

Data Management (IPPCR)

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Acronyms

- * GCP: Good Clinical Practices
- * CFR: Code of Federal Regulations
- * ICH: International Conference on Harmonisation
- * CRF: Case Report Form
- * FDA: Food and Drug Administration
- * IRB: Institutional Review Board
- * IND: Investigational New Drug
- * SOP: Standard Operating Procedure

Objectives

- * Define a source document
- * List regulatory documents to be kept at site
- * State how long records must be kept

Good Clinical Practices

- * The Rules of Research
- * International ethical and scientific quality standard for clinical trial conduct

Gapes

- * Code of Federal Regulations

 - 21 CFR 50

 - 21 CFR 56

 - 21 CFR 312

 - 45 CFR 46

- * State Laws

- * Institution Standards of Practice

- * ICH Guidelines

What Are Data?

- * Information (facts /figures)
- * An accounting of the study

Who Can Collect Data?

- * Investigators
- * Nurses
- * Research team
- * Participant
- * Participant's family
- * Participant's own physician

Where Are Data?

In the source documents

What is a Source Document?

- * It is the First Recording

- * What does it tell?
 1. It is the data that document the trial

 2. Study was carried out according to protocol

Source Documents

- * Original Lab reports
- * Pathology reports
- * Surgical reports
- * Physician Progress Notes
- * Nurses Notes
- * Medical Record

Source Documents (cont)

- * Letters from referring physicians
- * Original radiological films
- * Tumor measurements
- * Participant diary/ interview

What Do You Collect?

- * **Demographic data**
- * **Eligibility**
- * **Study agent given**
- * **Concurrent therapy**
- * **Assessments/tests/exams**
- * **Adverse Events**
- * **Response according to protocol**

Eligibility

- * Did participant meet eligibility criteria?
- * Signed and dated eligibility checklist
- * Consent obtained before study tests done
- * Consent obtained before study item given
- * Documented in Medical Record

Eligibility Checklist

_____ **Stage III or Stage IV epithelial ovarian cancer?**

_____ **Baseline CA-125 > 70 units/ml (drawn within 14 days)**

_____ **No prior chemotherapy or pelvic radiation**

_____ **ECOG Performance Status of 0-2**

_____ **Platelets >100,000**

Treatment According to Protocol

- * Drug/dose administered
 - Diary/pill count
- * Dose modification/reason
- * Delay in treatment
- * Were contraindicated drugs given?

Example of Study Drug Administration

Study Drug	Admin Dose	Unit	Freq	Route	Course	Start Date	End Date
Cure-All	250	mg	X 1	IV	1	1/5/2004	1/5/2004
						John Smith, MD	1/26/2004

Adverse Events Assessed According to Protocol

- * Did participant keep clinic visits?
- * How were Adverse Events assessed?
- * Was plan modified for Adverse Events?

Example of AE Reporting

C	D	Onset	Adverse event	Gr	Rel	Act	Ther	Out	Date Resolved
1	1	1/5/2004	Nausea	2	4	1	2	1	1/5/2004
1	2	1/6/2004	Pain: Headache	1	3	1	1	1	1/6/2004
					John Smith, MD				1/26/2004

Common Terminology Criteria for Adverse Events v3.0

		Grade				
Adverse Event	1	2	3	4	5	
Vomiting	1 episode in 24 hrs	2-5 episodes in 24 hrs or IV fluids indicated <24 hrs	6 or more episodes/ 24 hrs or IV fluids or TPN indicated for 24 hrs or longer	Life-threatening consequences	Death	

Adverse Event Attribution Categories

1	Unrelated	The AE is clearly NOT related to the intervention
2	Unlikely	The AE is doubtfully related to the intervention
3	Possible	The AE may be related to the intervention
4	Probable	The AE is likely related to the intervention
5	Definite	The AE is clearly related to the intervention

Concomitant Medications

C	D	Dose Date	Medication	Reason	End Date
-1	-126	9/1/2003	Psyllium	constipation	
1	1	1/5/2004	Prochlorperazine	Nausea	1/5/2004
1	2	1/6/2004	Diphenhydramine	itching	1/13/2004
			John Smith, MD 01/26/2004		

Response Assessed According to Protocol

- * Required tests done on time?
- * Interpreted on time?
- * Lab/tumor measurements done?

Response Assessed

Extent of Disease						
			Lesion # 1		Lesion # 2	
	How Measured		CT scan		CT scan	
Date	Measurements		2.5		3.5	
3/1/2004	Eval Number	Eval Code	0		0	
4/26/2004	How Measured		CT scan		CT scan	
	Measurements		2.0		3.5	
	Eval Number	Eval Code	1	D	1	S
			John Smith, MD 04/26/2004			

Managing the Data

- * Set up plan early: remember endpoints!
- * Plan CRFs to capture all needed data
- * Collect data as it happens
- * Standardize data entry procedures

Data Management Tools

- * Case Report Forms
- * Common Data Elements
- * Electronic Data Capture
- * e Source
- * Audits

Case Report Forms

- * Standardize
- * Plan CRFs to capture all needed data
- * Version the CRFs
- * Plan for all assessments
- * Limit text entries
- * Do not write in margins

Common Data Elements

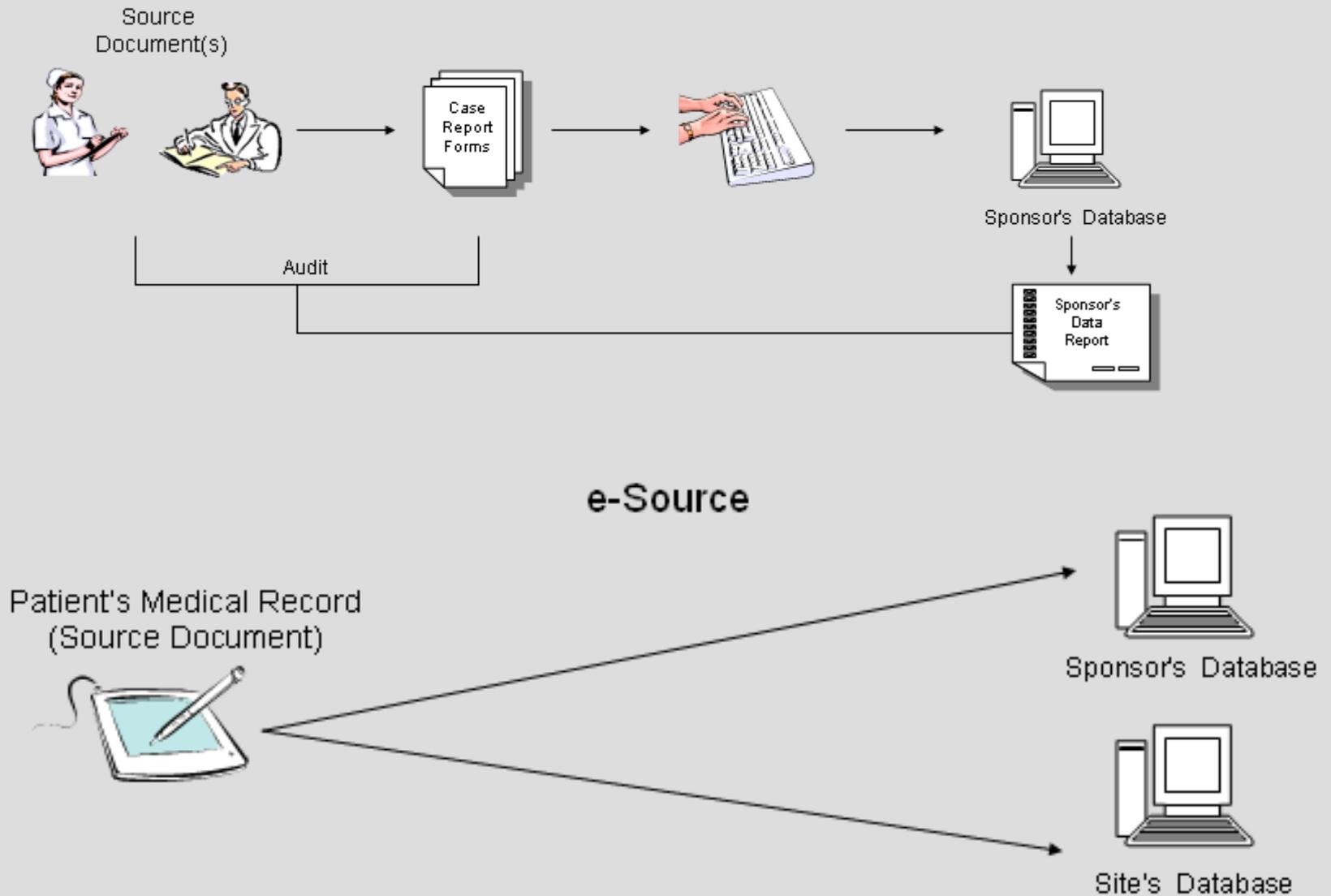
- * **Data elements that have been determined to be identical between projects or contexts**

caDSR

Data Quality

- * **Data entry procedures**
- * **Certification of data entry personnel**
- * **Edit checks**
- * **Ongoing quality checks**
- * **Different personnel QC data entries**
- * **Correction of errors**
- * **Data lock**

EDC –Electronic Data Capture



What Do You Do With the Data?

- * Ongoing monitoring
- * Safety/adverse event reporting
- * IRB reports/sponsor reports
- * FDA reports
- * Early analysis/late analysis

Examples of Documents to be Kept at Study Site

- * Signed FDA Form 1572
- * CVs of all investigators on 1572
- * Signed approved protocol and all amendments
- * Informed consent/all amended informed consents

Documents to be Kept (cont)

- * Investigator's Brochure
- * IRB approvals
- * IRB membership
- * Assurance number
- * Drug Accountability
- * IND safety reports from sponsor
- * Annual/interim reports
- * All information given to subject

Documents to be Kept (cont)

- * CRFs on each subject (signed/dated)
- * Adverse event reports
- * All source documents not kept in medical record
- * Meeting minutes/correspondence
- * Signature log/equipment logs

Documents to be Kept (cont)

- * Laboratory documentation
 - certification
 - normal range tables with dates
- * Specimen handling
 - instructions/labels/shipping
- * Staff education records

Documents to be Kept (cont)

- * Financial agreements
 - sponsor
 - subject
- * Signed study agreement grant
- * Letter of indemnification
- * Advertisements
- * End of study report

Audit Trail

- * Data show the study was conducted according to protocol

Data Discrepancies

- * Internal audits/monitoring
- * Sponsor audits/monitoring
- * Corrections documented

Example of Study Drug Administration

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Example of AE Reporting Discrepancy

C	D	Onset	Adverse event	Gr	Rel	Act	Ther	Out	Date Resolved
1	1	1/6/2004	Nausea	2	4	1	2	1	1/6/2004
1	2	1/7/2004	Pain: Headache	1	3	1	1	1	1/14/2004
					John Smith, MD			1/26/2004	

Concomitant Medications

Example of Discrepancy

C	D	Dose Date	Medication	Reason	End Date
-1	-126	9/1/2003	Psyllium	constipation	
1	1	1/7/2004	Prochlorperazine	Nausea	1/10/2004
1	2	1/7/2004	Diphenhydramine	itching	1/13/2004
				John Smith, MD 01/26/2004	

Example of Discrepancy in Adverse Event Reporting

C	D	Drug	Start Date	End Date
1	1	Cure-All	1/5/2004	1/5/2004

C	D	Drug	Start Date	End Date	Reason
1	1	<u>Prochlorperazine</u>	1/7/2004	1/10/2004	nausea
1	2	<u>Diphenhydramine</u>	1/7/2004	1/13/2004	itching

Electronic Database

- * Coding system
- * Relational database
- * Computer support
- * Passwords change periodically
- * Name of person entering data
- * Back-up tapes storage/QA plan
- * Security/confidentiality

Record Keeping (Regulatory)

- * Keep records: (21 CFR 312.62)
- * 2 years following the date the marketing application is approved for indication being investigated

OR

- * 2 years after investigation is discontinued and FDA notified

Record Keeping

- * ICH Guidelines
- * Site SOP
- * Sponsor SOP
- * IRB records 3 years
- * Follow-up/survival

Record Keeping NIH

- * Agency Records Officer
- * National Archives and Records Administration at <http://www.nara.gov>

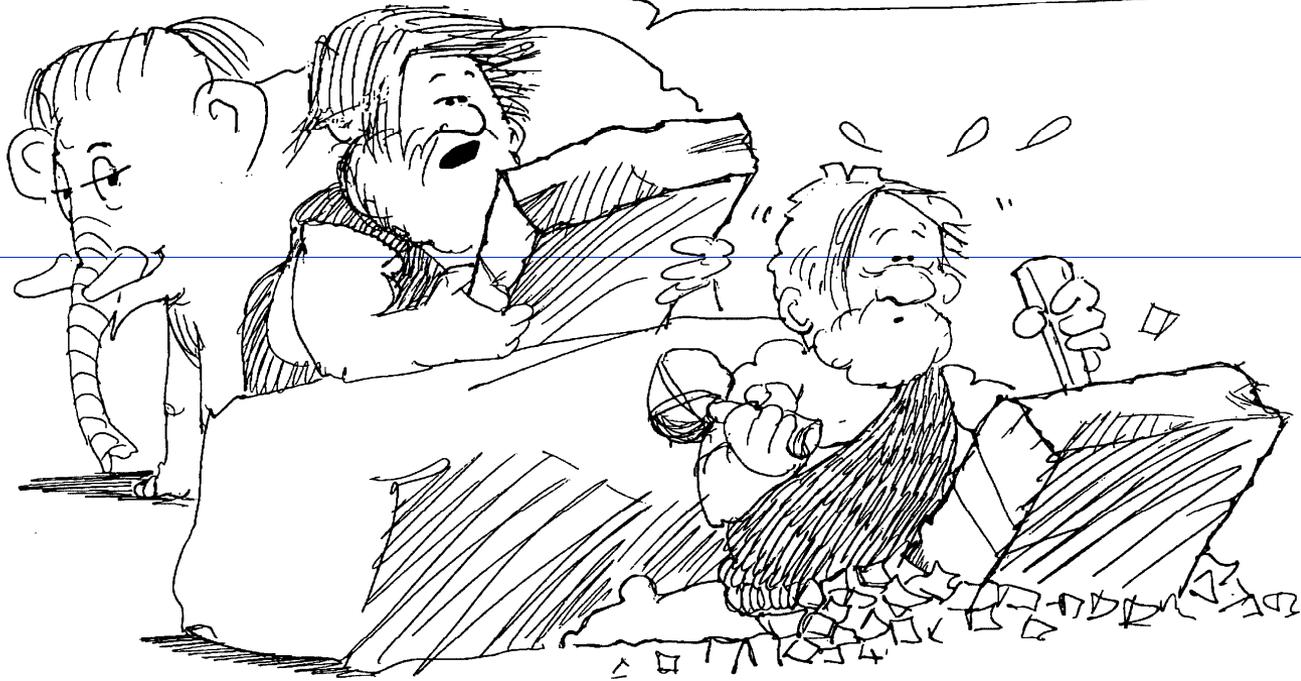
Developing Standards: Clinical Trials

- * Structured protocol
- * Defined elements
- * Human-readable
- * Machine-readable
- * Efficient review
- * Faster implementation
- * Easier analysis
- * Data mining across protocols

Outcome:

Clean data in a form you can analyze!

THE BOSS WANTS 10 COPIES BY 5:00



Quality

“Fast is fine, but accuracy is everything.”

(Wyatt Earp)

In God we trust!

Everyone else must show us the data!

Helpful URLs

FDA website:

<http://www.fda.gov>

Good Clinical Practices in FDA-regulated clinical trials:

<http://www.fda.gov/oc/gcp/>

Comparison of FDA and HHS Human Subject Protections:

<http://www.fda.gov/oc/gcp/comparison.html>

Guidance for Industry. E6 Good Clinical Practice: Consolidated Guidance:

<http://www.fda.gov/cder/guidance/959fnl.pdf>

Office for Human Research Protections:

<http://www.hhs.gov/ohrp/>

Cancer Therapy Evaluation home Page:

<http://ctep.cancer.gov/>

HIPAA:

<http://privacyruleandresearch.nih.gov/>

Cancer Data Standards Repository:

http://ncicb.nci.nih.gov/NCICB/infrastructure/cacore_overview/cadsr/

Helpful URLs

The International Compilation of Human Research Protections:

<http://www.hhs.gov/ohrp/international/HSPCompilation.pdf>

Device Advice: <http://www.fda.gov/cdrh/devadvice/>

Combination Products: <http://www.fda.gov/oc/combination/>

FDA Guidance: Supplements:

<http://www.cfsan.fda.gov/~dms/dsaergui.html>