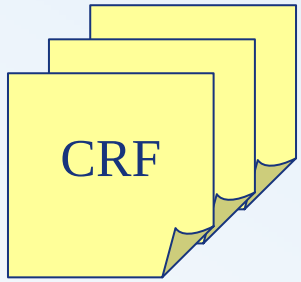
The 2nd Clinical Data Management Training

CASE REPORT FORM

September, 2010 at SMMU, Shanghai

What is the definition of CRF?

- A printed, optical or electronic document designed to record all of the protocol required information to be reported to the Sponsor on each trial subject. ---- ICH/GCP



If we take care in the beginning, the end will take care of itself !!

From CDASH

There is arguably no more important document than the instrument that is used to acquire the data from the clinical trial, with the exception of the protocol, which specifies the conduct of that trial. The quality of the data collected relies first and foremost on the quality of that instrument. No matter how much time and effort go into conducting the trial, if the correct data points were not collected, a meaningful analysis may not be possible. It follows, therefore, that the design, development and quality assurance of such an instrument must be given the utmost attention."

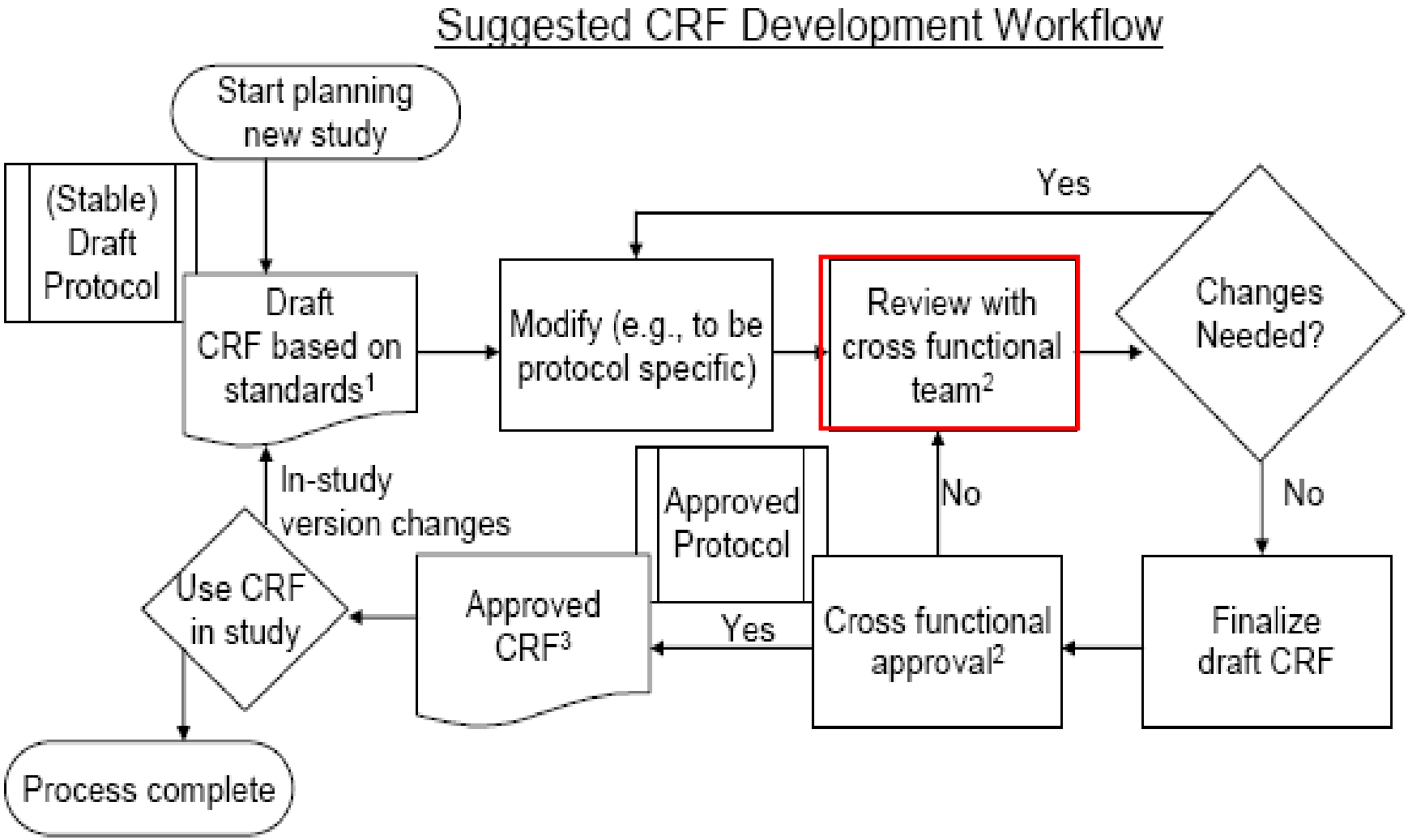
Purpose of the CRF

- Capturing all protocol-required information.
- Facilitates data collection and entry
- Benefits data management
- Benefits statistical analysis
- Simplifies database design and data validation processes as well as manipulation of data during statistical analysis.

Outlines

1. CRF Development Process
2. CRF Design
3. CRF Completion Guidelines
4. Take Home Message

CRF Development Workflow



What do we know from protocol?

- Study objectives – safety and efficacy
  - Efficacy parameters
  - Safety parameters
- Time and Event schedule
  - Study working flow
- Detailed procedures

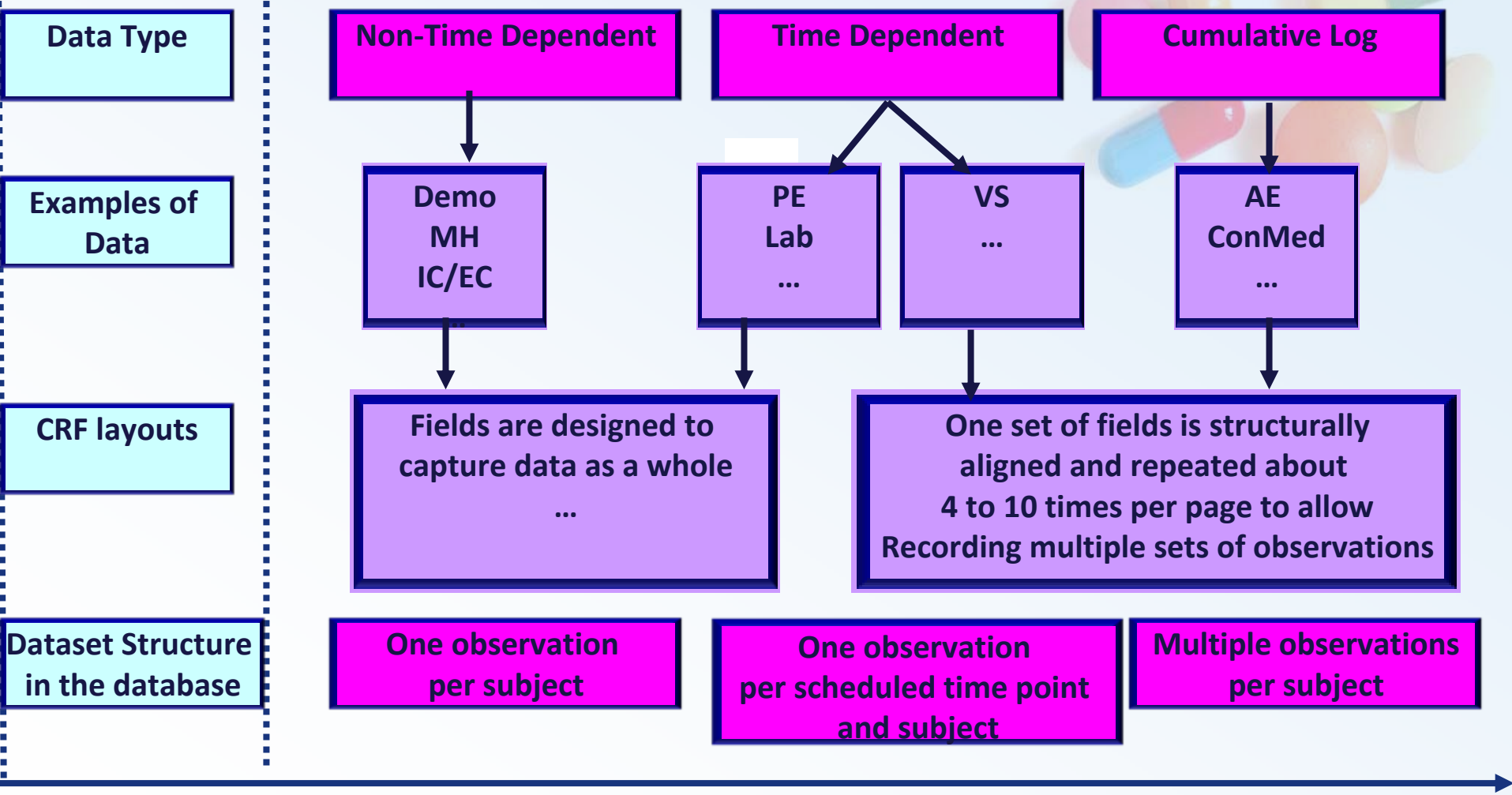
Some information out of protocol

- What data need to be collected if a subject dose not meet entry criteria (SF) or complete the study? (ET)
- How is dosing/compliance being measured?
- What population-specific data are needed?
- Lab (central vs local)
- Unscheduled procedures?

General Modules

- IC/DEMO
- INC/EXC (cross check? option of “NA”)
- Med Hx (specific Hx, general Hx)
- PE (body system)
- Vital Signs, 12-lead ECG, Chest X-ray, Holter, etc (data collected depends on the study)
- ConMed (time period)
- AE (definition, data collected, reported timeframe, follow-up period)
- Protocol deviations
- Comment Log
- Study drug administrationi/Study drug accountability log
- Study summary (reason for discontinuation)

Forms


Data Type
Examples of Data
CRF layouts
Dataset Structure in the database
Non-Time Dependent
Time Dependent
Cumulative Log
Demo
MH
IC/EC
PE
Lab
…
VS
…
AE
ConMed
…
Fields are designed to capture data as a whole
…
One set of fields is structurally aligned and repeated about 4 to 10 times per page to allow Recording multiple sets of observations
One observation per subject
One observation per scheduled time point and subject
Multiple observations per subject

Categories of Questions

- Open question
  - When, What, Where, Who, How
- Close question
  - Yes/No

How to Ask Questions?

- **When**
  - Date or time?
  - Duplicate recording
  - Protocol defined vs Actual Date/Time
  - Sample collection, Sample testing
- **Yes/No**
  - Double negative
    - E.g.
    - E.g. Wasn't the patient fasting before blood withdrawl?
  - Several options
    - Is the parameter A greater than 10 and the parameter B greater than 5?
- **Others**
  - Avoiding using words that have more than one meaning
  - Using single word to replace unnecessary phrases
  - Avoid passive voice
  - Break down
  - Leading questions
  - Notes and reminder

Answers

- Date/Time (format)
- Number (digits)
- Text (space)
- Units (per-printed or not)
- Options/Discrete Value Groups

Answers (cont.)

- Response order
  - Yes/no/unknown
  - Most likely options occur early
  - Grading performance – from good to worse
  - Numeric answers
- Tick box order
- Recording codes
- Exclusive options
- Combination questions
  - Other specify
  - None of the above

Analogue scales

- Provide clear instructions for marking the line
- Ensure the line is exactly 10 cm in length on return form the printers
- Copyright

1. 病人对疼痛的评估（过去一星期内）

在过去一星期内，您由于病症引起的疼痛有多严重？
请在下面的横线上画一个标记，来表示您疼痛的严重程度。

无疼痛 0 ——————————————— 100 可能出现的最严重的疼痛

2. 病人对疾病状况的总体评估（过去24小时内）

考虑目前的疾病和健康状况可能影响您的所有情形，请在下面的横线上画一个标记来表示您现在的状况。

很好 0 ——————————————— 100 很差

* 请勿填写以下部分

To be completed by site personnel:

Patient's Assessment of Pain Score: ☐☐☐ (mm)

Patient's Global Assessment of Disease Activity Score: ☐☐☐ (mm)

CRF Design (general)

- Study information (sponsor, protocol number, phrase, title)
- Subject information (site num, patient num, patient initials)
- Informative footer and header

CRF Design (specific)

- Diary Card (medical synonyms; domestic time; medication; structure)
- Specific data modules depends on individual
- **Translations**

  Translations of CRFs into other languages should be a parallel process following the same set of steps with separate reviews and approvals by the appropriate experts.

Precision – improve data quality

- Key dates and times
- **Necessary Data Only**
- Calculated data or derived data
- Objective measurements are the data of choice
- With multivariable information – focus on the factor of interest is present absent
- Standard ‘definitions’ exist when asking if a result is ‘normal’ or ‘abnormal’

Exercises (1)- Local Lab

	Result
Neutrophils	I____I
Lymphocytes	I____I

	Result	Unit If different
Neutrophils (%)	I____I	I____I
Lymphocytes (%)	I____I	I____I

Exercises (2)- PE

PHYSICAL EXAMINATION			
Body System	**Not Done**	**Assessment**	**If Abnormal, please specify**
1.Skin	☐	☐ Normal ☐ Abnormal	
2.HEENT	☐	☐ Normal ☐ Abnormal	
3.Neck	☐	☐ Normal ☐ Abnormal	
4.Lymph nodes	☐	☐ Normal ☐ Abnormal	
5.Thorax	☐	☐ Normal ☐ Abnormal	
6.Lung	☐	☐ Normal ☐ Abnormal	
7.Heart	☐	☐ Normal ☐ Abnormal	
8.Abdomen	☐	☐ Normal ☐ Abnormal	
9.Extremities	☐	☐ Normal ☐ Abnormal	
10.Musculoskeletal	☐	☐ Normal ☐ Abnormal	

Exercises (2)- PE

Physical examination

Perform a standard physical examination but specify only abnormalities.

normal ☐
abnormal ☐ → specify _____

Physical examination — [illegible]

ities on 'Adverse event/intercurrent illness'
date records of concomitant treatments.

Perform a standard physical examination and record any new abnormal
eform, update existing adverse events with follow-up information and up

Why employ standards

- Reduces production time for CRF design and reduces review and approval time.
- Reduces site re-training and queries and improves compliance and data quality at first collection
- Facilitates efficient monitoring, reducing queries
- Improves the speed and quality of data entry due to familiarity with standards and reduces the training burden in-house
- Enables easy reuse and integration of data across studies and facilitates “data mining” and the production of integrated summaries
- Reduces the need for new clinical and statistical programming with each new study

CRF Review

- CRF captures all of the data needed for analysis.
- Data are collected in a manner which should also be easy for the site to complete.

Key points for different functions

- CRF designer: review the protocol to ensure that it is possible to collect the proposed data.
- Statisticians: review the CRF against their planned analyses to make sure all required data will be collected in an appropriate form for those analyses.
- Clinical Operations staff: make sure the questions are unambiguous and that it is possible to collect the data being requested.
- Programmers: ensure that the manner in which the data are collected on the CRF will not adversely affect the programming function.
- Scientific experts: provide input on the efficacy and/or safety data collection fields, and educate the Clinical Data Management (CDM) staff on the type and methods of collecting those data.
- Regulatory: review the CRF for compliance with all applicable regulations.
- Data Entry is an important “user” of the CRF and their perspective should be included in the review as well.
- Pharmacovigilance should review to ensure appropriate data capture and process to support expedited reporting.

CRF Completion Guidelines

- Provide a set of instructions for the site to use during the process of filling out the Case Report Form for the study
- The instructions should be clear, concise, definite, consistent and correct.
- Significant reduce data entry errors (for EDC studies), query rate and eventually increase the accuracy and integrity of clinical data

CRF Completion Guidelines (cont.)

- CRF questions should be as self-explanatory as possible, thereby reducing the need for separate instructions.
- When instructions are needed, prompts and short instructions may be placed on the CRF page. More detailed instructions may be presented in a CRF completion guideline for paper CRFs, or in a context-sensitive help file for electronic CRFs (eCRFs).
- Instructions should be standardized along with the CRF as much as possible. This promotes standardization in that all sites will use the same conventions for completing the fields.

Q and A

- Should free text be an option for a response to a specific question?
- Should data be pre-populated in the CRF?
- Should location of measurement and position of subject *(e.g., oral temperature, blood pressure from right arm, etc.)* be collected for each assessment?
- Should sites be given guidance on how to record verbatim terms for adverse events, concomitant medications or medical history in the CRF?
- Should dosage to be recorded one by one?

Take Home Messages

- Keep questions, prompts and instructions clear and concise.
- Design the CRF to follow the data flow from the perspective of the person completing it.
- Avoid referential and redundant data points within the CRF whenever possible.
- Design the CRF with the primary safety and efficacy endpoints in mind as the main goal of data collection.
- Keep the layout (Font, table, etc.) consistent

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Thank You !