Late Clinical Trials in China

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Biography

- Huafang LI, M.D., Ph.D., Chief-Psychiatrist, executive director of Institute for clinical trial and Department of psychopharmacology and biochemistry, Shanghai Mental Health Center (SMHC), Shanghai Jiao Tong University School of Medicine.
- Dr. Li graduated from Shanghai Medical University and has worked in SMHC since 1990. She is major in clinical psychopharmacology and biomarker research of psychosis disorders. She has published more than 150 related papers. As the PI, she has conducted more than 80 clinical trials of various psychotropics, including global trials. Since 2008, as the PI, she has been being in charge of the “National Major Project for IND” (“Clinical tech-platform for evaluation of new drug in psychiatry”) in China and is dedicating to the development and improvement of clinical trials in psychiatry.

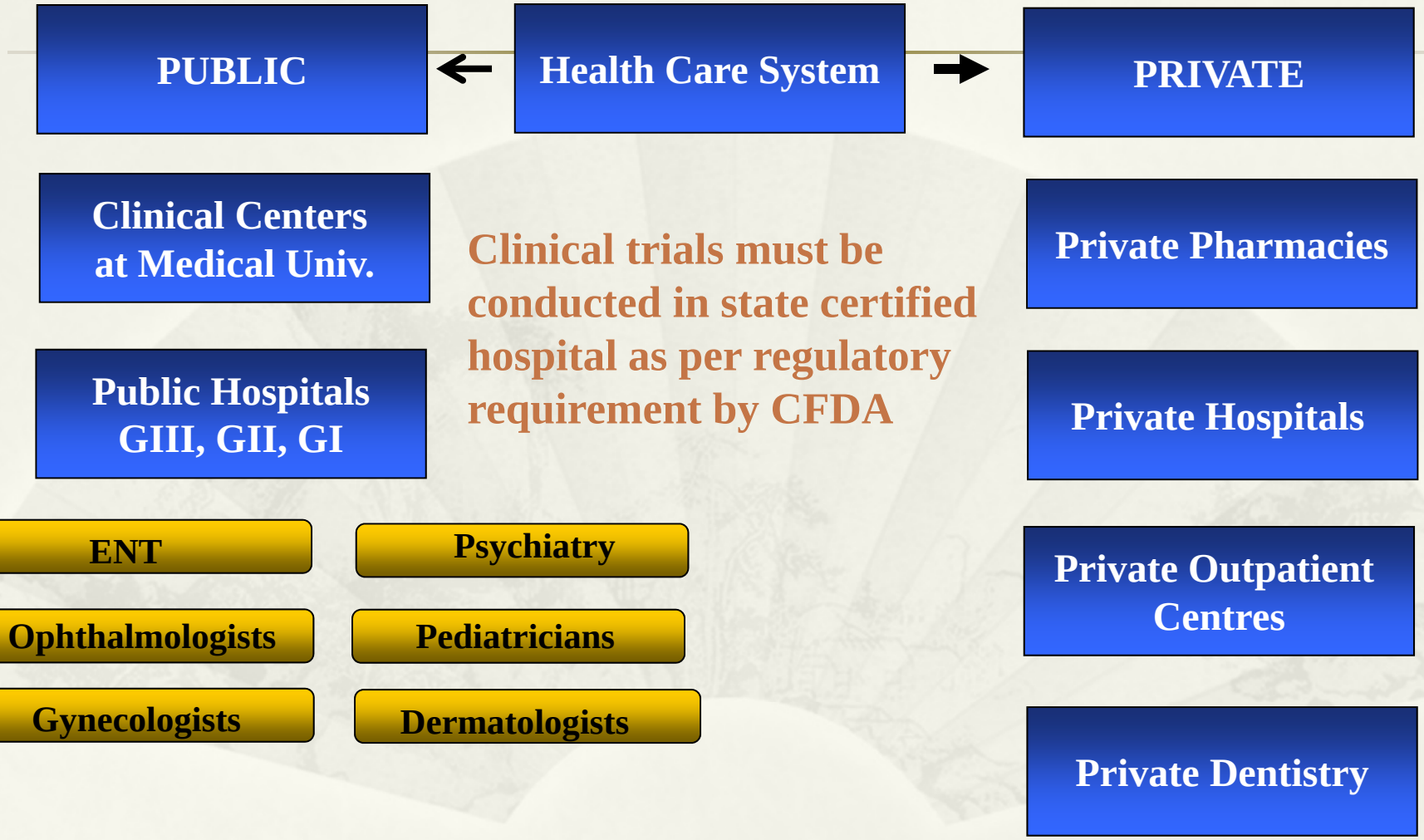
Disclosure

- Chief psychiatrist of Shanghai Mental Health Center
- Consultant of AZ, Eli Lily, Boehringer Ingelheim, Roche, Janssen, Pfizer and China domestic pharmaceuticals.
- No interest with the conference

Contents of the Presentation

- **Overview of Health Care System in China**
- **Regulatory Requirements for State certified sites**
- **One Stop Solution---The role of Administrative Office in the site**
- **Some of Details to Consider** (feasibility, study team, IRB, consent issues, patient recruitment, bias in evaluation).
- **Opportunities and Challenges when conducting global trials in China**

Overview of Health Care System in China



Number of Accredited Sites*--Major Therapeutic Areas

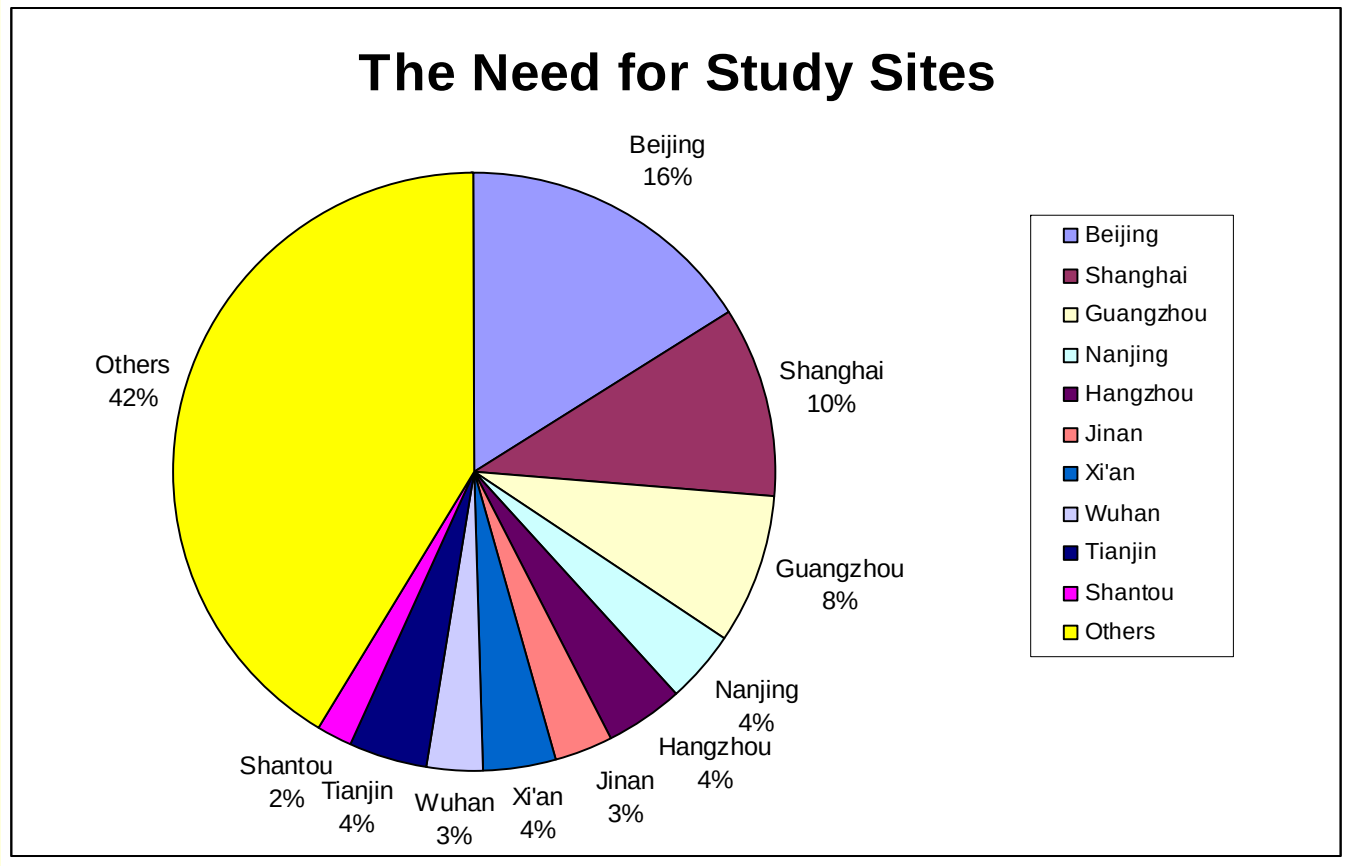
Therapeutical area	Number of sites
Cardiovascular	300+
Neurology/Psychiatry	240/ 35
Respiratory	300
Oncology	269
Endocrinology	221
Hemotology	158
Anti-infection	95
Hepatopathy	92
Rheumatology/Immunology	53

* 2013, 475 approved sites (hospital) for CT

The main certified sites for psychotropic clinical trials in China

1	中国人民解放军第四军医大学第一附属医院	1	20040010	Xi an
2	河北省精神卫生中心（河北省第六人民医院）	3	0033	
3	同济大学附属同济医院	3	0041	Shanghai
4	昆明医学院第一附属医院	3	0045	
5	哈尔滨医科大学附属第一医院	3	0050	
6	湖南省脑科医院	5	0080	
7	中南大学湘雅二医院	7	0110	
8	南京脑科医院	7	0116	Nanjing
9	西安市精神卫生中心（西安市第十医院）	10	0148	Xi an
10	浙江大学医学院附属第一医院（浙江省第一医院）	10	0150	
11	武汉大学人民医院（湖北省人民医院）	10	0155	
12	四川大学华西医院	13	0176	
13	中山大学附属第三医院	14	0181	
14	浙江大学医学院附属第二医院	15	0193	
15	首都医科大学附属北京安定医院	18	0224	Beijing
16	山西医科大学第一医院	18	0225	
17	西安交通大学医学院附属第一医院	20	0241	Xi an
18	上海市精神卫生中心	21	0247	Shanghai
19	北京回龙观医院	21	0250	Beijing
20	广州市精神病医院（广州市脑科医院）	23	0281	Guangzhou
21	天津市安定医院	23	0287	
22	中国医科大学附属第一医院	24	0297	
23	无锡市精神卫生中心	25	0302	
24	北京大学第六医院/精神卫生研究所	25	0305	Beijing
25	河南省精神病医院	28	0335	
26	广东省人民医院	28	0338	Guangzhou
27	武汉市精神卫生中心	36	410	
28	河北医科大学第一医院	36	414	

Number of Accredited Sites -- Geographic Distribution

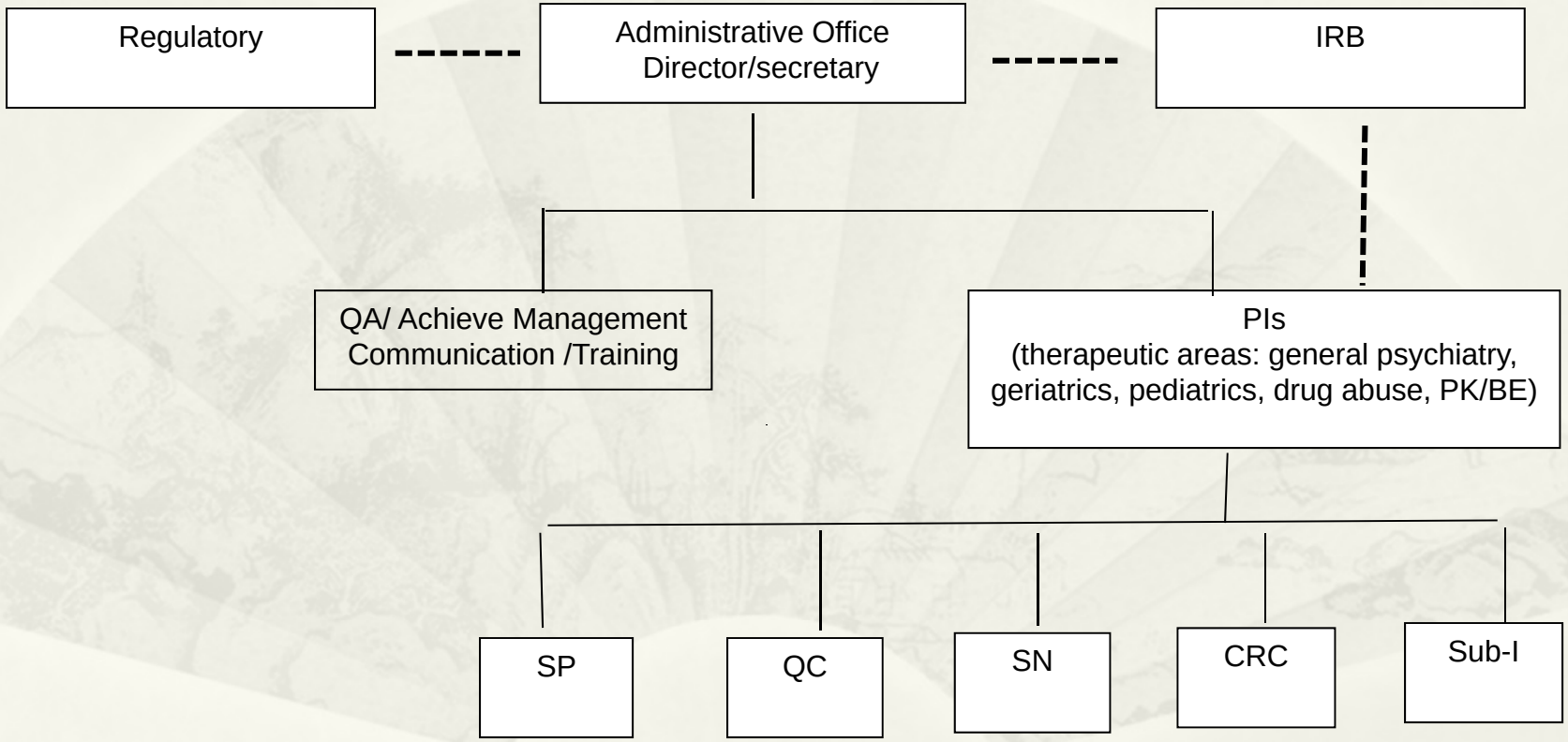


*www.sfda.gov.cn; Excludes institutions dedicated to traditional Chinese medicines

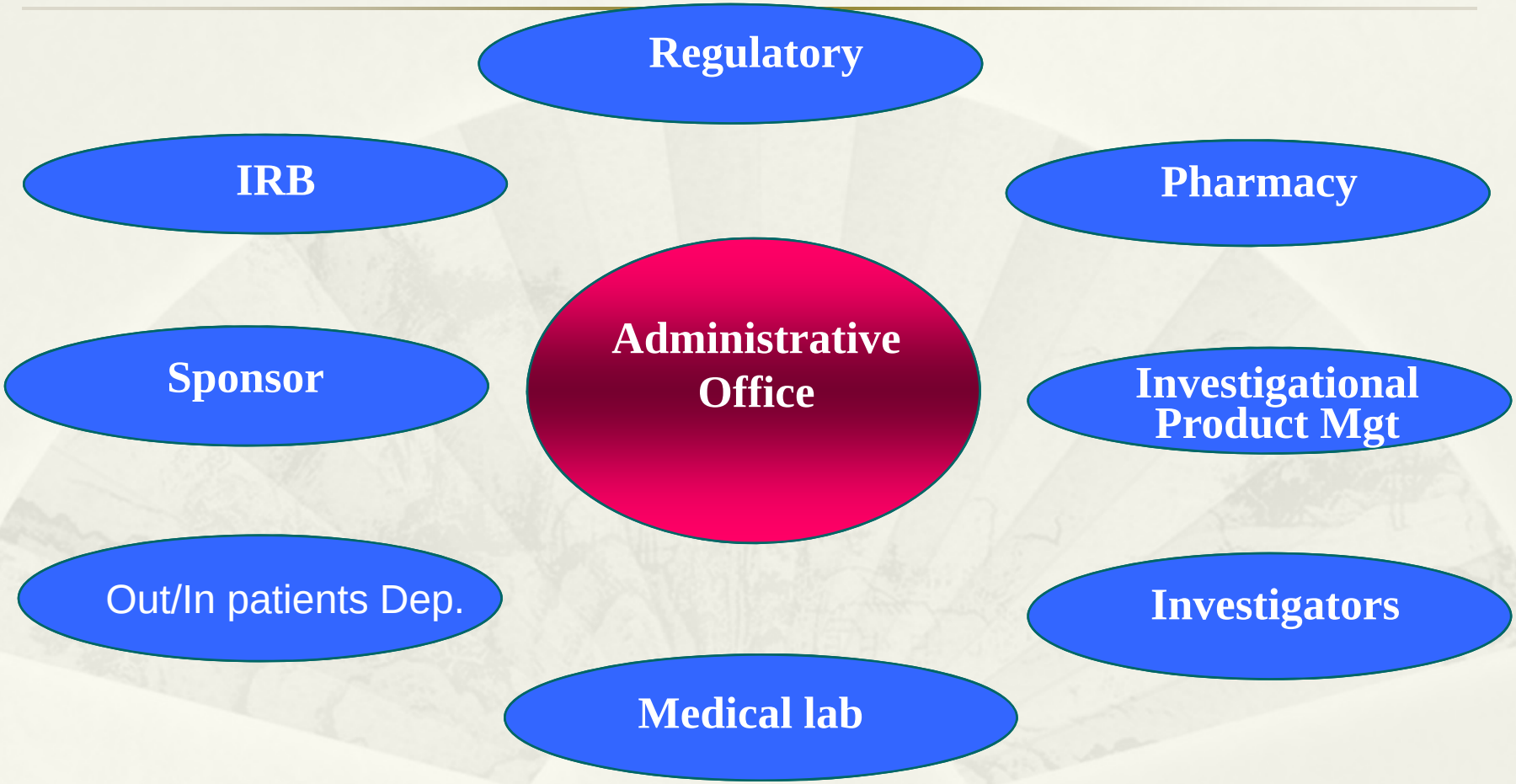
Process After the CFDA Approval for a Clinical Trial

2-6 weeks in average

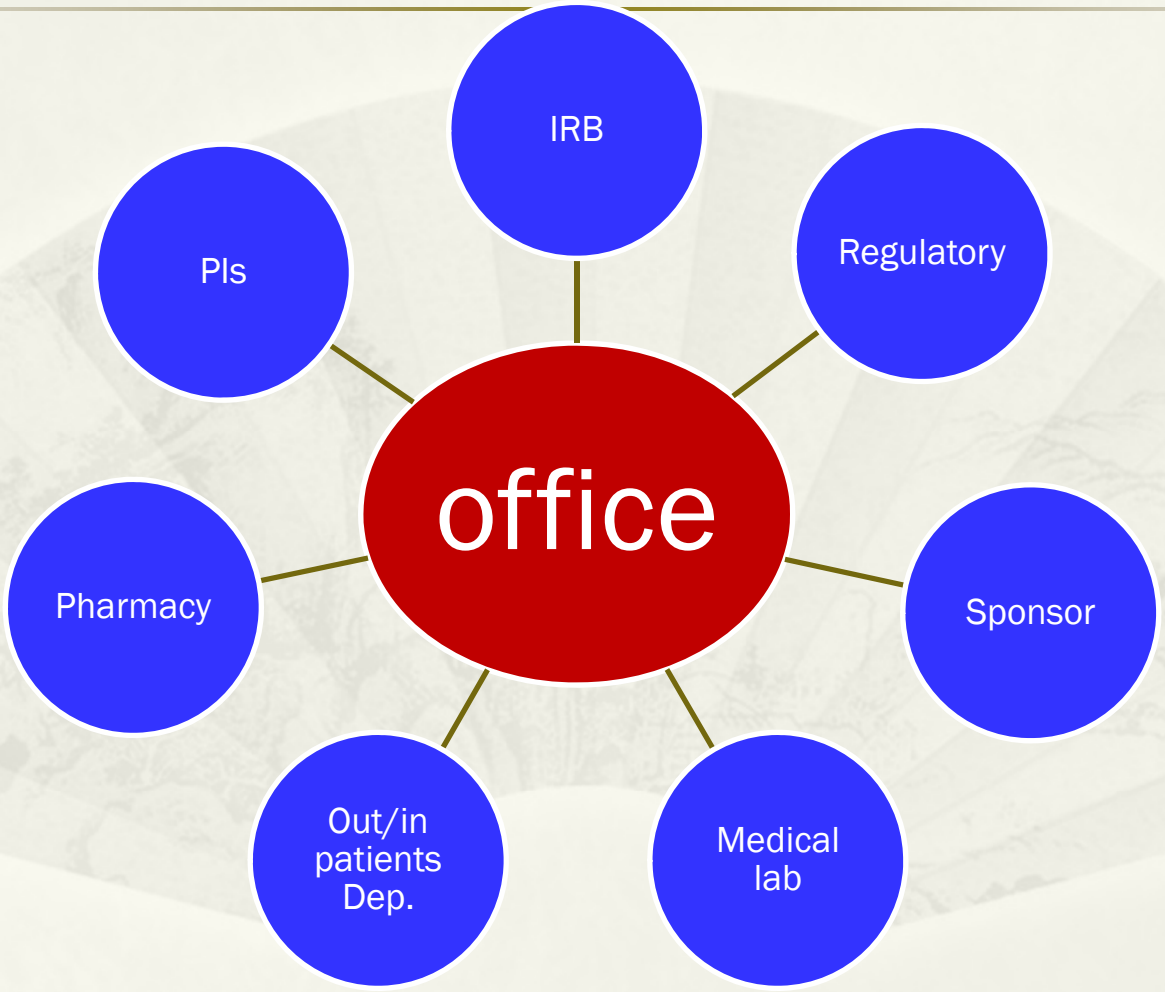
Organogram of Administrative Office and FTE



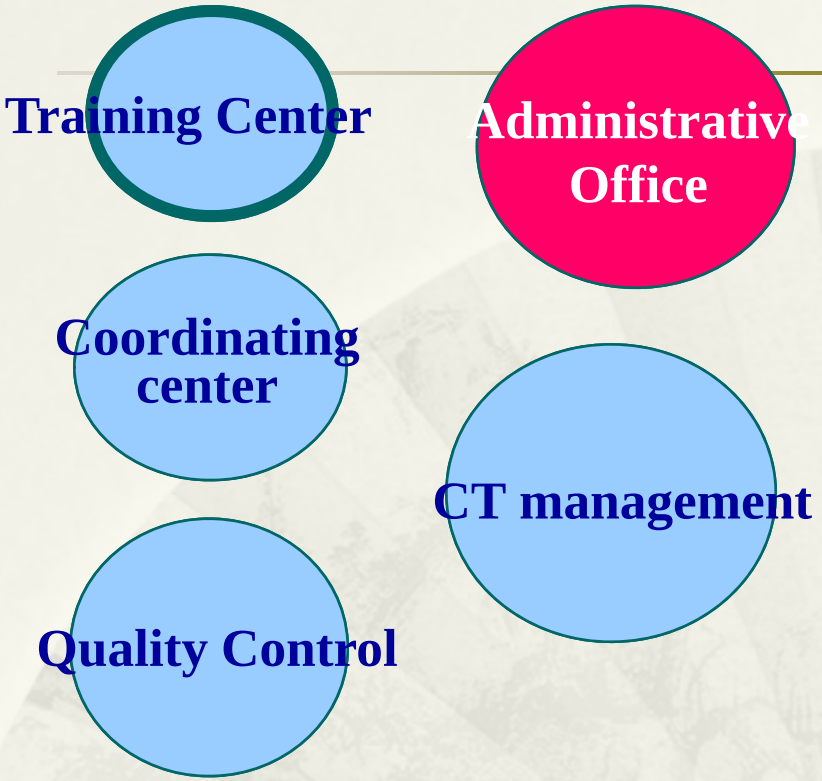
One Stop Solution: Role of administrative office



One Stop Solution: Role of administrative office



One Stop Solution: Role of administrative office (cont)

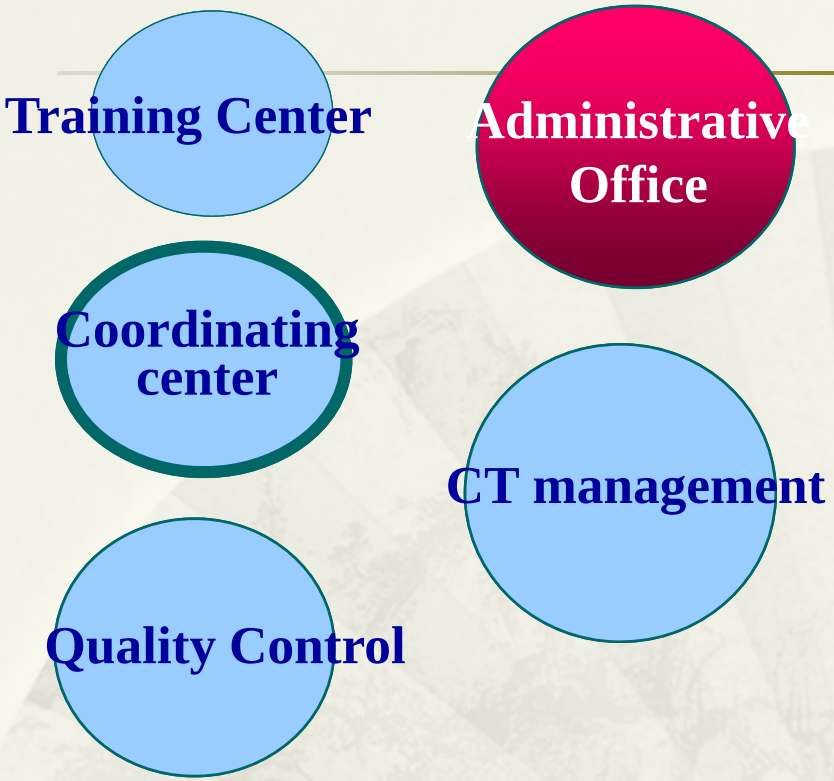


Training Center: (with PIs of therapeutics areas)

- Investigator/study coordinator/Trial staffs（GCP,SOP）
- Project specific training
  - Protocol
  - ICF
  - EDC
  - IVRS
  - Central ECG/Medical imaging/Lab
  - Psychometric rating scale et al.

* GCP training is sometimes organized by other training centers (eg, CFDA training center, and certificate of attendance is issued by CFDA), which usually takes 2 to 4 weeks, all investigators must have the certificate of GCP training.

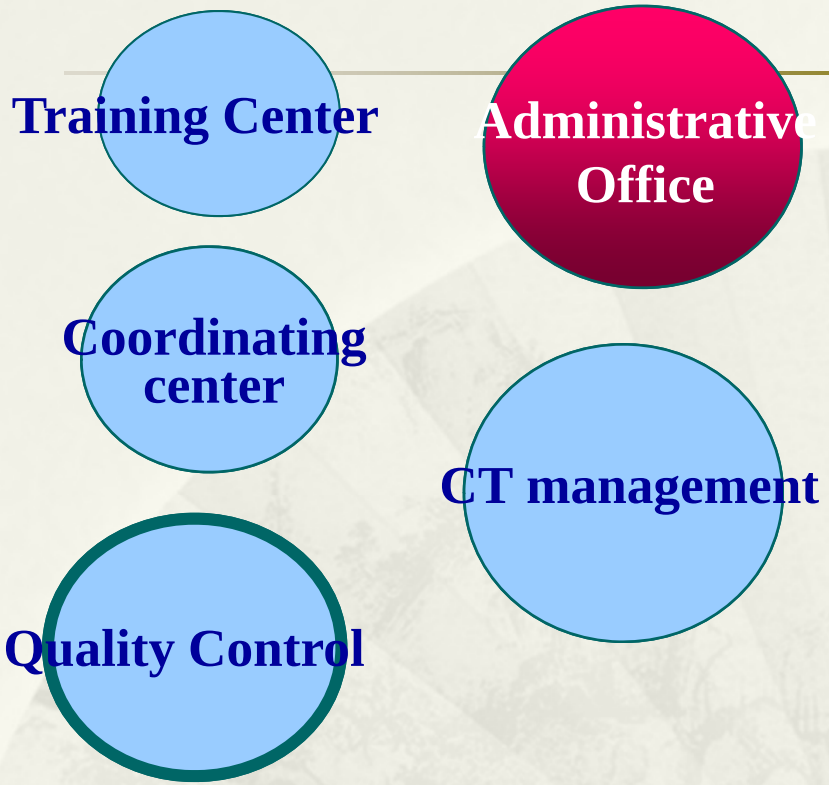
One Stop Solution: Role of administrative office (cont)



Coordinating Center: : (with PIs of therapeutics areas)

- Feasibility study
- Coordinating with sponsor, CRO and other venders
- Participating department (pharmacy, lab, other sites, etc)
- Leading site (sub PI) or participant site?
- Auditing, SIV and Close-out meeting

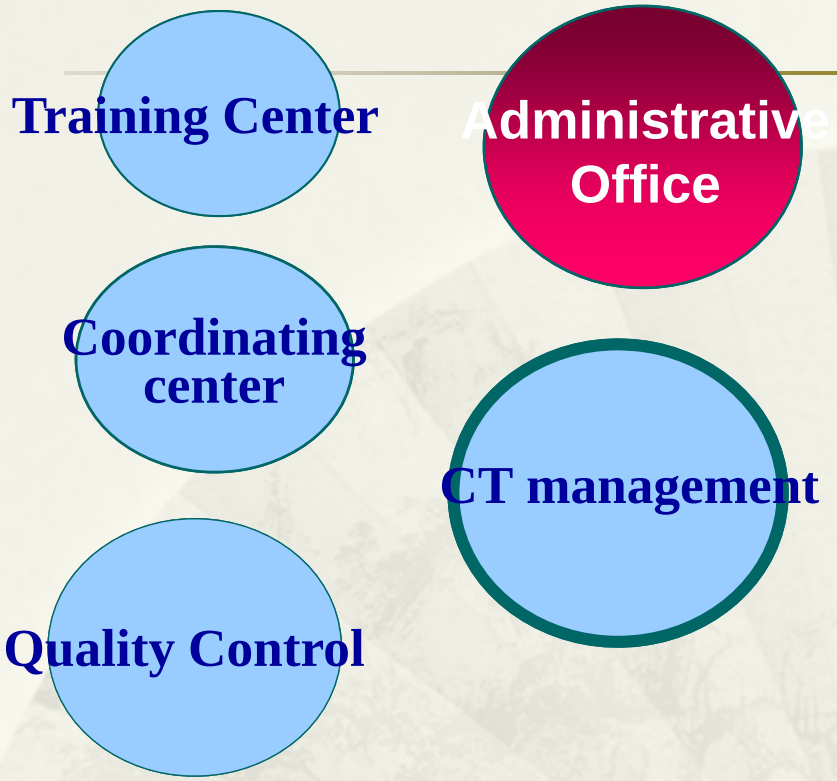
One Stop Solution: Role of administrative office (cont)



Quality Control:

- ICF signature, protocol compliance,
- AE/SAE reporting
- Study drug management
- Source data verification, etc.
- Check the study periodically
- Potential and existing problem
- Communication with sponsors, venders, other investigators, further training, etc
- Collecting feedback from sponsor

One Stop Solution: Role of administrative office (cont)



CT Management:

- Competing study, indication, subject resources, PI and manpower allocation)
- PI selection (background, experience, time, et al)
- Assisting PI to organize clinical trials
- IRB submission
- Subject recruitment
- Study grand negotiation/ Contract Management
- Timeline management
- Document Archive
- Study material preparation
- Sample collection

Some of the Details to Consider: Feasibility Study

- PI Selection Strategy
- IRB Submission (centralized IRB review?)
- Recruitment Strategy
- Blood Samples Export
- Contract Management
- Study Grant Management and Negotiation

Feasibility Study (cont)

- First step in study planning
- Determine the most suitable PI
- Pre-identify potential PI in therapeutic area and set up database
- Assess the workload (trials, clinic consultation, lecturing, other researches)
- Realistic recruitment projections
  - Details of how they present
  - Availability of patients
  - Inclusion/exclusion criteria & study design review
  - Competing trials

Feasibility Study (cont)

- Identify potential logistical problems
- Potential ethical obstacles
- Assess presence of competing studies
- Assess costs and timelines
- Assessment of investigator fees

Turnaround time: 2 to 4 days

Feasibility Study (cont): Challenges

- Repetition information (CROs for same or similar CT)
- General information (inpatient number, how many out pts, the incidence of disorders…)
- Without specific protocol, only the synopsis
- Without the operation process information, vendors? training?
- Without information about the budget
- Qualified CRO? CRA?

PI /Study Team Selection Strategy

- Minimal Requirement for PI: MD or Chief Physician (psychiatrists)
- Clinical research coordinator (CRC): resident or attending physician or study nurse
- Sub-I: physician
- Rater: physician
- Investigating drug management: pharmacist or nurse
- QC: independent to the CT
- Training Record (GCP, SOP etc)

IRB submission

Sequential Submission:

* Submission to IRB usually after approval by CFDA

The Mode of IRB Approval:

* Lead PI site IRB approval: accepted by other participating sites.
* All participating site IRB approval.
* Centralized IRB review?

As per specific requirements in site (usually occurring in registration trials or domestic trials)

Recruitment Strategy

Referral Strategy:

- Internal referral/in-house advertisements
- Understanding of CT in colleagues other than investigator
- External referral from other psychiatrists

Radio/TV advertisements are NOT encouraged !

ICF

- Public common sense of CT
- Relationship between pts and physician
- Where pts come from?
- Insurance?
- Compensation?
- Education level?
- Age?
- Indication?
- Protocol design? Placebo?
- Other medication for the indication?
- In/out pts?
- Description of AE in ICF

Evaluation bias?

- Diagnostic criteria?
- Baseline mood and behavior?
- Relationships? Family/social
- Communication: expression, gesture, dialect...
- Social support?
- Rater: psychiatrist/psychologist?
- Training process?
- Work load? Enough time?
- Rating scales: English/Chinese version?
- Demographic data at baseline? Age? Course? Acute or chronic? Severity? Education? Living status: single, married, divorced?

Blood Sample Export

Export of Blood/ Genetic Sample:

* Permission required from Office for Human Genetic Resource (OHGR)
  - This office is jointly managed by China Ministry of Science and Technology and Ministry of Health
  - This office is authorized to review and approve on the exportation of Chinese genetic resource like human organ, tissue, cell etc.
  - Review meeting is held on quarterly basis.

Export of Plasma/Serum:

weeks to obtain (ICF,

Contract/Study Grant

- Contract Management: Sponsor contact is accepted
- Study Grant Management and Negotiation
  with administration office and PI
- Financing: administration office, finance department of the site (hospital)

Opportunities and Challenges

Opportunities :

- Large Patient Pool --Many hospitals of grade III class A) in China have a large subject pool (eg, Shanghai Mental Health Center has 2000 inpatient beds, 2000+ outpatients/per day.
- State-certified sites warrant consistent standards with supportive, qualified medical infrastructure.
- Organization structure (e.g., administrative office) and practice in site are similar throughout China.
- Low cost?
- As per international standards, the central lab, logistic service provider, EDC, IVRS, central ECG and central imagine are available in China.
- More and more opportunities to join early phase trials.
- “National Key Project for IND” to support about 50 famous sites to optimize the global technique of CT (from 2008~) (these sites and their therapeutic areas, PIs are the best through China)

Opportunities and Challenges

Challenges:

- A good feasibility study may speed up recruitment rate
- Long regulatory approval process limit the chances to participate the global trials.
- As the CT is a new industry in China, public awareness for clinical trials has space to improve.
- Culture/language: Source docs are in Chinese.
- Medical system (training, diagnosis, quality, insurance).
- Blood sample/ Genetic sample transportation to overseas is still controlled by the government, the application and approval is tedious and complicated.
- Shortage of qualified/experienced PI, CRC, raters.
- Development of CRO is unbalanced.
- Shortage of qualified CRA and affect the quality of CT.
- CRA team is unstable.

Q & A

THANKS FOR YOUR ATTENTION!

谢谢！