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# Data Integrity

Requirements for a GMP-compliant Data Life Cycle

With an optional full-day pre-course session  
Audit Trail Review

Comments on the FDA Draft Guidance for Industry 'Data Integrity and Compliance with cGMP' and on the new GAMP Records and Data Integrity Guide from 2017



## SPEAKERS:



**Bob McDowall**  
*R.D. McDowall Ltd.*



**Karl-Heinz Menges**  
*Regierungspräsidium  
Darmstadt*



**Yves Samson**  
*Kereon AG*

## Workshops on:

- Which Audit Trail to Review?
- Identifying GMP-relevant Data
- Reviewing Audit Trail Entries
- Analysis of FDA Warning Letters
- Key Data Integrity Topics / Criteria
- How to write testable requirements for Data Integrity
- Assessing a System for Data Integrity

17 and 18 – 20 April 2018, Copenhagen, Denmark  
28 and 29 – 31 August 2018, Copenhagen, Denmark  
11 and 12 – 14 December 2018, Berlin, Germany

## LEARNING OBJECTIVES:

- Understand the regulatory requirements for an Audit Trails (review)
- Identifying GMP relevant data
- Review of Audit Trail entries
- Technical Controls to Aid Second Person Review of Audit Trails
- FDA Draft Guidance for Industry 'Data Integrity and Compliance with cGMP'
- WHO, MHRA and GAMP Data Integrity Guidances - Key Points
- Data Integrity – EU requirements
- Principles of Data Integrity
- Data Governance
- Role of Management in Data Integrity
- IT Support for Data Integrity
- Implementing Data Integrity Training
- Data Integrity and Cloud Computing
- Supplier Chain Data Integrity
- European Inspector's point of view
- Case study: Data Integrity questions as part of an inspection



# Audit Trail Review

17 April 2018, Copenhagen, Denmark | 28 August 2018, Copenhagen, Denmark | 11 December 2018, Berlin, Germany

## Objectives

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- You will learn the current regulatory requirements and regulatory expectations for an audit trail (review)
- All GMP-relevant data (changes and deletions) should be audit trailed – you will learn how to identify GMP-relevant data
- Event and audit logs: you will understand the differences between and what the regulators expect
- How should an audit trail review be performed? You will get familiar with the content and the frequency of an audit trail review

## Background

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Audit Trail Reviews are required by international regulations like US 21 CFR Part 11 and EU GMP Guide Annex 11. Clause 9 requests:

*“Consideration should be given, based on a risk assessment, to building into the system the creation of a record of all GMP-relevant changes and deletions (a system generated “audit trail”). For change or deletion of GMP-relevant data the reason should be documented. Audit trails need to be available and convertible to a generally intelligible form and regularly reviewed”*

Regulators focus on the (creation), modification and deletion of (GMP-relevant) data while many IT systems are not able to generate audit trails at all or they are not able to generate audit trails for GMP-relevant data.

Therefore, this course is designed to support you to identify GMP-relevant data and how to perform and document an Audit Trail review as part of a second person review.

## Target Audience for both courses

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This course is designed for managers and staff from health care industries as well for auditors who are responsible for the organisation and execution of audit trail (reviews) in their companies.

## Programme

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### Why Is An Audit Trail and Its Review Important?

- Part 11 and Annex 11 / Chapter 4 requirements for audit trail
- Regulatory requirements for audit trail review
- Guidance documents for audit trail review
- Do I really need an audit trail?

## Audit trail vs. system log

- Audit trail content
- Log files
- What and when should I review?
- Meaningful audit trails for a meaningful review

### Workshop 1: Which Audit Trail to Review?

Attendees will be presented with an overview of the audit trails within an application and the content of each one. Which audit trails should be reviewed and when?

## What are GMP-relevant Data?

- Annex 11 requires that audit trails monitor GMP-relevant data – what are GMP-relevant data?

### Workshop 2: Identifying GMP Relevant Data

Attendees will be presented with a list of records to identify if they are GMP records and how critical they are to help focus the second person review of audit trail data.

Examples from production, laboratory and QA examples of GMP-relevant data will be provided.

## Review of Audit Trail Entries

- Guidance for frequent is “frequent review” of audit trails
- Process versus system: avoiding missing data integrity issues when only focussing on a per system review
- What are we looking for in an audit review?
- Suspected data integrity violation - What do we need to do?

### Workshop 3: Reviewing Audit Trail Entries

Attendees will be provided with the output of an audit trail to review and see if any potential issues are identified for further investigation.

## Technical Controls to Aid Second Person Review of Audit Trails

- Technical considerations for audit trail review e.g.
- Identifying data that has been changed or modified – how the system can help
- Documenting the audit trail review has occurred
- Review by exception – how technical controls can help
- Have you specified and validated these functions?

# Data Integrity

18-20 April 2018, Copenhagen, Denmark | 29-31 August 2018, Copenhagen, Denmark | 12-14 Dec 2018, Berlin, Germany

## Objectives

- Understand the current FDA and EU GMP regulations and guidance impacting data integrity from paper records to hybrid and electronic systems.
- Understand the FDA requirements for data integrity, MHRA Data Integrity guidance July 2016 and WHO guidance from September 2015.
- Learn what is required for a data governance system from senior management through to staff in laboratories, manufacturing and quality assurance.
- Understand the data life cycle and how it is linked with the business process and where problems can occur for both paper records, hybrid systems and electronic systems.

## Background

Data Integrity is a global problem and currently a major concern with FDA and European Regulatory Agencies. Multiple FDA warning letters and EU GMP non-compliance reports have highlighted major data integrity failures and falsification in companies globally. The regulatory concern has been responded by the FDA issuing Compliance Program Guide that covers Pre-Approval Inspections. This document became effective in May 2012. The CPG objective 3 covers the laboratory data integrity audit. Furthermore in August 2014, the FDA issued Level 2 guidance on their web site about the sharing of login credentials for computerized systems and the use of test injections for testing into compliance.

In Europe, the UK's MHRA issued two versions of a Guidance for Industry on Data Integrity in January and March 2015. This document outlines a data integrity governance system and principles for defining quality and data integrity into processes and systems. In addition, the guidance defines 19 terms and provides expectations and examples for many of them and therein is where the document's value lies. A new draft version of the Guidance was published in July 2016. The WHO guidance is complimentary to the MHRA guidance in that it provides guidance for data governance and also expectations for records in both paper and electronic form.

As the regulators are tightening their inspection approaches it is important that managers, supervisors and users in regulated GMP laboratories understand the issues around data integrity and begin programs to ensure that their processes and systems ensure data integrity.

## Programme

### Why is Data Integrity Important? – Setting the Scene

- Summary of falsification observed by FDA and EU inspectors 2005 – to date
- FDAISA act 2012 and October 2014 Guidance for Industry and the impact on inspections
- Inspection of computerised systems is changing: from paper to on-line
- MHRA expectation for data governance; data integrity guidance documents 2016
- FDA Level 2 guidance on data integrity: 2010 and 2014 postings
- Impact of WHO guidance for data integrity

### Data Integrity – EU GMP Requirements

- EU GMP Chapter 4 – documentation
- EU GMP Annex 11 computerised systems
- Data integrity definitions
- Difference between paper and electronic systems

### Principles of Data Integrity

- The ALCOA+ criteria for data integrity
- Data life cycle in the process workflow – managing controls
- Paper versus hybrid versus electronic systems
- Validation of computerised systems for data integrity controls
- Scope: production information versus laboratory data: why are laboratory data higher risk?

### Facilitated Discussion / Workshop on Key Data Integrity Topics

- Recording results on paper
- Configuration of software applications
- Unique user identities for all users
- Unauthorised access
- Appropriate access privileges for each user role
- Is my chromatographic system ready? Role of “test” injections
- Audit trails – options for older systems
- Manual chromatographic integration
- Standalone versus network systems
- Protecting electronic records of standalone systems

### WHO, MHRA and GAMP Data Integrity Guidances - Key Points

- Data Governance System within the Pharmaceutical Quality System
- Data Life Cycle
- Spectrum of Systems: Paper to Electronic Systems with data integrity audit
- The GAMP Records and Data Integrity Guide

## FDA Draft Guidance for Industry 'Data Integrity and Compliance with cGMP'

- Background
- Questions and Answers regarding Data Integrity

## Role of Management in Data Integrity

- Role of Senior, Production and Department Management in ensuring data integrity within an organisation and its suppliers
- Data governance within a Quality System
- Failures to address poor data integrity practices and no training

## Development and Scope of a Data Governance System

- Within a PQS, what is the scope of a data governance system?
- Who are involved?
- What are their roles?

## Implementing Data Integrity Training

- Scope of data integrity training
- What cover in the training?
- Checking training effectiveness
- Integrating data integrity training with GMP training

### Workshop: Analysis of an FDA Warning Letter

- Working in teams, attendees will analyse one of several FDA warning letters to identify key areas of regulatory concern
- Group discussion of regulatory concerns identified

## US 21 CFR 211 and EU GMP Chapter 4: Complete data vs raw data vs primary record

- Why complete data and raw data are important for understanding data integrity
- EU GMP Chapter 4 requirements for raw data
- 21 CFR 211 requirements for laboratory records: complete data
- FDA Level 2 guidance: paper versus e-records
- Complete data / raw data / primary record example

## Case study: Data Integrity questions as part of an inspection

- Lab System
- QA System
- Manufacturing System

### Workshop: How to write testable requirements for Data Integrity

- Access control
- Archiving
- Technology constraints

## Data Integrity in paper documentation

- GMP requirements for good documentation practice
- Application to paper documents
- Common problems from FDA 483 observations and warning letters and how to avoid them

## User Account Management and Application Configuration

- Separation of roles and responsibilities between IT and the business
- Documentation of the configuration of an application e.g. audit trail, user types and access privileges
- User account management: the dos and don'ts
- User identities must be unique
- Regular review of each system users and privileges

## IT Support for Data Integrity

- IT facilities, environmental controls and physical security
- Qualified IT infrastructure and validated IT systems
- Backup and recovery / Change control
- IT support including database administration
- Impact of IT infrastructure on data integrity

## Software Suppliers Responsibility for Data Integrity Compliance

- Regulatory requirements for software systems: procedural and technical
- Role of software suppliers
- Regulations push v market needs pull
- Implementing technical requirements for software: architecture, database and application
- Marketing literature versus marketing bullshit

### Workshop: Assessing a System for Data Integrity

- Using a checklist based on the data integrity criteria, attendees will assess a system for data integrity

## Case study: Can Spreadsheets meet Data Integrity requirements?

- Problems with spreadsheets
- Good Practice for using spreadsheets in a regulated environment
- Building data integrity features into a spreadsheet

## Supply Chain Data Integrity – Organisational Interfaces

- Approaches to ensuring data integrity of your suppliers
- Role of technical agreements and audits

## Key Learning Points and Final Discussion

- Summary of Data Integrity Requirements and Key Learning Points
- Final Discussions and close of the course

## Fees Audit Trail Review (per delegate plus VAT)

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ECA Members € 790

APIC Members € 840

Non-ECA Members € 890

EU GMP Inspectorates € 445

The conference fee is payable in advance after receipt of invoice and includes conference documentation, lunch and all refreshments. VAT is reclaimable.

## Fees Data Integrity (per delegate plus VAT)

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ECA Members € 1,790

APIC Members € 1,890

Non-ECA Members € 1,990

EU GMP Inspectorates € 995

The conference fee is payable in advance after receipt of invoice and includes conference documentation, dinner on the first day, lunch on day 1 and day 2. VAT is reclaimable.

## Would you like to save money?

If you book both courses simultaneously, the fees reduce as follows:

## Fees Audit Trail Review + Data Integrity (per delegate plus VAT)

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ECA Members € 2,390

APIC Members € 2,490

Non-ECA Members € 2,590

EU GMP Inspectorates € 1,440

The conference fee is payable in advance after receipt of invoice and includes conference documentation, one dinner, lunch on all days and all refreshments. VAT is reclaimable.

## Accommodation

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CONCEPT HEIDELBERG has reserved a limited number of rooms in the conference hotel. You will receive a room reservation form when you have registered for the event. Reservation should be made directly with the hotel. Early reservation is recommended.

## Conference Language

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The official conference language will be English.

## Organisation and Contact

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ECA has entrusted Concept Heidelberg with the organisation of this event.

CONCEPT HEIDELBERG

P.O. Box 10 17 64, 69007 Heidelberg, Germany

Phone +49(0) 62 21/84 44-0, Fax +49(0) 62 21/84 44 84

info@concept-heidelberg.de, www.concept-heidelberg.de

### For questions regarding content:

Dr Andreas Mangel (Operations Director)

at +49(0) 62 21 / 84 44 41 or at

mangel@concept-heidelberg.de.

### For questions regarding reservation, hotel, organisation etc.:

Mr Rouwen Schopka (Organisation Manager)

at +49(0) 62 21 / 84 44 13 or per e-mail at

schopka@concept-heidelberg.de.

## Social Event

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On 18 April / 29 August / 12 December you are cordially invited to a social event. This is an excellent opportunity to share your experiences with colleagues from other companies in a relaxed atmosphere.

## Speakers

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### Dr Bob McDowall,

*R.D. McDowall Limited, UK*

Analytical chemist with over 40 years experience including 15 years working in the pharmaceutical industry and afterwards working for the industry as a consultant. Bob is an ISO 17025 assessor and

he has been involved with the validation of computerised systems for over 30 years and is the author of a book on the validation of chromatography data systems. He was also a contributor to the GAMP IT Infrastructure control & compliance and Lab System Validation 2nd edition Good Practice Guides. He is a core member of the GAMP Data Integrity SIG. He recently published the second edition of his book on Validation of Chromatography Data Systems: Ensuring Data Integrity, Meetings Business and Regulatory Requirements.



### Karl-Heinz Menges,

*Regierungspräsidium Darmstadt, Germany*

He is Inspector at the Regierungspraesidium Darmstadt in Germany. Mr Menges has been an Inspector for over 25 years and he is currently Head of the German Inspectors Working Group. He is also a member of GAMP D-A-CH steering committee and the German delegate of the PIC/S Expert Circle for computerised systems. Mr Menges has also contributed to Annex 11, PIC/S document PI 011 Recommendations on Computerised Systems and several GAMP CPGs.



### Yves Samson,

*Kereon AG, Switzerland*

Automation and system engineer with over 25 years experience, including 11 years as regulated user, Yves is the founder of Kereon AG, Basel. He supports his customers as consultant, trainer, and e-compliance auditor. He is member of GAMP Europe Steering Committees, chairman and co-founder of GAMP Francophone. He edited the French version of GAMP 4 and GAMP 5. Within ISPE he was an active member of the working group "IT Infrastructure Compliance and Control".

# Easy Registration



Reservation Form:  
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69007 Heidelberg, Germany



Reservation Form:  
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www.gmp-compliance.org



+ 49 6221 84 44 34

### Data Integrity

- 18-20 April 2018, Copenhagen, Denmark
- 29-31 August 2018, Copenhagen, Denmark
- 12-14 December 2018, Berlin, Germany

### Audit Trail Review

- 17 April 2018, Copenhagen, Denmark
- 28 August 2018, Copenhagen, Denmark
- 11 December 2018, Berlin, Germany
- Mr  Ms

Reservation Form (Please complete in full)

If the bill-to-address deviates from the specifications on the right, please fill out here:

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Company

Department

Important: Please indicate your company's VAT ID Number

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Zip Code

Country

Phone/Fax

E-Mail (please fill in)

#### General terms and conditions

- 1. If you cannot attend the conference you have two options:
  - We are happy to welcome a substitute colleague at any time.
  - If you have to cancel entirely we must charge the following processing fees: Cancellation
    - until 2 weeks prior to the conference 10 %
    - until 1 week prior to the conference 50 %
    - within 1 week prior to the conference 100 %.

CONCEPT HEIDELBERG reserves the right to change the materials, instructors, or speakers without notice or to cancel an event. If the event must be cancelled, registrants will be notified as soon as possible and will receive a full refund of fees paid. CONCEPT HEIDELBERG will not be responsible for discount airfare penalties or other costs incurred due to a cancellation.

**Terms of payment:** Payable without deductions within 10 days after receipt of invoice.

**Important:** This is a binding registration and above fees are due in case of cancellation or non-appearance. If you cannot take part, you have to inform us in writing. The cancellation fee will then be calculated according to the point of time at which we receive your message. In case you do not appear at the event without having informed us, you will have to pay the full registration fee, even if you have not made the payment yet. Only after we have received your payment, you are entitled to participate in the conference (receipt of payment will not be confirmed!) (As of January 2012).

German law shall apply. Court of jurisdiction is Heidelberg.

**Privacy Policy:** By registering for this event, I accept the processing of my Personal Data. Concept Heidelberg will use my data for the processing of this order, for which I hereby declare to agree that my personal data is stored and processed. Concept Heidelberg will only send me information in relation with this order or similar ones. My personal data will not be disclosed to third parties (see also the privacy policy at [http://www.gmp-compliance.org/eca\\_privacy.html](http://www.gmp-compliance.org/eca_privacy.html)). I note that I can ask for the modification, correction or deletion of my data at any time via the contact form on this website.

## Date and Venue April 2018

### Audit Trail Review:

Tuesday, 17 April 2018, 09.00 h – 17.15 h  
(Registration and coffee 08.30 h - 09.00 h)

### Data Integrity:

Wednesday, 18 April 2018, 09.00 h – 17.30 h  
(Registration and coffee 08.30 h - 09.00 h)  
Thursday, 19 April 2018, 08.30 h – 17.30 h  
Friday, 20 April 2018, 08.30 – 13.15 h

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Amager Boulevard 70  
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## Date and Venue August 2018

### Audit Trail Review:

Tuesday, 28 August 2018, 09.00 h – 17.15 h  
(Registration and coffee 08.30 h - 09.00 h)

### Data Integrity:

Wednesday, 29 August 2018, 09.00 h – 17.30 h  
(Registration and coffee 08.30 h - 09.00 h)  
Thursday, 30 August 2018, 08.30 h – 17.30 h  
Friday, 31 August 2018, 08.30 – 13.15 h

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Amager Boulevard 70  
2300 Copenhagen S, Denmark  
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Scandinavia.meetings.events@radissonblu.com

## Date and Venue December 2018

### Audit Trail Review:

Tuesday, 11 December 2018, 09.00 h – 17.15 h  
(Registration and coffee 08.30 h - 09.00 h)

### Data Integrity:

Wednesday, 12 December 2018, 09.00 h – 17.30 h  
(Registration and coffee 08.30 h - 09.00 h)  
Thursday, 13 December 2018, 08.30 h – 17.30 h  
Friday, 14 December 2018, 08.30 – 13.15 h

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