Data integrity
QA auditor's perspective

Tomasz Kosieradzki
QA Advisor
polpharma
www.linkedin.com/in/tomaszkosieradzki
gcp@kosieradzki.com

This presentation is intended for informational purposes only and does not replace independent professional judgment. Statements of fact and opinions expressed are those of the presenter individually and are not the opinion or position of the Polpharma .

What is the bigest risk to the data integrity?

Data „flow”



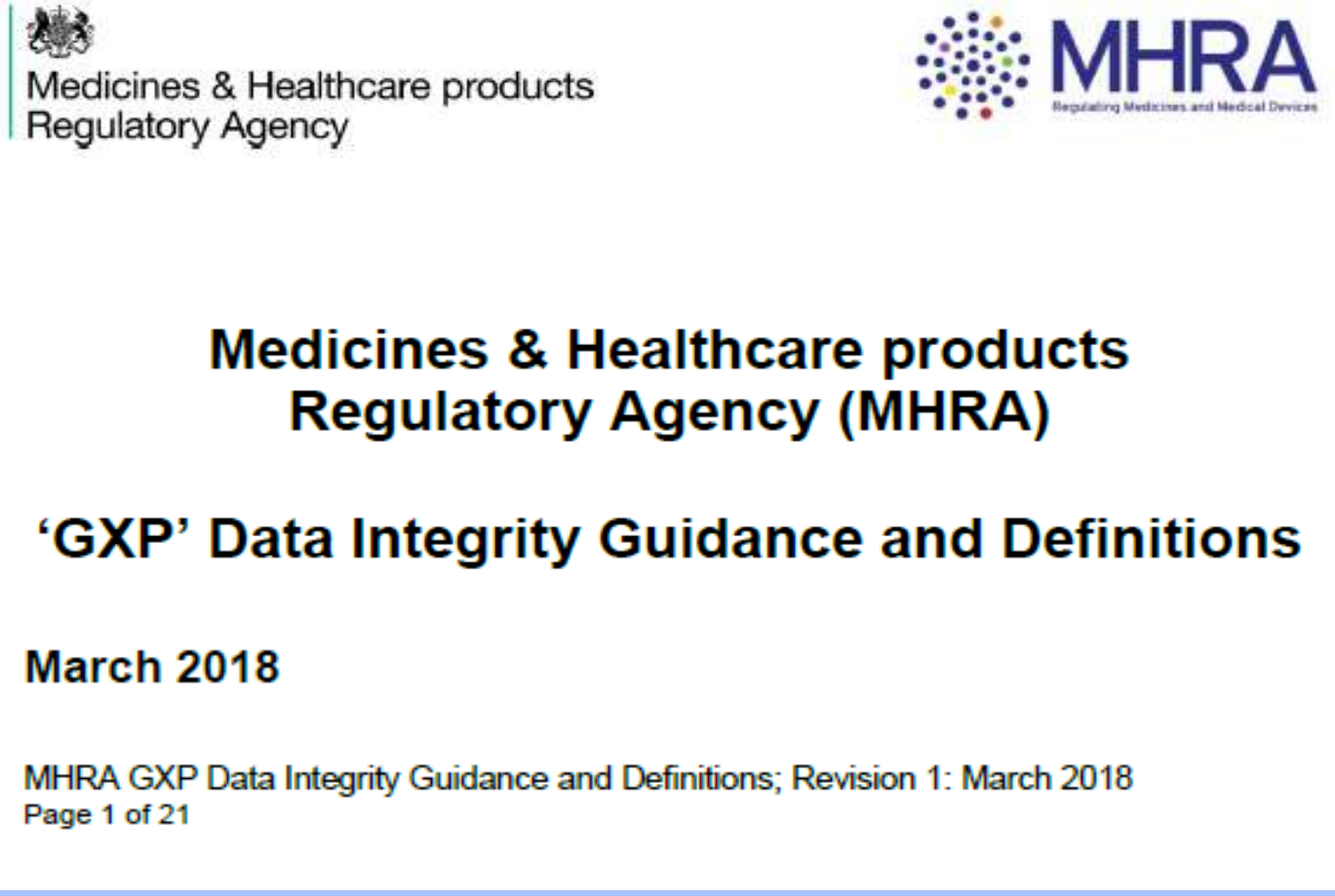




Are auditors able to verify the data integrity?

Are QA audits efficient in data integrity verification?

Data Integrity


Medicines & Healthcare products
Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

March 2018

MHRA GXP Data Integrity Guidance and Definitions; Revision 1: March 2018
Page 1 of 21

Data Integrity

Data Integrity

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable

Data Integrity

Consistent

1. Logically ordered and/or following the same pattern
2. Unchanging; steady
3. Being in conformity with a set of rules, guidelines or policies

http://www.businessdictionary.com/definition/consistent.html

Data Integrity

Complete

with all the parts

https://dictionary.cambridge.org/dictionary/english/complete

Data Integrity

Accurate

correct, exact, and without any mistakes:

http://www.dictionary.com/browse/reliable?s=t>

Data Integrity

Trustworth

deserving of trust, or able to be trusted

https://dictionary.cambridge.org/dictionary/english/trustworthy

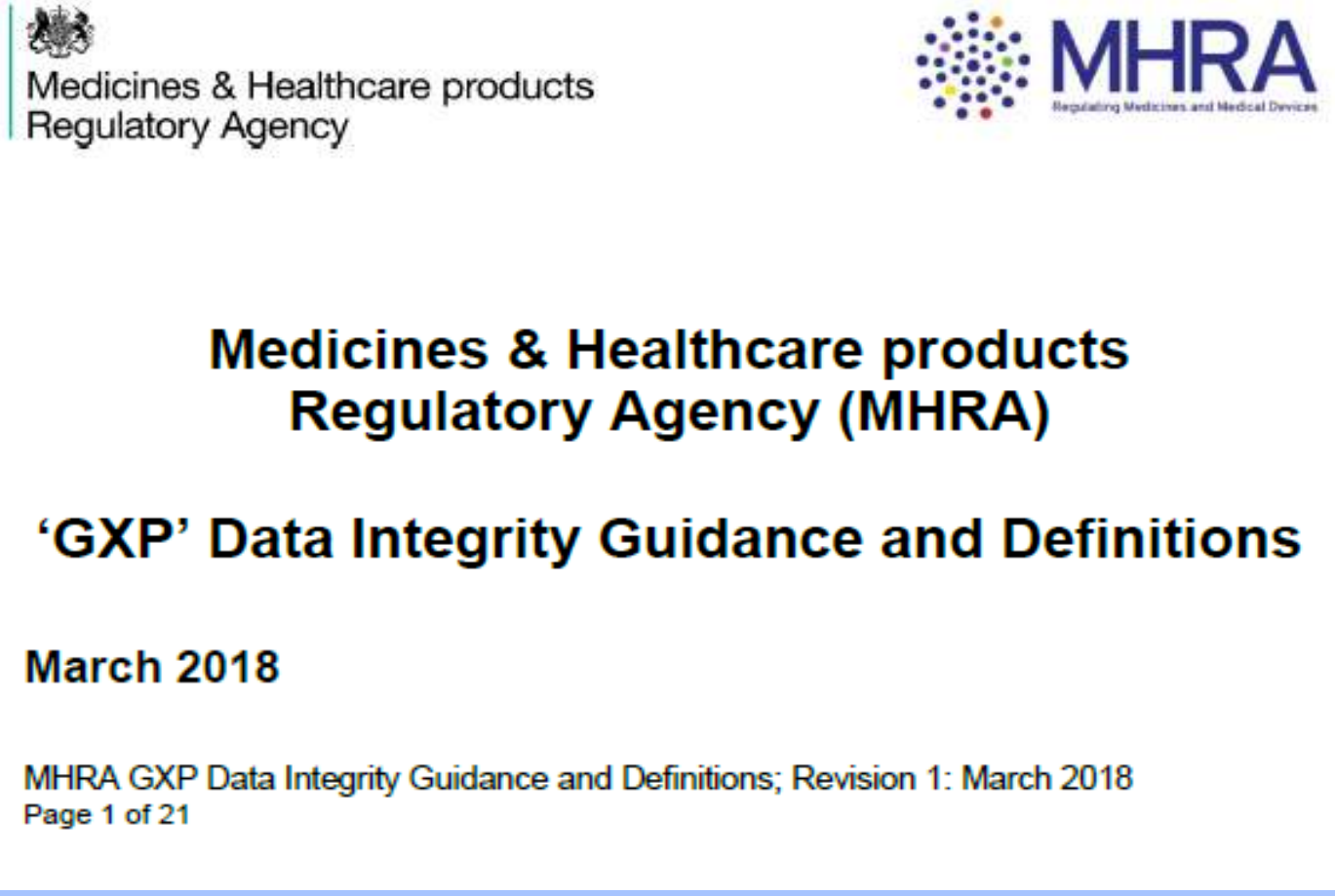
Data Integrity

Reliable

able to be trusted; predictable or dependable

https://dictionary.cambridge.org/dictionary/english/complete

Data Integrity


Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

March 2018

MHRA GXP Data Integrity Guidance and Definitions; Revision 1: March 2018
Page 1 of 21

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

6.4. Data Integrity

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. The data should be collected and maintained in a secure manner, so that they are attributable, legible, contemporaneously recorded, original (or a true copy) and accurate. Assuring data integrity requires appropriate quality and risk management systems, including adherence to sound scientific principles and good documentation practices

Data Integrity

Consistent

Complete

Accurate

Trustworthy

Reliable

Data Integrity

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable

≠

Data Qulity

Case Study

Phase 3 – dementia related study

Subject’s age > 65 y, all required support

Private outpatient clinic

100% IMP compliance over few months

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable


audit trail

Case Study

Terminally ill subjects – at home

Regular nurses' visits at home

At home - notebooks with AE information

No AE data from home in the hospital SD

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable

Case Study

Police investigation – documents and ePRO confiscated

ePRO of 2 subjects found at Investigator's home

Investigator entered the ePRO data instead of the subjects

Explanation – subjects had problems with ePRO

They called the investigator to inform him about their status

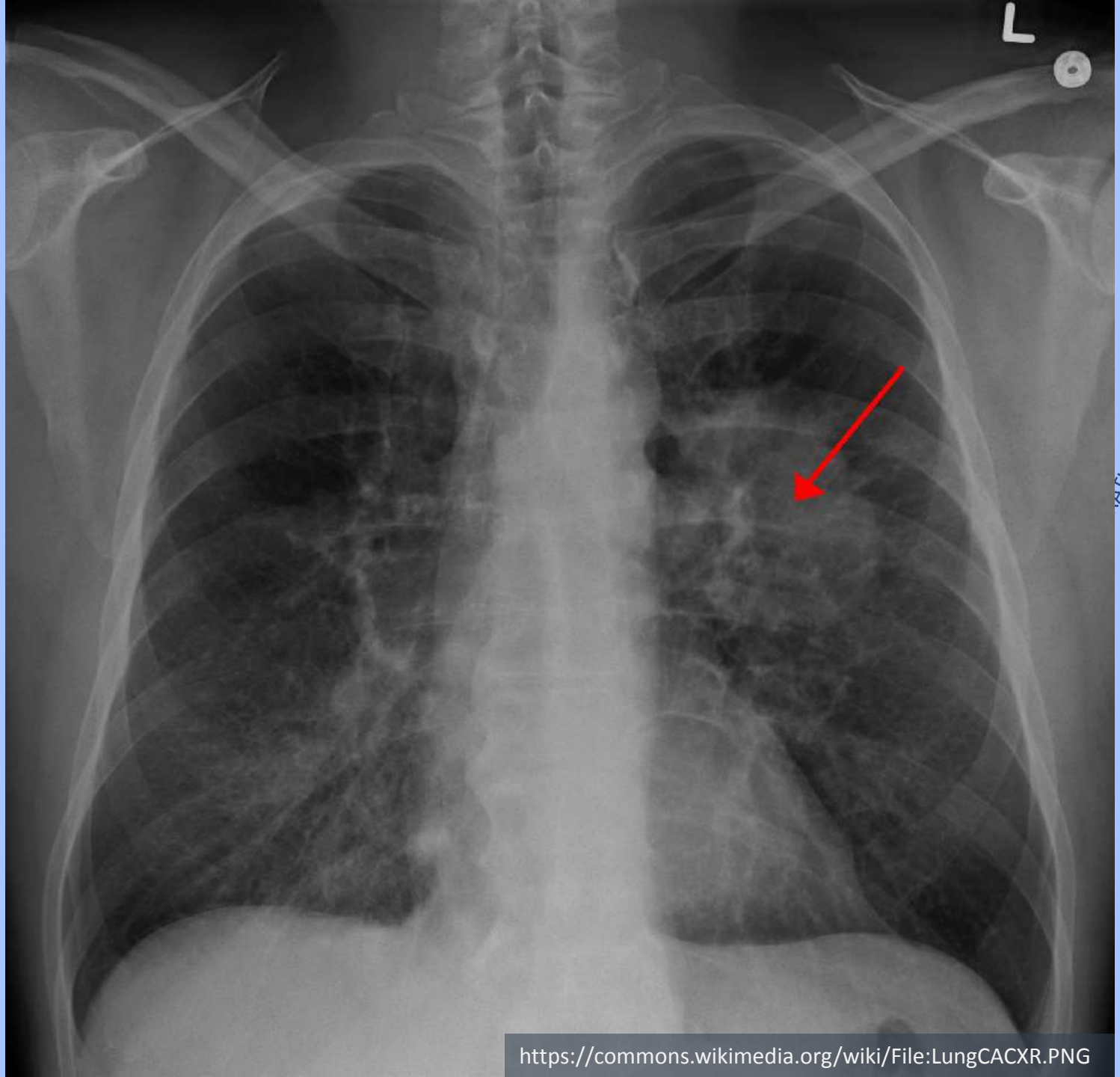
Case Study

ePRO Subject's logins – all subjects had the same logins

centralize monitoring detected inconsistency of the data

data were mixed (improbable change of the weight)

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable



https://commons.wikimedia.org/wiki/File:LungCACXR.PNG

Case Study

Eastern Cooperative Oncology Group – ECOG scale

Indication – lung cancer – advanced

All subjects – value of the ECOG – 0

ECOG Performance Status

Developed by the Eastern Cooperative Oncology Group, Robert L. Comis, MD, Group Chair.*

GRADE	ECOG PERFORMANCE STATUS
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities; up and about more than 50% of waking hours
3	Capable of only limited selfcare; confined to bed or chair more than 50% of waking hours
4	Completely disabled; cannot carry on any selfcare; totally confined to bed or chair
5	Dead

*Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol.* 1982;5:649-655.

Case Study

Eastern Cooperative Oncology Group – ECOG scale

Indication – lung cancer – advanced

All subjects – value of the ECOG – 0

High rate of SAE – deaths

Case Study

Doubts if the subjects exist

Check across all the SD available within hospital

SDV – additional, new information

Contradictory information – inconsistent with INC/EXCL

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable

Case Study

Cancer study with genetic profile

Central genetic laboratory tests

3 subjects with the same extreme rare mutation

Repeated testing and investigation

All 3 samples contained the same genetic material

2 of 3 randomized

Other sites – very high screen failure rate

Patological testing confirmed different type of the cancer

Case Study

Cancer study with genetic profile

Central genetic laboratory tests

According to the SD subject is male

According to the genetic tests subject is female

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable


F2
F3
F4
F5
num lock
F6
F7
F8
F11
F12
delete
W
E
R
T
Y
U
P
S
D
F
G
H
L
enter
return
Z
X
C
V
B
enter
page ▲
◄ home
page ▼

Case Study

eHealth Records - Source Documents

SDV – based on printouts from the eHR

CRA – has no direct access to the eHR

PI refuses access to the eHR to the auditors

Hospital management - hesitant – data privacy regulations

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable

What is the bigest risk to the data integrity?

Where are most frequently the data integrity issues located?

Data „flow”







Investigator

Investigator
one person – two roles

physician

investigator

≠

- Treatment
- Medical knowledge
- Long professional training

- Data
- Protocol & Guidelines
- few hours GCP course

Best people can make worst mistakes

What about quality management systems at the clinical sites?

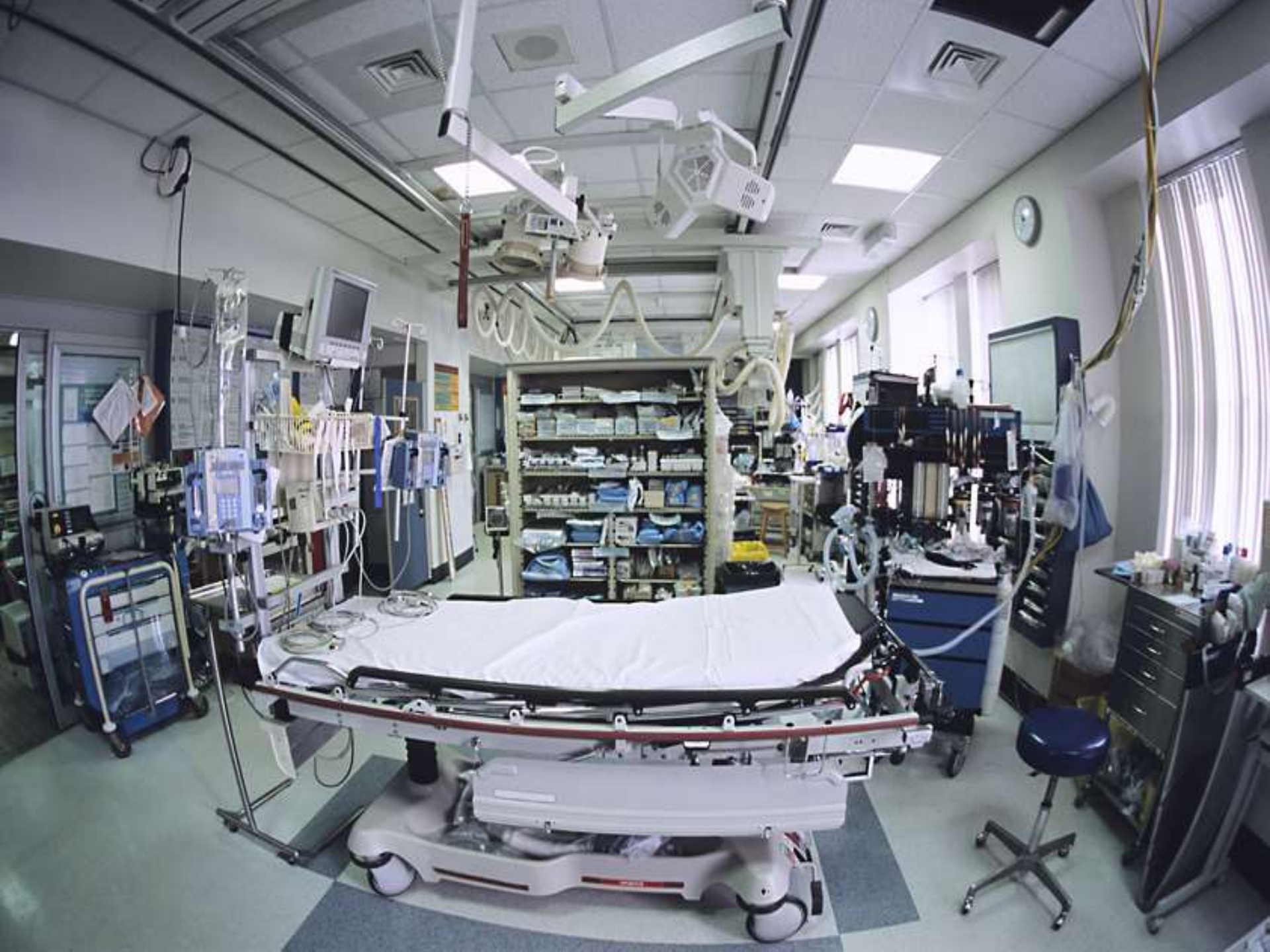
Quality

is the compliance with the references

is focused on subject’s security and rights

should lead to the integrity of the data

Quality is the method on how to achieve the data integrity in clinical trials



Case Study

Clinical Pharmacology Unit

Dedicated to bioequivalence and bioavailability studies

QMS based on Standard Operating Procedures

Emergency Procedure – EM bag & trolley – quality checked

One form without assignment to EM bag or EM trolley


TIME TO
LEARN

ICH HARMONISED GUIDELINE

INTEGRATED ADDENDUM TO ICH E6(R1): GUIDELINE FOR GOOD CLINICAL PRACTICE

E6(R2)

Current *Step 4* version

dated 9 November 2016

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definitions

- Consistent
- Complete
- Accurate
- Trustworthy
- Reliable

Data „flow”








Data „flow”








Data „flow”


Quality
Management
Systems


Jan Feb Mär Apr Mai Jun Jul Aug Sep Okt Nov Dez
M-DAX

Data Integrity

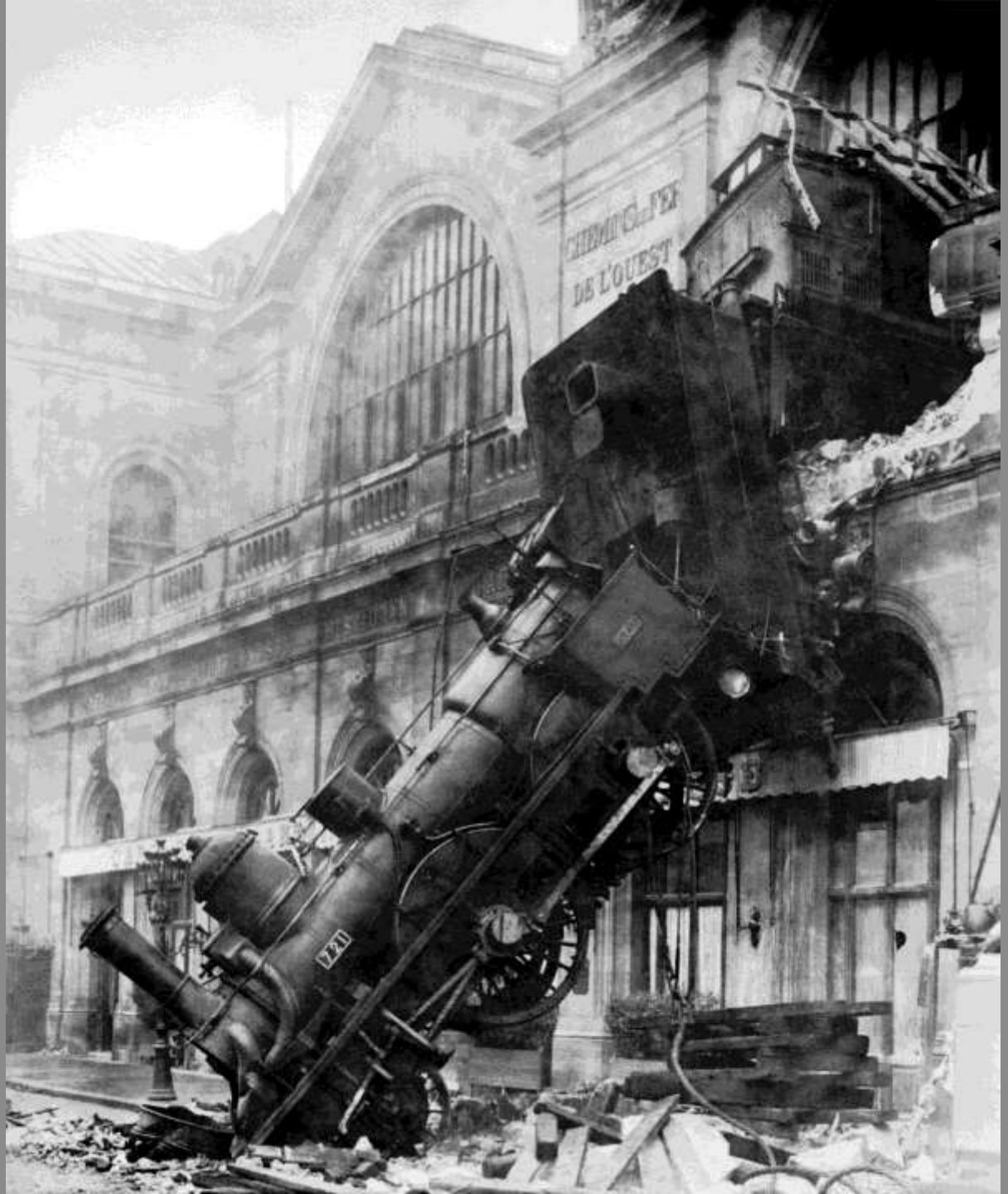
Consistent

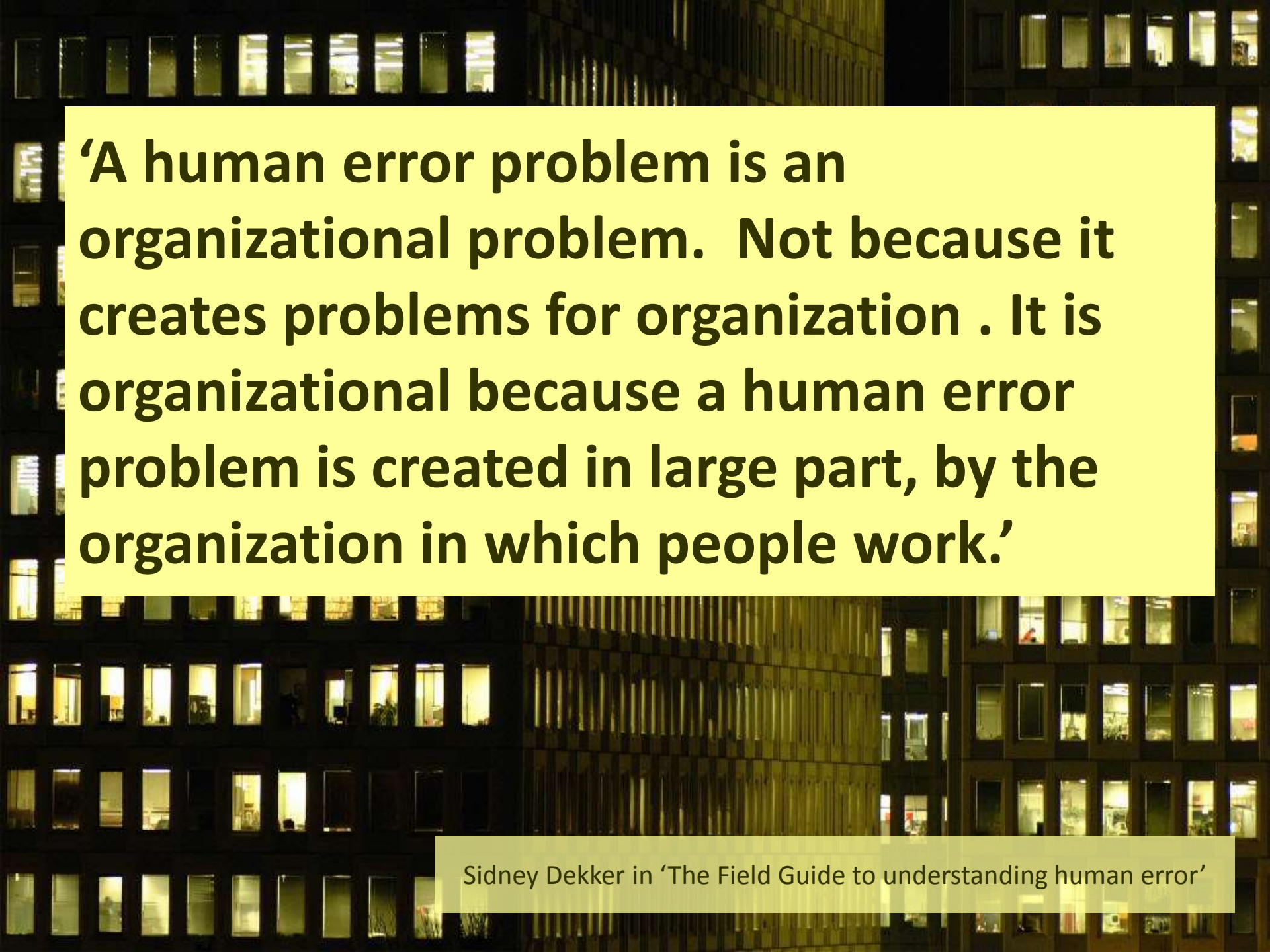
Complete

Accurate

Trustworthy

Reliable


CHEMIN DE FER
DE L'OUEST



‘A human error problem is an organizational problem. Not because it creates problems for organization . It is organizational because a human error problem is created in large part, by the organization in which people work.’

Sidney Dekker in ‘The Field Guide to understanding human error’

gcp@kosieradzki.com