China FDA's New Regulations and their Impacts on Data Management in China

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声明：此演讲只代表个人对演讲项目的理解。与本人所有任职单位以及培训组织者的观点立场无关

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New Regulations since 2015

Date	Announcements & Decree	
04-May-2016	总局关于发布化学药品新注册分类申报资料要求(试行)的通告(2016年 第80号)	Submission package requirement
29-Jul-2016	总局关于发布临床试验数据管理工作技术指南的通告(2016年第112号)	DM technical guideline
29-Jul-2016	总局关于发布药物临床试验数据管理与统计分析的计划和报告指导原则的通告(2016年第113号)	DMP/DMR guideline
29-Jul-2016	总局关于发布临床试验的电子数据采集技术指导原则的通告(2016年第114号)	EDC technical guideline
02-Dec-2016	总局办公厅公开征求《药物临床试验质量管理规范(修订稿)》的意见	China GCP
18-May-2017	总局关于发布仿制药质量和疗效一致性评价研制现场核查指导原则等4个指导原则的通告(2017年第77号)	BE on-site inspection guideline
24-May-2017	总局关于药物临床试验数据核查有关问题处理意见的公告(2017年第63号)	punishment and petition of inspection findings
30-May-2017	药品审评中心关于征求《药品电子通用技术文档结构(征求意见稿)》和《化学仿制药电子通用技术文档申报指导原则(征求意见稿)》意见的通知	eCTD guideline
10-Oct-2017	《国家食品药品监督管理总局关于调整进口药品注册管理有关事项的决定》（国家食品药品监督管理总局令第35号）	Accept clinical data outside China

DM Under CFDA's New Regulations

DMP(CFDA Announcement #80 in 2016)

- NDA
- CTA

DMP(CFDA Announcement #113 in 2016)

- China Specific: Blind Review Decision

DMR (CFDA Announcement #113 in 2016)

- China created

Contents of CFDA DMP

- Study Overview
- Roles & Responsibilities
- Type, format, source and flow of trial data
- Data capture system, data management system, data integration platform and data quality assurance and quality control systems
- Data management activities and its operation procedures
- Data management documentations
- Blind Review Decision

Related Data for “Blind Review Meeting”

Major Protocol Deviation

Major PD criteria

Prior to FPI, Medical, Biostats, Clinical pharm, Operation and DM confirm in writing

- *Inclusion/ exclusion Criteria*
- *Prohibited Therapies*
- *Treatment Compliance*
- *Developed withdrawal criteria but not withdrawn*
- *Other:*
  - *Time window of PK blood drawn*
  - *Time window of ECG measurement*
  - *Fasting status*

Related Data for “Blind Review Meeting” (2)

- Adverse Event listing
- Concomitant Medication listing
- Data listing of early termination
- Data listing of Abnormal lab data with clinical significant

Blind Review Practices (Domestic Enterprises)

Blind Review Meeting

Sponsor

Attend the meeting from beginning to the end,
know the progress of the trial data and decisions made by PI and biostats

Leading PI

1) Determine severity of protocol deviations, as basis of FAS, PPS datasets
2) Review Concomitant Medication listing
3) Review Safety data

CRA

1) Explain to the questions about site performance
2) Provide source documents

DM

1) Provide further details about query generation and resolution if there are questions from the meeting
2) Prepare for DBL

Biostats

1) Based on discussions with PI, decide FAS datasets and prepare “blind review decision”
2) Prepare final SAP

Define Populations in Statistics Analysis (MNC)

NO terminology called “Blind Review” OR “Blind Review Decision”

Similar Activities: Determination of FAS and PPS data sets

Activities owner : Biostatistician

Supporting functions: Medical, Operation, DM and SAS programming

Activities time: “On going”

General Practices of Identification Bio-statistical Population (MNC)

Define populations in Statistics Analysis

Investigator Answer queries from Medical, DM, Biostats

Medical
Review and confirm query generation and resolution;
Review and confirm data of major PD
Support FAS and PPS dataset review

CRA
Update on source data verification
Communications with investigational sites

DM
Collect, clean and integrate data
Provide listings per biostats request

Biostats Based on SAP to determine FAS, PPA datasets

Contents of CFDA DMR

Report key timepoints of major DM activities (DMP)

Summarize DM activities (DMP)

Roles and responsibilities of DM participants (DMP)

Outcomes of DM quality control activities (New)

Report results of inspection (New)

Data Query Status & External Data

Chapter	DMR	DM documents
5. Data Cleaning 5.1 Query Status	Data Cleaning 5.1Query Status (dataset domain with # of queries; High query frequency and reasons of question produced.	EDC/CDMS - Reports
5.2 Query Management	5.2 Query Management # of days of a query occurred to closed; Days of Midian ; Range of days	EDC/CDMS - Reports
5.3 Major problem in query management	5.3 Major problem in query management List problem types, clinical site information, # of query, days pf query occurred, reasons.	EDC/CDMS - Reports Information from CRA
7 SAE Reconciliation	7 ． SAE Reconciliation # of SAE， # of related to study drug ;Frequency of SAE Reconciliation ， # of SAE did not pass reconciliation (information list)	DMP
8. External Data Management	8 ． External Data Management (Name of external data External data provider information External data transfer agreement with version control information, transfer frequency and methods. If there are blinded data, provide blinded data management rules and process. External data reconciliation reports.	DMP

Data Quality Assessment and Audit

Chapter	DMR	DM documents
9. Data Quality Control and Audit 9.1 Data Quality Assessment	9. Data Quality Control and inspection 9.1 Data Quality Assessment Based on actual QC processes: list planned QC activities, planned times / volumes vs completed times/volumes. If there is difference, provide reason and explanations.	DMP EDC/CDMS Reports Data Quality Control Plan Protocol Deviation Documents Information from CRA
9.2 Data quality self inspection	9.2 Data Quality self inspection Based on actual QC processes: list QC activities, # of subject been assessed, Method of choose Subject for assessment; # of error of key data assessment, Error rate. # of error of other data and error rate	DMP
9.3 Audit Data management	9.3 Audit DM (Follow DM audit times. List audit organization. Full information of issues fund by audit and CAPA. Audit Report.	Audit/Inspection plan Audit/Inspection agenda Audit/Inspection report CAPA Plan and report Any Data Management related Audit/Inspection key documents

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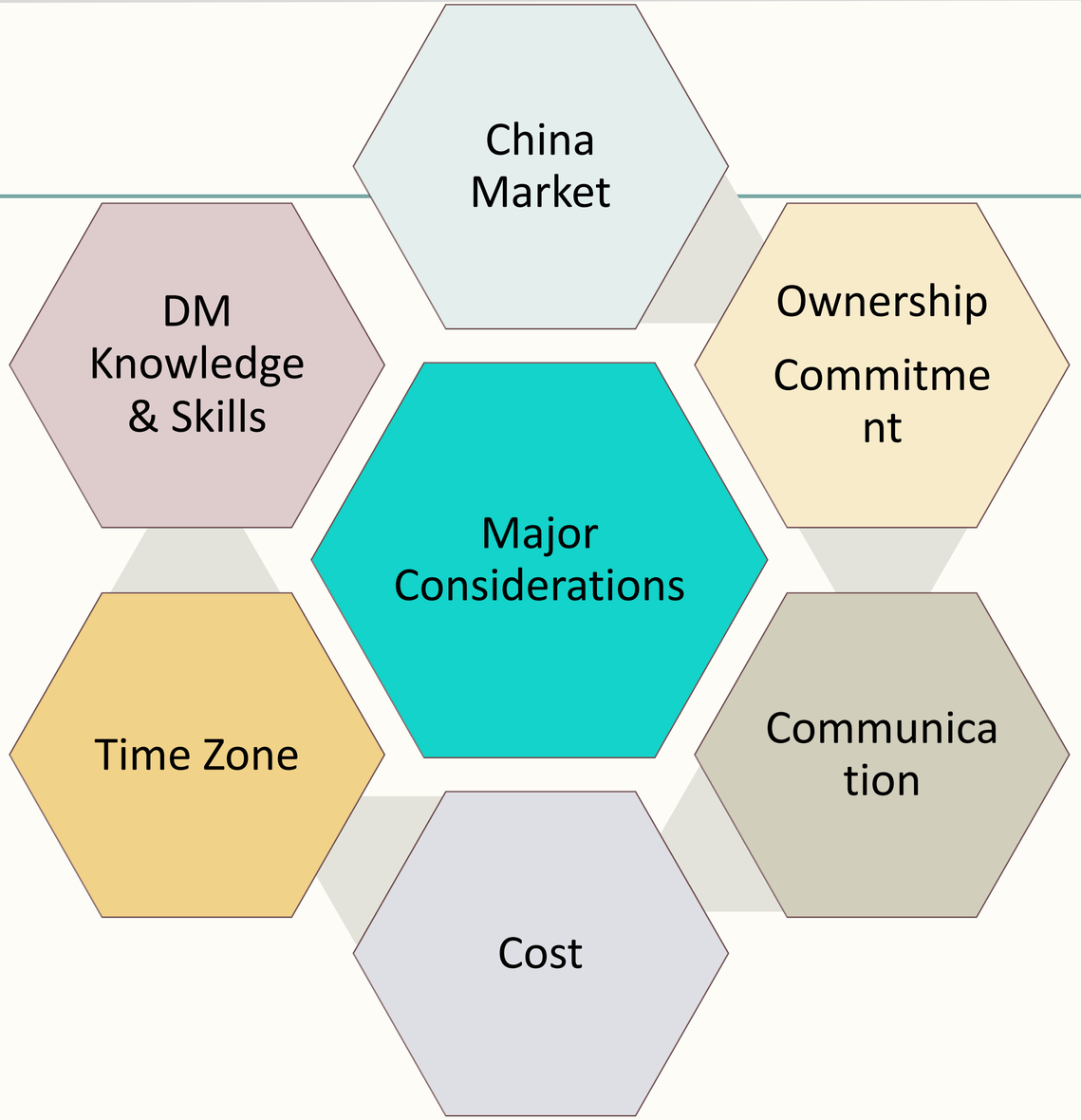
CFDA Decree #35 in 2017

- No CFDA verification required for a clinical site
- Support clinical sites, Medical schools and clinical research institutions conduct clinical trials
- Improve and perfect Ethic Committee system
- Improve efficiency of EC review /Approval process
- Optimize CTA review/approval process
- Accept clinical data that produced outside China
- Support Innovative clinical research

Position of MNC Data Management in China



Position of MNC Data Management in China

■China Only

- E2E knowledge + QC skills + PM
- Drug development (clinical trial) knowledge
- Various TA knowledge
- DM skills to support Clinical Development, Medical Affair, IIS ...
- Regulatory requirements /China submission knowledge (DMP/DMR. P21, eCDT ..)
- Inspection

➢ Small size group

➢ Work with CRO

□ Cost

□ Job market competition

Position of MNC Data Management in China (2)

China Only

- ~~E2E knowledge + QC skills + PM~~
- Drug development (clinical trial) knowledge
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- Inspection

➢Small size group

➢Work with CRO

☐Cost

☐Job market competition

Internal CRO

- Jr. - middle level – from 0 year exp.
- Simple trainings
- Not much English needed
- Ownership/ commitment
- 2nd tier cities

☐Labor intensive work

☐Career path

☐Engagement

☐Time zone

Position of MNC Data Management in China (3)

■China Only

- ~~E2E knowledge + QC skills + PM~~
- Drug development (clinical trial) knowledge
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- Regulatory requirements /China submission knowledge (DMP/DMR. P21, eCDT ..)
- Inspection

➢Small size group

➢Work with CRO

☐Cost

☐Job market competition

●**Global regional team**

- ~~Sr. level - Same work scopes as global peris~~
- Ownership/ commitment
- Talent development

☐E2E Knowledge and skills

☐Fluent English

☐Time zone

☐cost

☐Local pharm Competition

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