DATA INTEGRITY :
une perspective industrielle

Introduction

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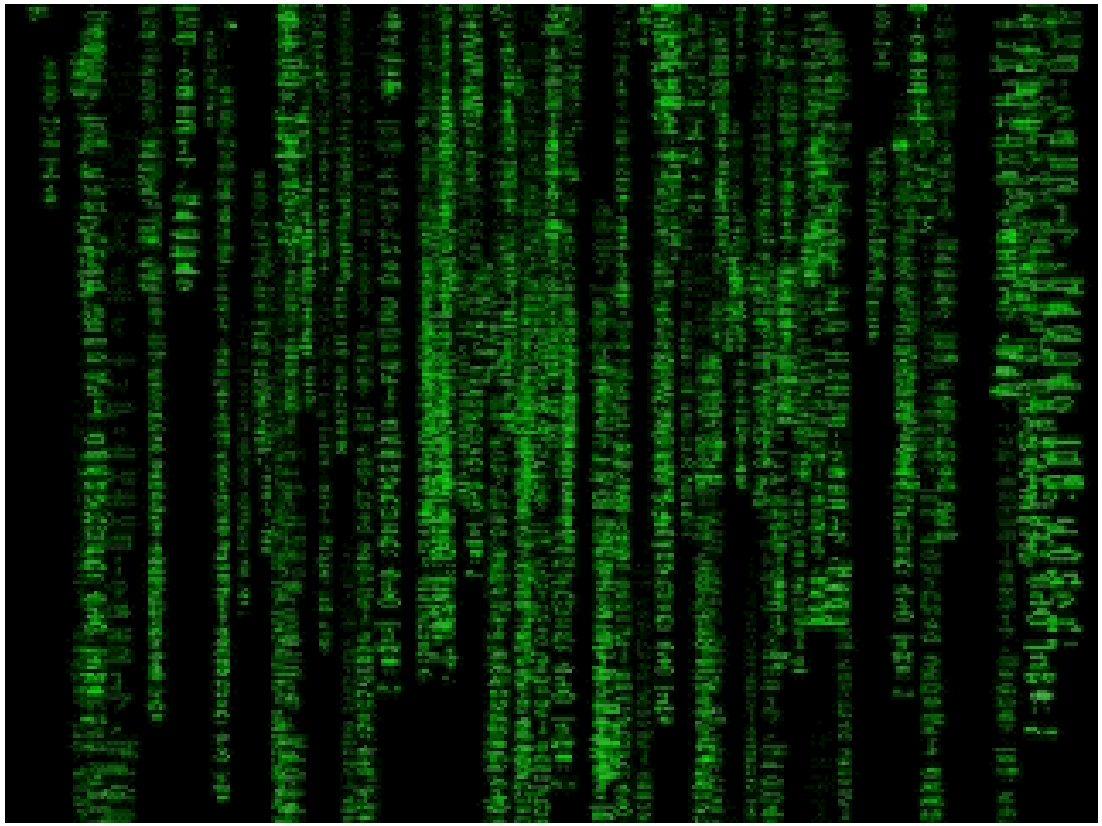
Integritas, -atis

- Etat de quelque chose qui a conservé sans altération ses qualités, son état originel

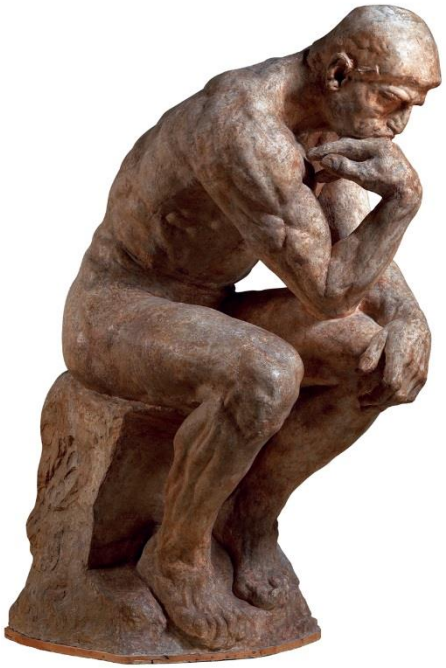
Data



Objectifs


Simple


CRITIQUE



Quelle est votre principale préoccupation ?

L’inspection

Contexte

2015/2016 – Data Integrity guidances

Augmentation des violations cGMP touchant à la **Data integrity**

- warning letters
- blocage des importations
- renforcement des contrôles
- sensibilisation

Contexte

Guidances sur le Data Integrity

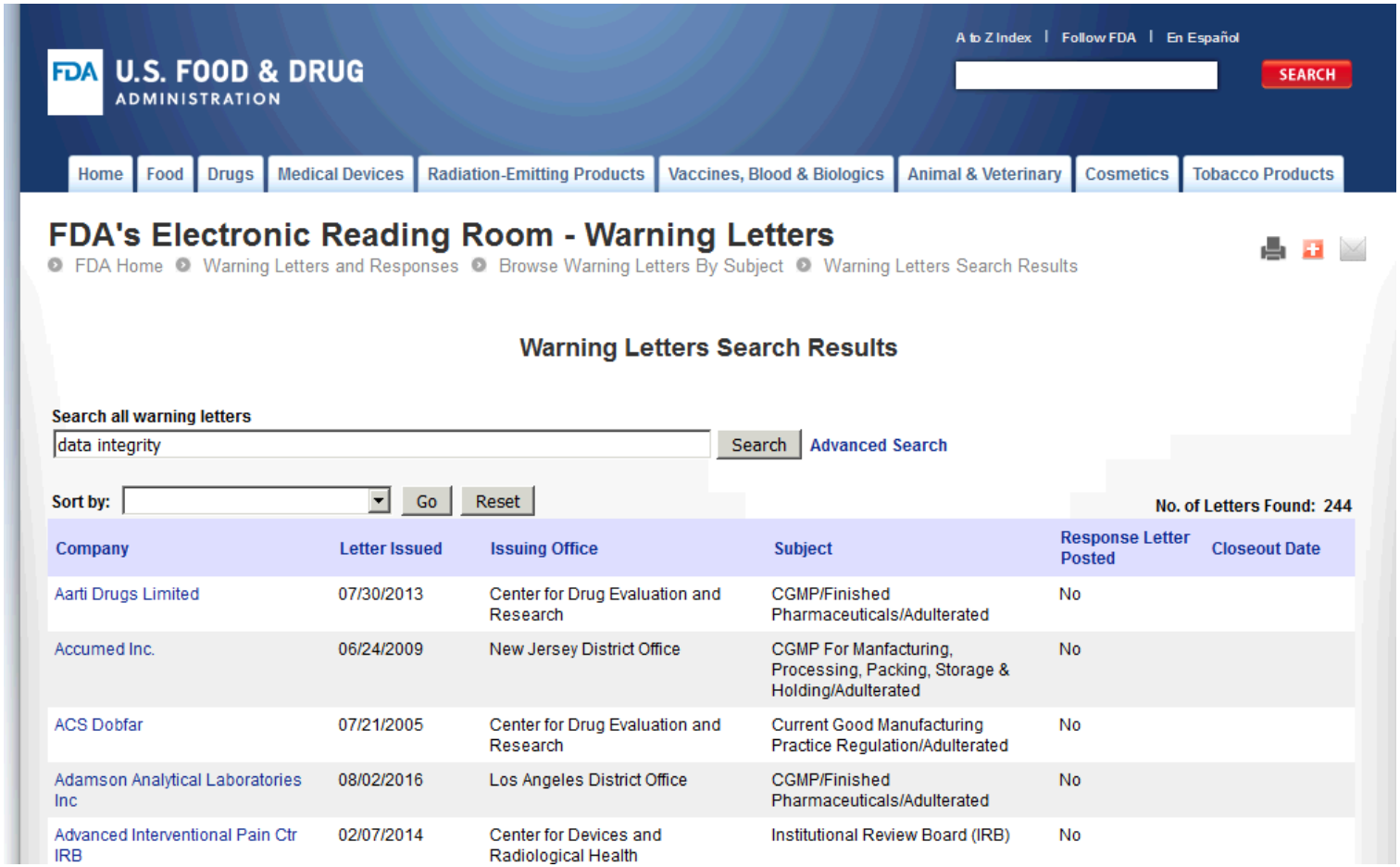
clarifier leurs exigences vis-à-vis des Industriels qui

« ***doivent mettre en œuvre des stratégies efficaces et significatives pour contrôler les risques autour de la Data integrity*** ».

~~une nouvelle réglementation~~

mais la façon de penser actuelle des Agences

Un réel enjeu en inspection



FDA U.S. FOOD & DRUG ADMINISTRATION

A to Z Index | Follow FDA | En Español

SEARCH

Home | Food | Drugs | Medical Devices | Radiation-Emitting Products | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Tobacco Products

FDA's Electronic Reading Room - Warning Letters

FDA Home › Warning Letters and Responses › Browse Warning Letters By Subject › Warning Letters Search Results

Warning Letters Search Results

Search all warning letters

data integrity | Search | Advanced Search

Sort by: | Go | Reset

No. of Letters Found: 244

Company	Letter Issued	Issuing Office	Subject	Response Letter Posted	Closeout Date
Aarti Drugs Limited	07/30/2013	Center for Drug Evaluation and Research	CGMP/Finished Pharmaceuticals/Adulterated	No	
Accumed Inc.	06/24/2009	New Jersey District Office	CGMP For Manfacturing, Processing, Packing, Storage & Holding/Adulterated	No	
ACS Dobfar	07/21/2005	Center for Drug Evaluation and Research	Current Good Manufacturing Practice Regulation/Adulterated	No	
Adamson Analytical Laboratories Inc	08/02/2016	Los Angeles District Office	CGMP/Finished Pharmaceuticals/Adulterated	No	
Advanced Interventional Pain Ctr IRB	02/07/2014	Center for Devices and Radiological Health	Institutional Review Board (IRB)	No	

Tendances en Inspection FDA

FDA a adressé **69**
GMP *Warning Letters* en 2017

12 / 20 USA

33 / 49 hors USA

Sont liées à une déficience de Data Integrity

65 %

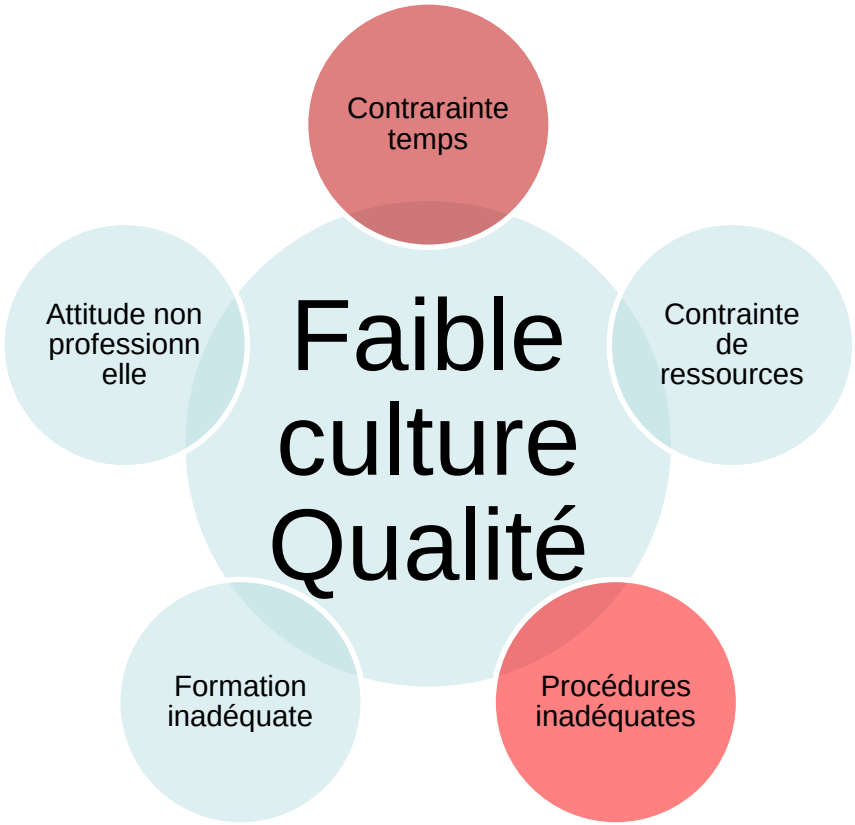
Warning letters -Exemples

Date	Companie	Pays	Domaine	Raison
11.08.17	Bicooya Cosmetics Limited	USA	Drug product	**système qualité** n'assure pas l'intégrité des données de la qualité des médicaments
16.05.16	BBT Biotech Gmbh	Germany	Drug product	**Audit trail** : pas suffisamment de **contrôles sur l'accès** ou les modifications des données
12.05.16	Tai Heng Industry Co., Ltd	China	API	**Pas suffisamment de contrôle** empêchant la manipulation et l'omission des données
03.03.16	Emcure Pharmaceuticals Limited	India	Drug product	Données d'enregistrements de laboratoire **incomplète**, **inexacte** ou **falsifiée**
02.03.16	Innovative Sterilization Technologies, LLC	USA	Medical Device	**Validation non documentée**
17.12.15	Sun Pharmaceuticals Industries Ltd	India	Drug	Manque **d'audit trail** et pas suffisamment de control sur le system
30.09.15	Merge Healthcare, Inc	USA	Software device	Manque de **validation**
28.09.15	Unimark Remedies Ltd	India	API	Manque de **contrôle d'accès** (identifiant et mot de passe unique) et données incomplètes
21.09.15	Genesis Biosystems, Inc.	USA	Medical Device	Manque de **validation**

[1] http://www.ofnisystems.com/fda-warning-letters/

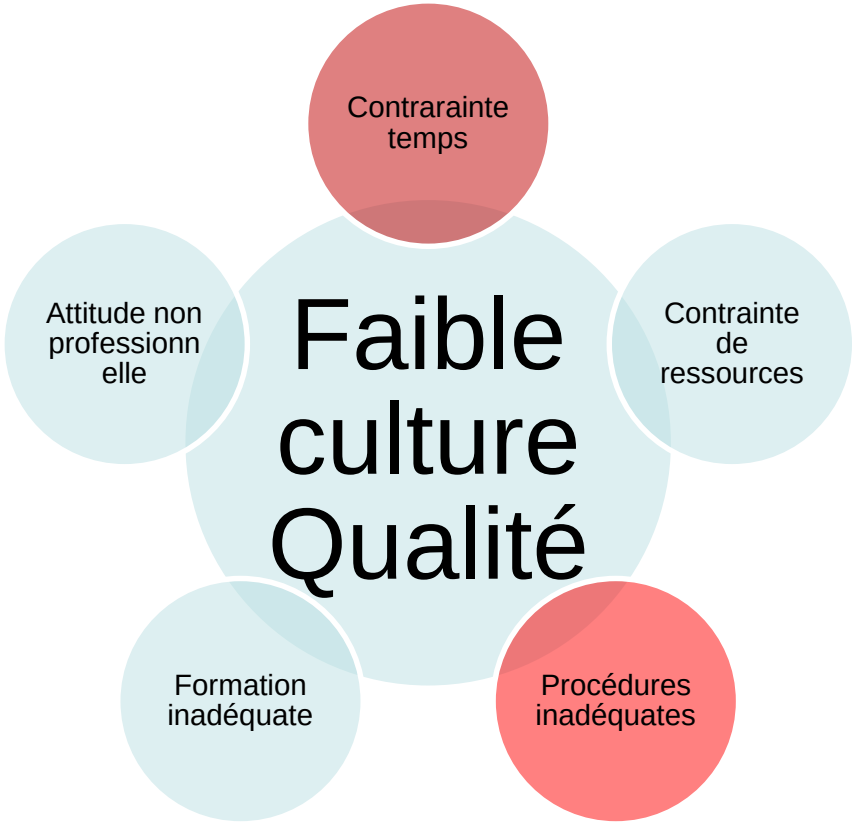
Culture Qualité

Les écarts sur le Data integrity ont été identifiées et reliées par les auditeurs comme un résultat direct de la faible culture qualité dans les organisations



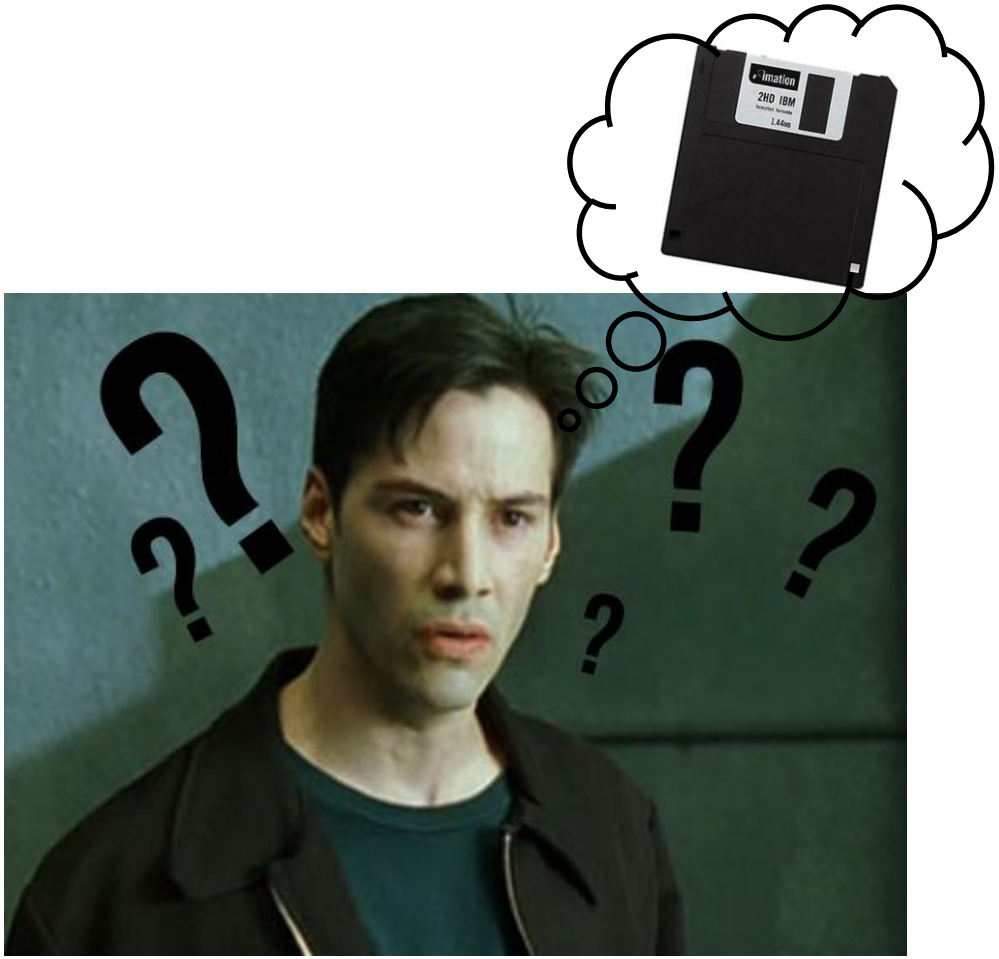
Culture Qualité

La culture qualité doit être promue à travers toute l'organisation



Quelle est ma principale préoccupation ?

La Décision Qualité



Manufacturing formula – Processing instruction – Batch processing record

Drago solution

0.025 mg per dosage

in 4.5 ml cartridges

Batch description: 9999205

Preparation size (ml): 80000

Batch production record no.: 0324-01

Batch production objective:

Order number:

Manufacturer:
Company name:
Manufacture of liquid forms:

Start of manufacture	Date of manufacture :	End of manufacture
Number of pages according to batch pro 19	Inserted pages	Facilities
Total number of pages:		

1. Staff responsible for compiling the batch production instructions/record

Date Signature (= Name =)

2. Head of production: Completion confirmed according to instructions

Date Signature (= Name =)

3. Responsible project manager

Date Signature (= Name =)

4. Manufacturing

Date Signature (= Name =)

5. Head of production

Date Signature (= Name =)

Comments:

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Data Integrity : Définition

MHRA

"The extent to which all data are **complete**, **consistent** and **accurate** throughout the data lifecycle"

MHRA* GMP Data Integrity Definitions and Guidance for Industry March 2015

World Health Organization

"The degree to which a collection of data is **complete**, **consistent** and **accurate** throughout the data lifecycle"

WHO Guidance on Good Data and Record Management Practices (draft version , 2015)

FDA

(IEEE*) The degree to which a collection of data is **complete**, **consistent**, and **accurate**

FDA Glossary of Computerized System and Software Development Terminology, 1995
* *Institute of Electrical and Electronics Engineers*

enregistrements papier

enregistrements électroniques

Concept FDA : ALCOA

Attributable

Legible

Contemporaneous

Original

Accurate

- 1990 : Invention du concept par Dr Stan Woolen aux Etats-Unis (inspecteur FDA)
- Introduction de notion ALCOA dans les « Good Laboratory Practice » par la FDA (réf. : 21 CFR 58.130 Part c et e)

Concept FDA : ALCOA

ATTRIBUABLE

Qui collecte, modifie ou manipule la donnée ?
Qui effectue une action et **quand** ?

Concept FDA :
ALCOA

La donnée est-elle **lisible**, **compréhensible**, **traçable** et permet-elle d'avoir une image claire du séquencement des étapes / évènements tout au long de son cycle de vie ?

LEGIBLE

Concept FDA :
ALCOA

CONTEMPORANEOUS

La donnée est-elle enregistrée à **l'instant ou est-elle générée / observée** ?

Concept FDA : ALCOA

L'information est-elle **l'enregistrement original** ou **une copie conforme** ?

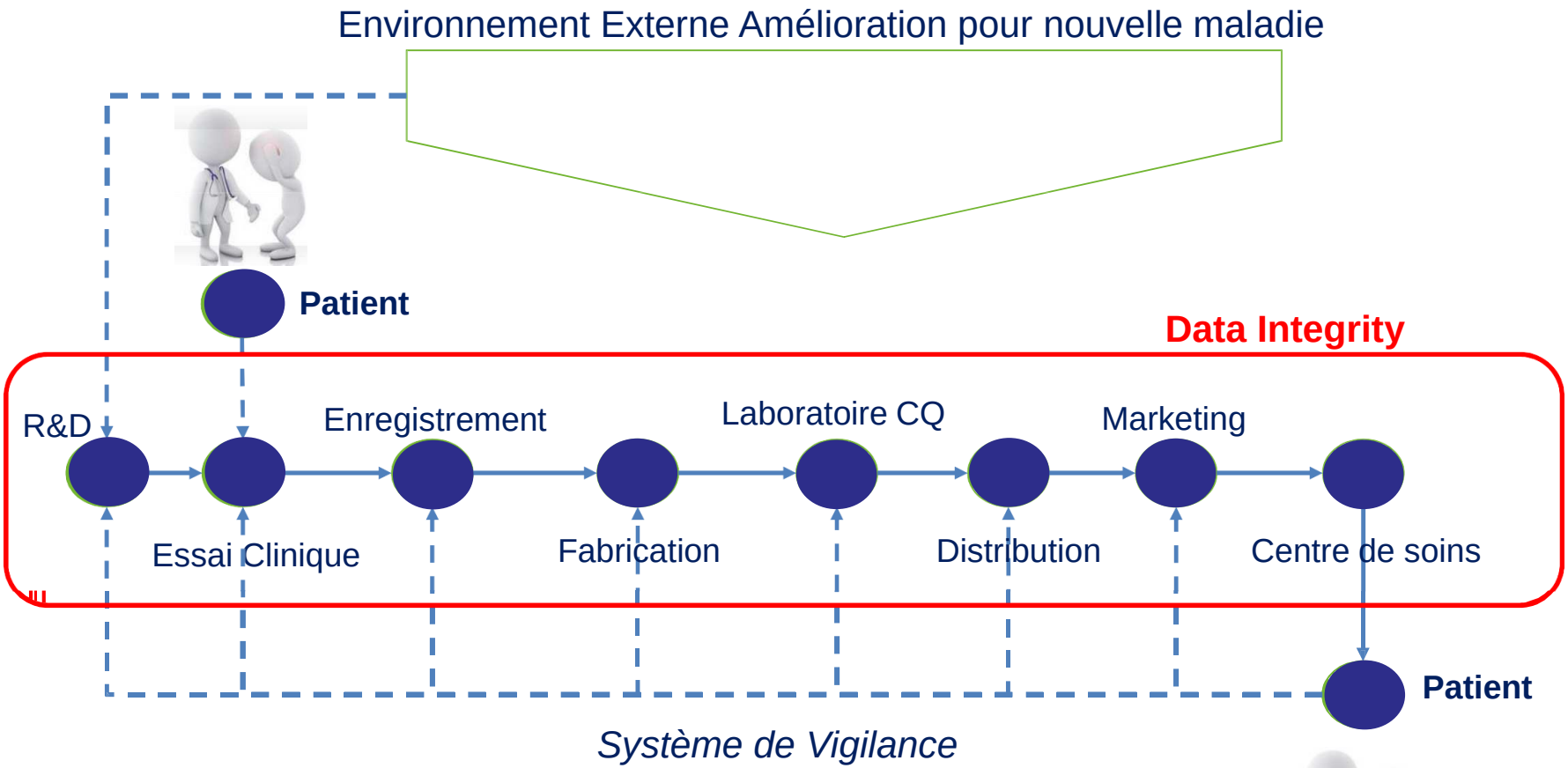
ORIGINAL

Concept FDA : ALCOA

ACCURATE

Les données sont-elles exemptes d'erreurs?
La donnée est-elle **correcte**, **vraie**, **valide**, **fiable** ?

Data Integrity et cycle de vie



Déploiement d'une démarche de data integrity

Déployer le data integrity

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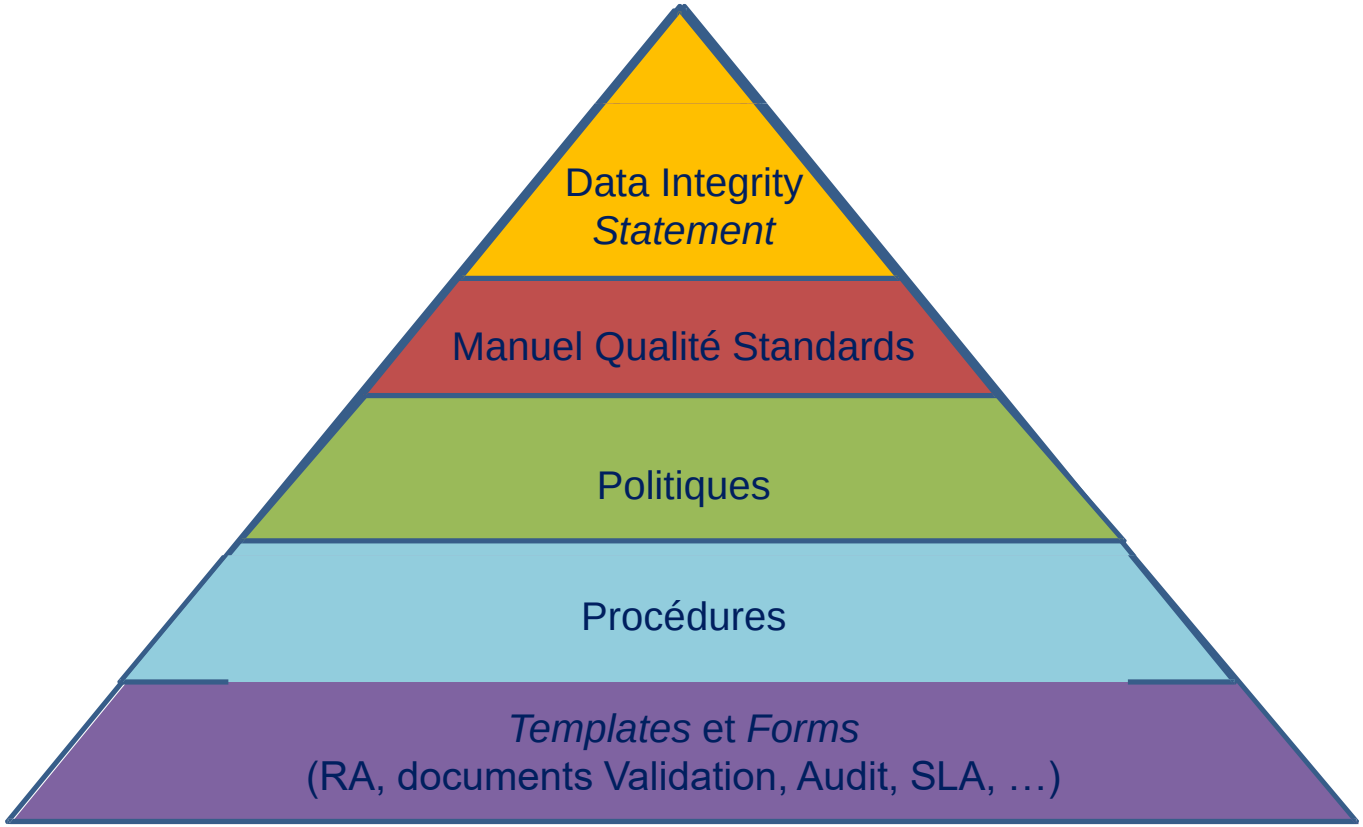
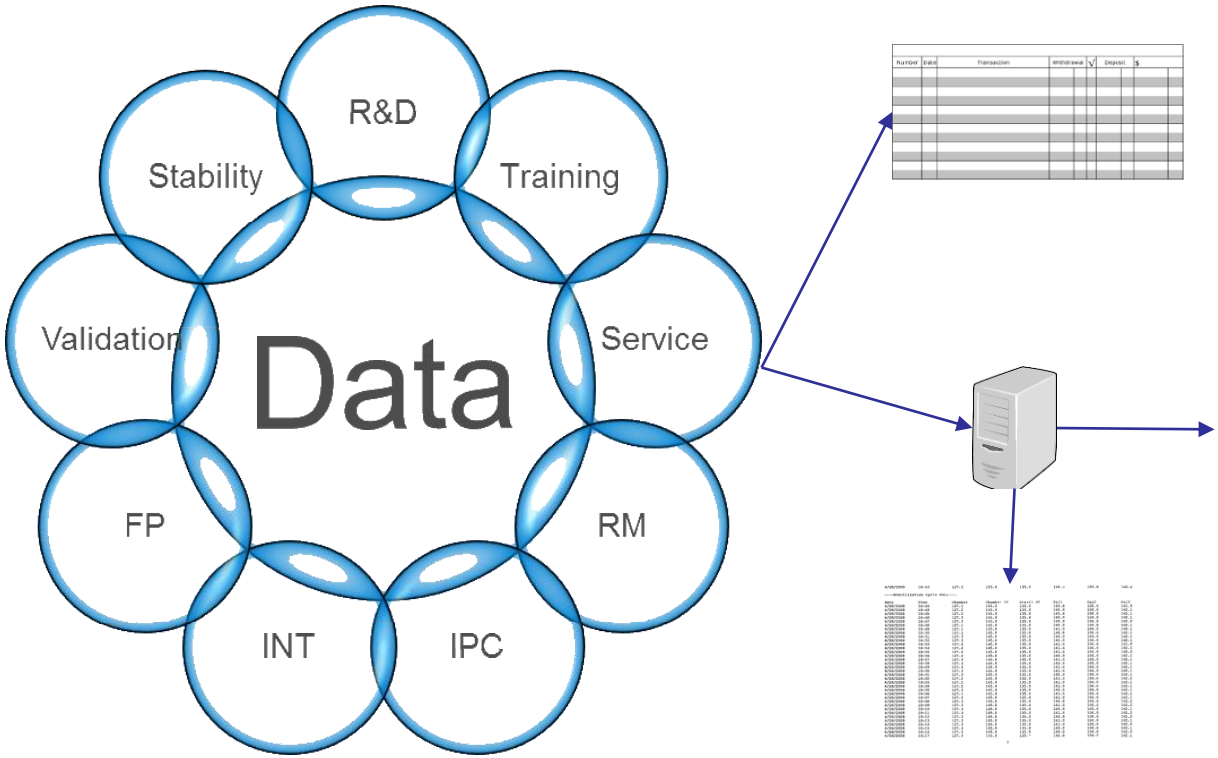
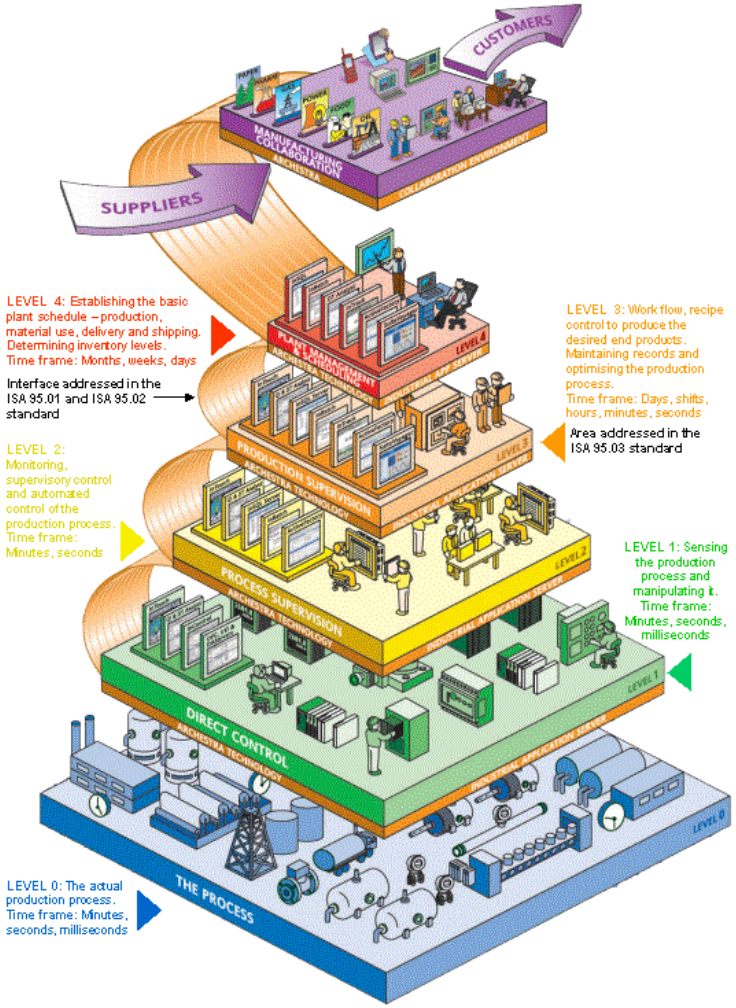

Data Integrity
Statement
Manuel Qualité Standards
Politiques
Procédures
Templates et *Forms*
(RA, documents Validation, Audit, SLA, …)

Identification des données

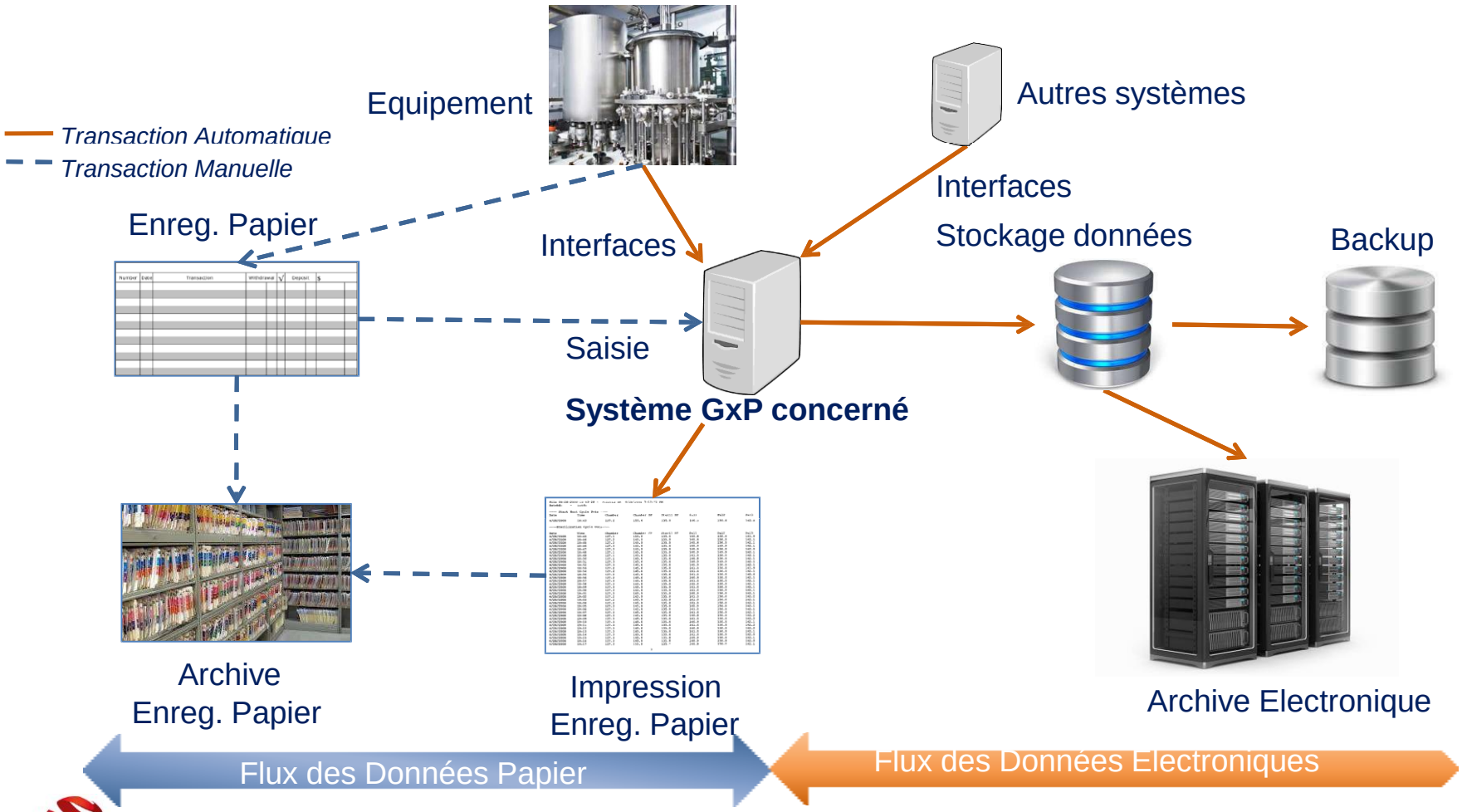
Quel type de données sont générées ?

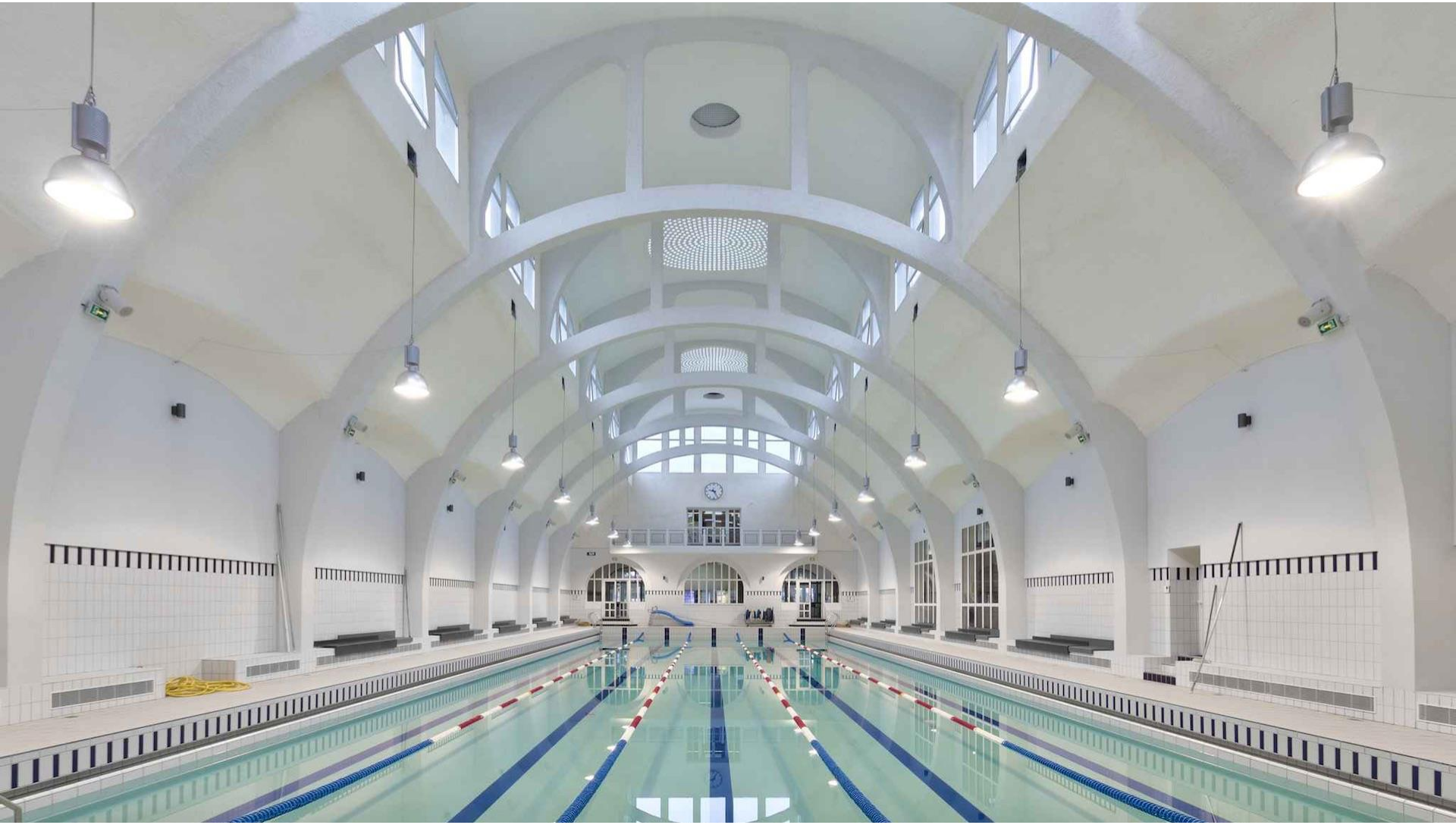


Comprendre son flux data



Identification des systèmes





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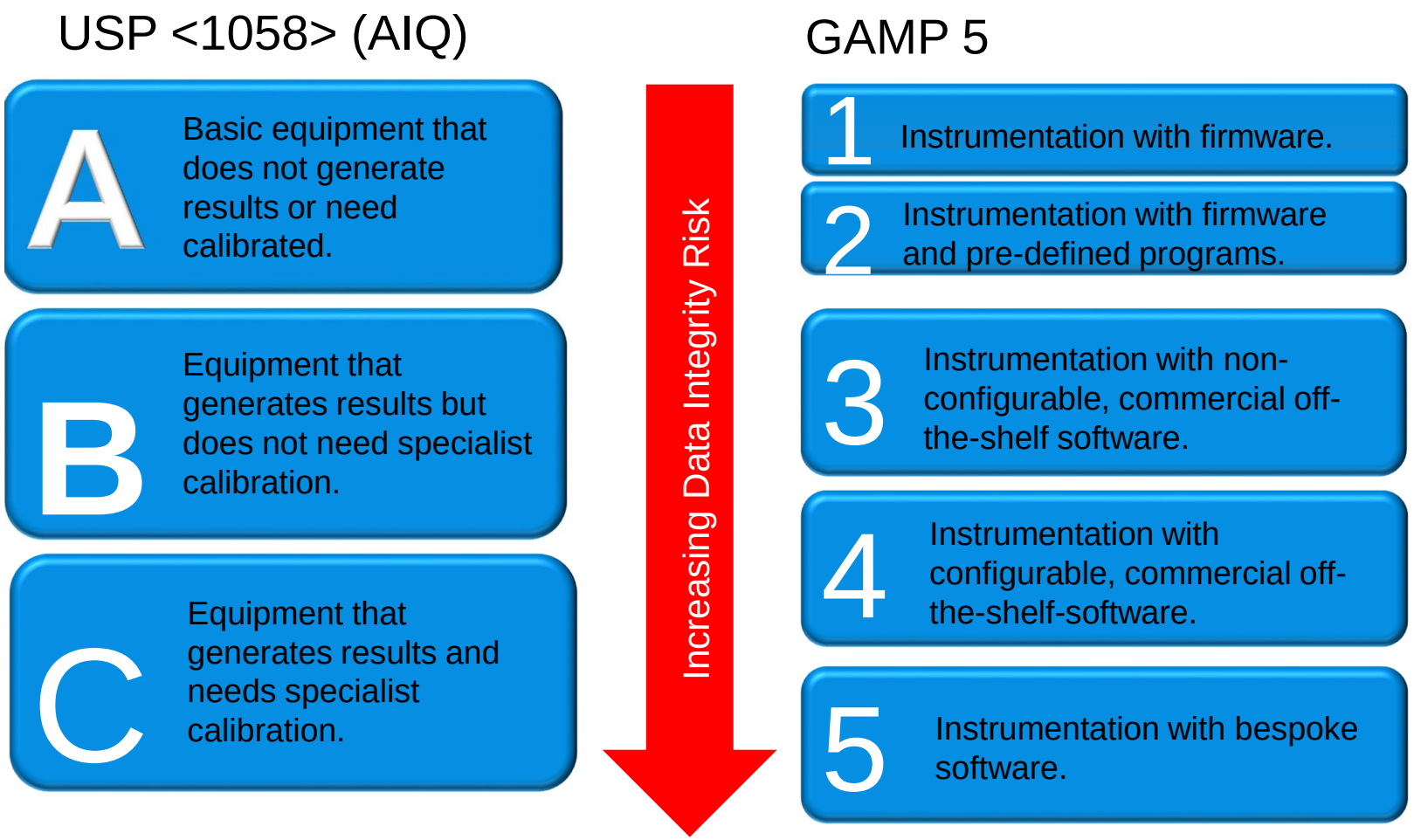
Analyse de risques



Analyse de risque

Instrument type	USP<1058> categorisation	GAMP5 categorisation	Data integrity risk
Balance	B	2	LOW
pH meter	B	2	LOW
FT-IR	C	3	MEDIUM
UV	C	3	MEDIUM
HPLC	C	4	HIGH
GC	C	4	HIGH

Plan d'action

- Validation Systèmes informatisés supportant le Data Integrity
- Qualification / Validation des équipements générant des données
- Mise en place de SOP's
  - IT policies.
  - System administration (CDS access, roles and privileges).
  - Data management and storage.
  - Data acquisition and processing.
  - Data review and approval.
  - Date archiving and back-up.
  - Monitoring anti-fraude
- Upgrade informatique

DATA INTEGRITY
Exemples d'écarts

6.2.2 short description, risk **Data integrity at risk - prone to adulteration of validated systems and laboratory work stations and risk of loss of data.**	**Statistical category:** Laboratory System

Observation:

6.2.2.1 Work station PCs with installed internet browsers (e.g. Firefox and MS Explorer) and internet connection were observed. Hence, data integrity is at risk as it is prone to unauthorized program installation and adulteration of validated systems and laboratory work stations or risk of loss of data. The SOP XXX does not define *raw data* and internet browsers are not listed as software applications.

6.2.2.2 For validated computerized laboratory systems the currently installed software versions are not documented (e.g. HPLC No. 13). This is prone to unauthorized program installation and adulteration of validated systems.

6.2.2.3 Development testing specifications lacking document and version control.

DATA INTEGRITY
Exemples d'écarts

6.2.2 Quality Control Laboratory	**Statistical category:** Laboratory System
Observation: A) No printer was available for the Brookfield Viscometer to record results. Values are read off the LCD display by eye and recorded in the documentation. No secondary check was performed to verify the observation.	

DATA INTEGRITY
Exemples d'écarts

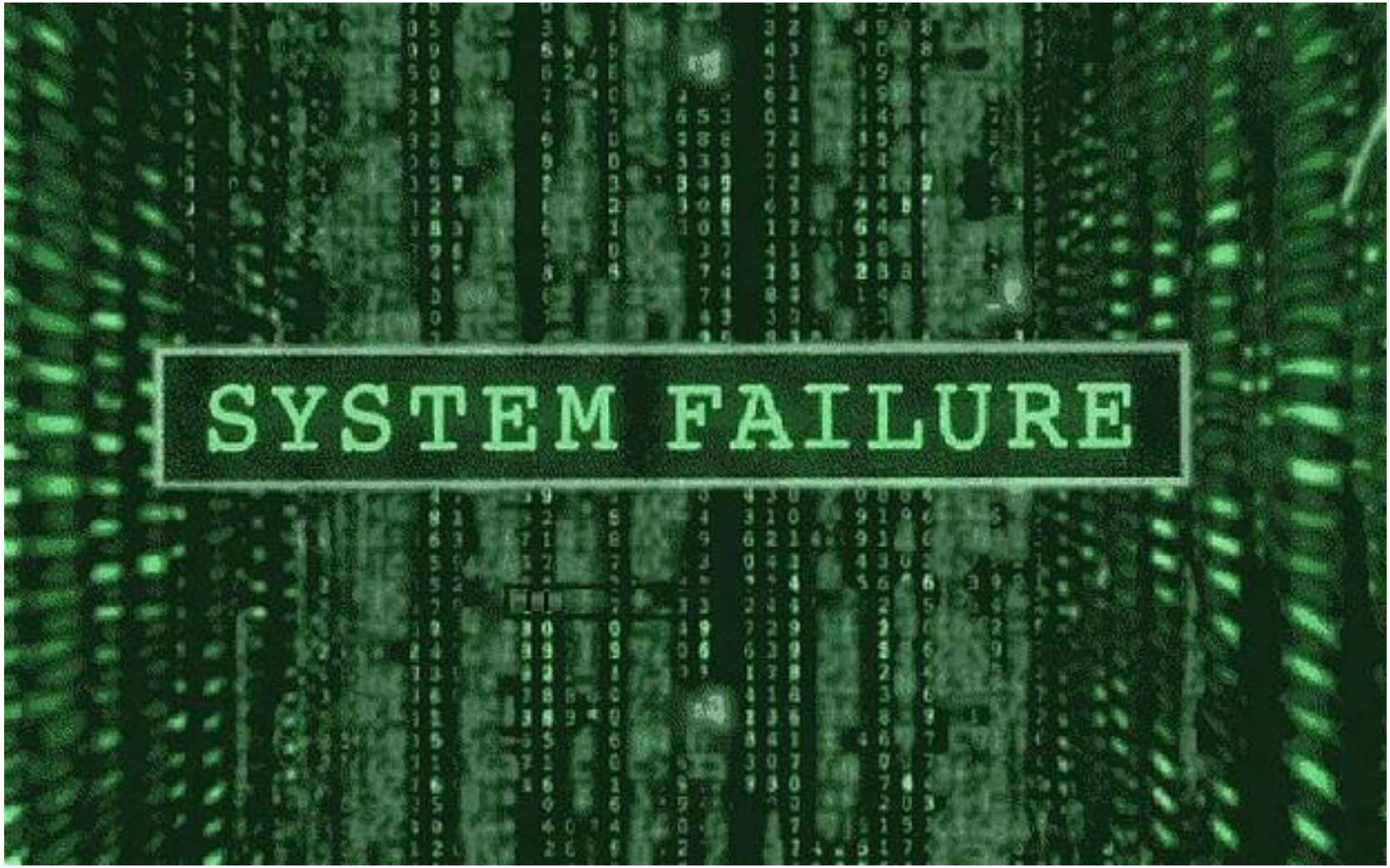
6.2.2 short description, risk **Data Integrity Issue**	**Statistical category:** Quality Systems
Observation: The balance calibration report XXX didn't content the weight tickets for the records of January and June 2016. This integration issue was the only one detected among the list of records reviewed during the audit.	


ARE YOU
READY?!

Etes vous prêts ?

- Selectionner un résultat (ou un enregistrement).
- Re-créer la séquence des évènements
- Essayer de connaitre et comprendre
  - QUI a réalisé l'analyse?
  - QUEL équipement a été utilisé pour réalisé l'analyse ?
  - QUAND l'analyse a-t-elle été réalisée ?
  - POURQUOI l'analyse a été réalisée ?
  - OU la donnée électronique est elle stockée ?

Données c'est Données
Reprendre c'est Voler


SYSTEM FAILURE

Sources of Data Integrity Information

MHRA
Regulating Medicines and Medical Devices

Data Integrity Guidance Document
www.gov.uk/government/publications/good-manufacturing-practice-data-integrity-definitions
Blog www.mhrainspectorate.blog.gov.uk

FDA

Warning Letters
www.fda.gov/ICECI/EnforcementActions/WarningLetters FDA Voice Blog
www.blogs.fda.gov

Health Canada

Inspection tracker
www.hc-sc.gc.ca/dhp-mps/pubs/compli-conform/tracker-suivi-eng.php

World Health Organization

Data Integrity Guidance Document
www.who.int/medicines/areas/quality_safety/quality_assurance/Guidance-on-good-data-management-practices_QAS15-624_16092015.pdf

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Sources of Data Integrity Information

Eudra GMP Data Base
http://eudragmdp.ema.europa.eu/inspections/gmpc/searchGMPNonCompliance.do

Data Integrity Specialist Interest Group (SIG) and Body of Knowledge tool (for members only). iSpeak blog (free to access)
www.blog.ispe.org

Data Integrity discussion group. Over 700 members.
Data integrity SME's regularly post information.

Guidances Data Integrity

MHRA* GMP Data Integrity Definitions and Guidance for Industry, July 2016
**Medecines & Healthcare products Regulatory Agency (UK)*

FDA* Data Integrity and Compliance With CGMP Guidance for Industry (draft April 2016)
**Food and Drug Administration (US)*

PIC'S* Good practise for Data management and Integrity in regulated GMP/GDP Environment (draft August 2016)
**Pharmaceutical Inspection Co-operation Scheme*

WHO* Guidance on Good Data and Record Management Practices (draft Sept. 2015)
**World Health Organization (OMS)*

ISPE* GPG Electronic Records and Data Integrity, (Draft June 2016)
**International Society for Pharmaceutical Engineering*