

Computer System Validation

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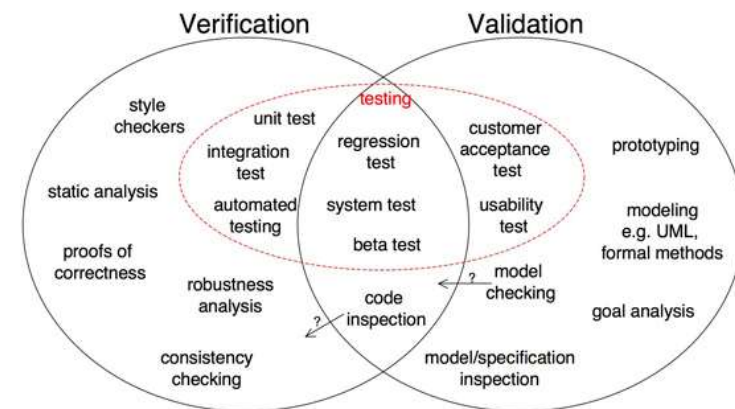
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Advanced Sponsor Oversight



Agenda

- Q&A from Day 3
- Computer System Validation
- Training & User Management



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Day 3 Q & A

A Brief Detour -ERES

Guidance and Updates

- August 2003
 - FDA Electronic Records; Electronic Signatures – Scope and Application
 - Narrower interpretation (predicate rules)
 - Enforcement discretion for legacy systems
 - Predicate Rule Requirements to be enforced
- 2011
 - EU Updated Annex 11 to its current Form
- 2012
 - Change of Scope – Does not apply to Food / Farms
- 11.100© - Updates to Certification Address
- Electronic Systems, Electronic Records and Electronic Signatures in Clinical Investigations: Q&A – October 2024
 - Reaffirming Computer Software Assurance / Validation Standard & Expectations
 - Some specifics for GCP

itions, reaffirming previous expectations / clarifications



Guidance and Updates

- 2016 – EMA Guidance on Data Integrity for GMP/GDP
- 2021 - TRS 1033 - Annex 4: WHO Guideline on data integrity (Replaced WHO Good data and record management (2016))
- 2021 – Updated ‘GXP’ Data Integrity Guidance and Definitions - MHRA
- 2021 – Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments – PIC/S
- EMA – Guideline on Computerised Systems and Electronic Data in clinical trials (Mar 2023)
- 2016 – Data Integrity and Compliance With cGMP - FDA
- 2024 - Data Integrity for In Vivo Bioavailability and Bioequivalence Studies – Draft
- 2026 – FDA Computer Software Assurance for Production & QMS Software

Predicate Rule

- A predicate rule is any FDA regulation that requires companies to **maintain** certain records **and submit information to the agency** as part of compliance. Examples can be found in in GxP regulations such as GLP (Good Laboratory Practices), GCP (Good Clinical Practices), and CGMP (Current Good Manufacturing Practices).
- Part 11 also applies to electronic records submitted to the Agency under the **Federal Food, Drug, and Cosmetic Act (the Act)** and the **Public Health Service Act (the PHS Act)**, even if such records are not specifically identified in Agency regulations (§ 11.1). **The underlying requirements set forth in the Act, PHS Act, and FDA regulations (other than part 11) are referred to in this guidance document as predicate rules.**

Open / Closed Systems

- Closed system means an environment in which **system access is controlled by persons who are responsible for the content** of electronic records that are on the system.
- Open system means an environment in which system access is not controlled by persons who are responsible for the content of electronic records that are on the system.
- - Source FDA – 21 CFR Part11 (11.3)

Open / Closed Systems - Considerations

- Who performs User Administration Tasks?
 - You
 - Vendor
 - Vendor Subcontractors
- Who has access to the Data
 - You
 - Vendor
 - Vendor Subcontractors
- Where are the Delegated Authorities Documented

Certified / True Copy

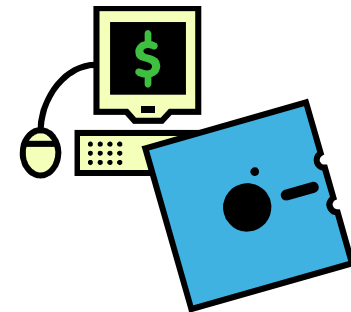
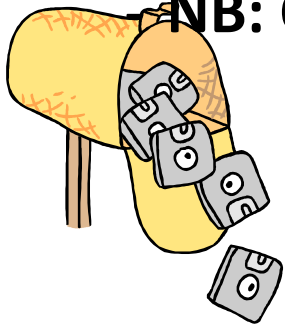
- A copy of original information that has been verified as an exact copy having all of the same attributes and information as the original, as indicated by a dated signature.
- FDA Guidance on Computerized Systems Used in Clinical Trials (CSUCT)
- Transformed Record following a Defined Process / Validated System to 'Copy' the record and ensure it is accurate and complete

Electronic Record

Means any combination of text, graphics, data, audio, pictorial or other information representation in digital form that is created, modified, maintained, archived, retrieved, or **distributed** by a computer system.

- **Where required by Predicate Rule**

NB: CSA Guidance applies Part 11 to Validation Evidence



Digital Signature

- Means an electronic signature based upon cryptographic methods of originator authentication, computer by using a set of rules and a set of parameters **such that the identity of the signer and the integrity of the data can be verified.**



Electronic Signature

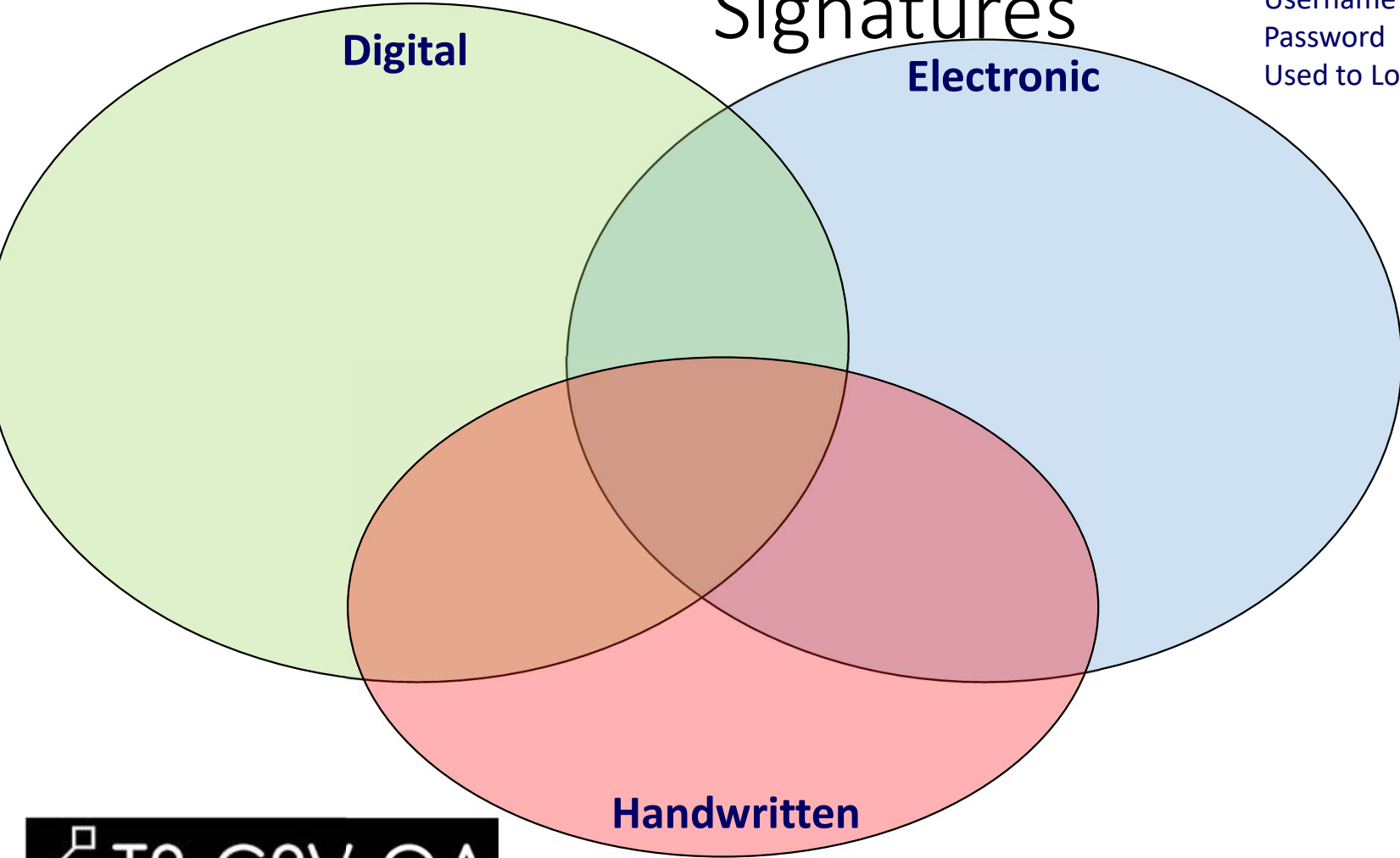
- Means a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the **legally binding equivalent of the individual's handwritten signature.**
 - Regulatory or Company Required
 - FDA
- Electronic records may be signed electronically. Electronic signatures are expected to:
 - have the **same impact as hand-written signatures within the boundaries of the company,**
 - be permanently linked to their respective record,
 - include the time and date that they were applied.



Handwritten Signature

- means the scripted name or legal mark of an individual handwritten by that individual and executed or adopted with the present intention to authenticate a writing in a permanent form. The **act of signing with a writing or marking instrument such as a pen or stylus is preserved**. The scripted name or **legal mark**, while conventionally applied to paper, **may also be applied to other devices that capture the name or mark**.

Signatures

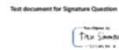


Network
Username /
Password
Used to Login

Network Username /
Password Required to
authorise....

Digital Signature used
to confirm
Authenticity of Data
being Transmitted

Spot the Signature



docusign

| Certificate Of Completion | | |
|--|---------------------------------------|----------------------------------|
| Envelope ID: 50C6A847-FFC7-4850-8214-0552A4F41F27 | Status: Completed | |
| Subject: Complete with DocuSign: 03 Test Doc | | |
| Envelope ID: [redacted] | Signatures: 1 | Envelope Originator: Tim Dimmons |
| Document Page: 1 | Pages: 2 | |
| Certificate Page: 1 | | |
| Author: (Hidden) | | IP Address: 91.108.102.221 |
| Envelope Signing Channel | | |
| Time Zone: (UTC-08:00) Pacific Time (US & Canada) | | |
| Record Tracking | | |
| Status: Original | Holder: Tim Dimmons | Location: DocuSign |
| Date: 9/15/2024 2:11:35 AM | IP Address: 91.108.102.221 | |
| Signer Events | Signature | Timestamp |
| Tim Dimmons | | Date: 9/15/2024 2:12:35 AM |
| tim.dimmons@docusign.co.uk | | Viewer: 9/15/2024 2:12:42 AM |
| Owner & Principal Consultant | | Signed: 9/15/2024 2:13:04 AM |
| Security Level: Email, Account Authentication (None) | Signature Adaptor: Pre-selected Style | Platform: Signing |
| | Using IP Address: 91.108.102.221 | |
| Details: Record and Signature Certificate Not Offered via DocuSign | | |
| In Person Signer Events | Signature | Timestamp |
| Editor Delivery Events | Status | Timestamp |
| Agent Delivery Events | Status | Timestamp |
| Intermediary Delivery Events | Status | Timestamp |
| Certified Delivery Events | Status | Timestamp |
| Carbon Copy Events | Status | Timestamp |
| Witness Events | Signature | Timestamp |
| Notary Events | Signature | Timestamp |
| Envelope Summary Events | Status | Timestamps |
| Envelope Sent | Notified/Encrypted | 9/15/2024 2:12:35 AM |
| Certified Document | Security Checked | 9/15/2024 2:12:35 AM |
| Signing Complete | Security Checked | 9/15/2024 2:13:04 AM |
| Completed | Security Checked | 9/15/2024 2:13:04 AM |
| Payment Events | Status | Timestamps |



Key Elements of Part 11

- Controls for closed systems (11.10)
- Controls for Open systems (11.30)
- Signature controls
 - Manifestation (11.50)
 - Signature / record linking (11.70)
 - General Requirements (11.100)
 - Signature components & controls (11.200)
 - **Identification Codes / Passwords (11.300)**

Key Elements of Annex 11

- Principle
- General
 - Risk management
 - Personnel
 - Supplier & Service Providers
- Project Phase
 - Validation
- Operational Phase
 - Data
 - Accuracy Checks
 - Data Storage
 - Printouts
 - Audit Trails
 - Change and Configuration Management
 - Periodic Evaluation
 - Security
 - Incident Management
 - **Electronic Signature**
 - Batch release
 - Archiving

Security & Identity Controls 11.10 (Closed)

- Validation of the Systems (a)
- Protected (Accurate, Retrievable) (c)
- Limiting System Access (d)
- Operational Sequence Checks (f)
- Use of Authority Checks (g)
- Use of device checks (h)
- Written Policy of accountability (j)
- Control over System Documentation (k)



Identification Codes and Password Controls (11.300)

- Uniqueness to an individual (a)
- Periodically checked (b)
- Loss management (c)
- Transaction Safeguards for unauthorised use (d)
- Testing of tokens / cards (e)

Signatures (11.100)

Uniqueness (a)

Identity verification (b)

Certified with the FDA (c)

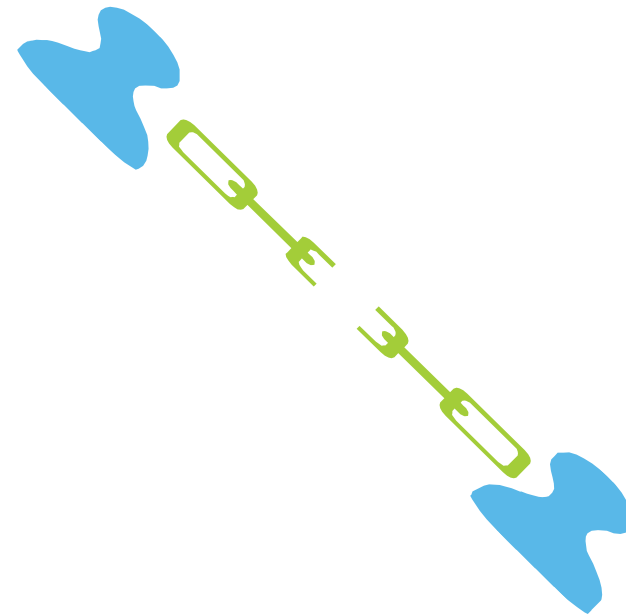


Signatures (11.200)

- Employ at least two distinct components (a)(1)
- Continuous Series of Signings (a)(1)(i)
 - First signing both components
 - Subsequent signings (one component)
- Non-Continuous Signings (a)(1)(ii)
 - All components every time
- Genuine Owner only (a)(2)
- Administered to detect falsification (a)(3)

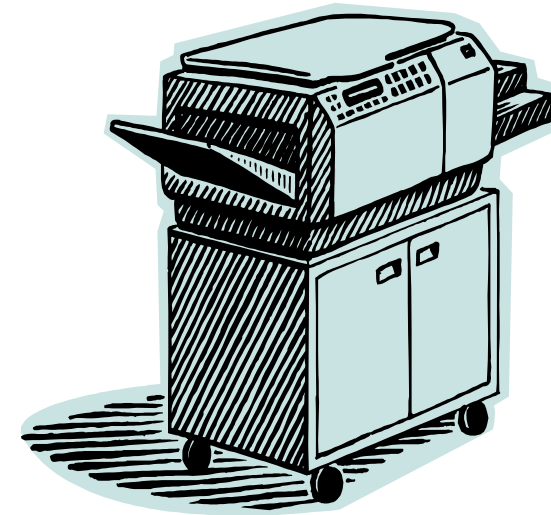
Signature Linking / Manifestation

- Signature / Record / Audit Trail Linking (11.70)
- Excised / Deleted
- Copied
- Otherwise transferred to falsify
- By ordinary means
- Secure (Non-editable)
- Signature Manifestations (11.50)
- Printed Name of the Signer (a)(1)
- Date and Time When Executed (a)(2)
- The Meaning (a)(3)
- **Suitable for Review & Copy by the Agency (b)**



Part 11- Miscellaneous

- Training Records (11.10) (h)(i)
 - Develop
 - Maintain
 - Use
- Generating Copies (11.10) (b)
 - Accurate & Complete
 - Human readable
 - And Electronic
 - Suitable for Review & Copy by the Agency



Audit trails – 11.10(e)

- Secure, Computer Generated Timestamp
- For operator Actions
 - Create
 - Modify
 - Delete
- Non-Obscuring
 - Before / After
- **Reason (Not in rule but in guidance)**
- Retained for as long as the Record
- Available for Agency Review & Copying



Annex 11 – Match-up

- Validation
- Personnel (Training Records)
- Legally Binding Signatures
- Electronic Record Audit Trails
- Meeting P11 supports compliance with the needs of annex 11.

What does it all mean?

- Built to support Nonrepudiation
- Who (did)
- What (to)
- What (record/data)
- When (did they do it)
- Why (did they do it)
- Should (they have / been able to have done it)

Audit trails – When an Audit Trail isn't an Audit Trail – Design Considerations

- Backend Database Changes / Triggers
- System Calls (Front-End / Middleware / BackEnd)
- May or May not be Part of / Separate to the 'Data Transaction'
- Implicit Reasoning
- Not always capturing Before / After in the Audit Trail
- Does the Audit Trail Reference Signatures? Or is it the actual 'record' of the signature
- Is authentication and user security data held in the Audit Trail or in other 'Logs'
- How many items actually constitute the Audit Trail



Audit trails – Availability



- Expected to be Available at the Point of Entry / Update
- Audit Trail SLA – 2 weeks, Immediate
- Who can see the Audit Trail? Blinding Implications?

Audit trails – Review

- Purpose of the Review?
 - QC Lab LIMS (1.8 Million Transactions)
 - Looking for ‘Repeat’ Analyses
 - Looking for Change that Alters Eligibility / Ineligibility, Safety /Non-Safety
- Reporting / Monitoring
 - Can it wait 12 weeks until next review?
 - Does it have to be a Human?
 - Automated System Alerts?



LEGACY SYSTEMS – CLINICAL TRIAL SUPPLY

| Audit Trail ID | REC ID | TABLE | FIELD | OLD VALUE | NEW VALUE | USER ID | TIMESTAMP | REASON |
|----------------|---------|-------------|--------------------|-----------|-----------|---------|---------------------|----------------|
| 1 | 234987 | BALANCE | MAKE | Sartorius | Mettler | SIMMTJ | 07/06/2019 08:51:23 | BALANCE_UPDATE |
| 2 | 126547 | DISPENSE | AMOUNT | 0 | 10000 | SIMMTJ | 07/06/2019 08:53:23 | WO_DISPENSE |
| 3 | 435734 | CALIBRATION | STATUS | FAIL | PASS | WELLERS | 07/06/2019 08:53:23 | RECALIBRATE |
| 4 | 123654 | INVENTORY | AMOUNT | 20000 | 10000 | SIMMTJ | 07/06/2019 08:53:24 | WO_DISPENSE |
| 5 | 9876556 | WORK ORDER | OUTSTANDING AMOUNT | 10000 | 0 | SIMMTJ | 07/06/2019 08:53:24 | WO_DISPENSE |
| 6 | 126548 | DISPENSE | AMOUNT | 0 | 5000 | SIMMTJ | 07/06/2019 08:53:54 | WO_DISPENSE |
| 7 | 9876554 | WORK ORDER | OUTSTANDING AMOUNT | 10000 | 5000 | SIMMTJ | 07/06/2019 08:53:54 | WO_DISPENSE |
| 8 | 126389 | INVENTORY | AMOUNT | 15000 | 10000 | SIMMTJ | 07/06/2019 08:53:54 | WO_DISPENSE |

LEGACY SYSTEMS – PATIENT DIARY

| Audit Trail ID | TIMESTAMP | ACTION | START TIME | END TIME | USER ID |
|----------------|---------------------|-----------|---------------------|---------------------|---------|
| 1 | 07/06/2008 08:51:23 | NEW EVENT | 07/06/2008 08:50:28 | 07/06/2008 08:51:23 | S1023 |
| 2 | 08/06/2008 08:53:23 | NEW EVENT | 08/06/2008 08:51:13 | 08/06/2008 08:53:23 | S1023 |
| 3 | 02/01/1970 12:53:00 | NEW EVENT | 02/01/1970 12:52:00 | 02/01/1970 12:53:00 | S1023 |
| 4 | 04/01/1970 13:45:22 | LOGIN | 04/01/1970 13:45:22 | NULL | INV001 |
| 5 | 15/06/2008 14:52:20 | TIME SYNC | 04/01/1970 13:48:52 | 15/06/2008 14:52:20 | INV001 |
| 6 | 15/06/2008 14:52:50 | LOGIN | 15/06/2008 14:52:50 | NULL | S1023 |
| 7 | 15/06/2008 14:54:50 | NEW EVENT | 15/06/2008 14:52:58 | 15/06/2008 14:54:50 | S1023 |
| 8 | 15/06/2008 14:55:20 | LOGIN | 15/06/2008 14:55:20 | NULL | INV001 |
| 9 | 15/06/2008 14:55:50 | ENROL | 15/06/2008 14:55:50 | NULL | INV001 |

LEGACY SYSTEMS – PATIENT DIARY

| Audit Trail ID | TIMESTAMP | ACTION | START TIME | END TIME | USER ID |
|----------------|-------------------------|--------------|-------------------------|------------------|---------------|
| 3 | 02/01/1970 12:53 | NEW EVENT | 02/01/1970 12:52 | 02/01/1970 12:53 | SI023 |
| 4 | 04/01/1970 13:45 | LOGIN | 04/01/1970 13:45 | NULL | INV001 |
| 1 | 07/06/2008 08:51 | NEW EVENT | 07/06/2008 08:50 | 07/06/2008 08:51 | SI023 |
| 2 | 08/06/2008 08:53 | NEW EVENT | 08/06/2008 08:51 | 08/06/2008 08:53 | SI023 |
| 5 | 15/06/2008 14:52 | TIME SYNC | 04/01/1970 13:48 | 15/06/2008 14:52 | INV001 |
| 6 | 15/06/2008 14:52 | LOGIN | 15/06/2008 14:52 | NULL | SI023 |
| 7 | 15/06/2008 14:54 | NEW EVENT | 15/06/2008 14:52 | 15/06/2008 14:54 | SI023 |
| 8 | 15/06/2008 14:55 | LOGIN | 15/06/2008 14:55 | NULL | INV001 |
| 9 | 15/06/2008 14:55 | ENROL | 15/06/2008 14:55 | NULL | INV001 |

Computer System Validation

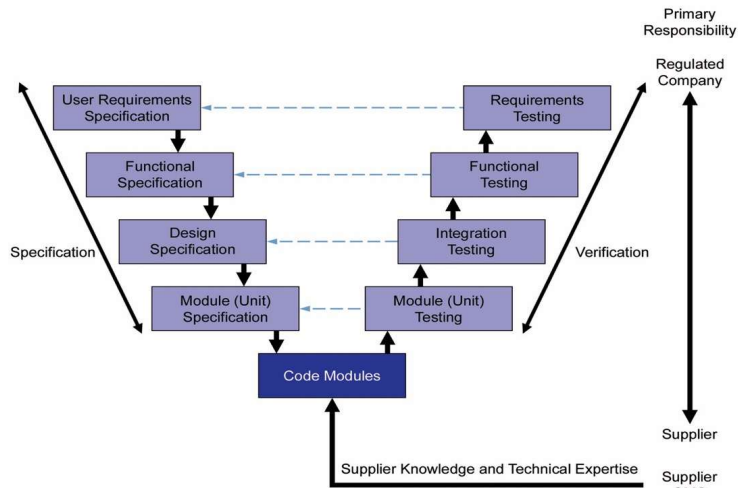
Computerised System Validation

- The process of establishing documented evidence, that provides a high degree of assurance, that a computer system consistently performs according to predetermined specifications and quality attributes [FDA]
- Validation - Confirmation by examination and through provision of objective evidence that the requirements for a specific intended use or application have been fulfilled. [ISO 9000]
- Proving that the system is **fit for purpose**

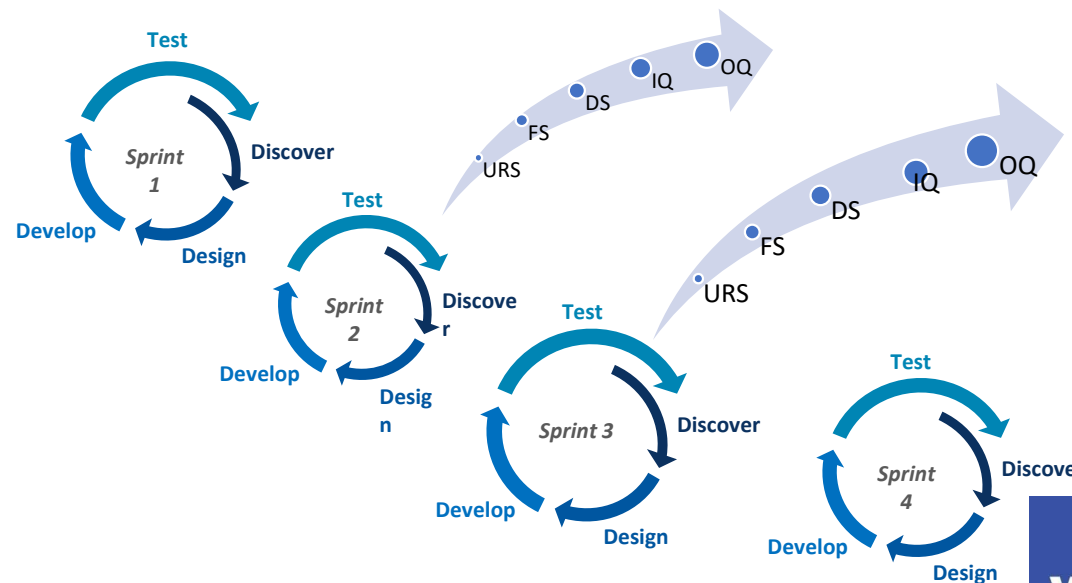
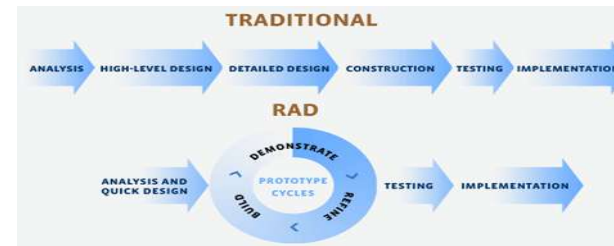
Objectives of Computerised System Validation

- CSV should demonstrate that accuracy and reliability are built into the software product (quality assurance), **without relying solely on testing** (quality control)
- To this aim CSV must be **addressed throughout the system development life cycle** from initiation through development, testing and production use to decommissioning

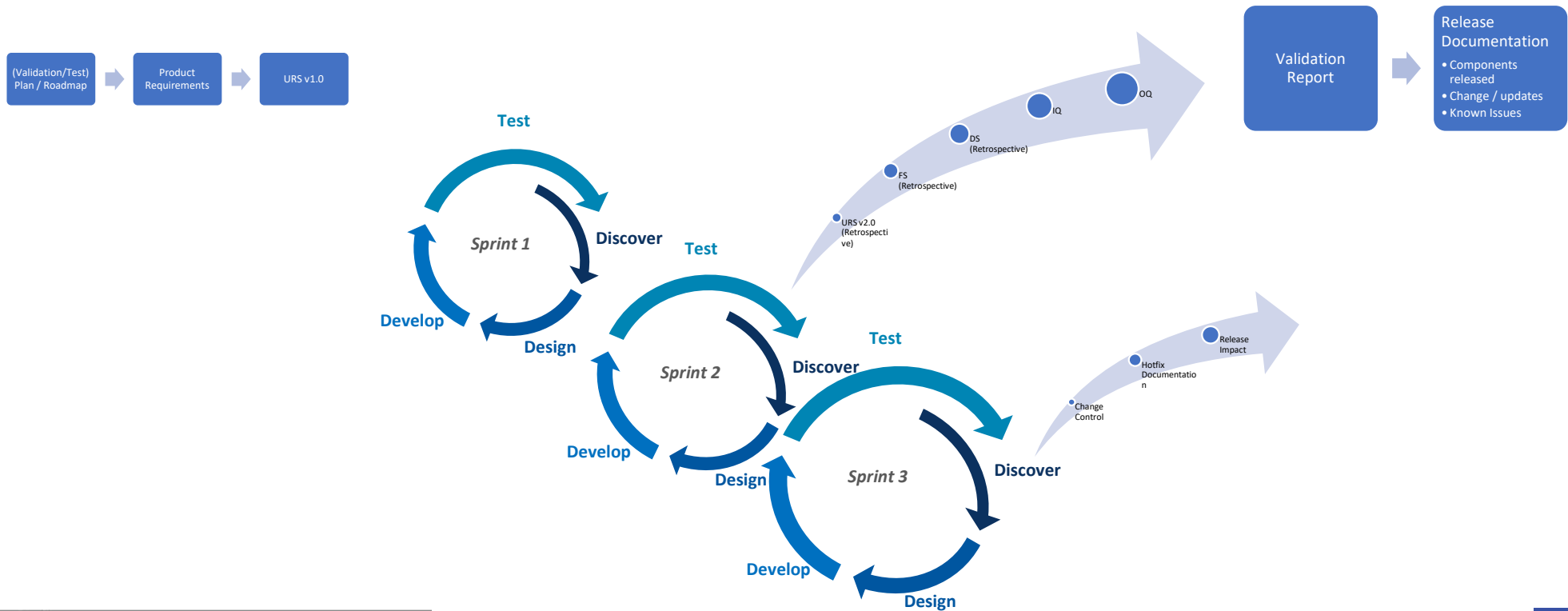
• GAMP 4 / 5 - Validation Lifecycle



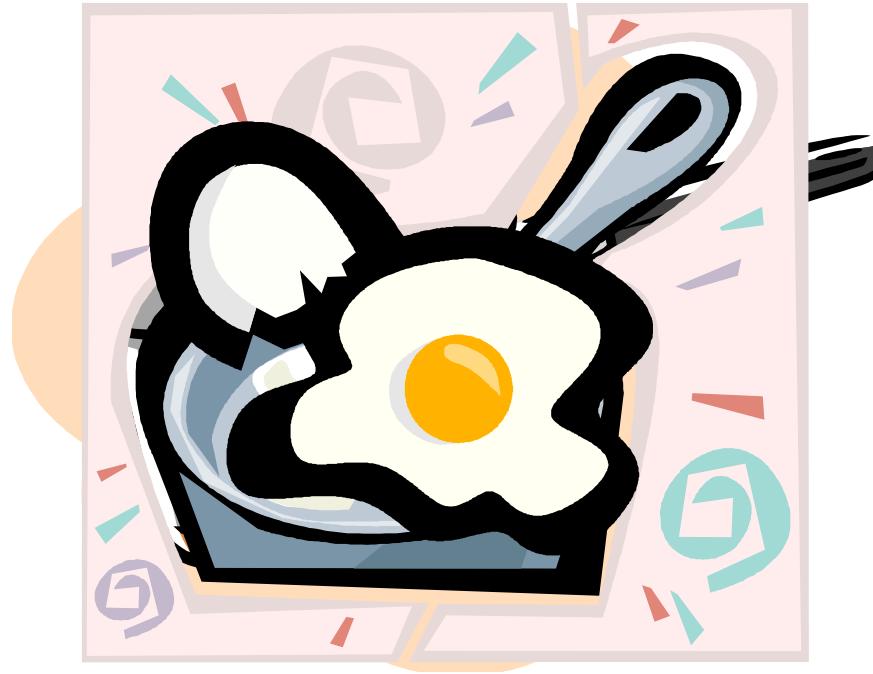
Source: Figure 4.4. GAMP 5: A Risk-Based Approach to Compliant GxP Computerized Systems, © Copyright ISPE 2008. All rights reserved. www.ISPE.org.



• GAMP 4 / 5 - Validation Lifecycle



What is a validated system?



Intended Purpose

- The User Requirements Specification (URS) details the required and desired functions and features from the end-users' perspective
- “SMART” requirements are:
 - Specific
 - Each requirement must be focused on a clear objective or broken down further
 - Measurable
 - The achievement of the requirement must be measurable by an objective test
 - Achievable
 - Requirements must be non-contradictory and be realistic in terms of the available functionality
 - Relevant
 - The requirements must be clearly related to a specific, agreed business need
 - Time-limited
 - It must be possible to meet all listed requirements within the time-frame of the current implementation
 - Testable
 - The requirement should be written such that it is easy to define a test to confirm the requirement has been met

Intended Purpose - Agile

- User Story
- Acceptance Criteria / Definition of Done

Intended Purpose - Agile

SMART

- The system should include a pre-defined role for CRA allowing:
 - read-only access to eCRFs for their allocated Site(s)
 - Ability to Raise Queries to Sites
 -

Agile

- As a Monitor I want to be able to access eCRFs for all my sites
 - eCRFs are available in my RemoteMonitoringView
 - Only my eCRFs are visible to me
- As a Monitor I wish to Raise Queries to be sent to the Site
 - Sites are notified of Queries by Email & within the System Alert Bar

Workshop - Requirements

- You have been tasked with Validating a new EDC for the study
- You have selected a vendor ClinicalTrialsForAll who operate the EDC as a PaaS solution within which you can manage EDCs and eTMF solutions
- Their EDC Solution allows the creation and re-use of:
 - Data Entry Fields (Labels, Data Types, Edit Checks)
 - Forms (Collections of Data Entry Fields)
 - Pages (Collection of Forms)
- Studies Consist of:
 - System & Study Specific Roles
 - Visit Schedule
 - Visits (Collection of Pages, Forms and Data Entry Fields)

Workshop - Requirements

- What are your EDC Platform Requirements?
 - Security
 - Data
 - Trial Design
 - Trial Execution
 - Regulatory

Workshop – Requirements Feedback

- Electronic Data Capture (EDC) platform requirements for clinical trials focus on ensuring data integrity, regulatory compliance, and user-friendly data entry to accelerate study timelines. Key requirements include support for electronic Case Report Forms (eCRFs), real-time data validation, secure audit trails, and, frequently, integration with external data sources like EHRs. [\[1, 2, 3, 4, 5\]](#)
- Here are examples of EDC platform requirements categorized by functionality:
- **1. Regulatory Compliance and Security** [\[1\]](#)
- **21 CFR Part 11 Compliance:** Strict adherence to FDA regulations regarding electronic records and signatures.
- **Audit Trails:** Secure, time-stamped records of all user actions—who, what, and when a change was made—including the original value.
- **Data Protection:** Compliance with GDPR and HIPAA for personal health information.
- **Access Control:** Role-based access control (RBAC) to ensure unauthorized users cannot access confidential data.
- **Data Security:** Data encryption in transit and at rest. [\[1, 2, 3, 4, 5\]](#)
- **2. Study Design and Data Entry**
- **Flexible eCRF Builder:** Tools allowing users to design and modify forms without requiring IT support.
- **Dynamic Logic & Data Validation:** Built-in edit checks, branching logic (if-then), and range checks to reduce human error at entry.
- **Diverse Field Types:** Ability to support multiple data types, including text, numeric, date, medical imaging, and lab results.
- **Offline Capability:** Ability to capture data without a live internet connection (essential for remote sites). [\[1, 2, 3, 4, 5, 6\]](#)
- **3. Data Management and Integration**
- **Real-time Monitoring & Reporting:** Dashboards to track recruitment, data accuracy, and query resolution in real time.
- **Electronic Medical Record (EHR) Integration:** Direct data import from hospital EMR systems to reduce manual transcription.
- **API Availability:** Open API for integration with other trial systems such as CTMS (Clinical Trial Management Systems) or RTSM (Randomization and Trial Supply Management).
- **ePRO/eCOA Support:** Integration with patient-reported outcomes. [\[1, 2, 3, 4, 5\]](#)
- **4. Performance and Usability**
- **Intuitive Interface:** A user-friendly interface to minimize training needs and encourage site adoption.
- **Multi-language Support:** Ability to support global studies in different languages.
- **Scalability:** Capacity to handle studies of varying sizes, from small pilots to large, multi-center trials.
- **Fast Deployment:** Fast database setup and quick turnaround for study amendments. [\[1, 2, 3, 4, 5\]](#)
- **Vendor:** Highly praised for its intuitive interface, 24/7 support, and fast study build times.



Advanced Sponsor Oversight



- How do you Validate – 4 Steps

1. A system of Quality Assurance
2. A GxP Risk / Critical Assessment as per 1
3. The Intended Purpose documented as per 1
4. Evidence that the System performs to 3 as per 1 and in accordance with 2

CONTROL

• Expectations of Validation

- Validation Plan
- User Requirement Specification
- Functional Specification
- Design Specification
- Module Specification
- Unit Test Specification
- Installation Qualification
- Operational Qualification / System Testing
- Performance Qualification / User Acceptance Testing
- Validation Report
- Disaster Recovery Plan
- Disaster Recovery Test Plan
- Business Continuity Plan
- Change Control Procedure
- Administration Procedure
- Incident Management Procedure
- Configuration Management Procedure
- System Usage Procedure
- Audit Trail Review Procedure
- User Security Review Procedure

It Depends

It Deepens



GxP Criticality / Risk

- Is the Data in the System related to a GxP Activity?
- Based on its nature what is its relationship with:
 - Patient Safety
 - Product Quality
 - Data Integrity
- Is it managing the Data Directly or it is an Indirect or Related System?
- This would link to YOUR QMS / YOUR POLICY for how you scale your validation lifecycle
- It is not ONE SIZE FITS ALL – It Must provide a Differentiation

GxP Criticality / Risk



Microsoft Excel
:ro-Enabled Worksl

Recap - What records should you see / have for a system

- Plans
 - Validation
 - Installation
 - Development
 - Testing
- Reports
 - Validation
 - Installation
 - Development
 - Testing
- Specifications
 - User Requirement Specification
 - Configuration Specification
 - Test Specification

**Understandable to
non-technical
Personnel**

VALIDATION PLAN

EXPECTATION

- **Activities Required**
 - **Specifications & Design**
 - **Build**
 - **Install / Configure**
 - **Test**
- How they will be performed & who is responsible
 - Documentation / Configuration
- What the output will be
 - Test Reports
 - Configuration Reports etc
- **Acceptance Criteria**
 - **Acceptable Bug levels**
 - **Performance metrics**
 - **Activity Completion**
- Mechanisms to maintain compliance in operations
 - Security and Usage SOPs
 - Audit trail / User Review
 - Periodic Review
 - Calibration / Servicing

TYPICAL CONTENTS

- Introduction & Scope
- System Overview
 - Software,
 - Servers
 - People
 - Data Flow
- **Organizational Structure**
 - **Project and Users**
 - **Frequently combined with Responsibilities**
- Quality Risk Management
 - Link back to policies and procedures
 - Area of GxP (May or may not be broken down for individual components)
- Validation Strategy
 - GAMP Categories / IQ/OQ/PQ etc
 - Quality Assurance & Supplier Assessment
- Deliverables
- Acceptance Criteria
- SOPs and Change Control

VALIDATION PLAN

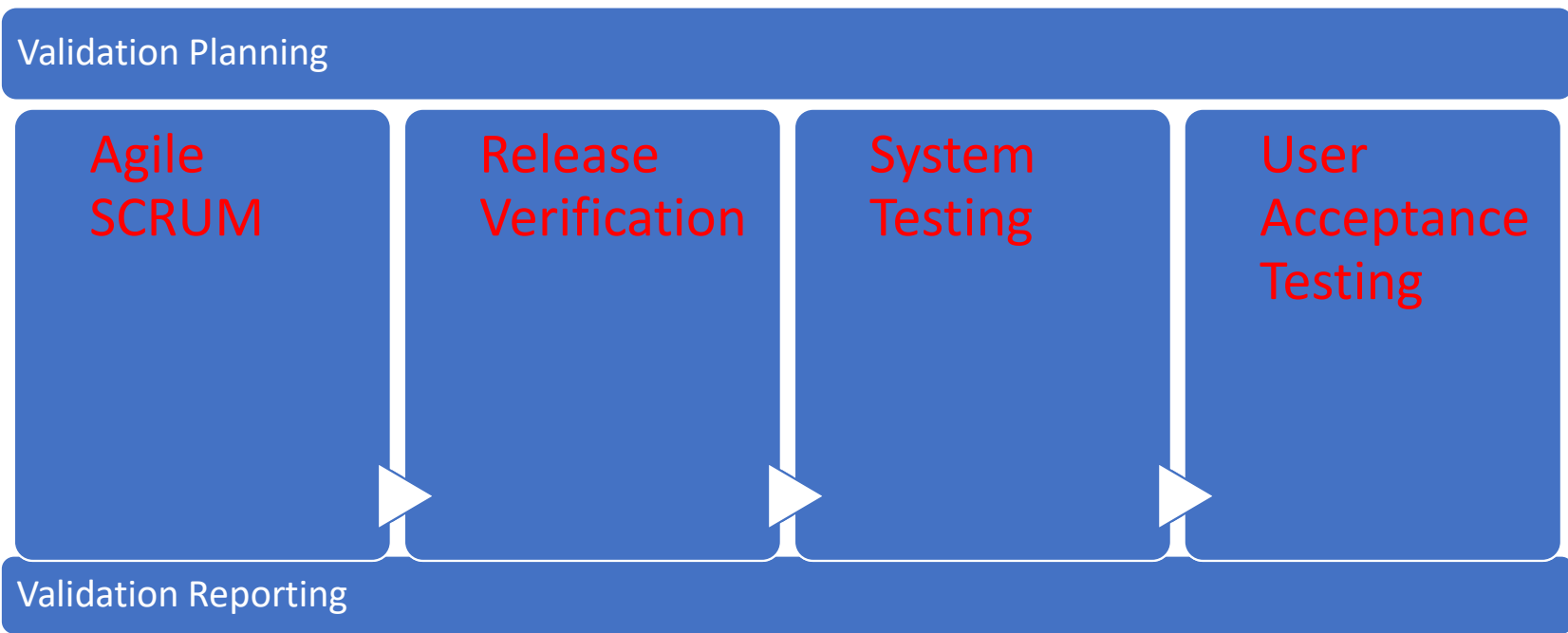
ORGANISATION

- Business Project Team
- Internal IT / Security
- Vendor(s)

KEY ELEMENTS

- Segregation of Duties
- SME Expertise
- Oversight
 - Audit / Assessment
 - Ongoing Monitoring
 - Vendor Stack Assurances
- Documentation Existence / Availability
 - What will you Check
 - What will you Trust
- Leverage
 - What will you Repeat / Verify
 - What will you leverage from the Vendor
- Assumptions
 - What has already been done
 - What aspects will still be being done
- Lifecycle Implications
 - Waterfall vs Agile
 - Mechanisms for CONTROL

What is required for Validation



What is required for Validation

Validation Planning

Performance
Qualification / UAT

Validation Reporting

Testing

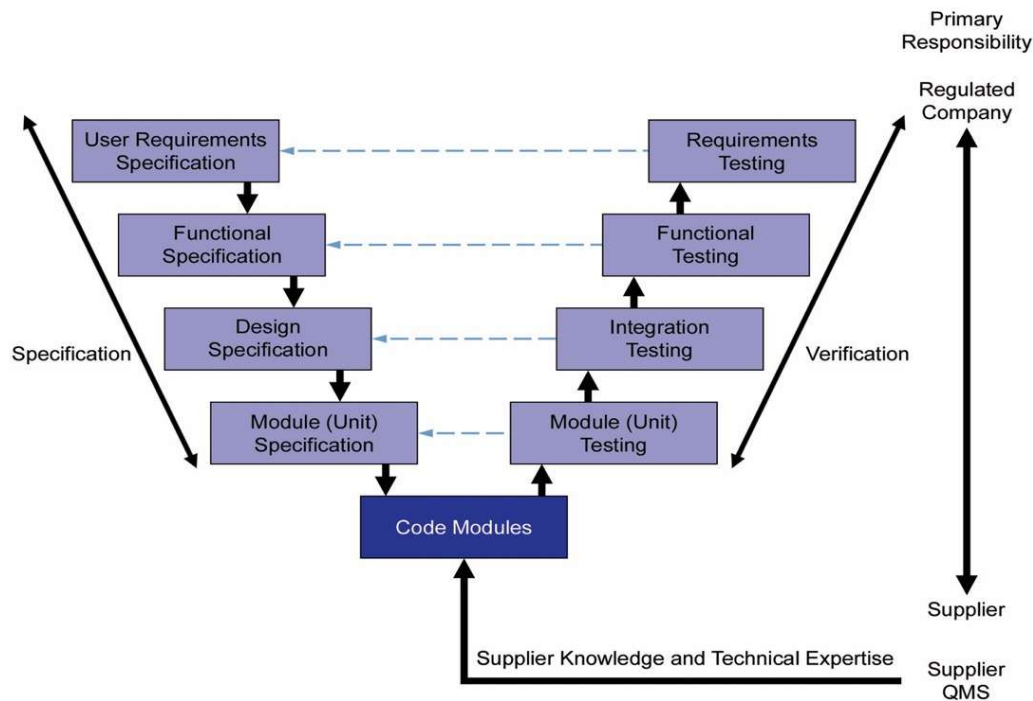
| | |
|-----------------------------|---|
| Unit / Developer Testing | Written by the Developer – with Full Knowledge of the Codes Design |
| Integration Testing | Verification that modules / components (e.g. Subject Enrolment, Visit Management) interact with each other correctly [White Box] |
| System Testing | System testing is a, [black-box software testing process] that evaluates a fully integrated application to ensure it meets specified requirements |
| Exploratory Testing | Typically Unscripted investigation looking for unexpected behaviours and usability issues |
| Performance Testing | System Performance and Behaviour under load...will it behave appropriately with 2 users AND 100 users |
| Security testing | Vulnerability tests, penetration tests |
| Smoke Testing | A Smoke Test is performed to verify core functionality within the system to reveal simple failures severe enough to reject a prospective software release. |
| (System) Acceptance Testing | System Acceptance Tests (SATs) ensure that the system works as expected. They potentially cover all User Requirements and include all tests that may also be referenced to as Performance Qualification (PQ) or Operational Qualification (OQ). |
| Regression Testing | A combination of Smoke and SAT tests to verify that pre-existing functionality has not been altered |
| Continuous Testing | Battery of Smoke, Unit, Security....that runs every time code is committed to the code branch |
| End to End Testing | Tests an entire application workflow from start to finish |

- Testing no longer requires a person, a computer and a Script
- Unit Testing is no longer run once before code is delivered
- System / Regression testing is Becoming Continuous
- The Days of Formal / Informal Testing has become Scripted vs Unscripted

Risk Management & Testing

- As per your organisations Defined Lifecycle
- The Higher the perception of Risk the more Formal / Scripted the Testing Approach
- The Source – your Documented Requirements
 - Risk Assessment for *every* Requirement (SPD or Critical/Optional)
 - Risks-Requirement is not a 1-2-1 Relationship
 - A matter of Scale (Time taken to do all the Risk Assessments vs Testing Effort ‘Saved’)

Validation Testing



Source: Figure 4.4, GAMP 5: A Risk-Based Approach to Compliant GxP Computerized Systems, © Copyright ISPE 2008. All rights reserved. www.ISPE.org.

- Everything should be tested somewhere by someone
- One good test is worth multiple bad ones
- You have to Rely on Oversight/Assessments
- Trust / Confirm that Templates were tested

Hidden Test Scripts

- Clinical Trial Protocol
- Clinical Project / Data Management SOPs
- ICH GCP
- ERES / Data Integrity

Test Type

- Functional Verification
 - Testing Boundaries (Max/Min, Age vs Number, Date (Of Birth, Today, last, next))
 - Configuration Confirmation

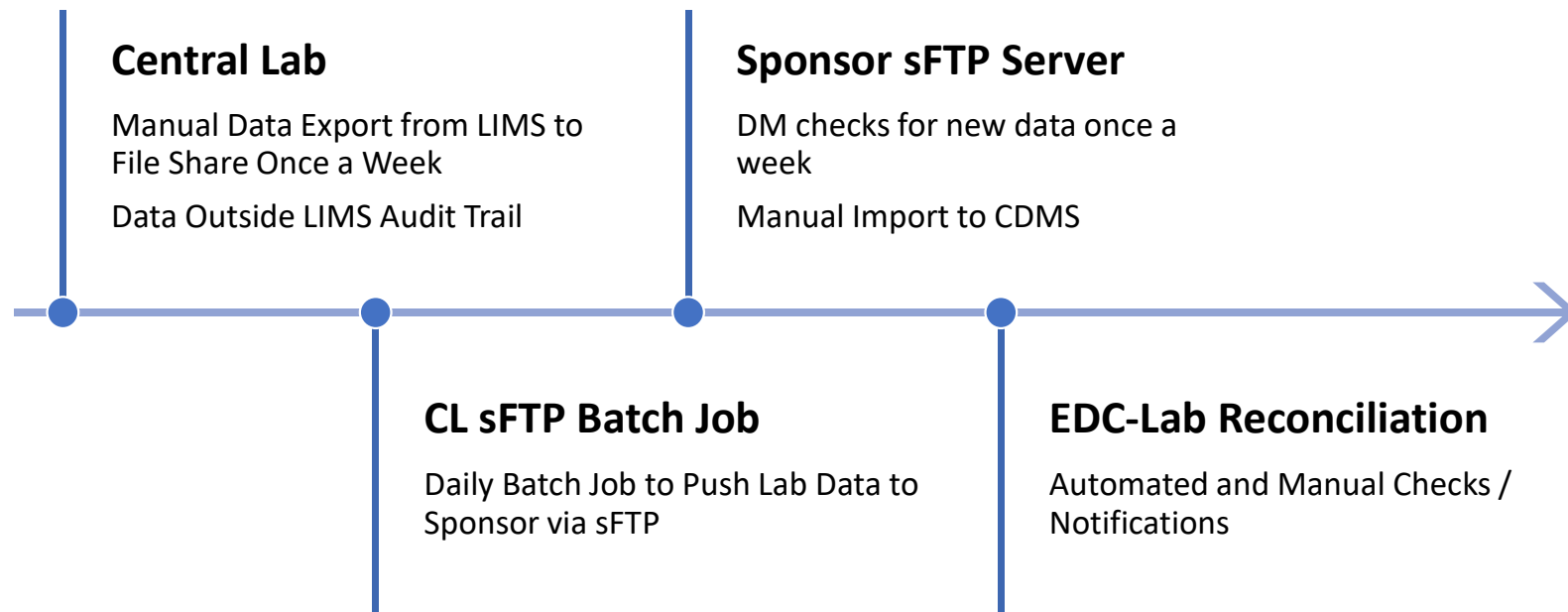
Key Tests to be Performed

- Critical Data / Processes
- EndPoints
- Safety Parameters
- Workflows / Sequences
- Data Sources / Devices
- Disaster Recovery / Backup
- Failback
- Security Configuration
- Audit Trails
- Interfaces
- Security Review
- Audit Trail Review
- Data Types / Data Lengths / Edit Checks
- Unleash your Negativity
- Understand and adapt to testing limitations (Can you test sequence / timing of 3 year study in a week)

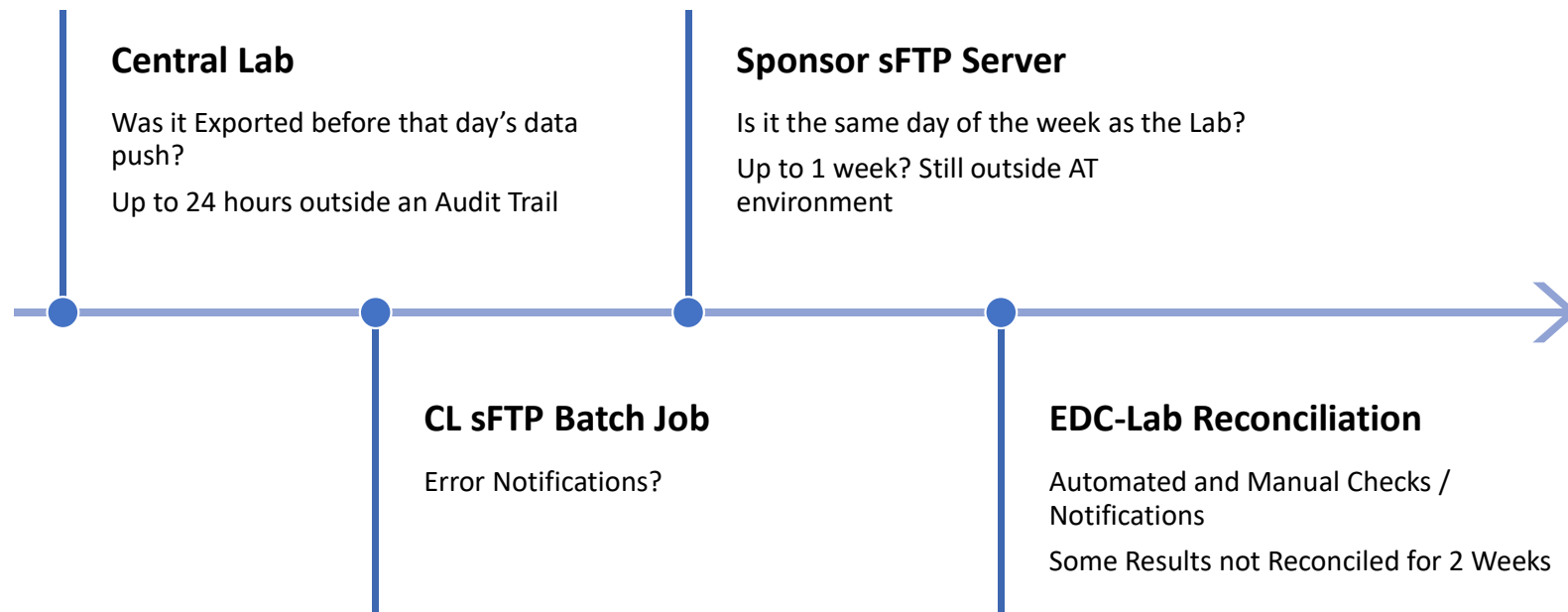
Spotcheck – Data Transfers in Clinical Trials

- Data Transfer Specifications
- One Test Transfer
- Often Lacks Detail on ‘Boundary Tests’
- Questionable Completeness
- Often assumes Data has been Cleaned prior to Transfer
- One Test Transfer does not allow for data that is transferred more than once
- Doesn’t include the audit trail

Spotcheck – Data Transfers in Clinical Trials



Spotcheck – Data Transfers in Clinical Trials



VALIDATION REPORT

- See Validation Plan (mostly) but Retrospective
- See 21CFRPart11
 - Who (did)
 - What (to)
 - What (document/component)
 - When (did they do it)
 - Why (did they do it)
 - Should (they have done it i.e. Was it in the plan or a Deviation)

Artificial Intelligence

AI Disclaimer

- I am deeply distrustful of supposed AI
- Computer Systems *CAN* outperform humans in many tasks (e.g. colour perception, data analysis with clear decision making, etc).
- Significant amounts of AI isn't
 - Application of Human Derived Logic
 - Machine Learning
 - Coded Simulations of Reasoning / Empathy

Artificial Intelligence vs Machine Learning

- AI answers are often – ‘Most likely’
- Need to understand the model being used.....
 - Structured (here are some answers we know which are right and wrong) vs Unstructured Learning (here is some data make some decisions about it)
 - Learnt and Fixed or continually adaptive
- Training Data
 - Sources (Anyone been offered an AI Training Position Recently?)
 - How verified
 - What are your feedback loops

Lies, damned lies and statistics – Mark Twain

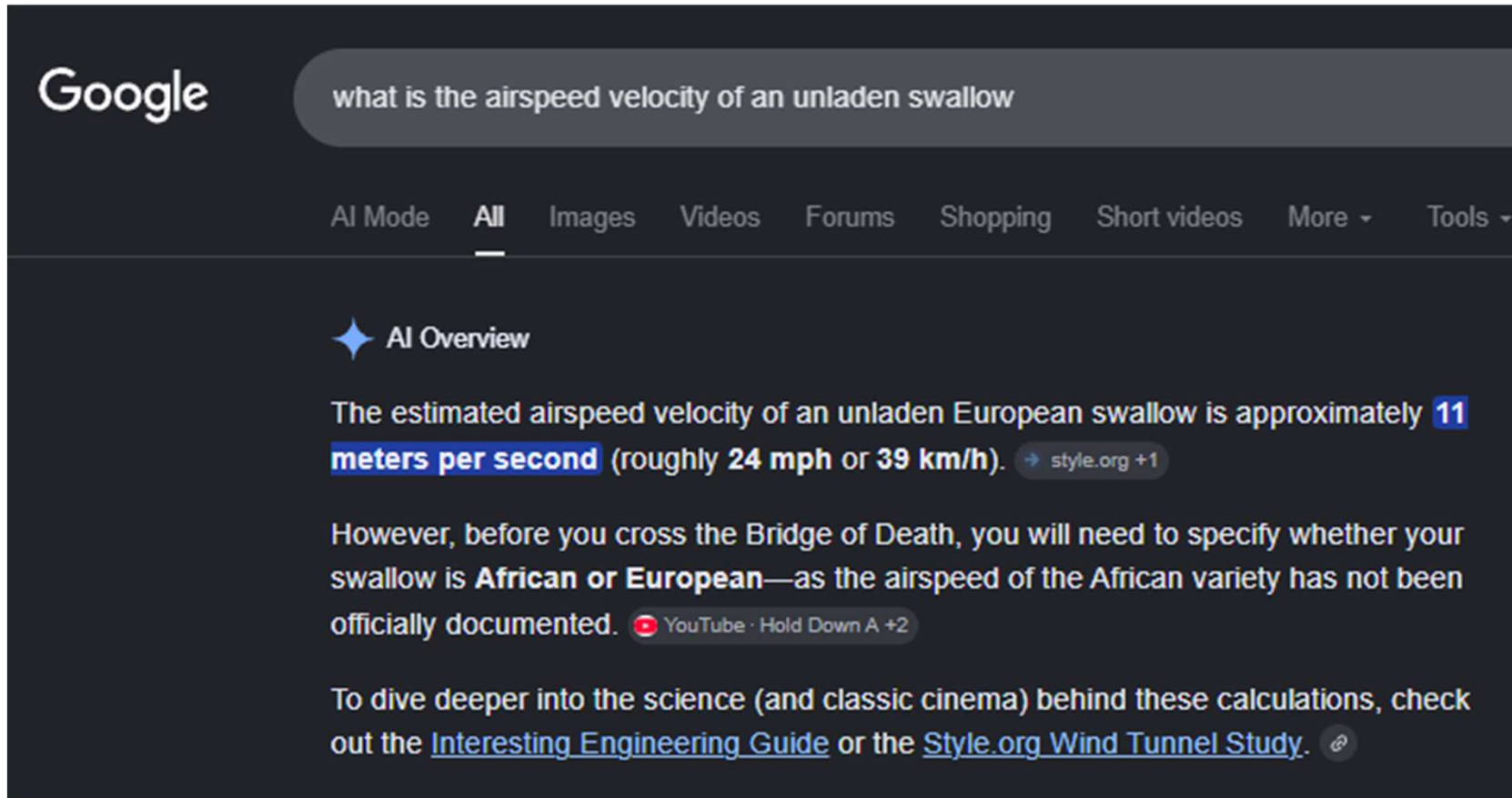
Artificial Intelligence vs Machine Learning

- Unstructured learning
 - Looks for patterns
 - Classifies and Groups
 - ‘Everyone else liked this so you will too’

Artificial Intelligence vs Machine Learning

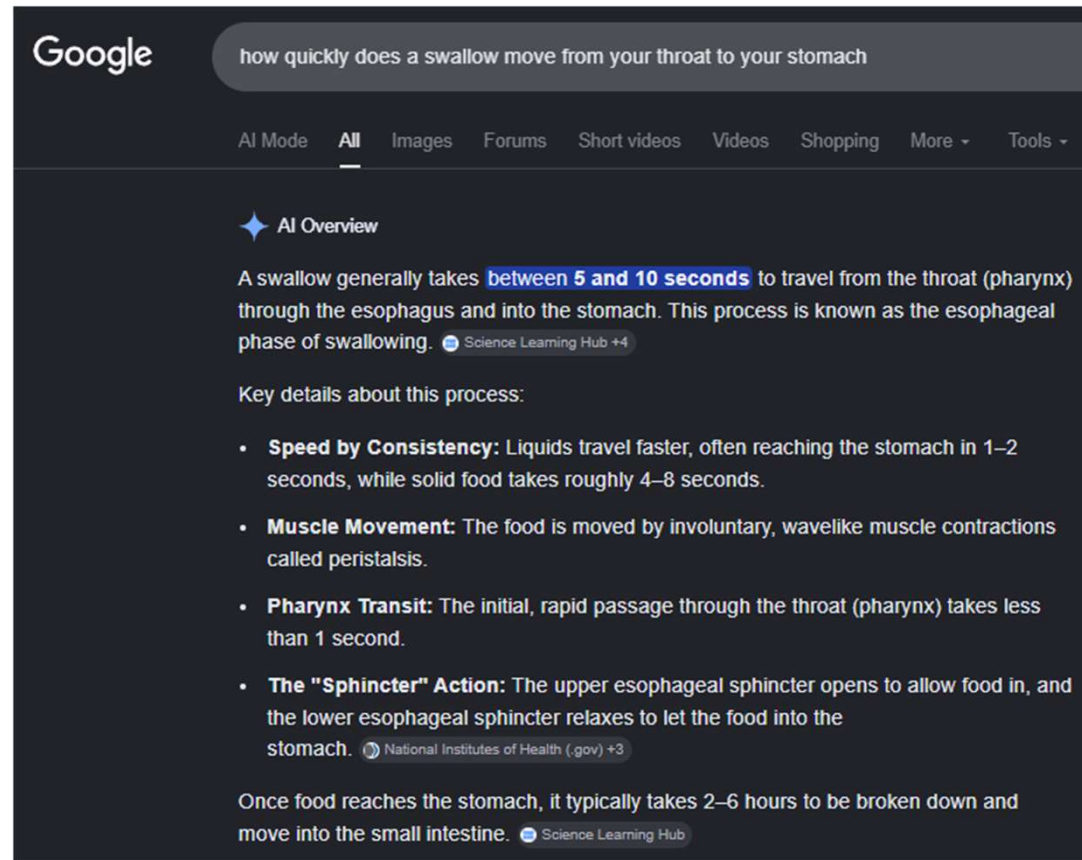
- There is still code – that needs to have been controlled / tested
 - Linear Regression ‘Best fit’ – Gradient Descent
 - Not one result that fits all its training data dependent
 - But did they code it correctly... how do you / they know
- The algorithms include ‘Decision limits’
 - Costs / Thresholds
 - Can you set your own tolerances
- There is a skill in being able to ask the question correctly

Artificial Intelligence vs Machine Learning



The screenshot shows a Google search interface with the query "what is the airspeed velocity of an unladen swallow". The search results are displayed in a dark theme. The "All" tab is selected. The first result is an "AI Overview" section. The text of the overview states: "The estimated airspeed velocity of an unladen European swallow is approximately **11 meters per second** (roughly **24 mph** or **39 km/h**). → style.org +1". Below this, a paragraph explains that the airspeed of an African swallow has not been officially documented, with a link to a YouTube video. A final paragraph suggests checking out the "Interesting Engineering Guide" or the "Style.org Wind Tunnel Study".

Artificial Intelligence vs Machine Learning



Google

how quickly does a swallow move from your throat to your stomach

AI Mode **All** Images Forums Short videos Videos Shopping More ▾ Tools ▾

◆ AI Overview

A swallow generally takes **between 5 and 10 seconds** to travel from the throat (pharynx) through the esophagus and into the stomach. This process is known as the esophageal phase of swallowing. [Science Learning Hub](#) +4

Key details about this process:

- **Speed by Consistency:** Liquids travel faster, often reaching the stomach in 1–2 seconds, while solid food takes roughly 4–8 seconds.
- **Muscle Movement:** The food is moved by involuntary, wavelike muscle contractions called peristalsis.
- **Pharynx Transit:** The initial, rapid passage through the throat (pharynx) takes less than 1 second.
- **The "Sphincter" Action:** The upper esophageal sphincter opens to allow food in, and the lower esophageal sphincter relaxes to let the food into the stomach. [National Institutes of Health \(.gov\)](#) +3

Once food reaches the stomach, it typically takes 2–6 hours to be broken down and move into the small intestine. [Science Learning Hub](#)

Artificial Intelligence vs Machine Learning

Google search results for "what is the average income of a human". The AI Overview section provides UK-specific data based on 2025–2026 data. It states that the median annual income for a full-time employee in the UK is approximately £39,039. Other measures show a mean average of roughly £40,269 to £45,836 for all employees, and £14,713 for part-time workers. The source is cited as the Office for National Statistics.

Key 2026 UK Income Statistics

- **Median Annual (Full-time):** £39,039
- **Mean Average (All Employees):** £40,269
- **Median Weekly (Full-time):** £766.60
- **Part-time Annual Median:** £14,713
- **Average Hourly Pay (All):** £18.00

Regional and Age Variations (2026)

- **Top 10% Earners:** Those earning over £76,903.
- **Age 22-29:** Median around £30,000–£34,724.
- **Age 40-49:** Peak earning years, with medians around £44,244–£50,927.
- **Region:** The North East generally sees lower averages (~£39,859) compared to other areas.

These figures show a 4.3% increase in median full-time earnings compared to 2024.

Note: The provided results focus on UK data based on the most recent available statistics (2025–2026).

Google search results for "what is the average income of a human worldwide". The AI Overview section provides global data. It states that the average annual income per person worldwide is roughly \$18,000 USD per year (approximately \$1,480 a month), according to data reported around 2012. However, more recent and regional data highlights that this figure varies heavily based on how it is measured.

- **Global Inequality:** In the poorest nations, average incomes are below \$1,000 per year, while in high-income countries, they are over 50 times higher.
- **Regional Disparities (GDP per capita 2022):** Global average GDP per capita is around \$17,000.
 - Latin America: ≈\$14,000
 - South & South East Asia: ≈\$9,000
 - Sub-Saharan Africa: ≈\$4,000
- **High-Income Examples (2024–2025):** Gross average monthly wages in high-income countries often exceed \$6,000–\$7,000 per month (e.g., Luxembourg, Iceland, USA).

Generative Artificial Intelligence

- Diverse Data Sets (Text, Codes Images)
 - Looks for patterns / Unstructured Learning
 - Analyses and develops rules
 - What makes a good novel (plots/sub-plots, twists, number of main characters and sub-plot interactions)
 - ‘Everyone else liked this so you will too’
- Remember Soft skill Training on the risks of GroupThink
- Where is your data going?
- Workshop examples
 - AI did come up (and arguable better wordsmith) similar responses to me
 - AI made declarative fixes including making (but not stating) assumptions and included potentially irrelevant actions because that’s what others did....

AI Summary

- Understand the AI you are using
- Understand its sources, limitations and tolerances
 - Does it offer answers before you have trained it
 - Does it admit it doesn't know
- Understand where the data is (and how that impacts future refinement / learning)
- Understand where you have 'Humans in the Loop'
 - Model Developers
 - Clinicians
- Understand who is making the decisions?
 - What data is the AI not bringing to your attention?
 - If you are not seeing all the information are you making an informed decision?

Training & User Management

Training (P11, A11, ICH)

- Who needs appropriate Training?
 - Users – SOPs, System User / Admin / Designer Training
 - Support / Maintenance Personnel – IT, ServiceDesk
 - Developers (Business Analysts, Coders, Testers.....)
- Role specific
 - Does an Oracle Clinical DBA need OC UI Training?
 - Do IST and Vendor Personnel need GCP / GPvP Training?
 - Awareness vs Detail?
 - Would ERES / Data Integrity Training with GCP Awareness suffice
 - A Developer does not need to understand an Adverse Event to develop a Generic EDC
 - They do need to understand not to change data and the need to implement appropriate integrity safeguards

Training (P11, A11, ICH)

- We aren't a regulated company / We cannot show you that for Privacy reasons
 - The Life Sciences Regulations are clear, if they wish to sell to Life Sciences
 - They need to adapt to meet the training requirements
 - IT Companies are not in the habit of hiring unskilled/unqualified workers

User Management

- Clear Process for Requesting, Authorising and Revoking Access
- Documentation / Tickets
- Periodic (Risk-based) Review
 - The Life Sciences Regulations are clear, if they wish to sell to Life Sciences
 - They need to adapt to meet the training requirements
 - IT Companies are not in the habit of hiring unskilled/unqualified workers
 - Training evidence is linked in to ISO accreditations etc.
- This is a mini-audit
 - Process was followed for all starters/leavers/changers

Day 4 Summary

- Only you know your purpose for a System
- Validation Supports your purpose and your choices, it should not block it
- Don't Overcomplicate things