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Considerations for Standard Library Development of Data Collection in Vaccine Trial

Presented by Yazhi Wang, Director of Clinical Data Management,
SDM Bio Service Inc.

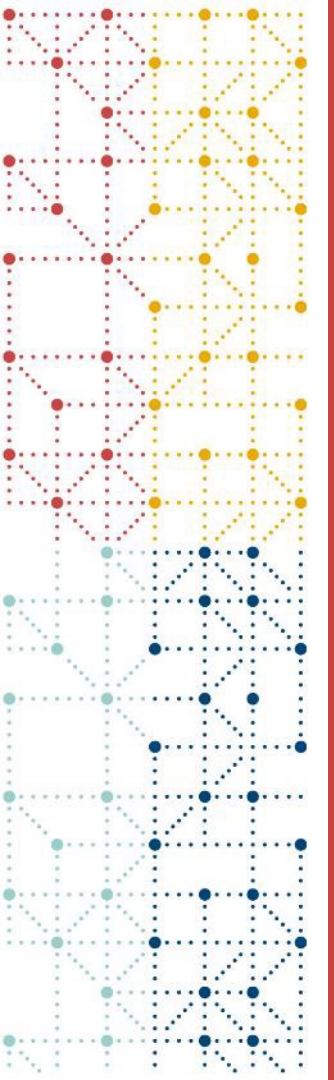
Meet the Speaker

Yazhi Wang

Title: Director of Clinical Data Manager

Organization: SDM Bio Service Inc.

Yazhi Wang has been working in clinical trials for 13 years, including 8 years in GDMS of MSD. She has participated in multiple global and local trials including vaccines (Gardasil 9, Gardasil, Rotateq, Zostavax), oncology, infection disease, diabetes, etc. Currently she is working in SDM Bio Service Inc, specializing in data management of vaccines trials. In June 2021, She established data management department, completed the construction of training, SOP, vaccine standard library, metrics, quality control, and supported more than 60 global and local vaccine trials with DM team.

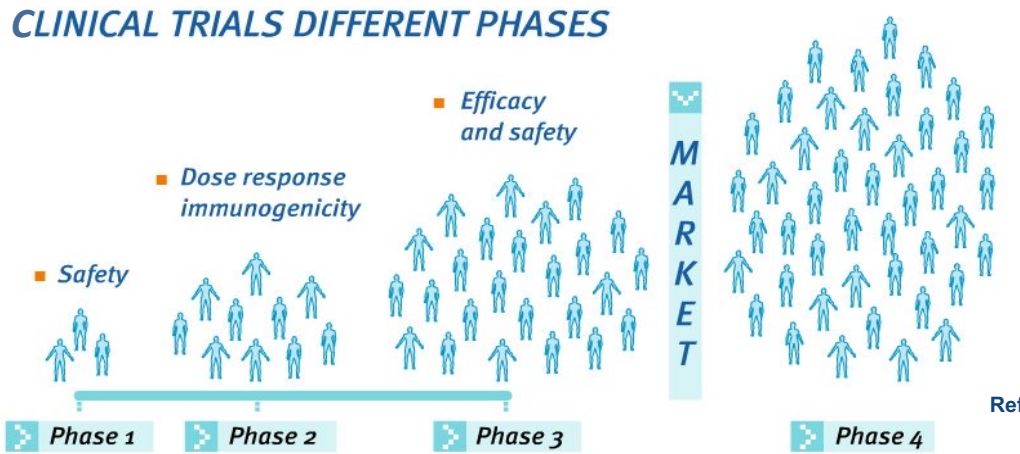


Agenda

1. Introduction of Vaccine Trial
2. Considerations of Data Collection in Vaccine Trial
3. Standard Library Development and Maintenance

Introduction of Vaccine Trial

Introduction of Vaccine Trial



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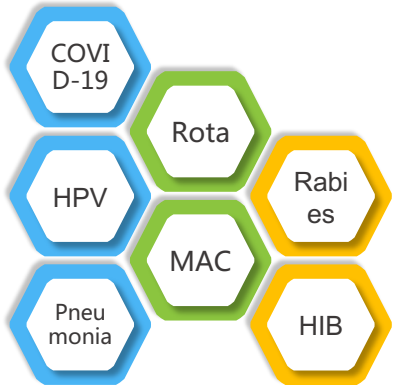


- **Phase I** focuses on the observation of **safety**, and the observation subjects should be **healthy adults**. Vaccines targeted at children and infants should be administered in the order of adults, children, and infants.
- The purpose of **Phase II** trials is to observe or evaluate whether the vaccine achieves the expected effect **(usually referred to immunogenicity)** and general **safety** information in the target population.
- **Phase III** trials are designed to fully evaluate the protective **efficacy and safety** of the vaccine, which is the basis for registration approval.
- **Phase IV** clinical trial is a comprehensive evaluation of the **safety and efficacy** of the vaccine in the actual population after registration and marketing.

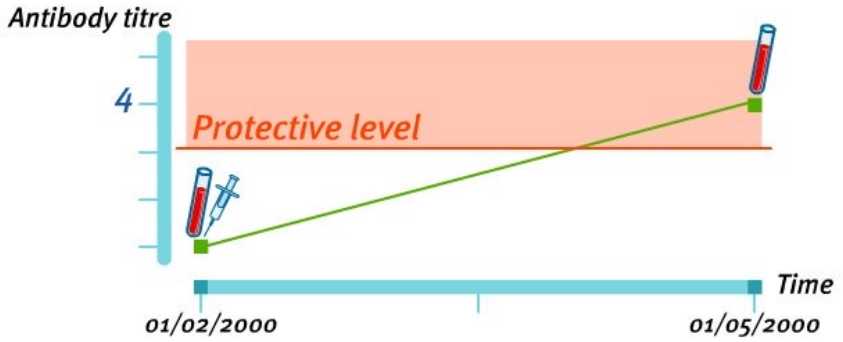
Introduction of Vaccine Trial

- **Immunogenicity Study**
  - Alternative endpoints exist - when widespread vaccination with an already approved vaccine reduces disease incidence to very low levels, **serological parameters** are recognized to be associated with clinical protection, and sample sizes are usually small

GMC	Geometric Mean Concentration 几何平均浓度
GMT	Geometric Mean Titer 几何平均滴度
SCR	Seroconversion Rate 血清转化率
SPR	Seroprotection Rate 血清保护率

- **Case Driven Study**
  - Clinical endpoints - Will the individual develop disease?
  - A large sample size is usually required

VE	**Vaccine Efficacy 疫苗效力**
	Vaccine Effectiveness 疫苗效果



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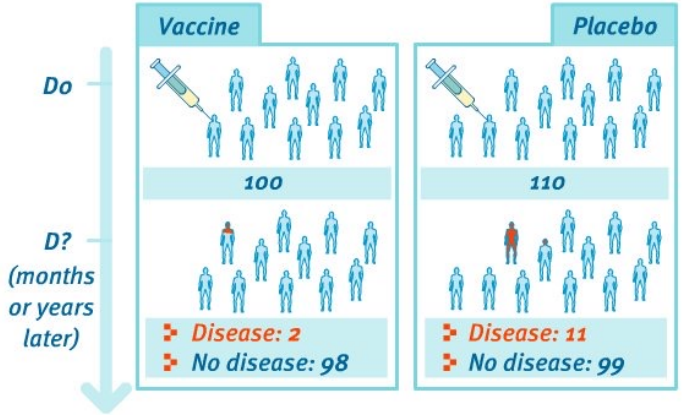


Ref.

Introduction of Vaccine Trial

➢ Safety Assessment

- Local: Injection Site Swelling
- Systemic: Fever

Solicited AE — 30min/7days

AE collected/reported proactively by the investigator or subject during a **specified follow-up period after vaccination**

Unsolicited AE — 28 days

AE other than solicited AE reported in clinical studies, solicited AE reported **outside the soliciited time window**

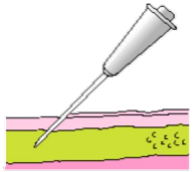
MAAE — Entire Study

Medical Attended AE: This includes visits to hospitals, emergency rooms, urgent care clinics, or medical staff

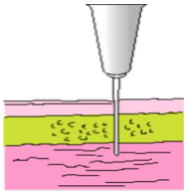
AESI — Entire Study

AE of Special Interest: SAE or Non-SAE, depends on long-term observation, an AESI list should be established in advance

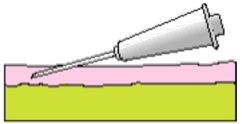
➢ Vaccination



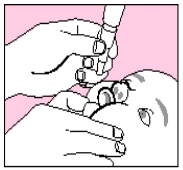
Subcutaneous injection



Intramuscular injection

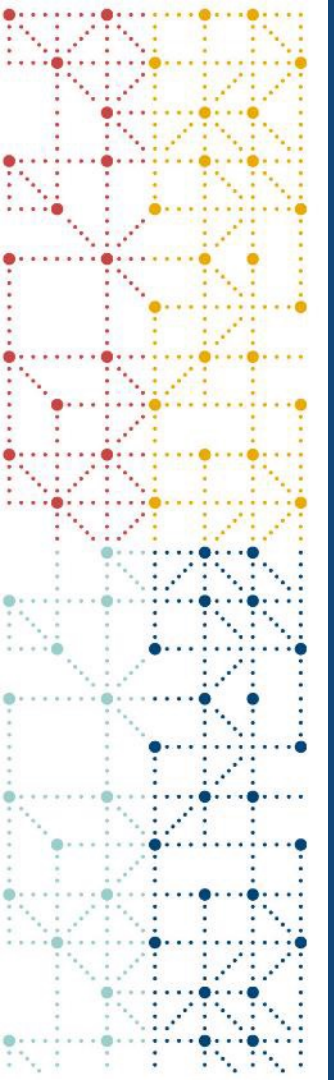


Intradermal injection



Oral

Ref. 7



Considerations of Data Collection in Vaccine Trial

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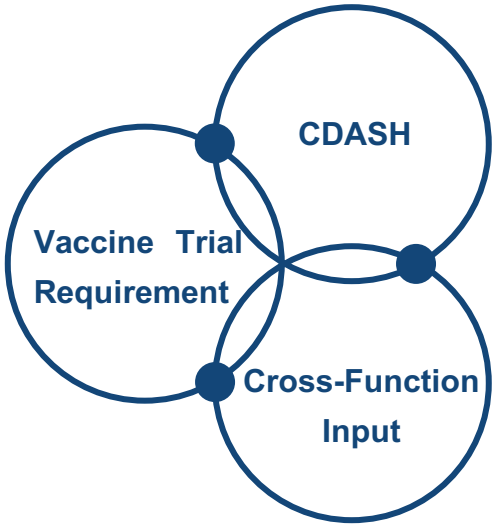


General Vaccine Trial

2 levels

In multiple TAs (COVID-19/HPV/ROTA)

CRF
Case Report Form
aCRF/UAT Script

DVP
Data Validation Plan
EC Testing Script

eCCI
e-CRF completion Instruction

DTS
Data Transfer Specification

CRF - Adverse Event

Solicited AE

- **Local Reactions**: Injection site pain, injection site redness, **injection site swelling** etc.

- **Systemic AEs**: Fatigue, headache, myalgia, arthralgia, anorexia, diarrhea, nausea, **fever**, **vomiting**, etc.

Maximum Size

|__|__|.|__| XX.X cm

Occurrence Site

○lateral deltoid of the left upper arm
○lateral deltoid of the right upper arm

Maximum Temperature

|__|__|.|__| XX.X ℃

Maximum Frequency

|__|__| XX times/day

CRF - Diary Card

Local Reactions

Injection Site Swelling

30min

7days

AE Intensity

Workload

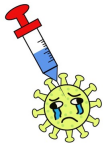
Data Integrity

Symptoms-Injection Site Swelling			
Associated Adverse Events*	_(Setting association)__		
Comments	____$200_____		
Time Point	Date*	Was there swelling at the injection site?*	Maximum Diameter*
Day 0	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm
Day 1	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm
Day 2	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm
Day 3	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm
Day 4	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm
Day 5	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm
Day 6	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm
Day 7	__/___/___ _DD/MMM/YYYY	○Yes ○No	|__|__|.|__| XX.X cm

CRF - COVID-19

COVID-19 Booster Dose Vaccine Efficacy Study (Case Driven)

- SARS-CoV-2 Vaccination History



Surveillance for COVID-19 Cases

- Symptoms/ Signs of COVID-19

- SARS-CoV-2 Antigen-RDT

- SARS-CoV-2 RT-PCR for COVID-19

- Results of SARS-CoV-2 RT-PCR for COVID-19

+/-

- Blood Sample Collection for COVID-19

CRF - HPV

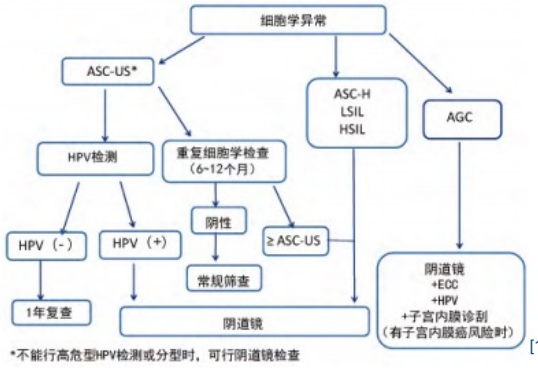
HPV Vaccine Efficacy Study (Case Driven)

Vaccination

Follow-up Visit

HPV DNA + TCT

- Gynecological Examination 妇科检查
- Cervical Exfoliated Cell Sample Collection/Test 宫颈脱落细胞样本采集/检测



[1]

- Colposcopy 阴道镜检查
- External Genitalia (Tissue Biopsy) 外生殖器（组织活检）
- Vagina (Tissue Biopsy) 阴道（组织活检）
- Cervix (Tissue Biopsy) 宫颈（组织活检）

- External Genitalia (Definitive Treatment) 外生殖器（确定性治疗）
- Vagina (Definitive Treatment) 阴道（确定性治疗）
- Cervix (Definitive Treatment) 宫颈（确定性治疗）

[1]中国优生科学协会阴道镜和宫颈病理学分会专家委员会.中国子宫颈癌筛查及异常管理相关问题专家共识(一)[J].中国妇产科临床杂志,2017(18):191.

CRF - HPV

Pregnancy Event

- Were there any pregnancy Events?*
- Number
- Date of Diagnosis of Pregnancy*
- First day of Last Menstrual Period*
- Estimated Delivery Date*
- Was there a pregnancy outcome?*
- Outcome Date*
- Outcome Type*
- Gestational Week*
- Delivery Type*
- Is there any abnormalities during delivery?*

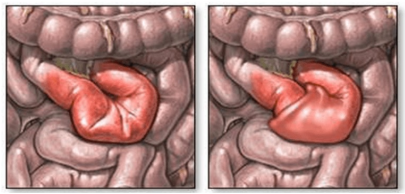
- Number (Automatically generated by the system)
- Birth Date
- Gender
- Neonatal State
- Other Neonatal Complications
- Neonatal Congenital Defects
- Weight
- Height
- Apgar Score (1 minute)
- Apgar Score (5 minutes)
- Apgar Score (10 minutes)
- Any congenital anomaly/abnormalities/complications?

CRF - ROTA

ROTA Vaccine Safety and Immunogenicity Study

- Fecal Rotavirus Test
  - Sample Collection Date
  - Age
  - Result
  - Clinical Significance
- Fecal Sample Collection
  - Sample Collection Timepoint

- AE of Special Interest AESI:
  - Acute gastroenteritis/diarrhea
  - Invagination
  - Kawasaki disease



DVP - Adverse Event

Edit Check

- **Solicited AE vs. Unsolicited AE**

AE	Adverse Events	Category of AE	"Start Date" of Adverse Events is within 0~XX days after "Date of Vaccination" of the First Dose, and "Was it an Injection Site AE?" select "Injection site AE", however "Category of AE" select "Unsolicited AE", please verify.

- **Solicited AE Start Date**

AE	Adverse Events	Was it happening within 30 minutes after the vaccination?	"Was it happening within 30 minutes after the vaccination?" select "Yes", "Start Date" of Adverse Events and "Date of Vaccination" are not on the same day, please verify.

- **Injection Site AE**

AE	Adverse Events	Was it an Injection Site AE?	"Adverse Events Term" select "Fever" or "Acute allergic reaction" or "Diarrhea" or "Anorexia" or "Vomiting" or "Irritation / Inhibition", "Was it an Injection Site AE?" select "Injection site AE", please verify.

Duplicated Subject Review for Global Trial

- Request: Potential duplicate subjects need to be reviewed as early as possible.
- Pain point: The duplicate subject review was limited to EDC data entry cycle time.The investigators start screening procedure as soon as they obtained a screening number in EDC, the data cannot be entered timely.
- Solution: According to the EDC workflow setting, the system will automatically assign a screening number only after the investigators have filled in the subject information page, so we added gender, date of birth and other fields to the subject information page, so that the investigators have to fill all informations of the subject at the beginning of enrollment.

CRF

4.1 Subject Information

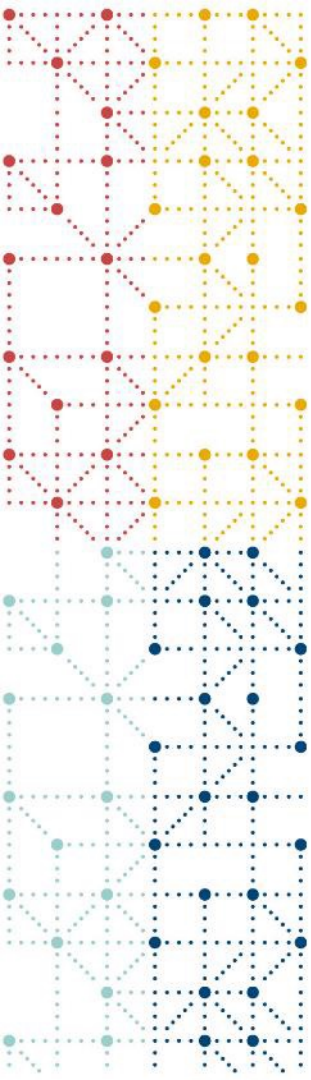
Subject Information	
Subject Screening	_____$7_____

4.1 Subject Information

Subject Information	
Subject Screening Number*	____$7____(Note: the system calculates automatically)
Birth Date*	___/____MMM/YYYY
Date of Informed Consent*	__/___/____DD/MMM/YYYY
Age*	XXX years (Note: the system calculates automatically)
Gender*	○Male ○Female

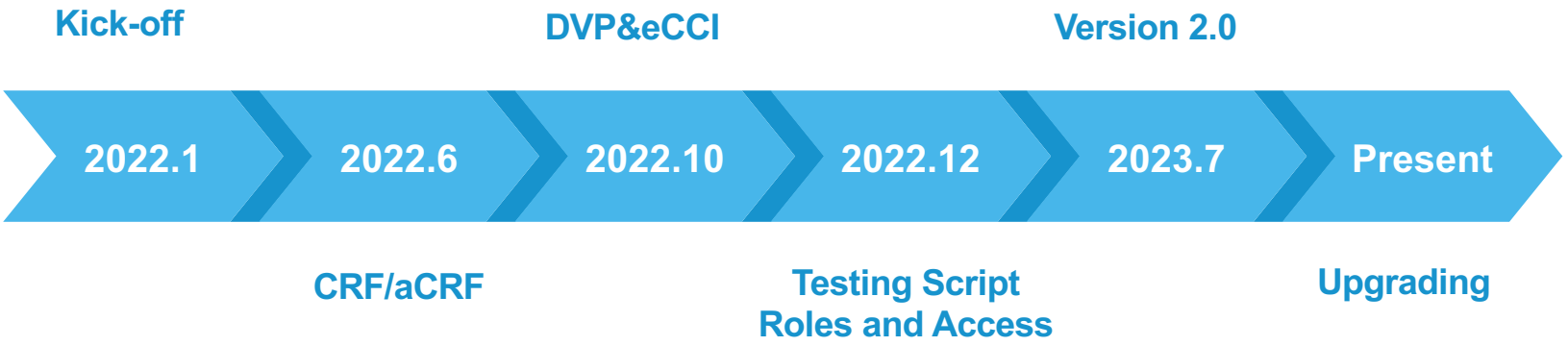
Manual Check

- Timely review for potential duplicate subjects: The Birth date and Gender of subjects are same.
- Regular review for potential duplicate subjects: The Birth date, Gender, Race and Ethnicity of subjects are same, the difference of height is within 5cm, the difference of weight is within 5kg.



Standard Library Development and Maintenance

Standard Library Development



- 100+ Vaccine Trials cross TAs
- Chinese and English Version

Standard Library Maintenance

update

Standard Request

DM SME Forum

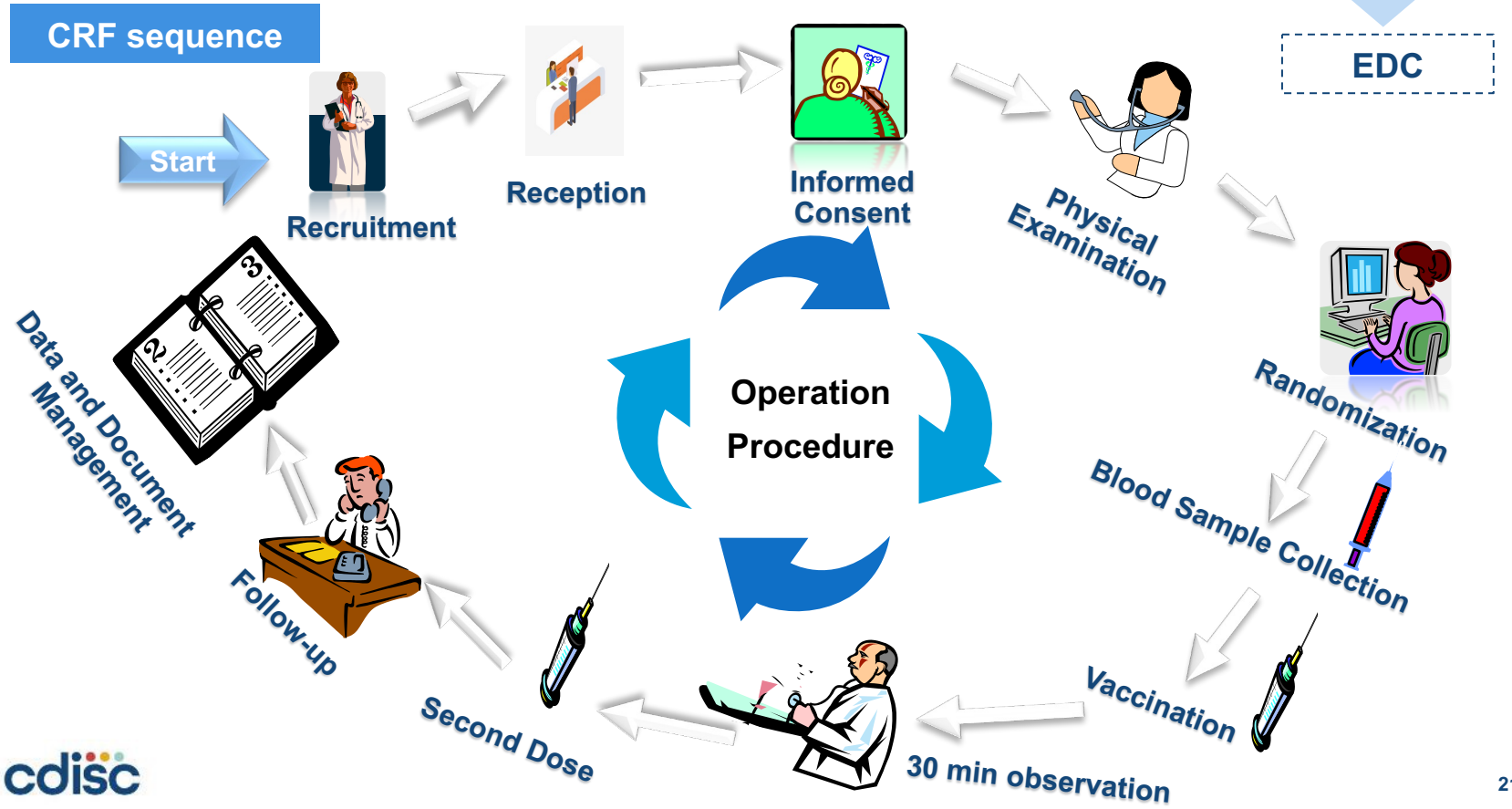
Cross Function Data Discussion

integrated Data Review Plan

How to use Standard Library?

Source Worksheet

EDC



How to use Standard Library?

Remark in Standard Library

- Required Item
- Optional Item
- Item could be modified
- Reminders for document design

For Interim Analysis

- 2 sets of common forms to avoid unlock
  - For leading question is answered as No
  - For new event

Data Submission

- AE Toxicity Grade in two standards
  - NMPA (National Medical Products Administration 国家药品监督管理局)
  - NIH (National Institutes of Health 美国国立卫生研究院)

Acknowledgement

- Standard Library Team for Vaccine Trial in SDM

Thank You!