



Medicines & Healthcare products  
Regulatory Agency



**U.S. FOOD & DRUG**  
ADMINISTRATION

# Effective Use of Audit Trails

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# Effective Use of Audit Trails

**How well designed and controlled audit trails can improve compliance and quality system performance.**

**Introduce strategies for effective use of audit trails.**



# Effective Use of Audit Trails

How they can aid our compliance and improve our systems

Design

Control

Review

Examples

**If only we had looked first...**



# Audit Trails: A Reminder

Audit trails are metadata that are a record of critical information (for example the change to or deletion of relevant data) that permit the reconstruction of activities.

The relevance of data retained in audit trails should be considered by the company to permit robust data review & verification.



# ICH E6 (R2) Good Clinical Practice

Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry **(e.g. via an audit trail)**. (4.9.0)

**Audit trail** - Documentation that allows reconstruction of the course of events. (1.9)



# ICH E6 (R2) Good Clinical Practice

Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data **(i.e. maintain an audit trail, data trail, edit trail).** (5.5.3)

Quality Management should identify risks to critical trial processes and data. (5.0.2)



## And do not forget

All clinical trial information should be recorded, handled, and stored in a way that allows its **accurate reporting, interpretation and verification**. This principle applies to all records (paper or electronic) referenced in this guideline.  
*(2.10)*



# A holistic approach to Data Integrity?

Which of the following is your favourite TV detective?

1. Ricardo Tubbs
2. Christine Cagney
3. Dirk Gently
4. Columbo
5. Jessica Fletcher







# A holistic approach to Data Integrity?

## **Dirk Gently's Holistic Detective Agency**

Dirk Gently, an eccentric "holistic" detective, who understands everything in the universe to be interconnected. He does not solve cases by conventional means, but rather by following fate.

*(Wikipedia, Douglas Adams)*



# A holistic approach to Data Integrity?

Is following GxP an effective way to ensure data integrity? Or is there a better way.....



Audit trails can support trial activities and identify problems that may not be obvious



# The good old days....

	Day	Month	Year
Date of Assessment	28	98	16

	Day	Month	Year
Date of Assessment	28	<sup>0</sup> <del>9</del> 8	16

*Entry error, ADF 28/09/16*



# eSystem Audit Trail

- What data parameter was changed

Data field/Variable Name, Visit Date

- What the change was

Field value **before and after**

- Who changed it

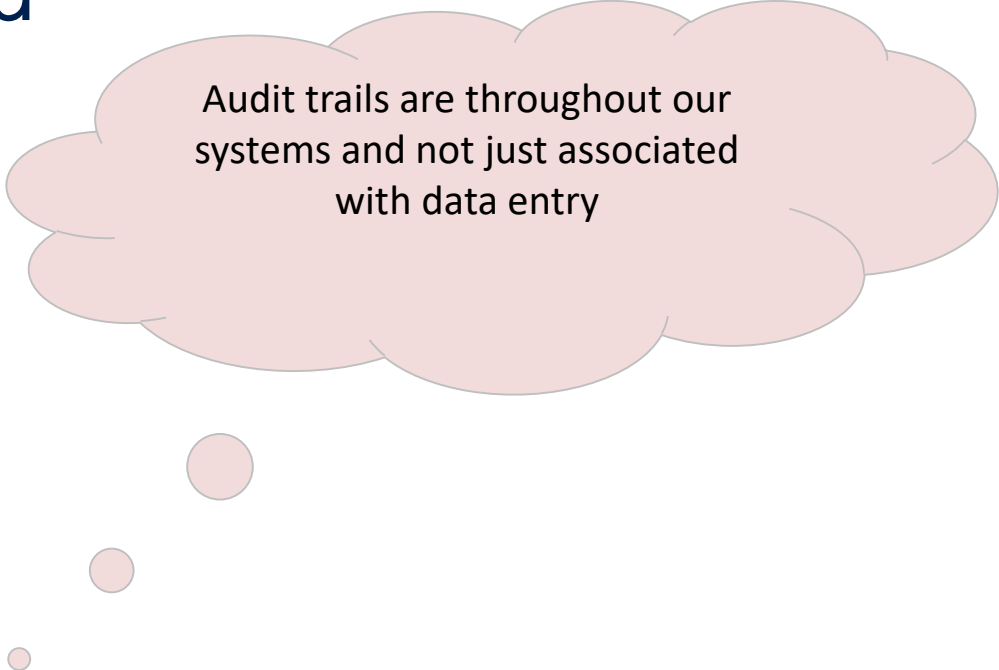
User names and roles and organisation

- When was it changed

Date and time (which time-zone?) of the change

- Why was it changed

Reason field or **link to the query** raised



Audit trails are throughout our systems and not just associated with data entry

It's an automatic function rather than reliant on the person to initial, date etc.



# eSystem Audit Trail

- eSignatures and invalidation if data changed
- Actions/workflows would involve other users and roles, not just the site users
- When database/eSystem was deployed into production (particularly if at country/site level) and how relates to approvals of updates
- To show user access history (addition/removal of users, changes of role, changes of role permissions)



# eSystem Audit Trail

- System actions (e.g. importation of electronic data)
- Authentication/Authorisation Audit (who was logged in & when)
- Logs of Back ups
- Changes to system properties – (e.g. turn off audit trail)



# eSystem Audit Trail in Practice

An authorisation form to make database updates was signed by management on 16 January.

However, on review of the electronic system audit trails changes to the data had been made before the authorisation had occurred (changes were made on 13 and 15 January respectively).



# Design



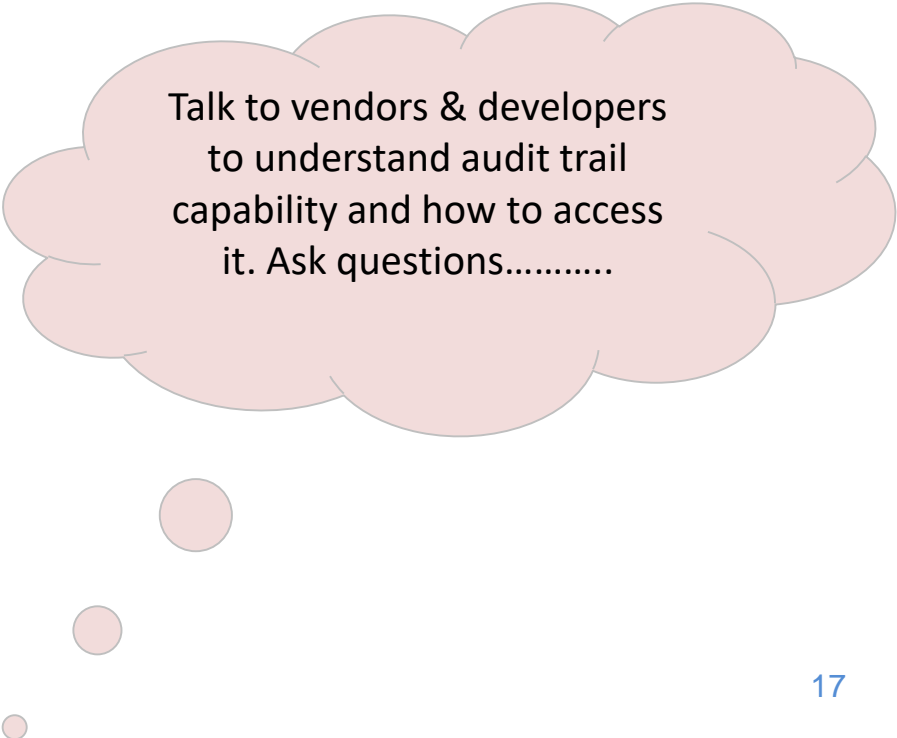




# Design Considerations

Make sure the audit trail works for you and is reliable.

- There is an audit trail and there can be more than one – don't forget system events
- Delivers regulatory requirements
- Fit for purpose
- Is it open to abuse?
- Security
- Archival



Talk to vendors & developers to understand audit trail capability and how to access it. Ask questions.....



# Design – Understand Outputs

	A	B	C	D	E	F	G	H	I
1	Study	CRTN	Patie	Visit	Visit Code	Eform	Eform Code	Eform Cycle	Question
2			1800	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
3			1800	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
4			1801	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
5			1801	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
6			1802	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
7			1802	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
8			1802	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
9			1803	Patient Initialization	ENROLL_EVT	Required Identifier Form	FENROLM		1 Patient code:
36			1807	Study Completion	V055_TERMINATIO	Death	FDIED1_1AI		1 Relationship of death to stu
37			2523	Study Completion	V055_TERMINATIO	Authorized Signature	FSIGN1_1AI		1 Date
38			2523	Study Completion	V055_TERMINATIO	Authorized Signature	FSIGN1_1AI		1 Authorized signature
39			2523	Study Completion	V055_TERMINATIO	Authorized Signature	FSIGN1_1AI		1 Authorized signature
40			2691	Study Completion	V055_TERMINATIO	Death	FDIED1_1AI		1 Date of death
41			2691	Study Completion	V055_TERMINATIO	Authorized Signature	FSIGN1_1AI		1 Date
42			2941	Study Completion	V055_TERMINATIO	Authorized Signature	FSIGN1_1AI		1 Date
43			2941	Study Completion	V055_TERMINATIO	Authorized Signature	FSIGN1_1AI		1 Authorized signature
44			2941	Study Completion	V055_TERMINATIO	Authorized Signature	FSIGN1_1AI		1 Authorized signature

To use the audit trail effectively the meaning of fields needs to be understood.



# Design – Understand Construction

Study Name	Subject Number	Question	Entered Reason	Current Value	Current Value Date/Time	Previous Value	Username
BIG TRIAL	123456	Present at dosing?	advice sought from PI		06-Oct-2014 10:00:14		JFLETCHER
		Weight	Transcription Error		06-Oct-2014 10:00:14	UNK	CGRIMES
		Was ECOG Performance Status as	Transcription Error	N	09-Oct-2014 13:51:52	Y	BCOX
	123888	Assessment type?	Transcription Error		17-Nov-2014 11:45:05		JMANGLE
	123457	QTcF interval #1 (msec)	Transcription Error	N	17-Nov-2014 11:45:05	Y	JMANGLE
	123458	Time performed #1	Transcription Error		17-Nov-2014 11:45:05	UNKNOWN	RGRIMES
	123459	Indication Type	as per query	PROPHYLAXIS	27-Nov-2014 11:40:49	MEDICAL HISTORY	DGENTLY
	123460	Indication	as per query		02-Dec-2014 15:34:00	No source information	DGENTLY
	123461	Reason for discontinuation of ass	Transcription Error	1.0	15-Dec-2014 10:52:07	Amend 1.0	GLEE

Within live system the data audit trail linked to queries. However in the data extract the link was lost. Only way to reconstruct activities post study would be via redeployment of database.

Merged cells in data extracts can cause problems when reviewing audit trails!



# Design – Transaction Times

Does Audit Trail Capture all data changes & could this be abused?

If several fields of a system (e.g. eCRF) can be completed prior to a submit action – would any data changes prior to this get captured in the audit trail?

BMI (18-25)	Weight (kg)	Height (m)	BMI	SUBMIT
	84.2	1.79	26.28	



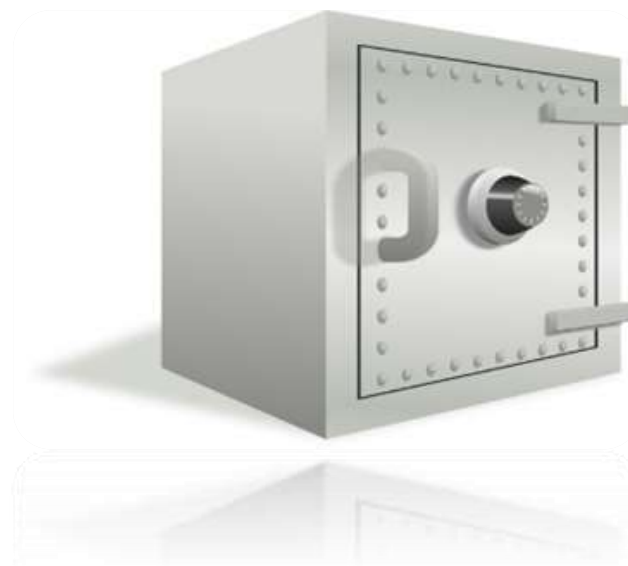
# Audit Trail in Practice

A volunteer for a study was borderline for the BMI criteria to be eligible for a bioequivalence study.

However, on review of the electronic system audit trails multiple changes to the data had been made to calculate the correct weight required for a volunteer to become eligible for the study. Volunteer returned at a later date for screening without oversight of the Investigator and in violation of company procedures.



# Control





# Control of Audit Trails

Security

Shared log ins for the system so it was not possible to attribute activities to any individual.  
No control of access permissions with multiple users being able to delete or amend audit trails.

Archival

Audit trails were not archived and the company was unaware that under the contract with the vendor all databases would be deleted on completion of the agreement.

Is it open to abuse?

Could be....



# Control of Audit Trails

PK Analysis Data reviewed on inspection



- Issues had been identified when trying to verify the conduct of laboratory analysis. Audit trails covering the six months containing the analysis were missing
- The laboratory could not explain what had happened to the data and did not have any procedures to review or manage audit trails effectively





# Review

## **The Bank of Life**

**Statement 2017/18**

**Balance:     \$100.00**

**Transactions:**

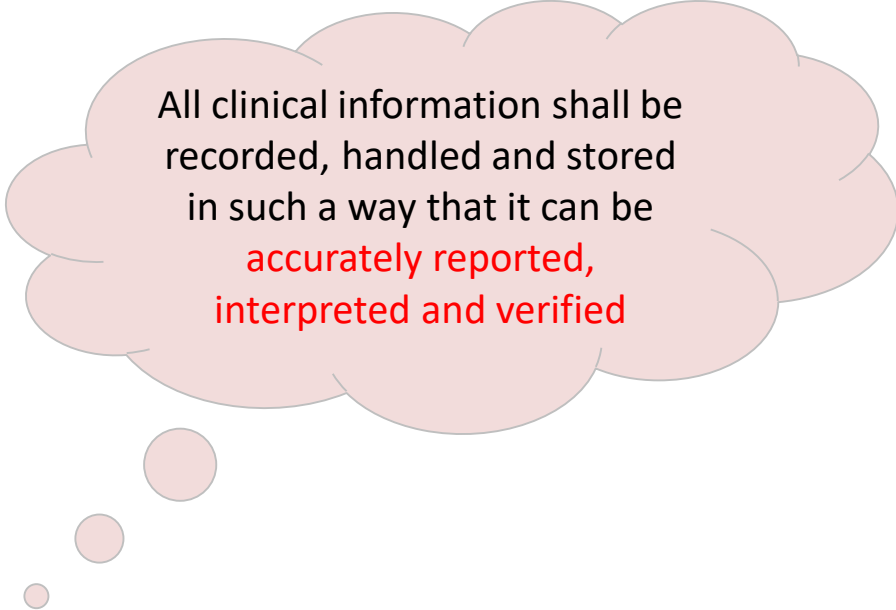
Don't worry everything is OK, nothing  
to see here.....



# Audit Trail Review

How can the audit trail be reviewed?

- In the system
- Via reports (e.g. in system or export)
- Maintain dynamic data



All clinical information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified



# Audit Trail Review

Using “Big Data” can give information across records

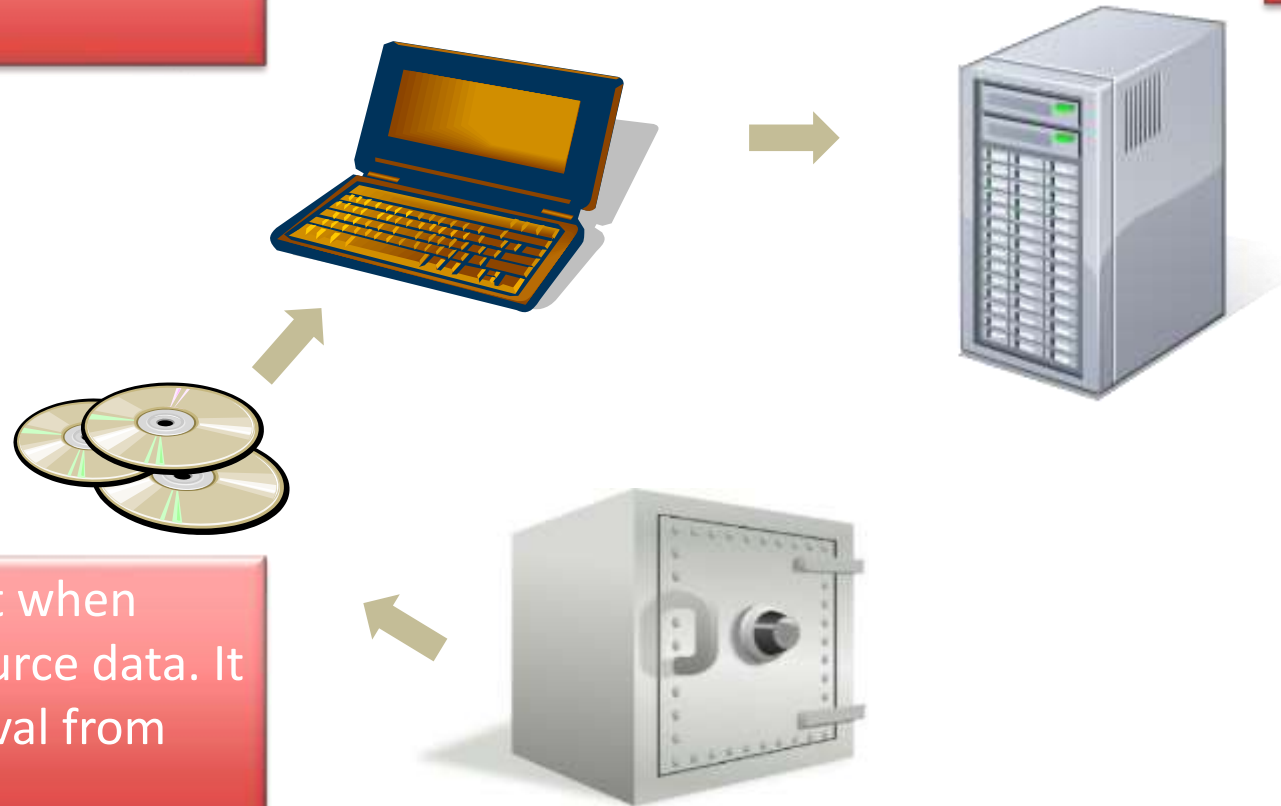
Study Name	Subject Number	Question	Entered Reason	Current Value	Current Value Date/Time	Previous Value	Username
BIG TRIAL	123456	Present at dosing?	advice sought from PI		06-Oct-2014 10:00:14		JFLETCHER
		Weight	Transcription Error		06-Oct-2014 10:00:14	UNK	CGRIMES
		Was ECOG Performance Status assessed?	Transcription Error	N	09-Oct-2014 13:51:52	Y	BCOX
	123888	Assessment type?	Transcription Error		17-Nov-2014 11:45:05		JMANGLE
	123457	QTcF interval #1 (msec)	Transcription Error	N	17-Nov-2014 11:45:05	Y	JMANGLE
	123458	Time performed #1	Transcription Error		17-Nov-2014 11:45:05	UNKNOWN	RGRIMES
	123459	Indication Type	as per query	PROPHYLAXIS	27-Nov-2014 11:40:49	MEDICAL HISTORY	DGENTLY
	123460	Indication	as per query		02-Dec-2014 15:34:00	No source information	DGENTLY
	123461	Reason for discontinuation of assessment?	Transcription Error	1.0	15-Dec-2014 10:52:07	Amend 1.0	GLEE
	123462	Diastolic Blood Pressure (mmHg)	Transcription Error	460	19-Dec-2014 09:50:00	125	CGRIMES
	123463	Systolic Blood Pressure (mmHg)	Transcription Error	460	19-Dec-2014 09:50:58	120	CGRIMES
	123464	Systolic Blood Pressure (mmHg)	Transcription Error	455	19-Dec-2014 09:51:28	116	RGRIMES
	123465	Indication	as per query trail	routine prophylaxis	13-Jan-2015 17:08:21		DGENTLY
	123466	Date of Visit	Transcription Error	11/11/2014	20-Jan-2015 12:32:15	11/25/2014	BCOX
	123467	Was a routine urinalysis and/or microscopy performed?	Transcription Error	Y	21-Jan-2015 11:11:38	N	ESHOESTRING
	123468	Present at dosing?	advice sought from PI	Y	23-Mar-2015 11:12:03	Y	ESHOESTRING
	123469	Was pulse rate (beats/min) clinically significant?	Transcription Error	1	23-Mar-2015 11:12:03	1.0	GLEE
	123470	Present at dosing?	advice from PI	1	14-Apr-2015 11:59:01		JMANGLE
	123457	Was temperature clinically-significant?	Transcription Error	Y	14-Apr-2015 11:59:01	N	ESHOESTRING
	123458	Present at dosing?	advice sought from PI	Y	14-Apr-2015 14:22:23	Y	PROBINSON
	123459	Assessment Date	Transcription Error	12/09/2014	14-Apr-2015 14:22:23	11/25/2014	GLEE
	123470	Date of assessment	Transcription Error	10/09/2014	14-Apr-2015 14:49:31	10/10/2014	NEGAN
	123471	AE Assessment	Transcription Error	RELATED	14-Apr-2015 15:02:21	NOT RELATED	NEGAN
	123471	AE Assessment	Transcription Error	NOT RELATED	14-Apr-2015 15:04:04	RELATED	RGRIMES
	123462	Present at dosing?	advice from PI	Y	05-May-2015 14:24:42	Y	BOUNCER



# Audit Trail Review

Inspection of data audit trail  
showed access by a systems  
engineer

CAPA  
Archive to server



No changes to data. But when  
inspectors looked at source data. It  
was corrupt after removal from  
archive





# Audit Trail Review

Use of eSystems is getting bigger so are audit trails, so when to look and how?

- Consider Risk
  - What is the purpose of the system and the data
  - What is a suitable level of review and how often
- How to review
  - As part of normal oversight activities to support review
    - Use audit trail in system and reports
  - By incident to support investigation



# Summary

Audit trails can be an important part of your quality management

Consider potential risks to identify what to look at and when

A combination of reviewing single data points and audit trail reports can aid audit, monitoring and incident investigation

Controlling access and archiving the audit trail preserves meaning to data and supports reconstruction



# Case Study



# An Audit Trail Inspected

An Inspection of an analytical laboratory

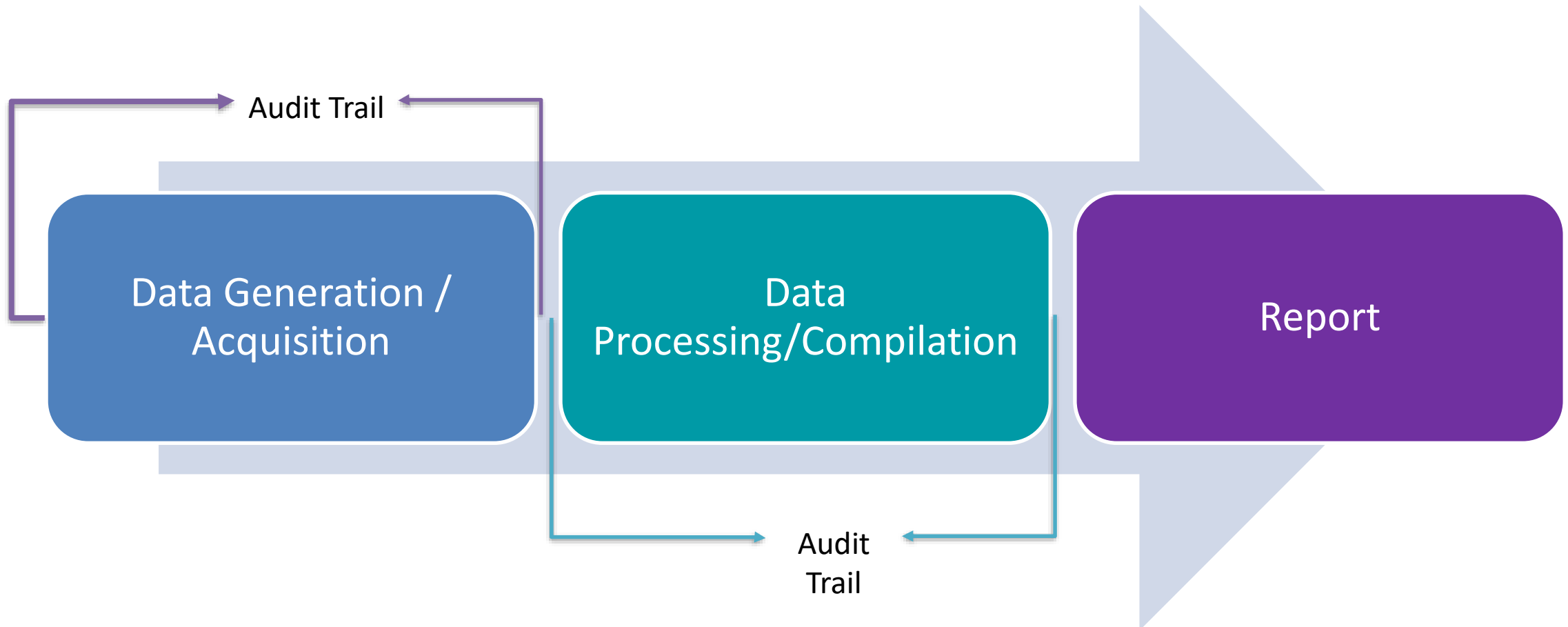
The final report for the study was found not to be fully reflective of the source data

The final report included data and information for work which had not been conducted as part of the study





# An Audit Trail Inspected





# An Audit Trail Inspected



Company procedures did not detail how the Data Generation software data (including audit trails) would be managed or archived following completion of a study.



The audit trail for the Data Generation software was not routinely reviewed and the organisation's procedures did not detail who should be responsible for this review or when/how this should be done.



# An Audit Trail Inspected

What was  
wrong with  
this data?

Review of the Audit Trails  
associated with the  
original Subject 02 and 03  
analysis confirmed that  
they had failed and  
therefore should have  
been repeated as run 42.

Data Run	Date	Name	Data Description
1	07 Aug 17	VAL01	Validation
2	14 Aug 17	Sub 01	Result 1
3	14 Aug 17	Sub 02	Result 2
4	15 Aug 17	Sub 03	Result 3
5	16 Aug 17	Sub 04	Result 4
6	16 Aug 17	Sub 05	Result 5
7	16 Aug 17	Sub 06	Result 6
8	16 Aug 17	Sub 07	Result 7
9	17 Aug 17	Sub 08	Result 8
10	17 Aug 17	Sub 09	Result 9
11	17 Aug 17	Sub 10	Result 10
12	17 Aug 17	Sub 11	Result 11
13	17 Aug 17	Sub 12	Result 12
14	17 Aug 17	Sub 13	Result 13
15	18 Aug 17	Sub 14	Result 14
16	18 Aug 17	Sub 15	Result 15
17	18 Aug 17	Sub 16	Result 16
18	18 Aug 17	Sub 17	Result 17
19	18 Aug 17	Sub 18	Result 18
20	18 Aug 17	Sub 19	Result 19
21	18 Aug 17	Sub 20	Result 20
22	18 Aug 17	Sub 21	Result 21
23	18 Aug 17	Sub 22	Result 22
24	21 Aug 17	Sub 23	Result 23

**The Data Generation  
audit trail for Run 42  
(repeat analysis) could  
not be found!**

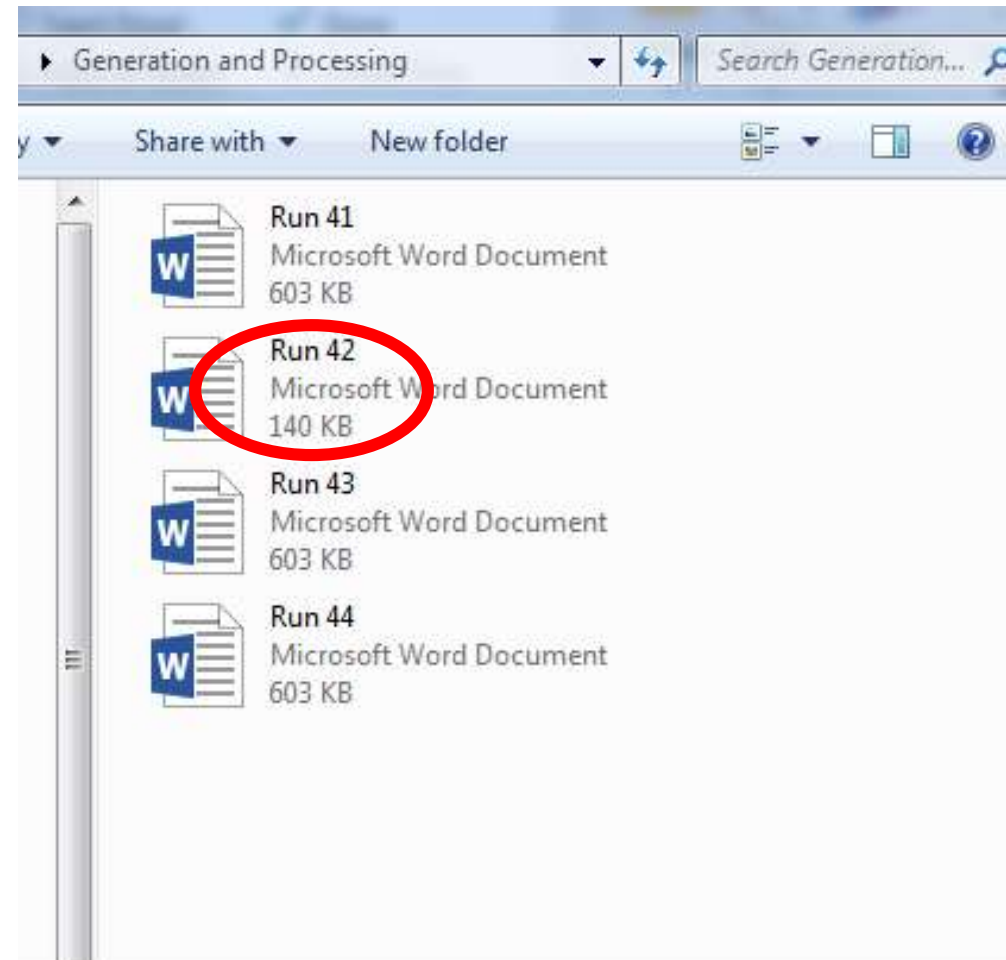
Data Run	Date	Name	Data Description
25	22 Aug 17	Sub 24	Result 24
26	22 Aug 17	Sub 25	Result 25
27	22 Aug 17	Sub 26	Result 26
28	22 Aug 17	Sub 27	Result 27
29	23 Aug 17	Sub 28	Result 28
30	23 Aug 17	Sub 29	Result 29
31	23 Aug 17	Sub 30	Result 30
32	23 Aug 17	Sub 31	Result 31
33	24 Aug 17	Sub 32	Result 32
34	24 Aug 17	Sub 33	Result 33
35	24 Aug 17	Sub 34	Result 34
36	25 Aug 17	Sub 35	Result 35
37	25 Aug 17	Sub 36	Result 36
38	28 Aug 17	Sub 37	Result 37
39	28 Aug 17	Sub 38	Result 38
40	28 Aug 17	Sub 39	Result 39
41	28 Aug 17	Sub 40	Result 40
42	04 Sep 17	Sub 02	Result 02
43	05 Sep 17	Sub 42	Result 42
44	05 Sep 17	Sub 43	Result 43
45	05 Sep 17	Sub 44	Result 44

Potential  
Repeat Data  
Generation



# An Audit Trail Inspected

Differences in file size noted  
between original runs and  
repeat run 42.





# An Audit Trail Inspected

42



**Review of Data Processing  
Audit Trail:**

**Software Super User had  
manually created Run 42  
(both the Data Generation  
file and Data Processing  
file) without analysis  
taking place.**

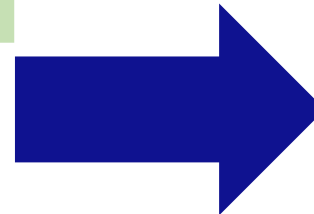
**WHY?**



# An Audit Trail Inspected

Subject	Time Point	Result	Date
2	0.125	Insufficient Vol	04 Sep 17
2	0.25	Insufficient Vol	04 Sep 17
2	0.5	Insufficient Vol	04 Sep 17

Run	Date of Extraction	Date of Analysis	Run Status	Gradient	R <sup>2</sup>
42	03 Sep 17	04 Sep 17	Accepted	0.6845	0.99999
2	1.5	Insufficient Vol	04 Sep 17		
2	2	Insufficient Vol	04 Sep 17		
3	0.125	Insufficient Vol	04 Sep 17		
3	0.25	Insufficient Vol	04 Sep 17		
3	0.5	Insufficient Vol	04 Sep 17		
3	0.75	Insufficient Vol	04 Sep 17		
3	1	Insufficient Vol	04 Sep 17		
3	1.5	Insufficient Vol	04 Sep 17		
3	2	Insufficient Vol	04 Sep 17		



Design of laboratory system meant that the study could not be closed with samples requiring re-testing. However couldn't re-test as was insufficient sample remaining.

Run 42 created to satisfy the requirement of the system to see a re-test created, and used original data for the subjects.

There was no impact on final results.

There was an opportunity to falsify data if so desired.

Quality Assurance didn't know...



# An Audit Trail Inspected

- The missing Audit Trail
- Irregularities in the file sizes
- Inappropriate use of Super User privileges
- Lack of controls and gaps in audit coverage
- System limitations



## Some Questions

- Are your current and planned audit trails designed to maximise use as a quality tool?
- Are your audit trails secure?
- Do you understand the content and meaning of your audit trails?
- Have you considered strategies to use audit trails to monitor performance and investigate issues?

**If only we had looked first...**





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