CRF-C
HRB Clinical Research Facility Cork

Data Management

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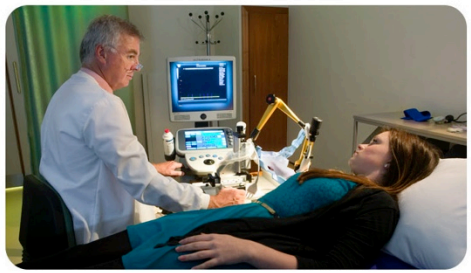


www.ucc.ie/en/crfc

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

HRB
Health Research Board

DATA MANAGEMENT OVERVIEW

- Role of the Data Manager in Clinical Trials
- General understanding of the principles underpinning data management for clinical studies.
- Overview of the data cycle in a clinical study.
- Case Report Form- Do’s and Don’ts
- Overview of data management plan.
- Sustainable data

Role of Data Management in Clinical Trials

Study Setup

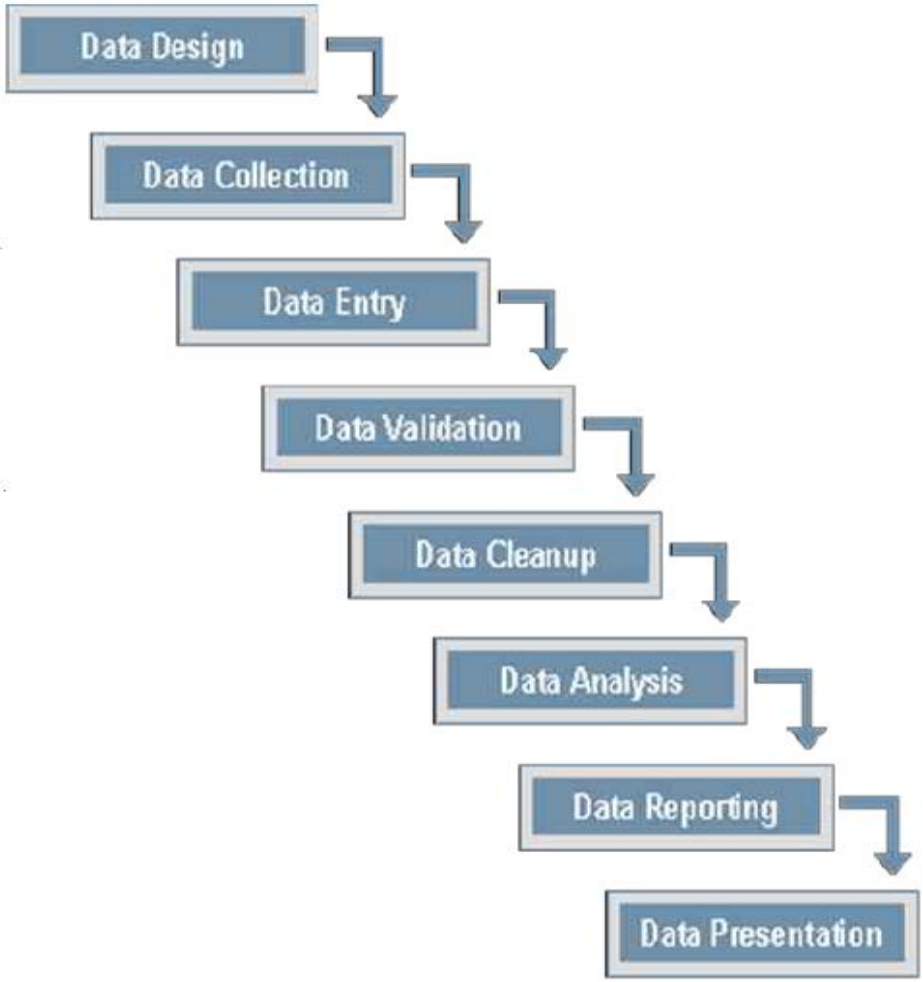
- CRF design and development
- Database build and testing
- Edit Checks preparation and testing

Study Conduct

- Data Entry
- Discrepancy Management
- Data review (Ongoing QC/QA)
- Query Reconciliation (Ongoing)
- Data Transfer

Study Closeout

- Query Reconciliation
- Quality Control
- Database Lock
- Electronic Archival
- Database Transfer



Regulations/ Guidance

REGULATORY FRAMEWORK

Good clinical practice is an international ethical and scientific quality standard for the design, conduct and record of research involving humans.

GCP is composed of 13 core principles, of which the following 2 applies specifically to data.

GCP – CORE PRINCIPLES FOR DATA

- The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

- All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

21 CFR Part 11

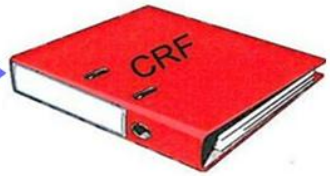
- Validation
- Record generation and copying
- Record protection
- Access
- Audit Trails
- Operational system checks
- Authority checks
- Device/Terminal Checks
- Training/User accountability
- System document control
- Controls for open systems
- Electronic Signatures

PLAN AHEAD TO CREATE HIGH-QUALITY AND SUSTAINABLE DATA


MAKE DATA
CLEAR TO
UNDERSTAND
AND EASY TO
USE

DATA SEQUENCE

Protocol design



CRF Design

Metadata design

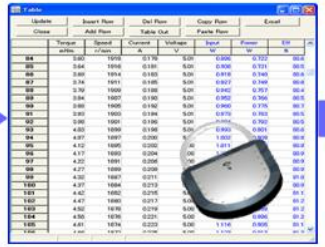
Database design

Database validation

Data collection

Data entry

Data cleaning



Dataset locked

Statistical analysis

Report writing

WHAT IS A CRF?

- A case report form (CRF) is a printed or electronic form used in a trial to record information about the participant as identified by the study protocol.

- CRFs allow us to:
  - record data in a manner that is both efficient and accurate.
  - Record data in a manner that is suitable for processing, analysis and reporting.

CRF Considerations

- CRF development:
  - First step in translating a protocol into data
  - Ideally occurs concurrently with protocol development
- Start EARLY!!
  - Enough time for drafts/reviews/changes/etc
  - To "Get it Right the First Time"
- PLAN AHEAD!!
  - With the END in mind!
  - Plan 'backwards'
    - What is the desired end product?
    - What is the best way to get there?
- Use draft protocol to design CRFs
  - Standard CRF modules
  - Project- and/or protocol-specific modules

CRF Considerations

- Collect precise data as required by protocol
  - Avoid collecting extraneous data
    - that "just in case" data
  - If you COLLECT it:
    - you have to CLEAN it
    - You have to ANALYZE it
    - You have to REPORT it
- Collect ONLY items needed in the database

CRF Design

- CRFs are only as good as their design
  - If unclear to the site personnel, will the data be accurate?
  - If unclear to DE operators, will entry into the database be accurate?
  - If not reflective of the protocol, will everyone know what to do with the resultant data?
- Must be easy to use
  - For site personnel
  - For Data Entry
  - Etc.
- Address needs of those who will work with the DATA
  - Database developers
  - Data Entry operators
  - Procedure programmers
  - Data managers
  - Statisticians
  - Clinical personnel
  - Etc.
- Consistency
  - CRF design consistency across studies

Consistent Format

- Consistent format throughout study
  - U.S. vs European vs Standard

DON'T:

	1c. Onset Date MM/DD/YY	1d. End Date MM/DD/YY
_____	☐☐/☐☐/☐☐	☐☐/☐☐/☐☐

Date: ☐☐/☐☐/☐☐ DD/MM/YY Recorder's Sign: _____ Da

NOTE: Elsewhere throughout this CRF Book, Dates are: ☐☐/☐☐/☐☐☐☐ DD/MM/YYYY

Consistent Format

- Use separate lines or combs (or boxes)
  - To display expected format
  - Include example of date in expected format

DON'T:

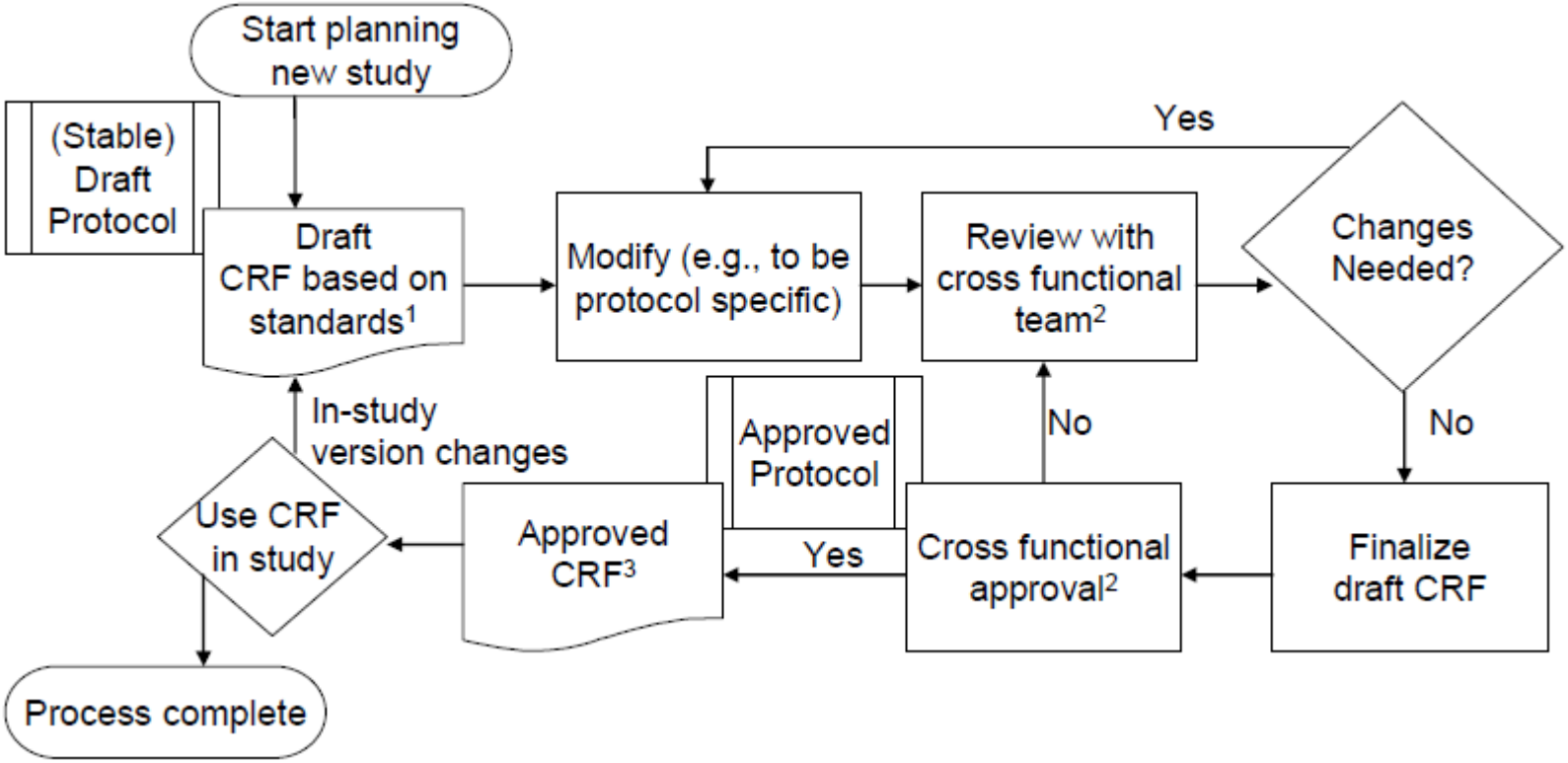
Date of Birth: _____

DO:

Date of Birth: | | | | | | | | |
dd MON yyyy *(Eg: 01-JAN-2007)*

Date of Birth: ____ / ____ / ____
dd MON yyyy *(Eg: 01/JAN/2007)*

Suggested CRF Development Workflow



High Level Overview of CRF Development Best Practices:

[1] Develop as early as possible with a stable draft Protocol, utilise standards

[2] Develop a cross functional team, reviewing from the perspective of the respective disciplines, including:

- Is all data for analysis collected?
- Is it possible to collect this way at the site?
- Are we collecting appropriate data to address safety?

[3] CRF is approved after Protocol is approved.

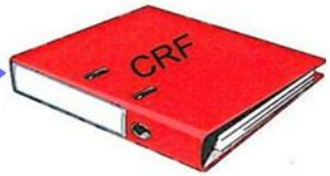
Designing CRFs, Key Questions

- What data is required to be collected?
  - Only data we specified in the proposal/protocol.
  - Only data required to answer the study question.

- When will this data be collected?
  - Baseline / follow-up .
- What Forms will need to be designed.
- Who is going to collect/complete this form.
- Are there validated instruments available?
- How is the data going to be analysed.

DATA SEQUENCE

Protocol design



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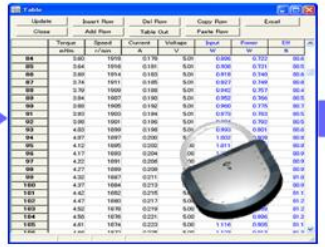

Dataset locked

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WHAT IS METADATA?

Metadata is structured data to organise and describe the data being collected.

It is a tool to control and maintain data entities:

- Content and variable definitions
- Validation rules

- Metadata consistently and effectively describes data and reduces the probability of the introduction of errors in the data framework by defining the content and structure of the target data.

Metadata File

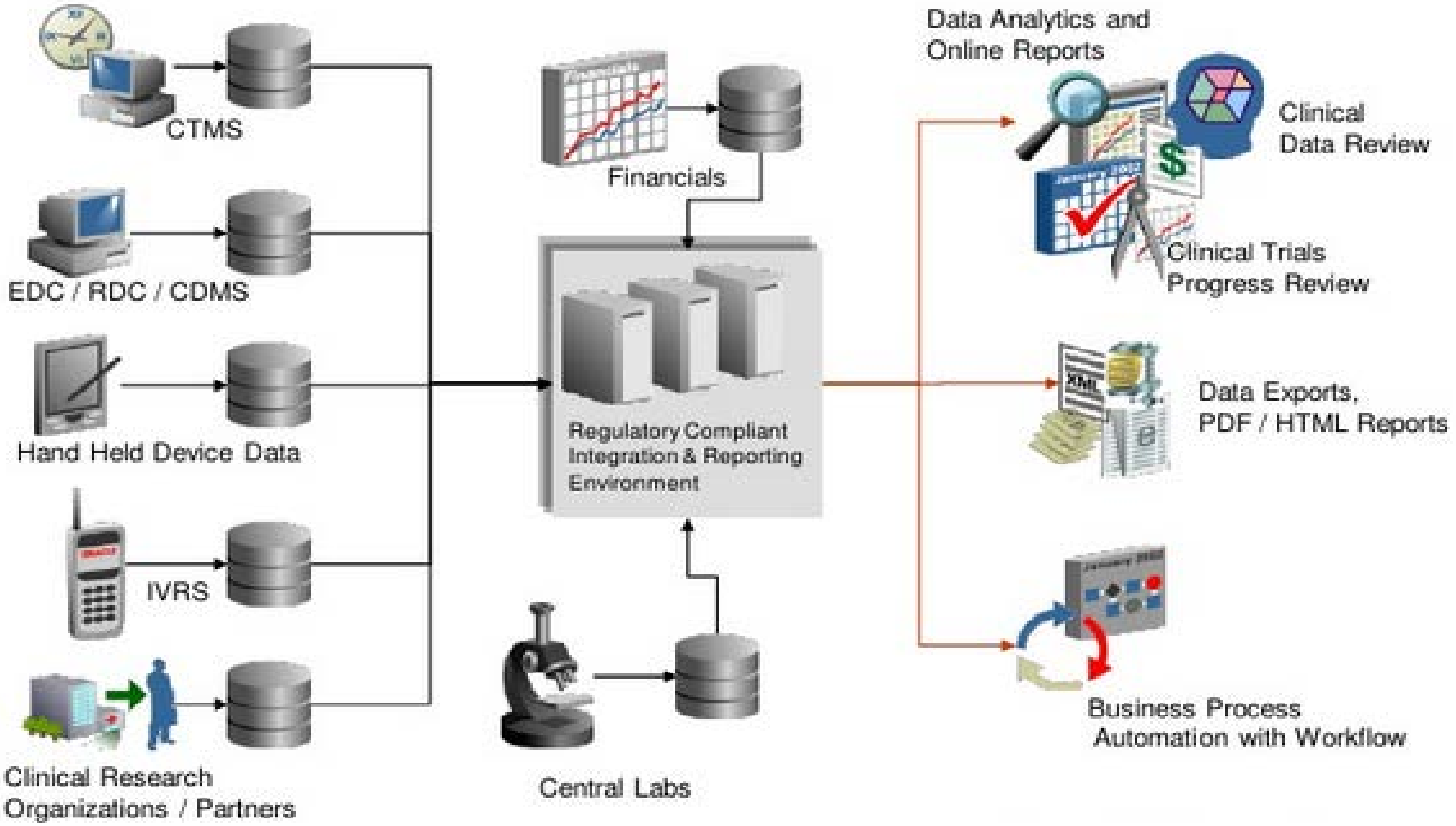
Name of Trial/Study: PAAD (Probiotics for Antibiotic Associated Diarrhoea) - stage 1

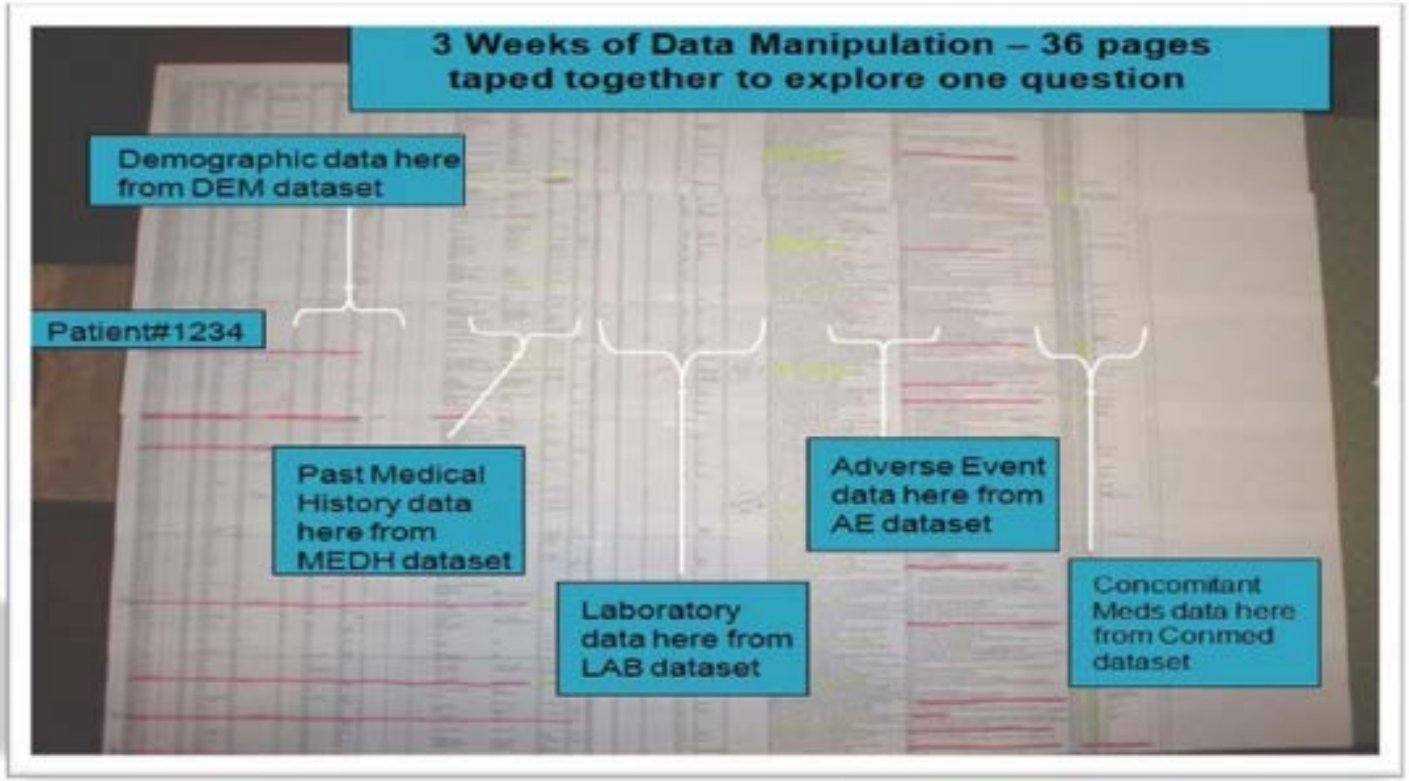
Metadata Author: H S	Number of Data Collection Forms for Trial/Study: 10

Name of File (Corresponding Data Collection Form): Recruitment CRF 02

Form Title	Variable Name	Variable Label	Data Type	Format		Length	Linked	Skip Condition	Validation Type	Validation
				Value Labels	Missing Codes					
Recruitment CRF 02	datecons	date of consent	date	dd/mm/yyyy		10			range	warn if <01.11.2010 > 01.06.2012
	sugender	service user gender	category	1 = Male, 2 = Female		1				
	consss1	consent for SS1	category	0 = no; 1 = yes		1				

Clinical Data Integration





Example of sophisticated review process of an FDA reviewer

Reference

1. http://www.globalsubmit.com/home/LinkClick.aspx?fileticket=ta1z74CpCQw=&tabid=260.

The Key Role of Data Standards

- Increase efficiencies of performing clinical trials
- Streamline data collection at investigator sites
- Higher quality data due to consistency of requirements
- Allow software development against a common standard
- Provide long-term means for electronic data archive
- Facilitate review of submissions

CDISC

DATA SEQUENCE

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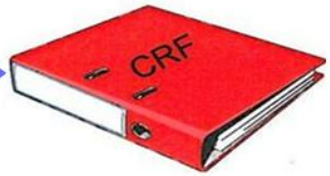

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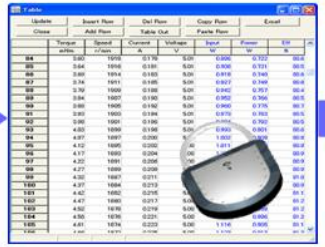

Dataset locked

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DATA COLLECTION

- Before starting data collection
  - Testing
  - SOP
  - Training
- During data collection
  - Monitoring/Audit

Testing the system

- Test
- Re- Test
- Re-Test again

DATA COLLECTION
AUDIT

- Maintain an audit trail of data changes made in the system.

- Procedure in place for when a study participant or other operator capturing data, realises that he / she has made a mistake and wants to correct data.

- Important that original entries are visible or accessible to ensure the changes are traceable.

Data Entry Process


Don’t over estimate your reader’s abilities

DATA ENTRY

- Different types of data entry exist, (manual /optical mark recognition system, online/offline, etc…).
- Type of data can also influence the method of data entry (numerical, free text, images etc…).
- It is important to have documented procedures (SOPs) defining who is performing data entry and how it is performed.

DATA ENTRY

- Data entry procedures should be tested at the earlier design stage, and testing adequately documented before sign-off.

- Adequate training on these procedures should be provided. Userguides/Data dictionary/Online recording

- Appropriate quality control procedures have to be set up.

AFTER DATA COLLECTION

- Regular backups should be made of your data, if outsourcing data collection or storage ensure that the company have backup systems in place.

- May need to archive whatever data you collect, includes both hard copy and electronic data, documents not archived need to be disposed of securely.

Putting the pieces together…

Photo by Dread Pirate Jeff
http://www.flickr.com/photos/justageek/2851643792

Data Management Plans (DMPs)

Importance of a DMP

- Make informed decisions to anticipate and avoid problems
- Avoid duplication, data loss and security breaches
- Develop procedures early on for consistency
- Ensure data are accurate, complete, reliable and secure
- Save time and effort – make your life easier!

HORIZON 2020

- Open Access to Research Data
- Data Management Plan a requirement
- What data will your project generate?
- How will it be exploited?
- Accessibility and verification
- Reuse
- Curation
- Long-term preservation

Funders' DM expectations

● Full Coverage ◐ Partial Coverage ○ No Coverage

	Policy Coverage		Policy Stipulations					Support Provided			
Research Funders	Published outputs	Data	Time limits	Data plan	Access/ sharing	Long-term curation	Monitoring	Guidance	Repository	Data centre	Costs
AHRC	●	●	●	●	●	◐	○	●	○	◐	◐
BBSRC	●	●	●	●	●	●	●	●	●	◐	●
CRUK	●	●	●	●	●	●	●	◐	●	○	○
EPSRC	●	●	●	◐	●	●	●	◐	○	○	●
ESRC	●	●	●	●	●	●	●	●	●	●	◐
MRC	●	●	●	●	●	●	○	◐	●	○	◐
NERC	●	●	●	●	●	●	●	●	●	●	◐
STFC	●	●	●	●	●	●	●	◐	●	◐	◐
Wellcome Trust	●	●	●	●	●	●	●	●	●	◐	●

DMP- Five common themes

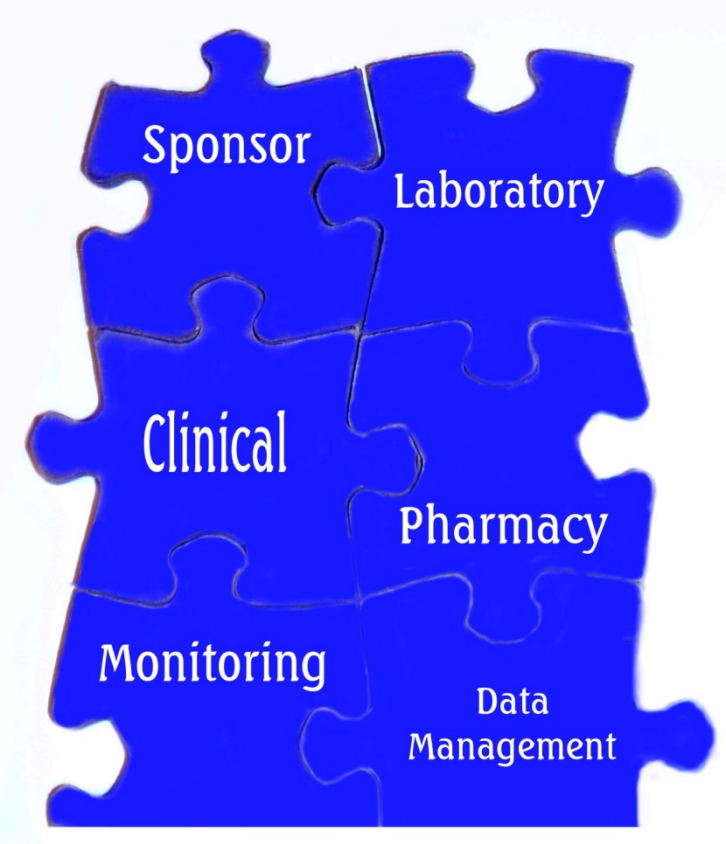
1. **Description of data to be collected / created**
   (i.e. content, type, format….)

2. **Standards / methodologies for data collection & management/ Short term storage**

3. **Ethics and Regulations**

4. **Plans for data sharing and access**
   (i.e. how, when, to whom)

5. **Strategy for long-term preservation**



When to plan?

- Recommended three versions:
  I. Minimal plan at the conceptualisation or grant application stage
  II. Core plan once the funding is in place covering issues up to the point of long-term management and preservation
  III. Full plan that adds issues of longer-term data management

Adherence and review

- The DMP should be regularly reviewed by the PI/DM
  - Once started, projects tend to change!
  - Develop habitual good practice
  - Use plan as a communication tool - with partners, funders and yourself!
- Make sure you know:
  - Who is responsible for making sure this plan is followed?
  - How often will this plan be reviewed and updated?

DMP advise

- Keep it simple, short and specific
- Seek advice - consult and collaborate
- Base plans on available skills and support
- Make sure implementation of the plan is feasible
- Justify any resources or restrictions needed

KEEP YOUR DIGITAL DATA SAFE,
SECURE AND RECOVERABLE

Sustainable Data

- LOOKING AFTER RESEARCH DATA FOR THE LONGER-TERM AND PROTECTING IT FROM UNWANTED LOSS REQUIRES HAVING GOOD STRATEGIES IN PLACE FOR SECURELY STORING, BACKING-UP, TRANSMITTING, AND DISPOSING OF DATA.

- Who knows what may happen in the future…….

THE TIMES

Max 20C, min 8C

Friday July 8 2011 | thetimes.co.uk | No 70306

£1

President Donald Trump pictured next to the American flag

Trump President

"An 'extremely credible source' has called my office and told me that Barack Obama's birth certificate is a fraud"

I speak to you today as a lifelong supporter and true friend of Israel. (CHEERS, APPLAUSE)
I am a newcomer to politics, but not to backing the Jewish state.

In 2001, weeks after the attacks on New York City and on Washington and, frankly, the attacks on all of us, attacks that perpetrated and they were perpetrated by the Islamic fundamentalists, Mayor Rudy Giuliani visited Israel to show solidarity with terror victims.
I sent my plane because I backed the mission for Israel 100 percent.

In spring of 2004 at the height of the violence in the Gaza Strip, I was the grand marshal of the 40th Salute to Israel Parade, the largest-single gathering in support of the Jewish state.

It was a very dangerous time for Israel and frankly for anyone supporting Israel. Many people turned down this honor. I did not. I took the risk and I'm glad I did.

But I didn't come here tonight to pander to you about Israel. That's what politicians do: all talk, no action. Believe me.

I came here to speak to you about where I stand on the future of American relations with our strategic ally, our unbreakable friendship and our cultural brother, the only democracy in the Middle East, the state of Israel.
Thank you.
My number-one priority is to dismantle

Popular journalism is crucial to a free society
Leading article, page 2

Staff wept as they were told the news
News, pages 3-10

Convicted in the court of public opinion
William Rees-Mogg; Opinion, page 29

What journalists do — and what readers expect
Letters, page 31

I have been in business a long time. I know deal-making.
And let me tell you, this deal is catastrophic for America, for Israel and for the whole of the Middle East.
The problem here is fundamental. We've rewarded the world's leading state sponsor of terror with $150 billion, and we received absolutely nothing in return.

I've studied this issue in great detail, I would say actually greater by far than anybody else.

Believe me. Oh, believe me.
And it's a bad deal.
The biggest concern with the

Key points for data management planning in research:

- Know your legal, ethical and other obligations regarding research data, towards research participants, colleagues, research funders and institutions
- Incorporate data management measures as an integral part of your research cycle
- Implement and review data management throughout research as part of research progression and review

Thank you!