



# FINDING YOUR WAY THROUGH THE MATRIX OF DATA INTEGRITY

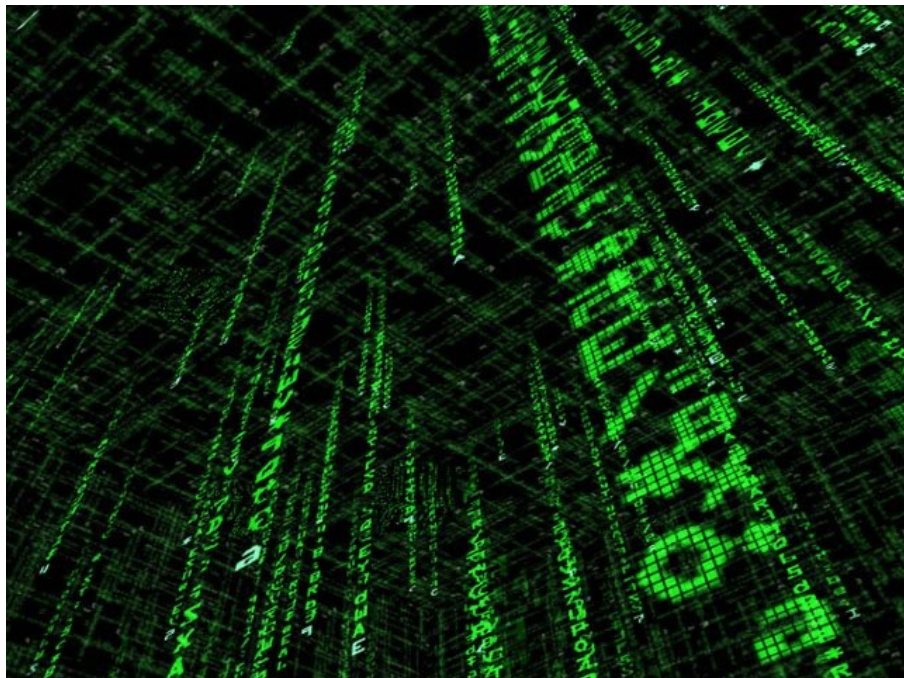
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# Topics



01. What is Data Integrity?

02. ALCOA+ Principles

03. Planning for the Why

04. Audit Lessons Learned

# POLL One: What is data integrity?



- A. Clean data with integrity
- B. Something that involves IT
- C. A guide on quality culture
- D. None of the above

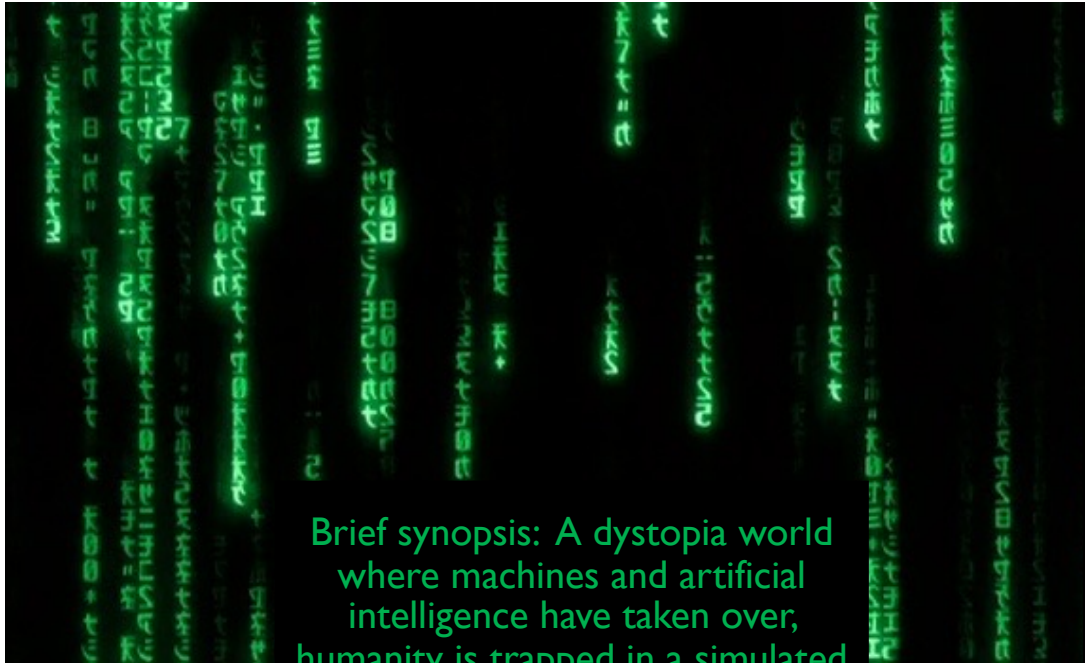


## Poll Two: What is The Matrix?



- A. The world we live in.
- B. A 90s movie
- C. A.I. used to distract humans
- D. An environment or material
- E. All of the above

# The Matrix Movies



Brief synopsis: A dystopia world where machines and artificial intelligence have taken over, humanity is trapped in a simulated reality, and a computer hacker named Neo sets out to free humanity from The Matrix



The Matrix - 1999

The Matrix Reloaded – 2003

The Matrix Revolutions – 2003

The Matrix Resurrections - 2021

Thomas Anderson “Neo” a computer hacker

Morpheus leader of resistance

Trinity another hacker

Smith a super software program

The Agents more software programs

The Merovingian

The Oracle

The Architect creator of The Matrix

The Analyst creator of the new Matrix



# WHAT IS DATA INTEGRITY?

# What is Data Integrity?

**Data integrity** is the *maintenance of, and the assurance of, data accuracy and consistency over its entire life-cycle<sup>[1]</sup>* and is a critical aspect to the design, implementation, and usage of any system that stores, processes, or retrieves data. The term is broad in scope and may have widely different meanings depending on the specific context – even under the same general umbrella of computing. It is at times used as a proxy term for data quality,<sup>[2]</sup> while data validation is a prerequisite for data integrity.<sup>[3]</sup> Data integrity is the opposite of data corruption.<sup>[4]</sup> The overall intent of any data integrity technique is the same: ***ensure data is recorded exactly as intended (such as a database correctly rejecting mutually exclusive possibilities). Moreover, upon later retrieval, ensure the data is the same as when it was originally recorded.*** In short, ***data integrity aims to prevent unintentional changes to information.*** Data integrity is not to be confused with data security, the discipline of protecting data from unauthorized parties.

Source: [https://en.wikipedia.org/wiki/Data\\_integrity](https://en.wikipedia.org/wiki/Data_integrity)







EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH



MHRA  
Regulating Medicines and Medical Devices

What do the regulators say about data integrity?...



独立行政法人  
医薬品医療機器総合機構

Pharmaceuticals and Medical Devices Agency



Name of Regulation	Relevancy to GCP
1. US Code of Federal Regulations 21 – 21 CFR Parts 50, 54, 56, 312, 314	50 - Protection of Human Subjects 54 - Financial Disclosure by Clinical Investigators 56 - IRBs 312 - IND App 314 - Applications for FDA Approval to Market a New Drug
2. US Code of Federal Regulations 21 - 21 CFR Part 11	Defines the criteria under which electronic records and electronic signatures are considered “trustworthy, reliable, and equivalent to paper records
3. FDA BIMO Checklist	Use as a guide to ensure that all documents are present in the TMF and meet ALCOA+ standards

Sources:

- 1 – [https://www.ecfr.gov/cgi-bin/text-idx?SID=2cc29fbfc3d3d0911f6fc94d2c658917&mc=true&tpl=/ecfrbrowse/Title21/21tab\\_02.tpl](https://www.ecfr.gov/cgi-bin/text-idx?SID=2cc29fbfc3d3d0911f6fc94d2c658917&mc=true&tpl=/ecfrbrowse/Title21/21tab_02.tpl)
- 2 – <https://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm125125.pdf>
- 3 - <https://oprs.usc.edu/wp-content/uploads/sites/3/2021/07/FDA-BIMO-Checklist-Copyrighted-pdf.pdf>

Name of Regulation	Relevancy to GCP
4. Good Clinical Practice Guide, 2012	Chapter 10 - Discusses that the same controls must be in place for managing both a paper TMF and an eTMF: Appropriate security, Audit trail, Passwords, Training, Metadata, Digital signatures...
5. UK Statutory Instrument 2006 No. 1928 Medicines for Human Use (Clinical Trials) Amendment Regulations, UK Clinical Trials Amendment Regulation	18. in 31A Discusses importance of TMF and archiving and what is required as well as who, including if transfer of ownership of documents (or data) occurs.
6. MHRA GXP Data Integrity Guidance, March 2018	Data integrity is the degree to which data are <b>complete, consistent, accurate, trustworthy, reliable</b> and that these characteristics of the data are maintained throughout the data life cycle". "Data governance should [...] comply with the principles of data integrity including <b>control over intentional and unintentional changes to information.</b> " Governed by the ALCOA (+) principles.

Sources:

4 – MHRA Grey Guide, Chapter 10 – available for purchase, no direct URL content

5 – [http://www.legislation.gov.uk/ukxi/2006/1928/pdfs/ukxi\\_20061928\\_en.pdf](http://www.legislation.gov.uk/ukxi/2006/1928/pdfs/ukxi_20061928_en.pdf)

6 - [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/687246/MHRA\\_GxP\\_data\\_integrity\\_guide\\_March\\_edited\\_Final.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/687246/MHRA_GxP_data_integrity_guide_March_edited_Final.pdf)



Name of Regulation	Relevancy to GCP
7 - EU Directives 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products	Chapter 2 - The Ethics Committee- Article 6 <b>Chapter 4 - The Trial Master File and Archiving - Articles 16-20</b> Chapter 5 - Inspectors Chapter 6 - Inspection Procedures - Article 24, “make publicly available within their territories the documents relating to the adoption of GCP principles.”
8 - EU Regulation 536/2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC	Will replace 2001/20/EC <b>Article 57 - Clinical trial master file</b> <b>Article 58 - Archiving of the clinical trial master file</b>
9 - EMA Guideline 2018	<b>Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic).</b> <b>Discusses email and eTMF content.</b>
10 - EMA Reflection Paper on Source Data 2010	<b>Reflection paper on expectations for electronic source data and data transcribed to electronic data collection tools in clinical trials. Attributes considered of universal importance - ALCOA+. Also outlines expectations for GCP inspectors.</b>
11 - ICH Guideline on Good Clinical Practice E6 (R2) 2016 INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R2)	<b>6.10 - Direct Access to Source Data/Documents</b> <b>6.13- Data Handling and Records Keeping</b> <b>8 - Essential documents</b>

Sources:

7 - [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir\\_2005\\_28/dir\\_2005\\_28\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2005_28/dir_2005_28_en.pdf)

8 - [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg\\_2014\\_536/reg\\_2014\\_536\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf)

9 - [https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-content-management-archiving-clinical-trial-master-file-paper/electronic\\_en.pdf](https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-content-management-archiving-clinical-trial-master-file-paper/electronic_en.pdf)

10 - [https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/reflection-paper-expectations-electronic-source-data-data-transcribed-electronic-data-collection\\_en.pdf](https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/reflection-paper-expectations-electronic-source-data-data-transcribed-electronic-data-collection_en.pdf)

11 - [https://www.ich.org/fileadmin/Public\\_Web\\_Site/ICH\\_Products/Guidelines/Efficacy/E6/E6\\_R2\\_Step\\_4\\_2016\\_1109.pdf](https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2_Step_4_2016_1109.pdf)



Name of Regulation	Relevancy to GCP
Reliability Standards	<p><b><u>Accuracy:</u></b> The data should be prepared accurately based on the results of trials.</p> <p><b><u>Completeness:</u></b> All CSRs should be able to traced to raw data. All data obtained in trials should be described in the NDA/sNDA documents, including data which is less favorable, to the dossier.</p> <p><b><u>Retention:</u></b> All data which contributed to the NDA/sNDA documents and other related data should be archived.</p>
PMDA Checklist	<p><b>Created to help sponsors to be ready for site inspection and compliance review of GCP, carried out based on the MHLW GCP Ordinance - Ministerial Ordinance on Good Clinical Practice for Drugs [Ordinance of the Ministry of Health and Welfare No. 28 of March 27, 1997 (As last amended by the Ordinance of Ministry of Health, Labour and Welfare No. 161 of December 28, 2012)]</b></p> <p>References “records” throughout and necessity to <b>store</b> records, <b>maintain</b>, <b>retain</b>, and <b>archive</b>.</p>

Sources:

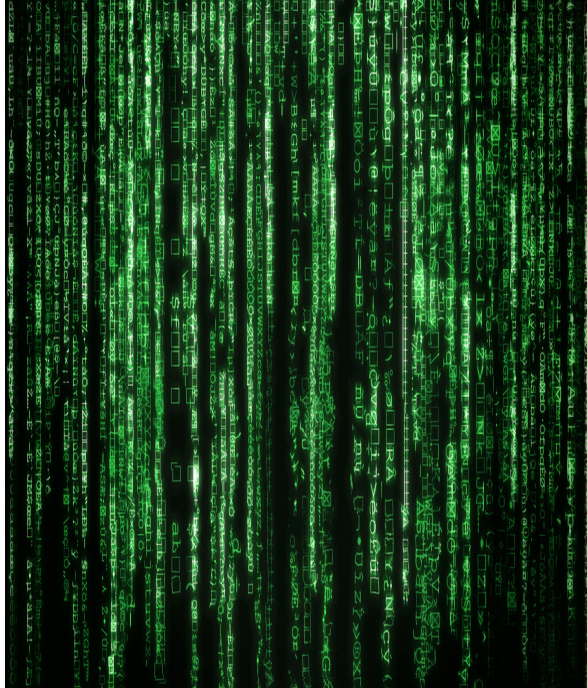
12 – <http://www.pmda.go.jp/english/index.html>

13 - <https://www.pmda.go.jp/files/000152996.pdf>

The background features a complex, abstract pattern of green and yellow lines and circles, resembling a circuit board or a network diagram. The lines are thin and vary in color, with some being bright yellow and others a muted green. The circles are also in these colors, some solid and some outlined. The overall effect is a sense of connectivity and technology. A solid black rectangular box is positioned on the right side of the image, containing the text "ALCOA+ PRINCIPLES" in white, sans-serif, uppercase letters.

# ALCOA+ PRINCIPLES

# ALCOA+



<b>A</b>	<b>Attributable</b>
<b>L</b>	<b>Legible</b>
<b>C</b>	<b>Contemporaneous</b>
<b>O</b>	<b>Original</b>
<b>A</b>	<b>Accurate</b>
<b>+</b>	<b>Available, Complete, Consistent, Enduring, Corroborated</b>

The background features a complex pattern of glowing green and yellow lines and dots, resembling a circuit board or a network diagram. A solid black rectangular box is positioned on the right side of the image, containing the text "PLANNING FOR THE WHY" in white, uppercase letters.

## PLANNING FOR THE WHY



# The Why?



***“Causality is action, reaction, cause and effect... [it’s] important to understanding the why”.***

- Merovingian to Neo in “Matrix Reloaded” (the second installment of “The Matrix”)

***The same holds true for data!***

# Poll Three: Have you been through a Data Integrity Audit?



- A. Yes.
- B. No.
- C. What is that?
- D. One is coming soon.
- E. I do not know.



# DATA INTEGRITY AUDIT LESSONS LEARNED



Inspections are coming...are you  
ready?...



The Matrix has you...

Do not panic...





Prepare yourself...

# Authorized Access - Electronic

## Inputs

Who has access to your system?

How is access granted?

How is access revoked?

What kind of recertification process is in place for user accounts?

What is the turnaround time for granting and revoking access?

How often is recertification done and by whom?

How is the recertification process confirmed?

Listing of all users who have access including the type of access?

Are there existing reports that can be run?

Do reports need to be created?

Are there work instructions in place?

Create a checklist by system for inspections

Know which reports need to be run periodically to check and confirm access rights

Create an access report to produce for an audit or inspection that shows date of request, date of activation, type of access, modifications to access, date of deactivations due to changes or terminations

Create necessary work instructions

## Outputs

# Authorized Access - Paper

## Inputs

Who has access to the paper records?

How is paper retrieved?

Is the retrieval timely?

When is the last time paper record retrieval was tested?

Is there an electronic inventory of the paper records?

Is the paper the original source or back up to the electronic records?

Create a checklist by file room/paper storage area for inspections

Know which reports need to be run periodically to check and confirm access rights.

Run tests of data integrity of the paper records to confirm timeliness for retrieval, accessibility and durability of the paper records

Create necessary work instructions.

## Outputs



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Are you ready now?...

# Audit Trails

## Inputs

Have you looked at the audit trail?

Are there errors found?

Is data truncated or not visible?

Is the audit trail in a human readable format to read and also print if needed?

What kind of sampling will be done?

Which fields must be displayed in the audit trail?

Has a test run of an audit trail pull been conducted?

Which fields will be reviewed during a periodic check?

Are there work instructions in place?

Conduct a periodic check of data throughout the life of the data

Document (in a plan or process) how such a check will be conducted and when

Validate the process for the pull of an audit trail

Create an escalation plan if there are issues with data or if data is not being entered when and as it should

Create a checklist by system and include this in inspection readiness prep and in periodic reviews

Create necessary work instructions

## Outputs

# Transfers/Migrations

## Inputs

What is the rationale for data migration or conversion?

Is the migration / conversion process validated?

What kind of quality check will be done before / during / after transfer or migration?

Have the audit trails from the source and target systems been included in the migration / conversion?

Are there work instructions in place?

Create a migration / conversion plan

Create a (QC) checklist to confirm the data integrity of the migration / conversion along each lifecycle as needed

Create work instructions

## Outputs





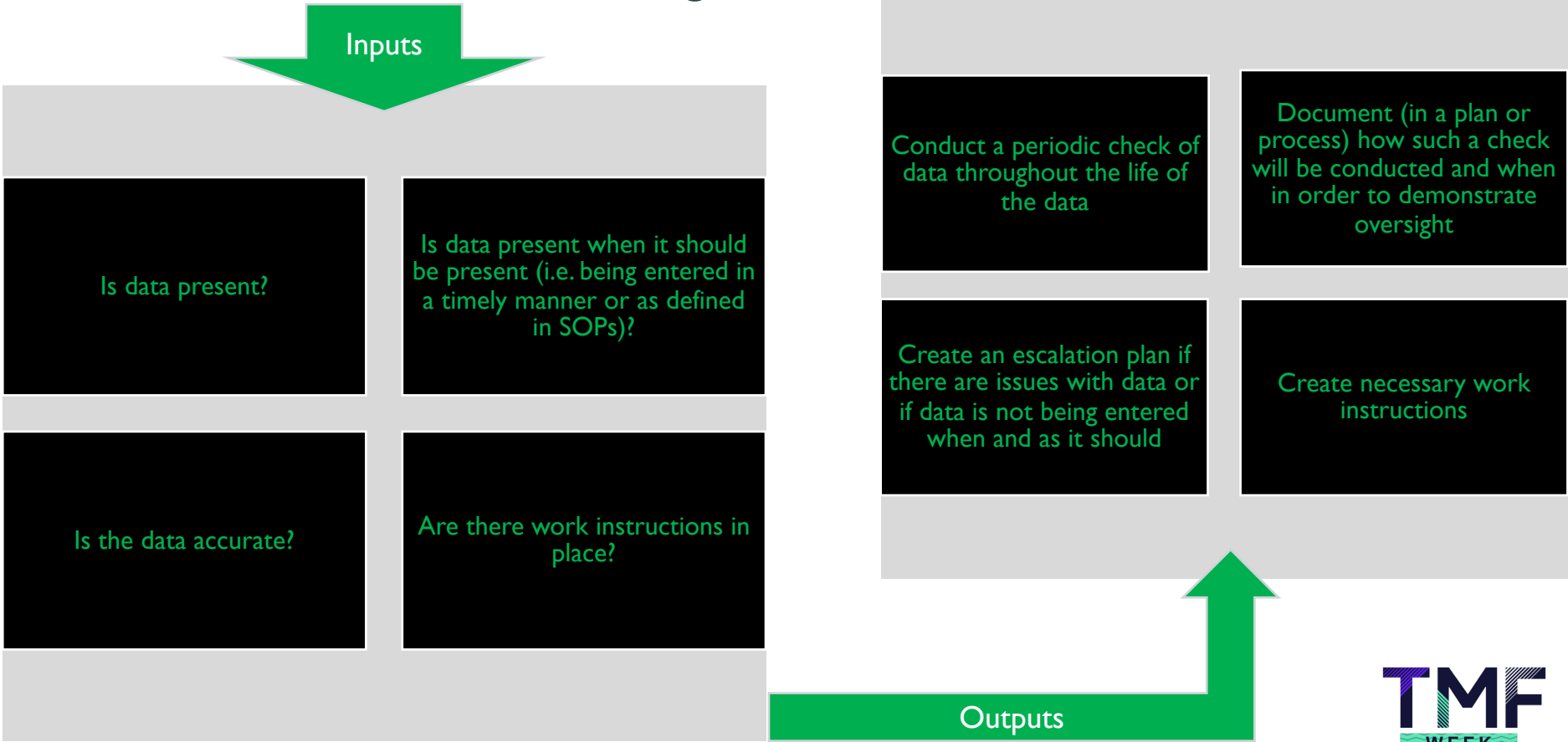
Are you getting the hint?...



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Create those work instructions...  
if it's not documented it didn't  
happen...  
even in The Matrix...

# Escalation Process & Oversight



# Training

Inputs

Do users who are entering data into systems or viewing data, have the proper training?

Is the training documented and filed in the appropriate training system?

Are there work instructions in place?

Create a checklist for onboarding new users / employees that includes training on relevant systems

Create a training report for inspection readiness

Create necessary work instructions

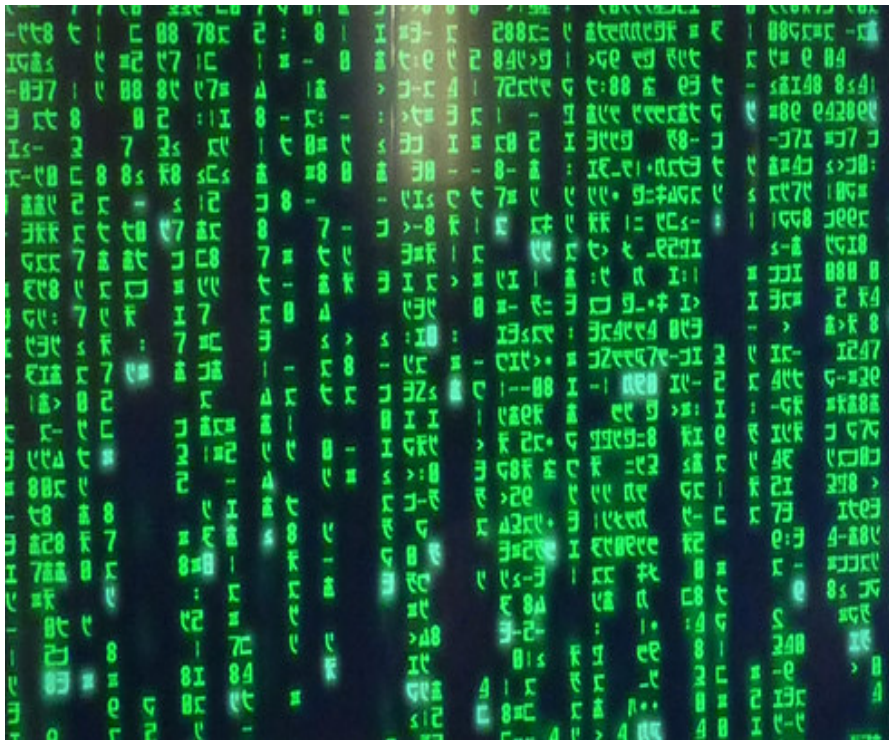
Outputs

The background is a gradient of green and yellow, overlaid with a complex pattern of glowing circuit lines and nodes. A solid black rectangle is positioned on the right side of the image, containing the text "IN CONCLUSION" in white, uppercase letters.

IN CONCLUSION



# Summary



To make it through The Matrix you need to...

Understand the regulations

Ensure ALCOA+ standards are being followed

Get to the WHY of your data

Put in place regular checks to ensure data integrity  
and...

**DOCUMENT IT ALL**

in well defined work instructions



# Thank you!



Thank you for joining me in The Matrix of Data Integrity...

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