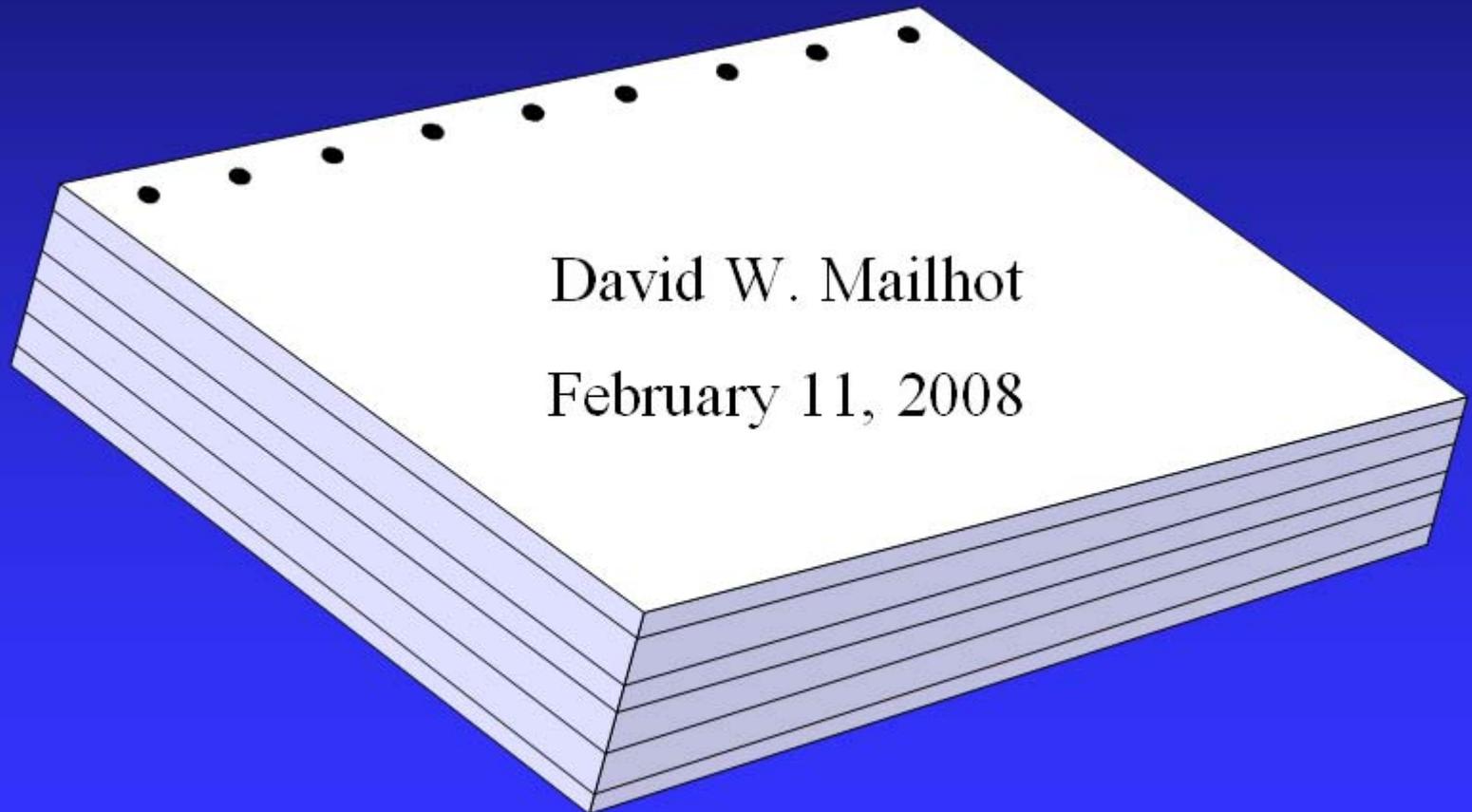


Design of Case Report Forms



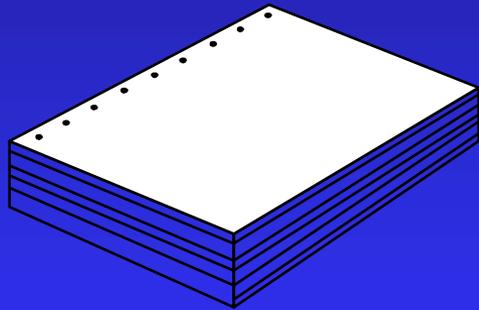
David W. Mailhot

February 11, 2008

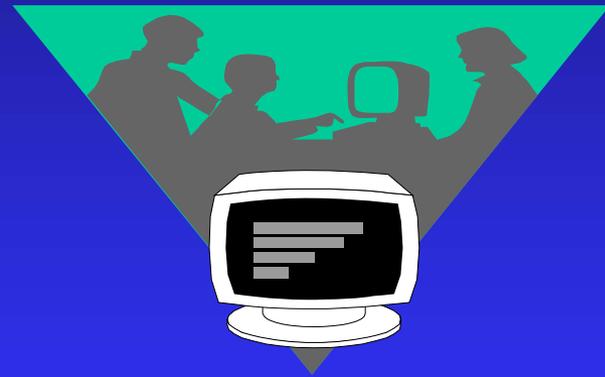
Case Report Form

* CRF

- Official clinical data-recording document or tool used in a clinical study



PAPER



**RDC/RDE (Remote Data Capture,
Remote Data Entry)**

Purpose

- * Collects relevant data in a specific format
 - in accordance with the protocol
 - compliance with regulatory requirements
- * Allows for efficient and complete data processing, analysis and reporting
- * Facilitates the exchange of data across projects and organizations esp. through standardization

CRF Relationship to Protocol

- * Protocol determines what data *should* be collected on the CRF
- * All data *must* be collected on the CRF if specified in the protocol
- * Data that will not be analyzed *should not* appear on the CRF

CRF Development

* Guidelines

- Collect data with all users in mind
- Collect data required by the regulatory agencies
- Collect data outlined in the protocol
- Be clear and concise with your data questions
- Avoid duplication
- Request minimal free text responses

CRF Development

* Guidelines (con't)

- Provide units to ensure comparable values
- Provide instructions to reduce misinterpretations
- Provide “choices” for each questions
 - * allows for computer summarization
- * Use “None” and “Not done”

CRF Development

- * Guidelines (con't)

- Collect data in a fashion that:

- * allows for the most efficient computerization

- * similar data to be collected across studies

- * CRF book needs to be finalized and available before an investigator starts enrolling patients into a study

Take the time to get it right the first time

Elements of the CRF

- * Three major parts:

- Header
- Safety related modules
- Efficacy related modules

- * **Module** block of specific questions

- * **CRF** module(s) make up a single CRF page

- * **CRF Book** series of CRF pages

Header Information

* Key identifying Information

* ***MUST HAVES***

- **Study Number**

- **Site/Center Number**

- **Subject identification number**

Creating Safety Modules

- * Usually come from a standard library
- * Select modules appropriate for your study
- * Keep safety analysis requirements in mind
- * Safety Modules usually include
 - Demographic
 - Adverse Events
 - Vital Signs
 - Medical History/Physical Exam
 - Concomitant Medications
 - Patient Disposition

Efficacy Modules

- * Designed for each therapeutic area based on the protocol
- * Considered to be “unique” modules and can be more difficult to develop
 - Use existing examples from similar protocols where applicable
 - Consider developing a library of efficacy pages
- * Design modules following project standards for data collection

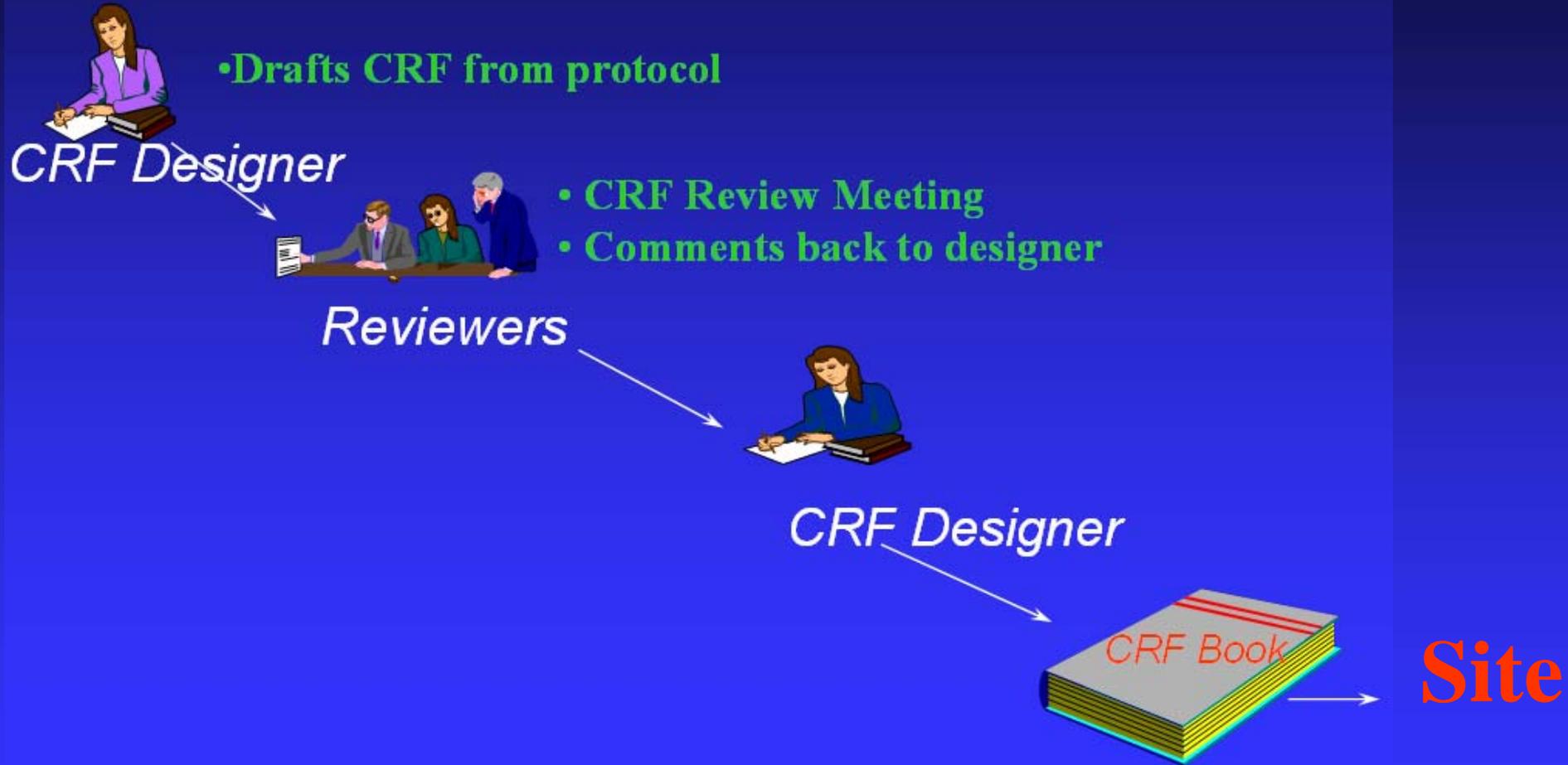
Creating Efficacy Modules

- * Follow general CRF design guidelines
- * Use pages or modules from the therapeutic library
- * Define diagnostics required
- * Include appropriate baseline measurements
- * Repeat same battery of tests
- * Define and identify
 - key efficacy endpoints
 - additional tests for efficacy

Importance of Standard CRFs

- * Prepares the way for data exchange
- * Removes the need for mapping during data exchange
- * Allows for consistent reporting across protocols, across projects
- * Promotes monitoring and investigator staff efficiency
- * Allows merging of data between studies
- * Provides increased efficiency in processing and analysis of of clinical data

CRF Development Process



- * Updates CRF to incl. comments
- * Review and Sign off
- * Coordinate printing and distribution

CRF Development Process

- * Responsibility for CRF design can vary between clinical research organizations (CRA, data manager, specialty role)
 - Include all efficacy and safety parameters specified in the protocol using standards libraries
 - To collect ONLY data required by the protocol
 - Work with protocol grid/visit schedule

CRF Development Process

- * Interdisciplinary review is necessary
 - each organization has its own process for review/sign-off
 - Should include relevant members of the project team involved in conduct, analysis and reporting of the trial
- * Begins
 - As soon in the study prep process as possible

CRF Development Process

* Review Team (example)

- Project Clinician
- Lead CRA
- Lead Statistician
- Lead Programmer
- Lead Data Manager
- Others

* Database Development, Dictionary
Coding, Standards

CRF Development Process

* *After the CRF book is approved*

- Initiate the process for printing

Note: the Protocol must be approved before the CRF book is approved and printed

* *After it is printed*

- Stored according to organizational guidelines
- Printed and distributed to research sites

Properly Designed CRF

- * Components/All of the CRF pages are reusable
- * Saves time
- * Saves money

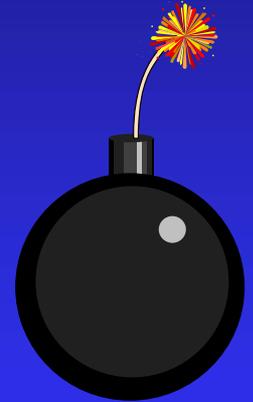


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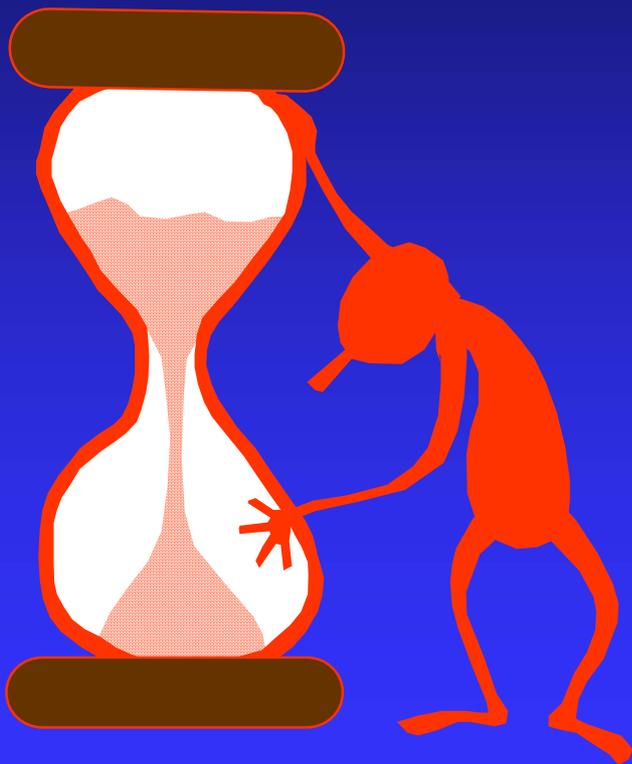


Poorly Designed CRF

- * Data not collected
- * Database may require modification
- * Data Entry process impeded
- * Need to edit data
- * Target dates are missed
- * Collected too much data – *Wasted resources in collection and processing*



Poorly Designed CRF Issues



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The Case Report Form

* How do we use it?

- Collect data from the investigational sites
- Helps project team and study site team
 - * Reminder to investigator to perform specific evaluation
 - * CRA uses to verify protocol is being followed and compare with source documents
 - * Biometrics uses it to build database structures, develop edit checks and programming specs

The Case Report Form

* Used for

- Subject tracking
- Data analysis and reporting
- Reports to FDA on subject safety
 - * e.g.. APR
- Promotional materials
- New Drug Application submissions
- Support of labeling claims
- Articles in medical journals

Electronic CRFs

- * The use of RDC is increasing
- * In general, the concepts for the design of electronic CRFs/RDC screens are the same as covered for paper
- * Electronic CRFs will impact the following:
 - Review of CRF is different (screen review)
 - No need to print and distribute paper

Examples

Protocol ID:

CENTER

--	--	--	--

SUBJECT ID

--	--	--	--	--	--	--	--

DATE OF VISIT

				-			-		
--	--	--	--	---	--	--	---	--	--

YYYY

MM

DD

Visit: Screening

Subject Initials:

--	--	--

PAGE 1

Please print all details, and INITIAL and DATE all corrections. Indicate ☒ where applicable.

DATE OF BIRTH: (yyyy-mm-dd)

				-			-		
--	--	--	--	---	--	--	---	--	--

SEX AT BIRTH:

- (1) Male
- (2) Female

RACE:

- (1) White
- (2) Black
- (3) Asian
- (4) Other

**IF SUBJECT IS FEMALE,
HORMONAL STATUS:**

- (1) Premenarchal
 - (2) Premenopausal
 - (3) Postmenopausal
-

SMOKING STATUS:

- (1) Current Smoker
 - (2) Ex-Smoker
 - (3) Non-Smoker
-

SIGNIFICANT MEDICAL/SURGICAL HISTORY: (1) NOT DONE (1) No Significant History

	Past (1)	Present (2)
Specify:	<input type="checkbox"/>	<input type="checkbox"/>
Specify:	<input type="checkbox"/>	<input type="checkbox"/>
Specify:	<input type="checkbox"/>	<input type="checkbox"/>

VITALS NOT DONE:

(1)

Weight:

.

(1) lb
 (2) kg

Height:

.

(1) in
 (2) cm

**Blood Pressure,
(1) Sitting:**

/
Systolic Diastolic

mmHg

**Heart Rate,
(1) Sitting:**

beats/minute

Body Fluid/Matrix:

SERUM

Analyte:

(1) PK NOT DONE

Date (yyyy-mm-dd)	Not Done	Time Post Dose (Hours)	Actual Time (24 hour clock)	Unique Sample ID	Comments (Keep brief and legible)
<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/>	<input type="checkbox"/> (1)	0	<input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/>		
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PRIOR AND CONCOMITANT MEDICATIONS:

(1) NONE

Drug Name (Generic preferred but use brand name for combination product)	Start Date (yyyy-mm-dd)	End Date (yyyy-mm-dd)	Continuing (1)
	□□□□ - □□ - □□	□□□□ - □□ - □□	<input type="checkbox"/>
	□□□□ - □□ - □□	□□□□ - □□ - □□	<input type="checkbox"/>
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Questions ?