reserve Samples Management
- Audit Management
- Quality System Review

Quality Control

Main Responsibilities

- Test of raw materials, intermediates and final products
- Stability Test
- Environmental Monitoring
- Purified Water Monitoring



- Standards Management
- Calibration





Main SMPs

- Documentation Management
- Suppliers Audit
- OOS
- Deviation and CAPA
- Change Control
- GMP Self-audit
- Stability Test
- Validation Management
- Customer Complaint
- Recalls and Returns

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- Established Year: 1990
- Site Area: 166,500 M²
- Employees: 810
- Product Area: Intermediates, Veterinary, Formulation, CMO
- Regular product: Cephalosporin intermediates

- Established Year: 1991
- Site Area: 477,000 m².
- Employee: Around 2400
- Product areas: APIs, Advanced intermediates, CMO
- Regular product: Metoprolol, Bupropion, etc.

Zhejiang Apeloa Kangyu Pharmaceutical Co., Ltd

- Established Year: 1993
- Site Area: 460,000m²
- Employee: Around 1300
- Product areas: Bio-fermentation, chemical drugs, Intermediates
- Regular product: Colistin sulfate, etc

Thank You!

