NHS Scotland Pharmaceutical 'Specials' Service (PSS)

Data Integrity Analysis

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NHS Scotland Pharmaceutical 'Specials' Service

October 2024

Purpose

"Based on feedback last year … Attendees want to learn a new skill or have their understanding updated"

Purpose

Objectives

1. What
2. Why
3. Compliance
   - S10 and MHRA
4. Guidance
5. Making a start

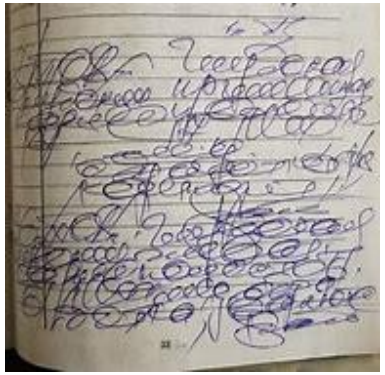
Questions

- Provide items or a service for use in patients?
- S10 aseptic unit
- QA
- MHRA authorisation

- Data Governance policy?
- Current issues?

Questions

- You confidently know what ALCOA is?



Data Integrity

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

Data - "Facts, figures and statistics collected together for reference or analysis..."

ref: MHRA Guidance 2018

Examples

- Initials on worksheets
- Time or duration of activities
- Log books – equipment / cleaning / activity
- Transcriptions from ingredients
- Transcriptions of physical parameters – pressures etc
- Analysis printouts – pH / conductivity / etc
- Equipment printouts – balances / autoclaves
- Lab books
- Dispatch
- etc

Why should we care?

- To comply?
- Effective decision making relies on trustworthy data
- Culture

Why is it important?

Field Safety Notice **Ref: SRC**	Diffuplast S.r.L. Via Piave 48, 21057 Olgiate Olona (VA), Italia

April 20, 2021

Dear customer,

Diffuplast is conducting a Field Safety Corrective Action for:

- Parenteral nutrition bags (ExactaMix eva, Exacta Mix multilayer, DiMix eva, Di Mix multilayer, Nutri-bag eva, Nutri-bag multicapa, KabiHelp uno, KabiHelp advance plus, KabiHelp duo)
- Enteral nutrition bags (Di Eto, Nutri-bag enteral)
- Connection sets
- Filling sets
- Transfer sets
- Preparation sets
- Extension sets

See Annex 1 for full lists of all impacted products (REFs) and batches (LOTs).

Diffuplast has been informed by its EO sterilisation supplier that a member of the company's staff has intentionally falsified records relating to sterilisation processes carried out from 2010 onwards. The EO sterilisation supplier has provided raw data for sterilisation cycles carried out in 2018, 2019, 2020 and 2021, downloaded by an external independent company from the supplier's SCADA system. No data has been received for sterilisations carried out in previous years. Diffuplast conducted an analysis of the raw data, but some information is still missing or incongruent and not completely reliable. Based on our post market surveillance, no incident has occurred and no notification has been received about infection since 2010.

For the batches listed in Annex 1:

Why is it important?

Part 3

Nature of non-compliance:
Following inspections on 25 July 2023 and 8 April 2024, critical deficiencies were identified in relation to data integrity, good distribution practice, lack of protection from microbial and other contamination, and inadequate control of packaging changes. This Statement of Non Compliance does not include the manufacture of critical products. Such products should be agreed in writing with individual National Competent Authorities.

Withdrawal of current valid GMP certificates:
UK MIA 17907 INSP GMP 17907/13988-0035[H]

Part 3

Nature of non-compliance:
The Inspection in December 2019 identified failures in the measures to prevent and detect cross-contamination and presented a risk that cross-contamination between products could occur and would not be detected the vendor approval process did not adequately consider the risk of contamination to existing products when introducing new raw materials; the integrity of reported data could not be relied upon; the site had contravened the restrictions on the 2014 GMP certificate.

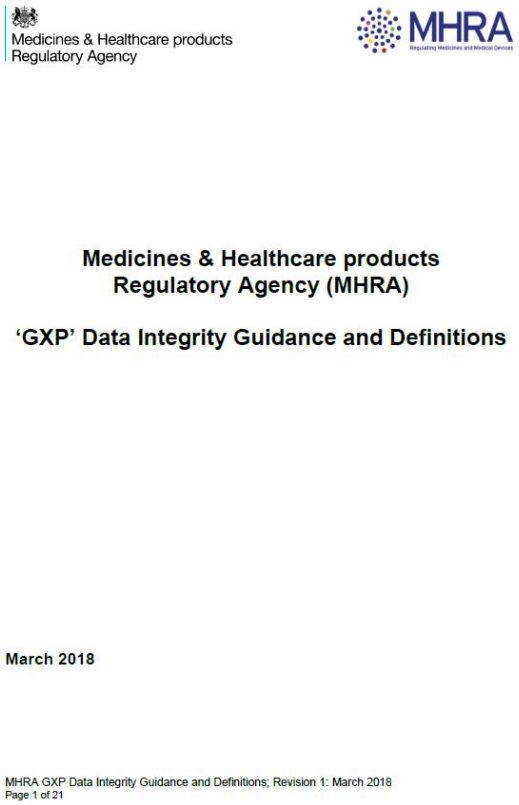
Recall of batches:
Member states should contact the site to determine the level of risk associated with specific products released to market. MHRA would recommend determining the criticality of the products on the market and to assess if a precautionary recall is appropriate.

Prohibition of supply:
No batches to be supplied to EU markets whilst this statement of non-compliance remains in force.

What do the standards say?

QAAPS

- 1 ref only in computerised system validation – PQ. But...
- 8.5.2-4
  WkS traceability
- Ch 11
  Monitoring
- 14.10
  Product approval


Medicines & Healthcare products Regulatory Agency

MHRA

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
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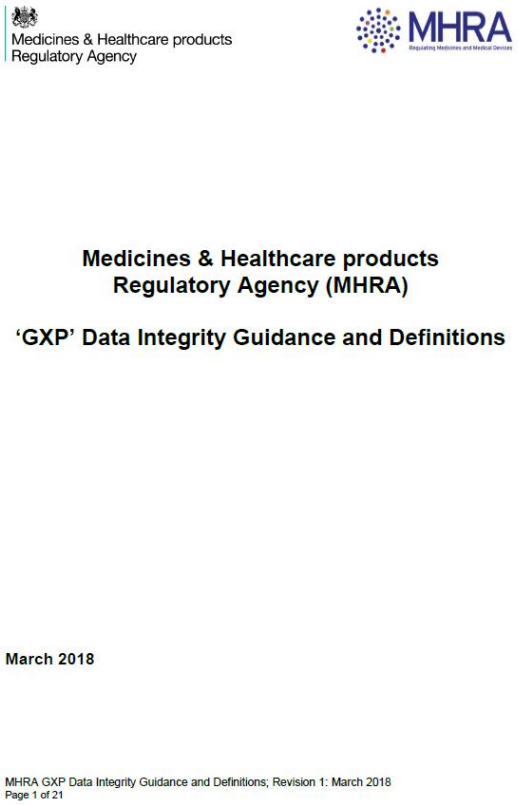
What do the standards say?

"...manufacturers and analytical laboratories are **not expected to implement a forensic approach** to data checking on a routine basis, but instead **design and operate a system which provides an acceptable state of control based on data criticality and inherent risk.**"



Medicines & Healthcare products Regulatory Agency

MHRA

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'GXP' Data Integrity Guidance and Definitions

March 2018

MHRA GXP Data Integrity Guidance and Definitions; Revision 1: March 2018
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What do the standards say?

- Section 8 – paper records

2.	**Expectation** The document design should provide sufficient space for manual data entries. **Potential risk of not meeting expectations/items to be checked** • Handwritten data may not be clear and legible if the spaces provided for data entry are not sufficiently sized. • Documents should be designed to provide sufficient space for comments, e.g. in case of a transcription error, there should be sufficient space for the operator to cross out, initial and date the error, and record any explanation required. • If additional pages of the documents are added to allow complete documentation, the number of, and reference to any pages added should be clearly documented on the main record page and signed. • Sufficient space should be provided in the document format to add all necessary data, and data should not be recorded haphazardly on the document, for example to avoid recording on the reverse of printed recording on the reverse of printed pages which are not intended for this purpose.

PIC/S

PHARMACEUTICAL INSPECTION CONVENTION
PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

PI 041-1
1 July 2021

PIC/S GUIDANCE

GOOD PRACTICES FOR DATA MANAGEMENT AND INTEGRITY IN REGULATED GMP/GDP ENVIRONMENTS

Editor: PIC/S Secretariat

e-mail: info@picscheme.org
web site: https://www.picscheme.org

How to get started?

- Read the MHRA blog and guidance
- Read your Data Governance Policy / SOP

Be curious...

- Explore your organisational culture and understanding
- Perform a Data Integrity Risk Assessment (DIRA)

DIRA 1

1. Identify data and how it is used
2. Define criticality
3. Assess risks
4. Prioritise
5. Accept / mitigate using QMS

1. Grouped lists
2. Release > EM > LB > error logs > business
3. Life-cycle, ALCOA
4. High>Medium>Low
5. Action Plans / CHG / risk assessments

NHS SCOTLAND

NHS Scotland Pharmaceutical 'Specials' Service (PSS)

DIRA 2

Department	Data obtained	Form	Main use for data	Critical	Is data backed-up?	Is raw data manipulatable / this detectable?	ALCOA compliant	ALCOA non-compliant	Risk	Combined risk	Comments
Production	Bag filling machine reports	H	GXP requirement. Product quality - assurance of equipment cleanliness.	1. High	N	N/Y	N/A	N/A	1. High	1. H/H	Unable to print CIP cycle information - not available. RSK-13
QA	Data in analytical instruments	E/P/H	GXP requirement. Used to decide release and trend results	1. High	N	Variable	Variable	Variable	1. High	1. H/H	RSK-12
QA	Micro spreadsheets	E	GXP requirement. Trend analysis of FD.	1. High	Y	Y/N*	L	ACOA	1. High	1. H/H	*data is not locked. Data is generated from raw data. There is potential for it to be manipulated or lost without detection. (note moving to MRS) RSK-14
Stores	Master records (forms)	E	To record information from inputs (e.g. delivery proforma)	1. High	Y	Y/N*	ALCOA (QPulse)	ALCOA (non-QPulse)	1. High	1. H/H	*Mixture - some forms on QPulse, some in G: drive. **Risks higher for non-QPulse forms if no controlled copy exists. AP**
Sales Office	Record of new customer approval	H	GDP archive	1. High	N	E-Y/N P-N/Y	E-L P-ALCOA	E-ACOA	2. Medium	2. H/M	Excel spreadsheet (editable) high risk. Record of approval on customer 1st order - printed copy low risk. Retained and detectable.
Estates	In-house utilities maintenance records	P	Reference	1. High	N	N/Y	ALCOA		2. Medium	2. H/M	P copy - potential for loss of data. Data is not checked. No other copies
Production	Belimed reports - PSS	H	GXP requirement. Reviewed for batch release.	1. High	Y - 168hrs only	N/Y	ALCOA		2. Medium	2. H/M	
Production	Autoclave reports - PSS	H	GXP requirement. Reviewed for batch release.	1. High	Y	N/Y	ALCOA		2. Medium	2. H/M	Original full records manually downloaded with USB and entered in Onedrive. Not editable. **Risk relates to accessing and availability of critical data**
Production	Autoclave cycle info (FLS/PLS + PSS)	P	Reference for investigation of issues	1. High	Y (not raw data)	N/Y	ALCO	A	2. Medium	2. H/M	P copy - potential for loss of data. Information not checked. No other copies
Production	Housekeeping activities - cleaning etc	P	GXP requirement	1. High	N	N/Y	ALCOA		2. Medium	2. H/M	P copy - potential for loss of data. Periodic checking by Supervisors. Archived. No other copies
Production	Pressure differentials (TP)	P	GXP requirement	1. High	Y (not raw data)	N/Y	ALCO	A	2. Medium	2. H/M	P copy - potential for loss of data. Info also on BMS (note only accessible by NHST Estates)

DIRA 3

Printed on: 15 October 2024

Risk Management

Details

Number	Product/ Ref		
RSK-12			
Status	**Raised Against (Department or Supplier)**	**Raised Date**	**Target Date**
Risk assessment for review	QA	30/10/23	27/12/2024
Severity	**Raised By (Person or Customer)**	**Fault Category**	
2 Medium	Boag, Peter	Internal Audit / Management	

Details

Interim approach to data integrity for QA analytical software packages

Process	Product Service
Testing	QA

Owner	Root Cause
Boag, Peter	Software

Approval Date	Closed Date	Closed By	Resolution
01/01/0001		Admin, LH	Rectification

Risk Assessment

Target Date	Owner	Closed Date	Closed By
02/11/2023	Boag, Peter	31/10/2023	Boag, Peter

Details

Assess the risk using the work flow below

Owner	Details	Response	Target	Completed
Boag, Peter	What is the likelihood (probability) it will go wrong?	1. Data destruction by accident can always be considered a possibility, just bit clicking the wrong buttons. Avoiding wilful manipulations comes down to good training and trust in staff - Medium	02/11/2023	31/10/2023

Summary

- Take a risk commensurate approach
- Read the guidance (MHRA and PIC/S)
- Undertake an initial assessment and move forward
- Focus on
  - Organisational culture
  - Process design

Thank you

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