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

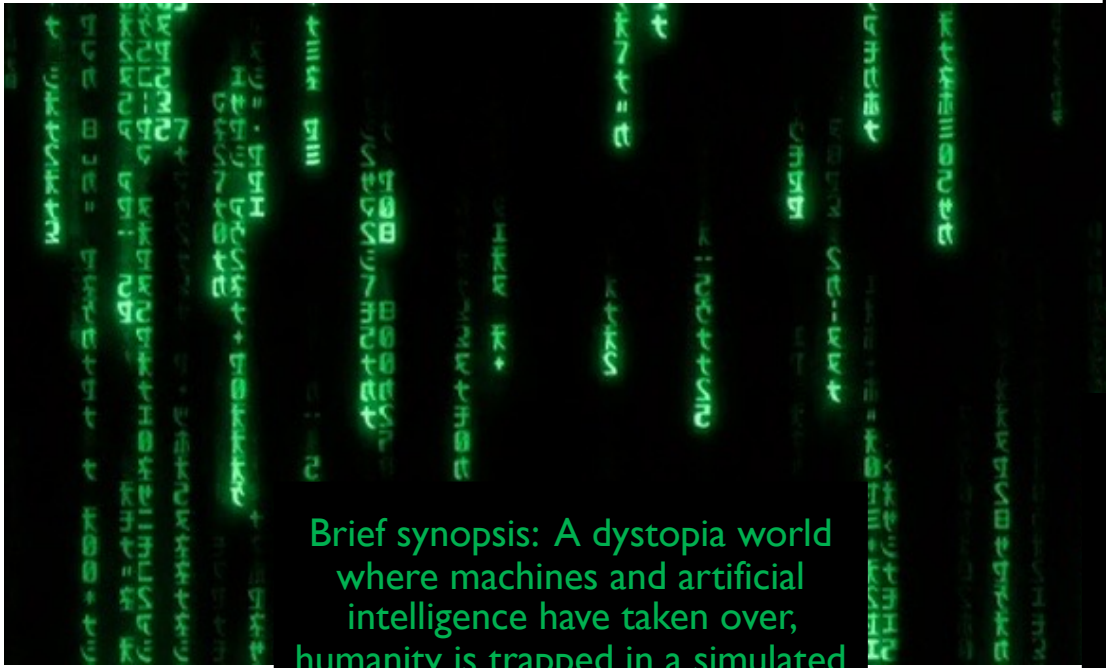
POLL One: What is data integrity?

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



The Matrix - 1999

The Matrix Reloaded – 2003

The Matrix Revolutions – 2003

The Matrix Resurrections - 2021

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

Thomas Anderson "Neo" a computer hacker

Morpheus leader of resistance

Trinity another hacker

Smith a super software program

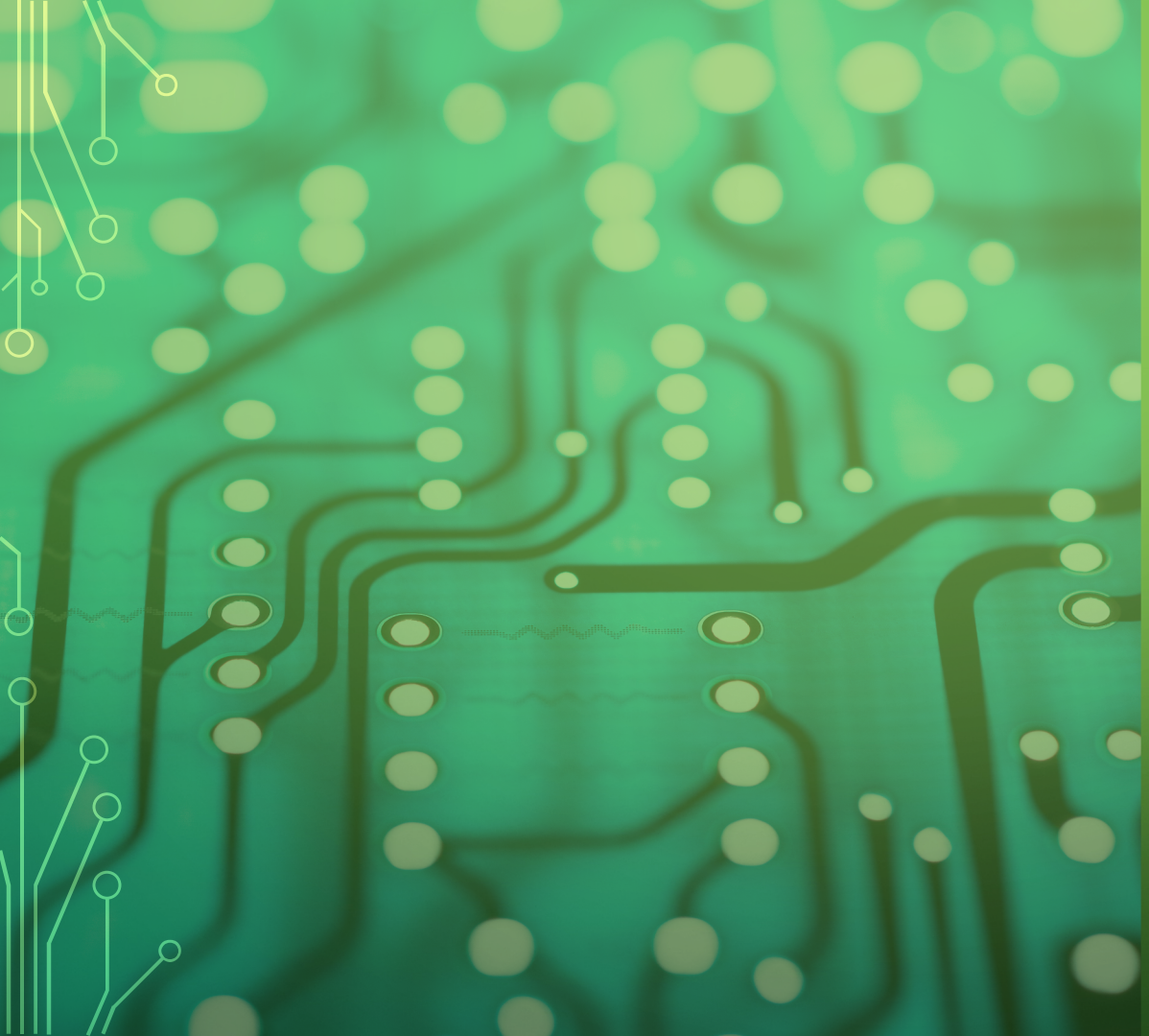
The Agents more software programs

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***[1] 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,[2] while data validation is a prerequisite for data integrity.[3] Data integrity is the opposite of data corruption.[4] 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

EUROPEAN MEDICINES AGENCY
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MHRA
Regulating Medicines and Medical Devices

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

FDA

Pmda 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
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 Trails) 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 **complete, consistent, accurate, trustworthy, reliable** 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 **control over intentional and unintentional changes to information**." 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/uksi/2006/1928/pdfs/uksi_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

EUROPEAN MEDICINES AGENCY
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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 **Chapter 4 - The Trial Master File and Archiving - Articles 16-20** 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 **Article 57 - Clinical trial master file** **Article 58 - Archiving of the clinical trial master file**
9 - EMA Guideline 2018	**Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic).** **Discusses email and eTMF content.**
10 - EMA Reflection Paper on Source Data 2010	**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.**
11 - ICH Guideline on Good Clinical Practice E6 (R2) 2016 INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE E6(R2)	**6.10 - Direct Access to Source Data/Documents** **6.13- Data Handling and Records Keeping** **8 - Essential documents**

Sources:
7 – 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
9 - 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
11 - https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4_2016_1109.pdf

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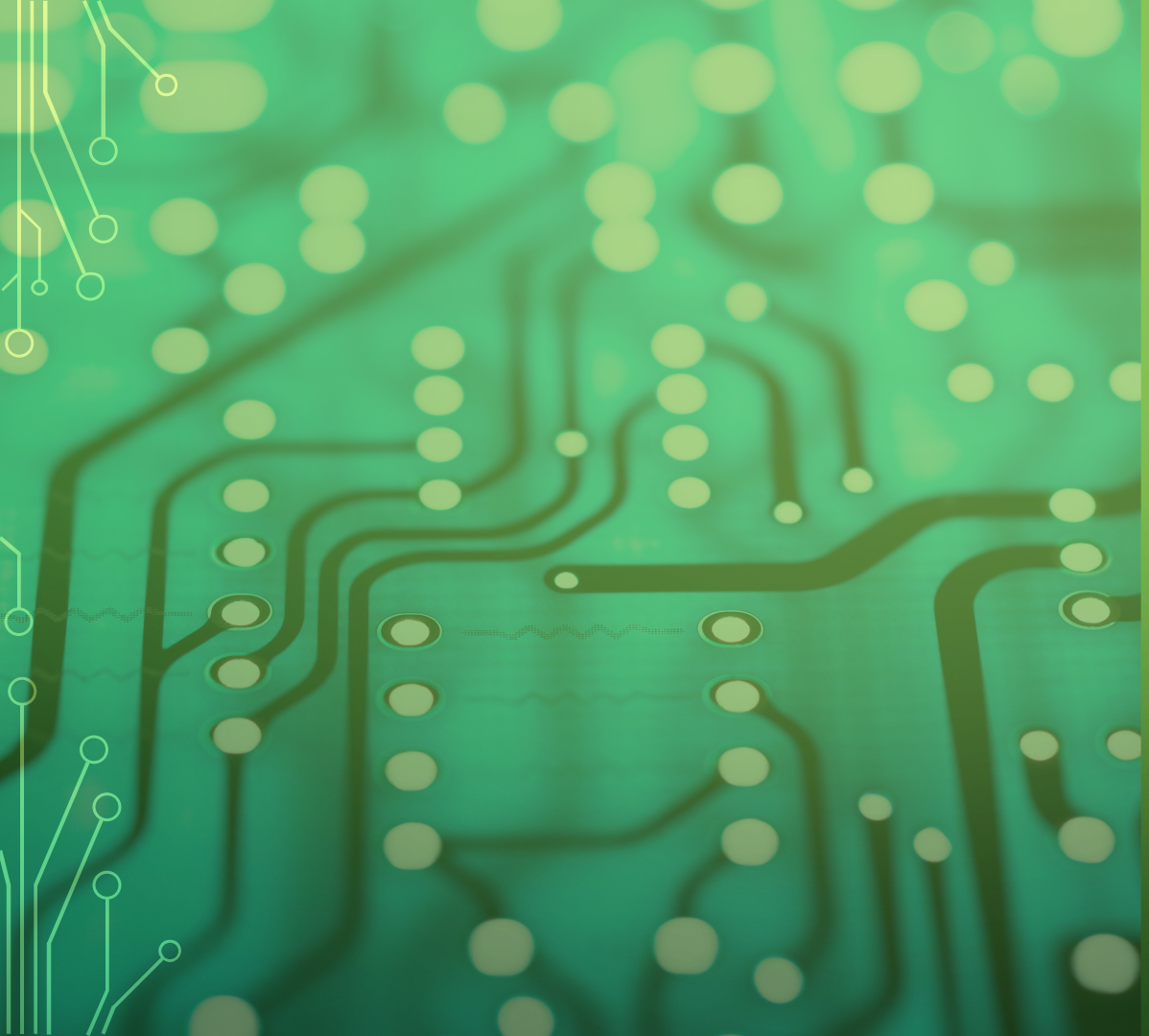
Pharmaceuticals and Medical Devices Agency

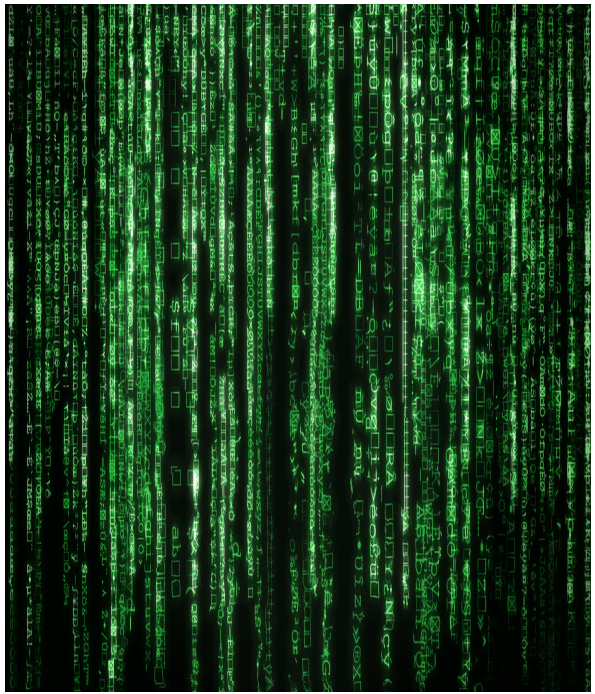
Name of Regulation	Relevancy to GCP
Reliability Standards	**Accuracy**: The data should be prepared accurately based on the results of trials. **Completeness**: All CSRs should be able to traced to raw data. All data obtained in trials should be described in the NDA/sNDA documents, including data which is less favorable, to the dossier. **Retention**: All data which contributed to the NDA/sNDA documents and other related data should be archived.
PMDA Checklist	**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)] References “records” throughout and necessity to **store** records, **maintain**, **retain**, and **archive**.

Sources:
12 – http://www.pmda.go.jp/english/index.html
13 - https://www.pmda.go.jp/files/000152996.pdf

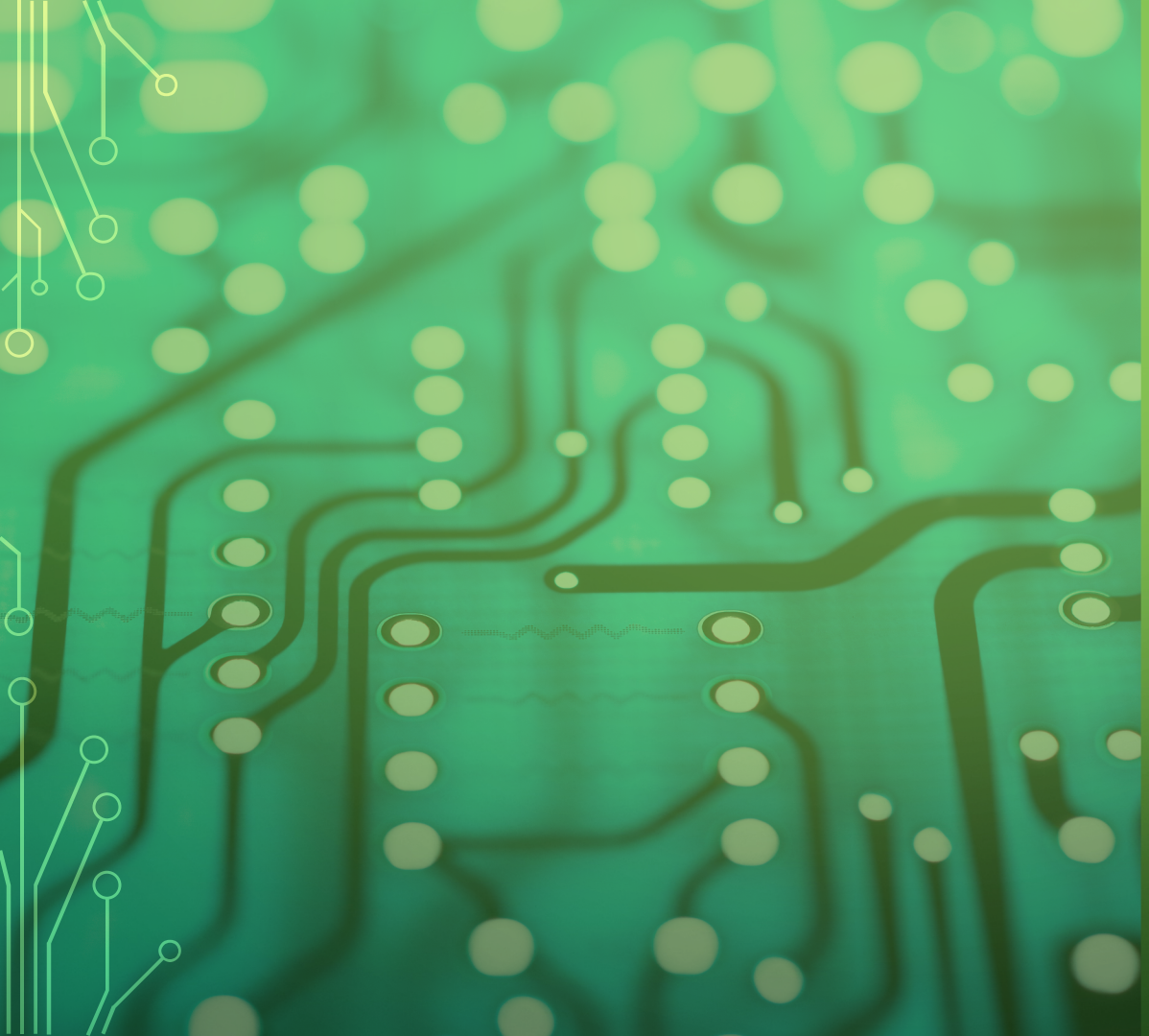


ALCOA+ PRINCIPLES

ALCOA+

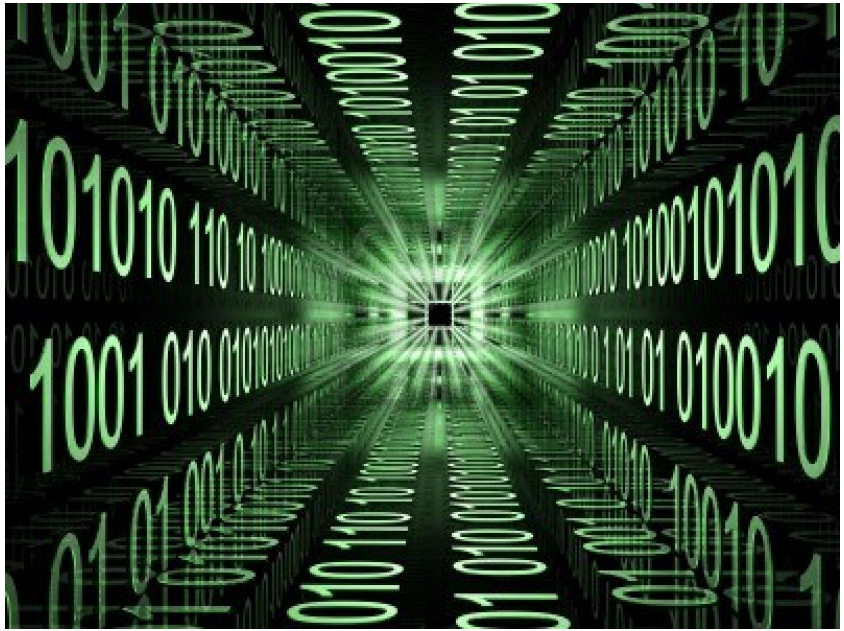


A	Attributable
L	Legible
C	Contemporaneous
O	Original
A	Accurate
+	Available, Complete, Consistent, Enduring, Corroborated



PLANNING FOR THE WHY

The Why?



"Causality is action, reaction, cause and effect… [it's] important to understanding <u>the why</u>".

- 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?

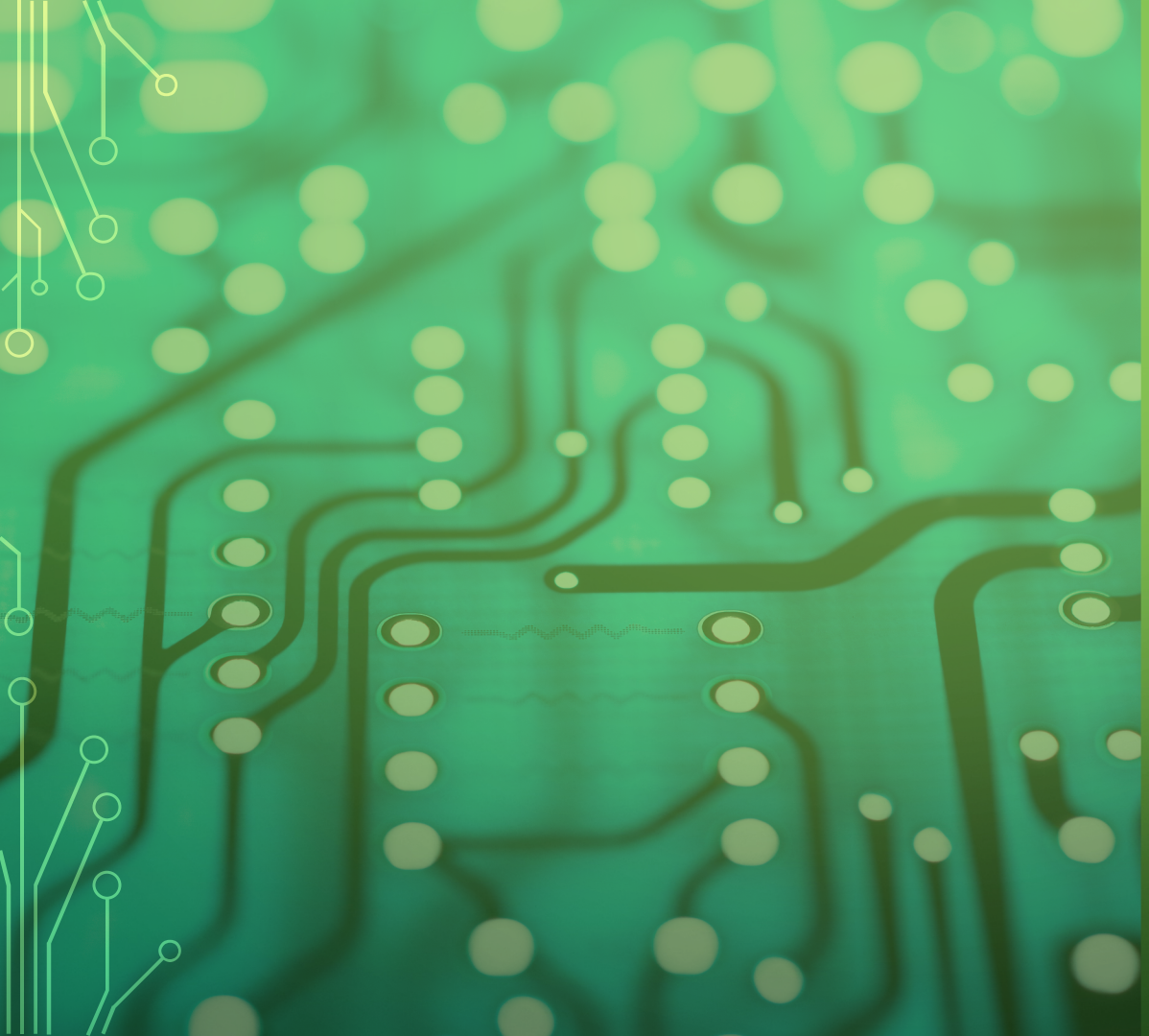
A. Yes.

B. No.

C. What is that?

D. One is coming soon.

E. I do not know.



DATA INTEGRITY AUDIT LESSONS LEARNED

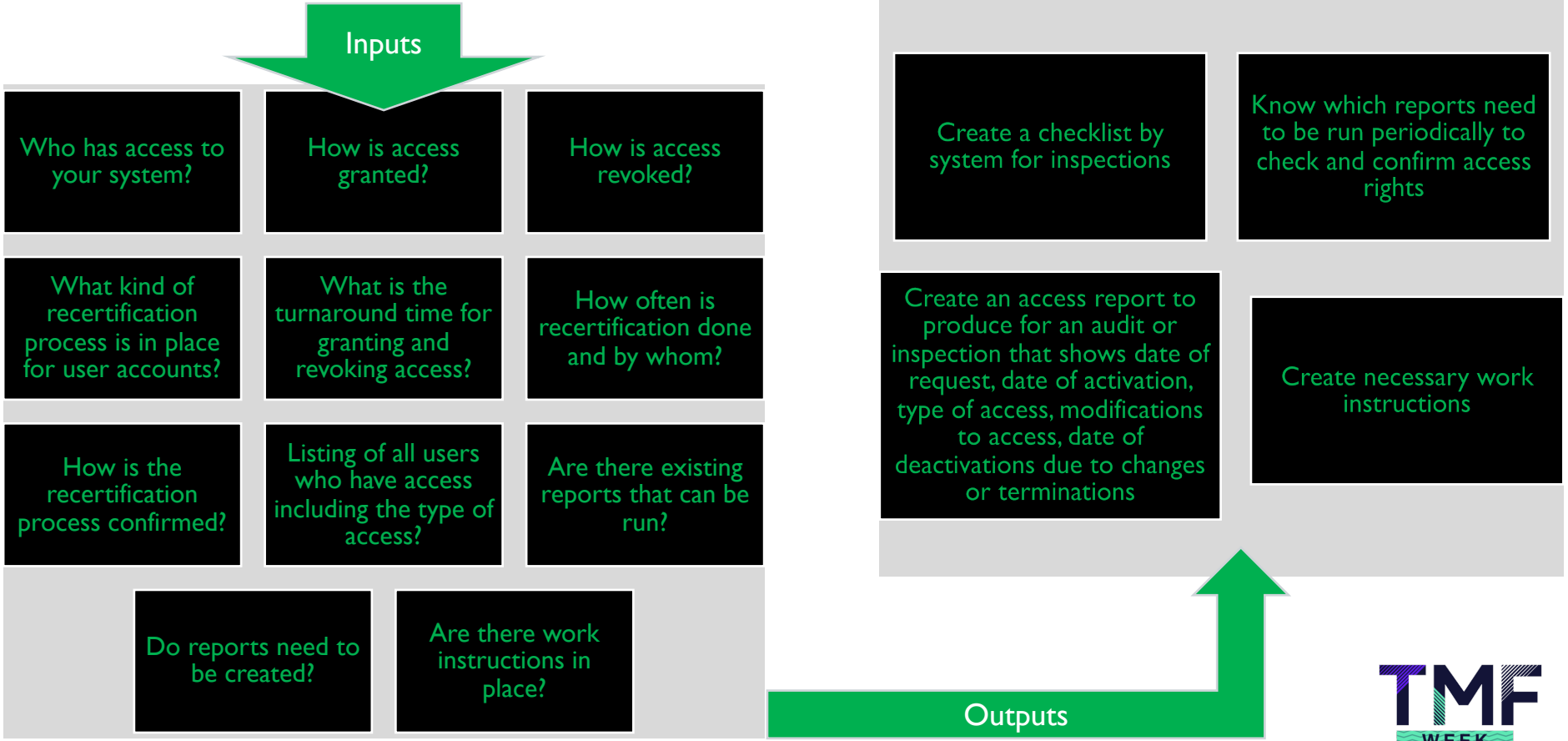
Inspections are coming…are you ready?...

The Matrix has you…

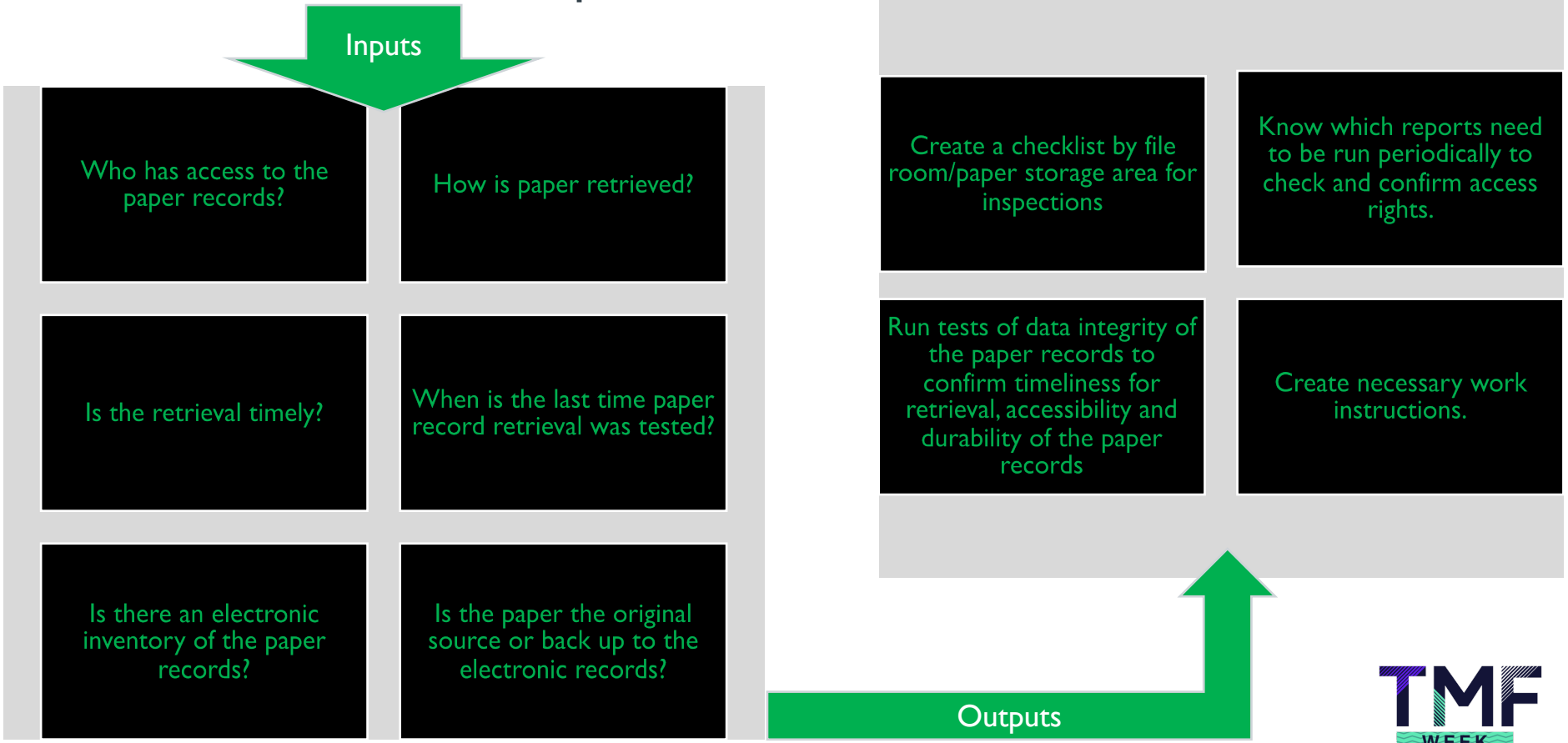
Do not panic…

Prepare yourself…

Authorized Access - Electronic

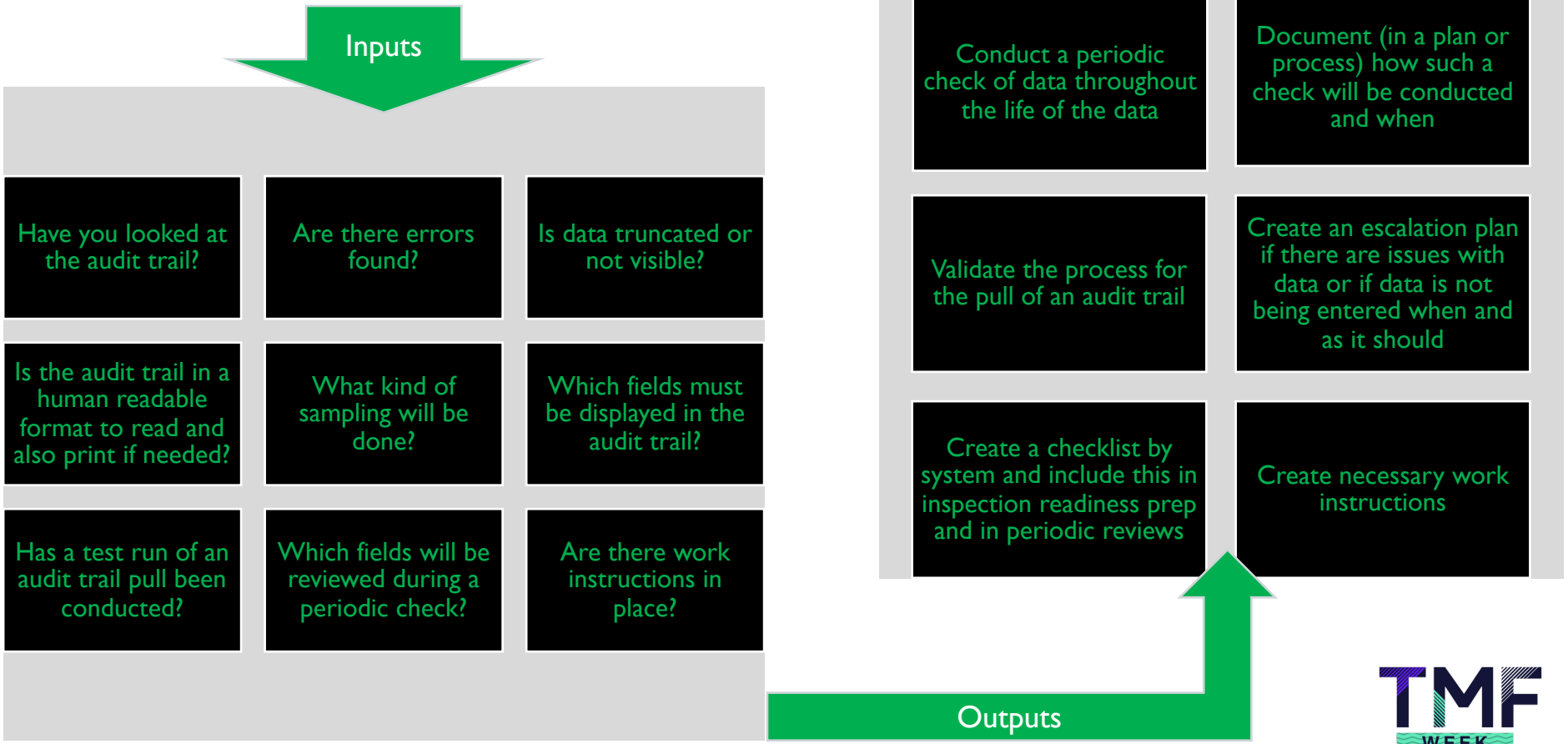


Authorized Access - Paper

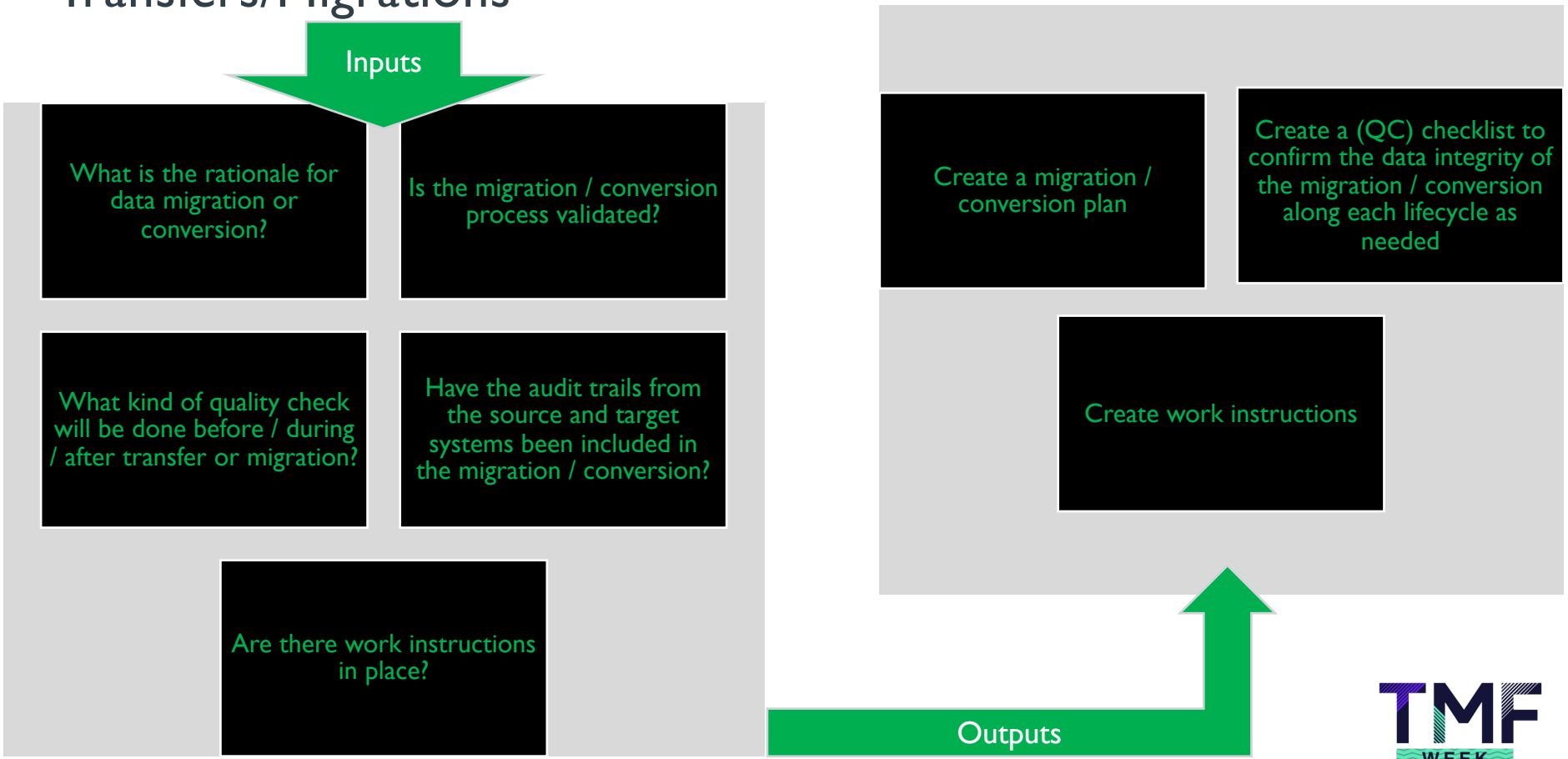


Are you ready now?…

Audit Trails



Transfers/Migrations



Are you getting the hint?…

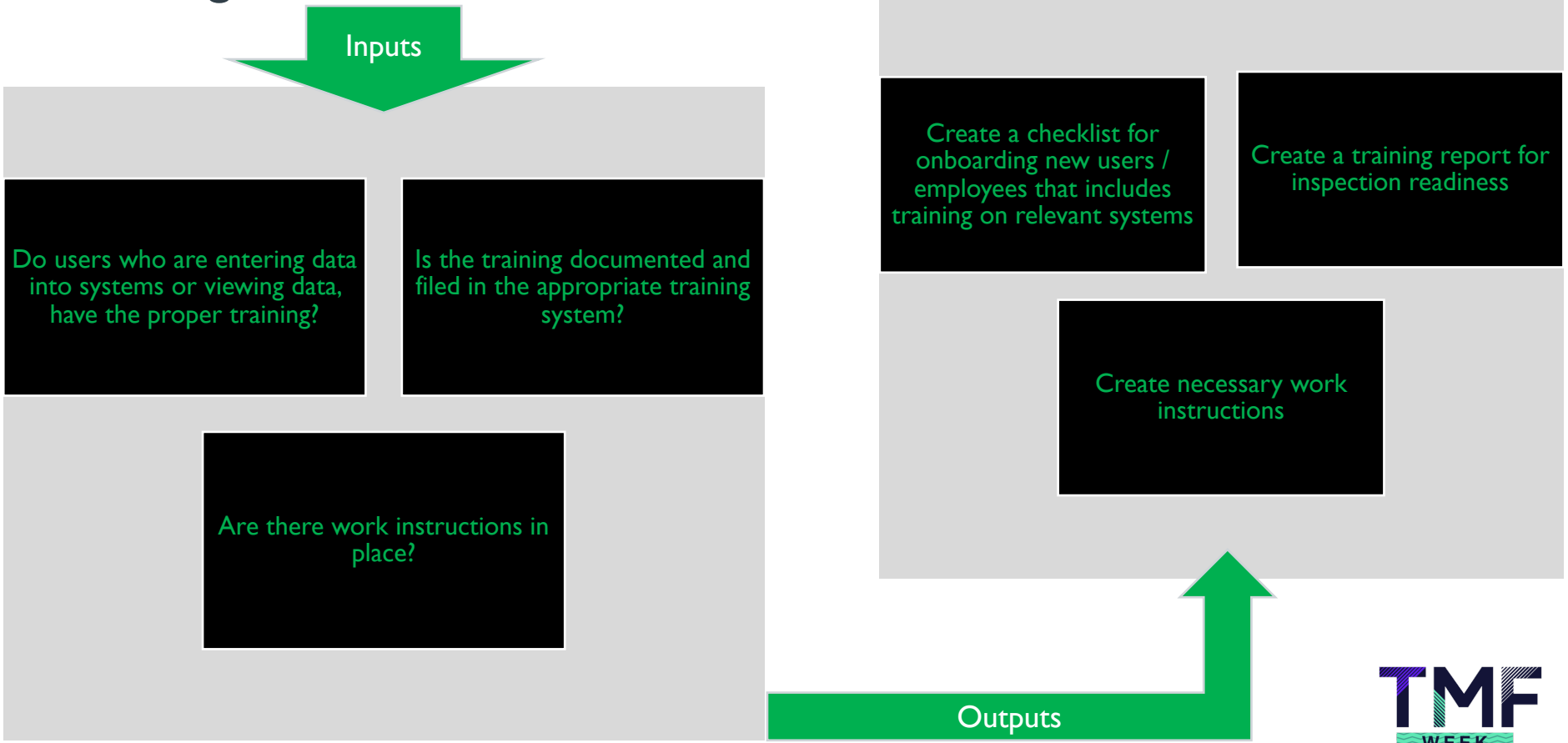
Create those work instructions…

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

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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