Study Documentation

NHS Grampian Research and Development

Rory Lynch

Agenda

- Introductions
- Study set up
- Trial Master Files/Investigator Site Files
- Approvals/amendments
- Source data/Case Report Forms
- Good documentation Practice
- Progress/Safety reporting
- Deviations/breaches
- End of study
- Monitoring hints and tips

Introductions

- Rory Lynch– Research Monitor
  rory.lynch@nhs.scot

What kind of trials are you working on?

Non-commercial/commercial

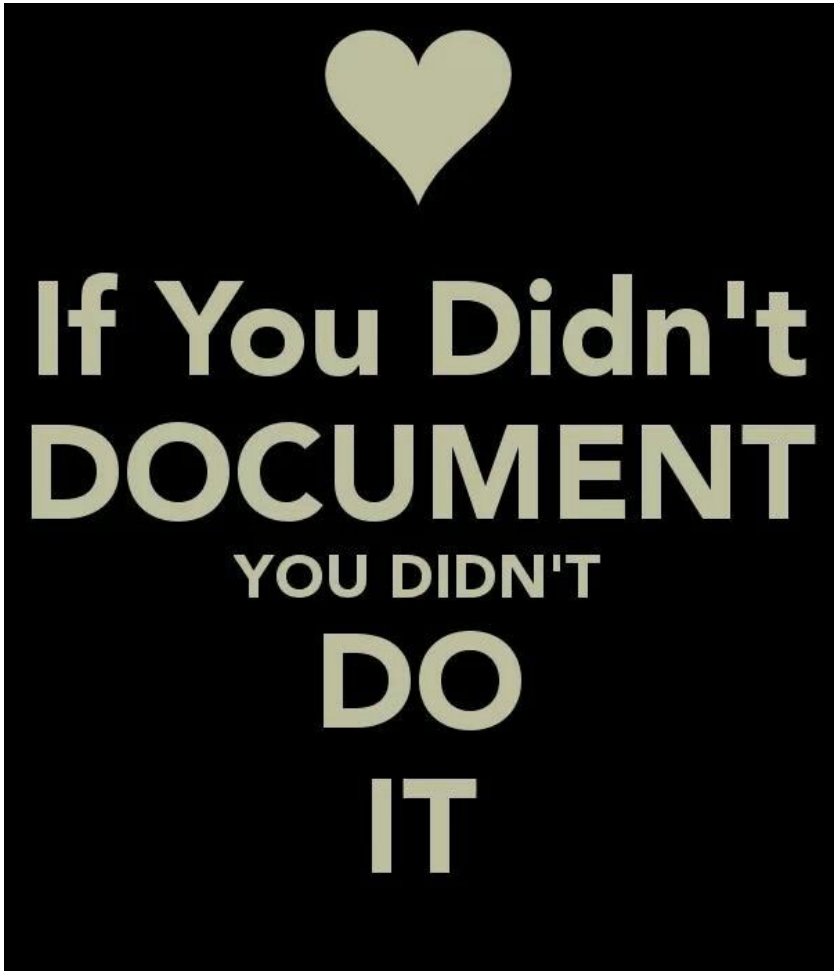
CTIMPs/non CTIMPs

Locally sponsored (UoA/NHSG)/hosted (externally sponsored)

Study Documentation

- ✓ Based on local procedures (SOPs)
- ✓ Relevant to both drug and non-drug research
- ✓ Aimed at new researchers /those setting up a study for the first time/changed role within research


THE
GOLDEN
RULE


If You Didn't
DOCUMENT
YOU DIDN'T
DO
IT

Fallacy

Researcher *(thinking)*: ‘I will remember everything about this visit.’

Monitor: ‘What happened at this visit? Why was BP not recorded?’

R: ‘Well, when the participant arrived …’

M: ‘It is not documented in medical records/study file and no file notes to explain.’

Not documented – did not happen

Study Documents

- A Study File is a collection of documents which ‘tell the story’ of the study
- These documents serve to demonstrate the compliance of Research staff with GCP
- Each site should set up a Study Site File at the start of study which will then be archived at the end of the study

Study Files and Documentation

- Trial Master Files (TMF)
  - Sponsor
  - Pharmacy
  - Investigator Site File
  - Laboratory
- Source Documentation
- Database

At end of study it will be closed out and archived.

Study Set Up

- Where can I get help?
- https://www.abdn.ac.uk/grampian-research-office/
- https://www.nhsgresearchanddevelopment.scot.nhs.uk
- http://www.hra.nhs.uk
- Speak to
  - Sponsor
  - QA Manager
  - Monitors
  - Ethics Committee

Local SOPs for Establishing and Maintaining Study Files

- https://www.abdn.ac.uk/grampian-research-office/sops/index.php
- Trial Master File: SOP-QA-7
- TMF index
- Investigator Site File: SOP-QA-8
- ISF non CTIMP index
- Applies to all staff conducting or supporting studies sponsored or co-sponsored by UoA / NHS

Local Sponsor contact: researchgovernance@abdn.ac.uk

Study Set Up: What documents do I need?

- Submissions, approvals and amendments
- Protocol
- Participant documents: Information sheets and consent forms, GP letter
- Delegation log
- CVs/GCP
- Training logs
- Enrolment logs
- Lab sample logs
- IB/SmPC for CTIMPs
- Templates for safety reporting
- General correspondence (e.g. email
- Case Report Forms

Establishing and Maintaining a TMF or ISF (Study File) tips

- Responsibility of the CI (TMF)/PI (site) – can be delegated to research team – Delegation Log
- Set up a TMF/ISF using a file index template
- Hosted studies may use the ISF file index template if not provided with one by external sponsor
- If index sections not applicable mark this as N/A on index
- Clearly state the location of all documents which are retained in different places (e.g. electronic)
- Keep secure in a lockable cabinet or room with restricted access

(Help available from Monitors if required)

Medicines for Human Use (Clinical Trials) Regulations 2004 (SI:1031)

"All Clinical Trial information should be **recorded, handled and stored** in a way that allows its accurate reporting, interpretation and verification"

"The **confidentiality of records** that could identity subjects shall be protected, respecting the privacy and confidentiality rules in accordance with the requirements of the **Data Protection Act 1998** and the law relating to confidentiality"

**** If you are ever notified of selection of MHRA inspection let R&D know immediately****

Submitting for Approval

- Protocol
- PIS & IC form/s
- Any other patient/participant documentation e.g. Invite letter/GP letter etc.

- IRAS forms
  - Study details
  - Research Team details

  - Local team completes OID for R&D approval.

Submissions

University of Jura

Bridge over Troubled Water
Main Street
Isle of Jura

GP Notification Letter

Date

GP ADDRESS

Dear Dr

Re: Patient details

Study title: Is there a link between chocolate consumption and depression?

Your patient has recently agreed to participate in the above study, which is taking place at the Psychiatric Unit, Jura Hospital. The study is investigating whether a regular intake of chocolate can improve mild depression. This involves consuming 2 bars of chocolate very day and attending the study clinic twice where a questionnaire is completed and a small blood sample will be taken on each occasion to check cholesterol levels.

I have attached the Patient Information Sheet, if you require any further information please do not hesitate to contact me.

Yours sincerely

University of Jura
Bridge Over Troubled Water
Main Street, Isle of Jura

Patient Identification Number for this trial: 001

CONSENT FORM

Title of Project: Is there a link between chocolate consumption and depression?

Name of Researcher: Dr Art Garfunkel

		Please initial box
1	I confirm that I have read and understand the information sheet dated .....1st December 2009 (version .....1.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	HG
2	I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	HG
3	I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from the University of Aberdeen or from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	HG
4	I agree to my GP being informed of my participation in the study.	HG
5	I agree to take part in the above study.	HG

HOLLY GOLIGHTLY — 27/2/10 — Signature

University of Jura
Bridge Over Troubled Water
High Street, Isle of Jura

1

Participant Information Sheet

Title of the research:

Is there a link between chocolate consumption and depression?

You are being invited to take part in a research study being conducted in Jura. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information and discuss it with your family or friends first. If there is any thing that is not clear or if you would like further information, please ask. Please take time to consider whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?

The purpose of this study is to determine if regular intake of chocolate can improve mild depression. Other studies have shown that eating fruit regularly may improve mild depression but there have been no studies looking at the effect of chocolate consumption.

Why have I been chosen?

You have been chosen because you suffer from depression and do not require medication at present. Your participation is voluntary.

Do I have to take part?

No it is up to you to decide whether to take part. If you do decide to take part, you will be given this information sheet to keep and if you decide to participate you will be asked to sign a consent form. If you decide to take part you are free to withdraw at any time without giving reason and without detriment to yourself.

What would I be asked to do if I took part?

If you agree to be in this study, we will ask you to eat two bars of chocolate every day for the period of the study. The study will last two months. You will attend the study nurse on two occasions, at the start of the study and at the end of the study. You will be asked to complete a questionnaire, give a blood sample to check your cholesterol and also have your weight checked at each visit.

What are the possible disadvantages and risks of taking part?

The study has been reviewed by an independent ethics committee who have decided there are no unacceptable risks and the study may go ahead.

The possible risks are:

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DO YOU SUFFER FROM DEPRESSION?

If so, you are not alone. More than five million people suffer from depression in the United Kingdom.

Will eating Chocolate help you?

This study has been launched to find out if there is a link between chocolate consumption and depression.

All GP Practices in Jura are taking part.
ıu are aged 18 or over and are NOT currently taking medication to treat your depression, you may be able to help with this research.

tact Penelope Cruz, Research Nurse, Psychiatric Unit, Jura Hospital, of Jura.Telephone: 09876 555552

TELEPHONE INTERVIEW QUESTIONS

1. hfhfdhjdfjgdjtfhjngtfnmjgfjmngfjgfgfnhgfjrdghfuhrshydrhtfkjtfk

2. fgjfgkmfghdrydrtjftk,tfjmbmkghkjyfgklylytly

3. dgjnmdkmfgtkftkjyfirgfylylkytiky

4. fkjhfktduhyrdsjrjyytklikdrutujedujtrututuryhfrthjtjfgjtfujtityutr

5. dfjtfgkmytkuylytujrdghrd

Approval Documentation - by who?

Sponsor

- Ethics
  - NHS
  - CERB
  - Rowett Institute
  - RGU
- R&D Management
- MHRA
- Research Passport
- Other
  - e.g. ARSAC

Amendments

- Process: follow the SOP – SOP QA 19
- Amendment log
  - Amendment number and details
  - Versions of documents approved at each amendment
  - Approvals received for amendment

- Filing:

  - Supersede old versions of documents

  - Newest and current version filed on top

  - If keeping a separate working file, then only have current documents within this

- Documents should all have version number and date in footer of page.

Study Registration

- *ALL* studies need to be registered on a public database prior to consenting
- They need to be kept updated
- Good practice to identify a member of the Research team on the delegation log who is responsible for this task

Recommended sites are:

www.researchregistry.com or clinicaltrials.gov


Good Practice

Source Data – What is this?

"All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial."

ICH GCP Guidelines

The first place trial data are documented.

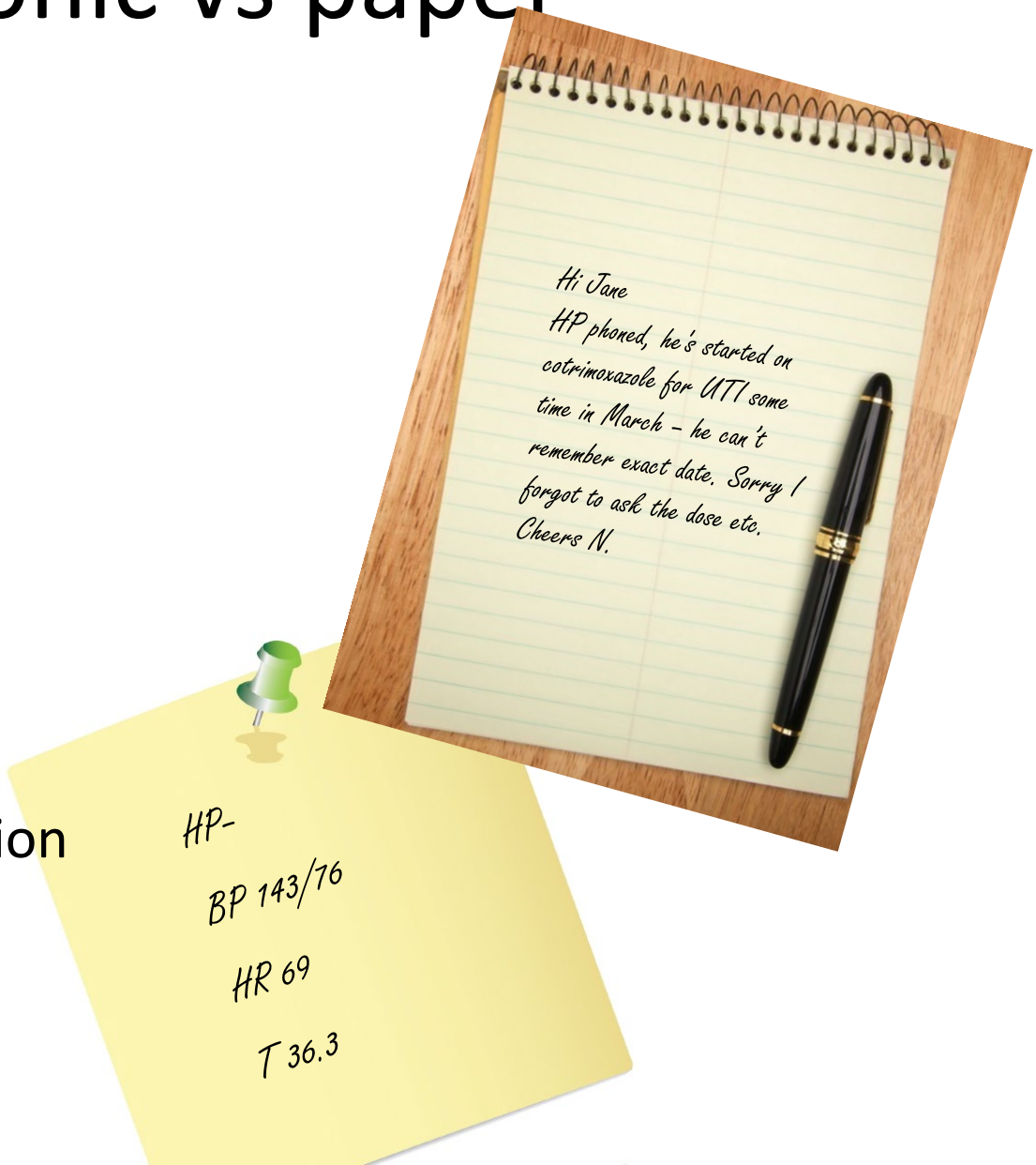
Source data what should be recorded?

- Consent process
- Eligibility confirmed by a medic (CTIMP)
- CRF data capture points (medical history, physical exam, con meds, demographics, vital signs etc..)
- Subsequent visits document that participant is happy to remain in trial.
- Any changes from last visit e.g. medications
- Adverse events and corresponding documents
- Any follow up communication with participant: phone calls, emails

Electronic vs paper

Examples:

- Patient notes
- Laboratory test results
- X-rays
- Scan results
- Record of drug administration
- Electronic data
- Primary care – information from participant but verified by GP.



Completion of a Case Report Form

- Requires consistency on all pages of an individual document
- Writing must be ***legible***
- Complete all appropriate fields OR
- State why an entry was not made e.g. N/A or Not Done (ND)
- Date formatting as per Sponsor request

  -i.e. 30/03/2023 OR 30/MAR/2023

Good Documentation Practice
SOP-QA-27

- All records must be attributable, legible and completed at the time of the event (contemporaneously).
- Errors: crossed out with a single line; the corrected value inserted alongside, initialled and dated
- Correction fluid not permitted
- Attachments and printouts from instrument – signed and dated
- Permanent ink (where requirements for medical records e.g. black ink is necessary then this must be complied with)
- Legible writing
- All sections must be completed or have explanation why not completed; use N/A for not applicable

Data Entry

- Source data should match data entry
- Test databases / dummy participant?
- CRF guidance document
- Data ranges?
- Data queries
  - Try to keep on top of them
  - If illogical tell Trial Manager/CRA

Safety & Progress Reporting Documentation

Annual Progress Reports Development Safety Update Reports APRs and DSURs *SOP-QA-21*

- Development Safety Update Reports – for CTIMPs locally sponsored or externally sponsored.

Safety Reporting (Pharmacovigilance)
Adverse Events in CTIMPs (*SOP-QA-22)*

- Applies to all studies
- Guidance as per protocol
  - SAEs to be reported to Sponsor within 24 hours
  - Medic oversight required for confirming relatedness
- For local studies contact RG office on pharmaco@abdn.ac.uk

- Guidance on Reporting SUSARs via eSUSAR website
  - https://**esusar**.mhra.gov.uk/
- SAE reporting form
- Trial Log (SAEs)
- Pregnancy Form
- AE Form

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Serious Adverse Event Form

Internal Sponsor Reference:		**R&D Reference:**	
Study Title:			
EudraCT:		**Centre:** (if multicentre trial)	
Participant Number:			

Do not send identifiable data or source documents with this report

Is this a possible SUSAR? Yes ☐ No ☐

Date of report D D M M Y Y Y Y

Initial Report ☐ **Follow Up Report** ☐

Subject Details

Initials ☐☐☐ Date of Birth D D M M Y Y Y Y Gender: Male ☐ Female ☐

Serious Adverse Event

Seriousness criteria (Check all that apply):

Resulted in death ☐	Life-threatening ☐	Hospitalisation/Prolongation of hospitalisation ☐
Persistent/Significant Disability/Incapacity ☐	Congenital anomaly/ Birth defect ☐	Other medically important condition ☐

If Resulted in Death

Date of Death:	Cause of Death:	Cause of Death determined by Autopsy:
D D M M Y Y Y Y		Yes ☐ No ☐

Action taken:	Drug withdrawn ☐	Dose reduced ☐	Dose increased ☐
	Dose not changed ☐	Unknown ☐	Not applicable ☐

Expectedness: Expected ☐ Unexpected ☐ Onset Date: D D M M Y Y Y Y

Diagnosis:

Relationship to Study Drug: None ☐ Possible ☐ Probable ☐ Definite ☐

Deviations and Breaches
SOP-QA-25

Applies to all studies locally sponsored and externally sponsored.

Definitions, Procedure, Sponsor assessment and investigation, Notification, Reporting, and Corrective and Preventive Actions (CAPA)

- Log of Deviations, Breaches and Urgent Safety Measures
- Breach Report Form

Research Project Closure
SOP-QA-31

Research Project Closure
SOP-QA-31

- **Including procedure for project suspension and early termination**
- Responsibility of the CI to ensure that the 'end of study/trial' is clearly defined in the protocol - any change to this is a substantial amendment
- Locally sponsored studies: Contact R&D so they can have trial close out monitoring visit
- Declaration of End of Trial form must be sent to Sponsor, MHRA and REC within **90 days** of the trial ending (copy to R&D)
- Check for completeness of TMF & Data Collection
- Final reports & dissemination of results - SOP-QA-33 Research Project Publications and Dissemination

Archiving
(*SOP-QA-32)*

- Applies to all research.
- Sponsor and CI must ensure essential documents are retained for an appropriate period of time - and made available for Audit & Inspection.
- CTIMPs =25 years minimum (unless 3rd party obligations differ).
- Defined on REC application in IRAS form.
- Multicentre studies- as per sites procedures or returned to Sponsor?

Archiving SOP – cont.

- For externally sponsored studies - sponsor remains responsible for archiving.
  - PI – check contract to establish if archiving has been delegated from the Sponsor to PI
- Electronic data files:
  - held on a UoA or NHSG secure networked server using a validated system
  - 'locked' in a read only format
  - restricted access as documented in the TMF
- Access to archive – controlled & restricted
- Destruction of Archive – agreed with named archivist

- **Do not destroy early or take with you if you leave – must be retained within the Sponsors locality**

Essential / Source Documents

- TMF / ISF
- Data
- Hospital Records
- Clinical and office charts
- Lab notes
- Memoranda
- Subjects diaries
- Case Report Forms
- Evaluation checklists
- Recorded data from automated instruments
- Data Queries
- Copies of transcriptions

- Records kept at pharmacy / Labs
- X-Rays / reports
- Photographs / microfilm
- Other – if appropriate

Hospital Health Records

- Health records and source data therein should be retained throughout the archiving period
- NHSG policy – scanned & destroy after 6 years inactivity or 3 years after death
- New SOP – Procedure for Retention of Health Records – to include alert on TrakCare® to back up retention sticker

- Adhere sticker to front of 'pink cover sheet' (or inside cover of health record if no pink sheet) documenting:
  - Patient Name:
  - CHI number:
  - Research Study:
  - Do not destroy until:
  - Contact:
  - Signature:

SOP-QA-36 – Retention of Health Records of Clinical Trial Patients – includes details of alert on TrakCare® to back up retention sticker

Hints & Tips from our Monitor

Monitoring purpose

- Safety and wellbeing of participants
- Data is accurate and verifiable
- Protocol, GCP and SOPs being followed
- Sponsor oversight

What is involved?

- TMF/ISF reviewed
- Consent forms reviewed
- If CTIMP/high risk trial -> source data and case report forms reviewed.
- If CTIMP pharmacy file reviewed

Monitoring Findings

Non-conformances

- A sample log was not filed and no details of storage locations
- The recruitment is not as per the protocol
- Documents not version controlled. Superseded documents were not marked as such
- The CI had pre-populated the date of when the participant had signed consent form
- The delegation log and a number of CVs GCP/GRP certificates were not filed
- Lack of clear documentation in the medical notes.

Monitoring Findings

Observations

- Incomplete documents and some missing documents from the ISF
- Correspondence not filed
- A file note should be used where necessary
- APR to be submitted to REC
- Protocols not signed
- Incorrect sequence of filing of documents.

Breaches/Deviations

- Any departure from approved study documentation or GCP.
- Deviations refer to divergences that do not significantly impact patient rights, safety, well-being or outcomes.
- Breaches refer to divergences that may significantly impact patient rights, safety, well-being or outcomes/ impact the reliability, completeness and accuracy of the study data.

Monitoring Findings

Deviations

- The date of PI signing consent form precedes the date of the patient's signature.
- Participant reported forgetting to take Trial medication for a day.
- Patient receiving an MRI scan 2 weeks later than planned due to other commitments.

Monitoring Findings

Breaches

- Patient consented to trial prior to regulatory green light being issued.
- Trial medication lost by ward staff before patient could collect it.
- Monitoring visit was meant to occur following the registration of 1st patient. However, monitors were not informed until 10 patients had been recruited.

Tips: Do!

- Update site file on a regular basis
  - Includes Delegation log/CVs/GCP certificates
- Review your CV annually and update if required e.g. when new training attended (GCP)
- Keep *all* superseded documents
- Mark superseded document appropriately: score through them with single line, date, sign, write superseded by version 2...
- Electronic TMF/ISF should be stored on secure server (not researchers own secure folder)

Tips: Do!

- Check consent forms are completed appropriately
  - File note if any issues
- Insurance and indemnity letters are issued on annual basis via R&I (if study longer than a year, then delegated research team member should contact Sponsor to get a copy of one to include into the TMF/ISF if applicable)

FILE NOTES

- Should be signed and dated by person who wrote it – may need approval and signature of PI (proves oversight of need of file note)
- Change of PI/CI – substantial amendment

Tips: Do not!

- Hand write on official documents (scribbling phone numbers etc..)
- Write on post-it notes and attach to these documents
- Don’t fill in stop dates on delegation log until end of study or staff member leaves

Key Points

- Have one person responsible for maintaining TMF/ISF within the research team
- Follow template index
- Keep your documentation inspection-ready: file everything in the appropriate place, update delegation log, training records, AE logs etc.
- Don’t forget about safety, progress and end of study reporting

Finally Remember

“If it isn’t documented, it didn’t happen”

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Thank You
Any questions

NHS Grampian R&D

Ensuring quality of research,

providing guidance and training