MHRA
Regulating Medicines and Medical Devices

Good Documentation Practices

Documentation Requirements For Regulated Environments

Medicines and Healthcare Products Regulatory Agency

Agenda

- Example Deficiency 2014
- Result Of Poor Record Creation
- Data Integrity
- EU GMP Chapter 4 Requirements
- Non GMP Compliant Record
- Date Stamped Entry In QPulse
- Example Policy

Agenda

- **Example Deficiency 2014**
- Result Of Poor Record Creation
- Data Integrity
- EU GMP Chapter 4 Requirements
- Non GMP Compliant Record
- Date Stamped Entry In QPulse
- Example Policy

Example Deficiency 2014

The Trusts' Quality Management System lacks adequate controls to ensure a common understanding of the requirements of good documentation practice

Example Deficiency 2014

Records are not always made or completed at the time each action is taken and in such a way that all significant activities undertaken are traceable

ie contemporaneous records to identify who conducted an activity and when

Example Deficiency 2014

There was no awareness that the records for good practice compliance require either a handwritten signature and date or an equivalently controlled record generally with a date stamp within a document control system

Examples include but are not limited to:

- The Change Control process, including approvers of change proposals
- Approvals of incident management events (Quality Deviations) and associated Corrective and Preventative Actions. (CAPA)
- Qualification records including the Diamed analysers

Example Deficiency 2014

There are records where alterations made to the entries on the documents are not signed and dated

The alterations do not ensure that the original information may be read and they lack explanations for the alterations

Obliteration (including Tippex tape (or stickers) and overwriting) had been used to amend original entries

Example Deficiency 2014

The document control system is deficient in that:

- Historically procedures had been made Active in QPulse without using the approvals process

- The active dates on Policies and Procedures can differ for example, xxx xxx xxx 007 had an active date of 1 December 2013 on the document but had an active date of 22 January 2014 in QPulse

Agenda

- Example Deficiency 2014
- **Result Of Poor Record Creation**
- Data Integrity
- EU GMP Chapter 4 Requirements
- Non GMP Compliant Record
- Date Stamped Entry In QPulse
- Example Policy

Result of poor record creation

Issues over the past year in Pharma side of our Regulated organisations

(Reuters) - Britain's MHRA drug regulator has halted the sale of 16 medicines …….after it identified manufacturing deficiencies.
The medicines that are affected have *not been manufactured to Good Manufacturing Practice (GMP) standards*, U.K. inspectors cited

- Inadequate record keeping and production controls

Findings over the year have included:

- Evidence of "forged documents relating to staff training records"
- Deletion of key analytical data from hard drives

- Data generated lacked reliability and accuracy
- Laboratory records are not in compliance with established standards

Result of poor record creation

Consequences

Questions raised over the reliability and accuracy of tests

…….inability to implement a robust and sustainable quality system?

Evidence of falsification can lead to a lack of reliance on ANY data presented

Therefore any attempts at mitigating risk through presentation of other information cannot be relied upon

Patient safety could be at risk, chance of regulatory action increases, and the organisations credibility and integrity as a whole might be called into question

Could lead to increased interest from other organisations with whom we share regulatory information (such as CQC)

December 2013

MHRA expectation regarding self inspection and data integrity

The MHRA is setting an expectation that pharmaceutical manufacturers, importers and contract laboratories, as part of their self-inspection programme will need to review the effectiveness of their governance systems to ensure data integrity and traceability

Agenda

- Example Deficiency 2014
- Result Of Poor Record Creation
- **Data Integrity**
- EU GMP Chapter 4 Requirements
- Non GMP Compliant Record
- Date Stamped Entry In QPulse
- Example Policy

Data integrity from Wikipedia!

Data integrity refers to maintaining and assuring the accuracy and consistency of data over the entire life-cycle:

- ensure data is recorded exactly as intended
- upon later retrieval, ensure the data is the same as it was when it was originally recorded

Agenda

- Example Deficiency 2014
- Result Of Poor Record Creation
- Data Integrity
- **EU GMP Chapter 4 Requirements**
- Non GMP Compliant Record
- Date Stamped Entry In QPulse
- Example Policy

EU GMP Chapter 4

Principle

- The Quality Management System should include sufficient instructional detail to facilitate a common understanding of the requirements, in addition to providing for sufficient recording of the various processes and evaluation of any observations, so that ongoing application of the requirements may be demonstrated.

- There are two primary types of documentation used to manage and record GMP compliance: instructions (directions, requirements) and records/reports. Appropriate good documentation practice should be applied with respect to the type of document.

- Suitable controls should be implemented to ensure the accuracy, integrity, availability and legibility of documents…… The term ‘written’ means recorded, or documented on media from which data may be rendered in a human readable form.

EU GMP Chapter 4

- ***Record/Report type:***

- **Records:** Provide evidence of various actions taken to demonstrate compliance with instructions, e.g. activities, events, investigations, and in the case of manufactured batches a history of each batch of product, including its distribution.
  Records include the raw data which is used to generate other records.
  For electronic records regulated users should define which data are to be used as raw data. At least, all data on which quality decisions are based should be defined as raw data

- **Reports:** Document the conduct of particular exercises, projects or investigations, together with results, conclusions and recommendations.

EU GMP Chapter 4

Good Documentation Practices

4.7 Handwritten entries should be made in clear, legible, indelible way.

4.8 Records should be made or completed at the time each action is taken and in such a way that all significant activities …… are traceable.

4.9 Any alteration made to the entry on a document should be signed and dated; the alteration should permit the reading of the original information. Where appropriate, the reason for the alteration should be recorded.

Blood Good Practice Guide

(link below)

http://www.edqm.eu/site/good_practice_guidelines_dec_2013pdf-en-31298-2.html

GMP quotations used are aligned with those in the new standard

Agenda

- Example Deficiency 2014
- Result Of Poor Record Creation
- Data Integrity
- EU GMP Chapter 4 Requirements
- **Non GMP Compliant Record**
- Date Stamped Entry In QPulse
- Example Policy

Non GMP Compliant Record

[redacted] Hospital Services NHS

NHS Trust

Pathology Change Control Proforma for Improvement Ideas

Number: INC4171	Originator: [redacted]	Department: Blood Transfusion	Date: 26/3/2013

Title of Change: Replacement of [redacted] with GelStation Plus

Reason for Change: Current [redacted] grouping analysers are old and experiencing re-current problems requiring an engineer to visit.

Description and Intent of Change (costings):
One [redacted] has already been replaced by an IH-1000 see INC3444 as part of a managed service contract with DiaMed/Bio-Rad. The GelStation Plus will serve as a back-up instrument but will also be used routinely to cover IH-1000 downtime as a result of maintenance. Once the IH-1000 has been fully implemented delivery of the GelStation Plus will be arranged at the same time as removal of one of the existing [redacted] instruments by DiaMed/Bio-Rad. Once the GelStation Plus is fully validated the remaining [redacted] will also be removed.

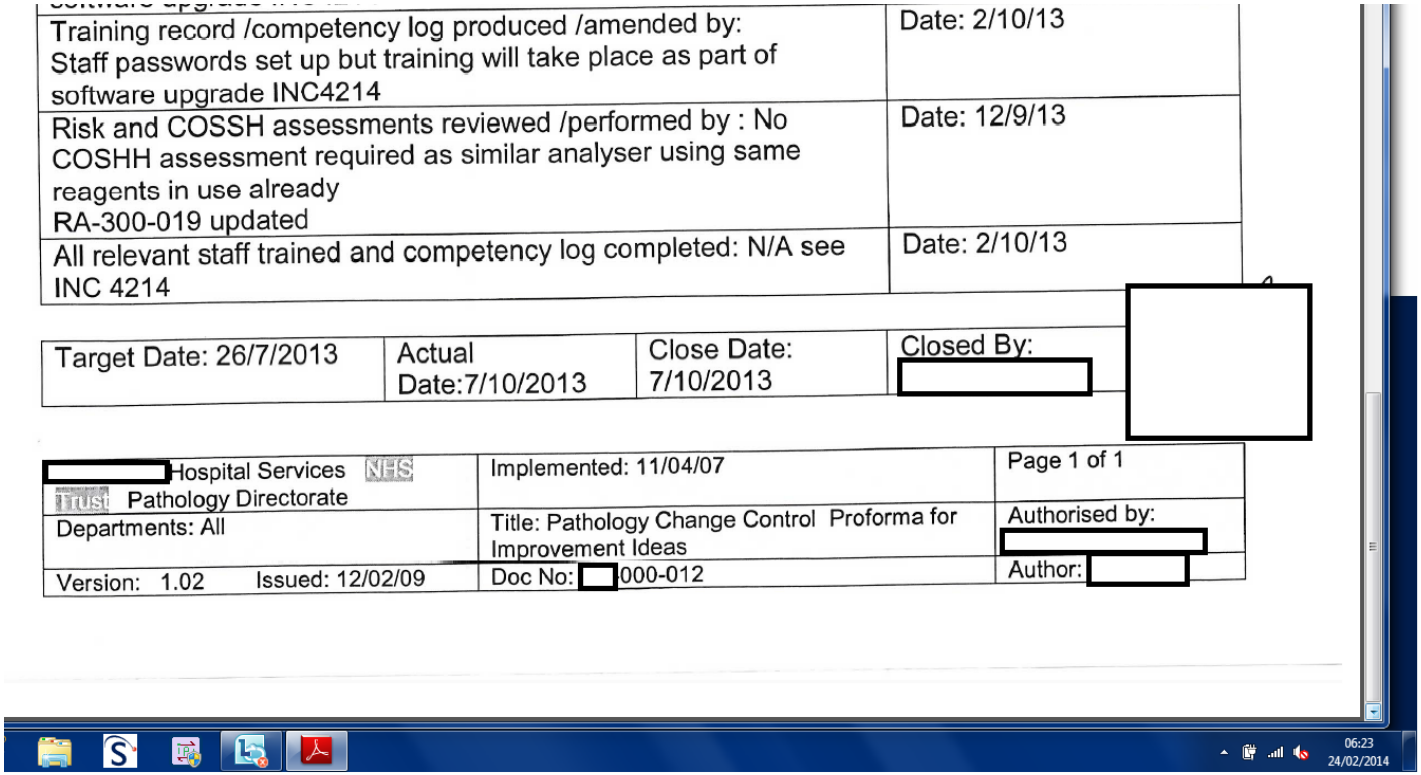
Impact of Change (including staffing & revenue implications):

Non GMP Compliant Record

GelStation Plus is fully validated the remaining [redacted] will also be removed.	
Impact of Change (including staffing & revenue implications): Staff will require a limited amount of training on the instrument in order to become familiarised with any modifications present. The instrument has been purchased as part of a managed service contract. See full validation for further documentation.	
Risk Assessment: [redacted]	
Responsible Person: [redacted]	
Approved by: [redacted]	Date: 26/3/13
Validated by: [redacted] as part of project for Bio-medical scinec degree at [redacted] under the supervision of [redacted]	Date: 17/9/13
Procedure/ SOP/ written / amended by: SOP's to be written after software upgrade INC4214	Date: 2/10/13
Training record /competency log produced /amended by: Staff passwords set up but training will take place as part of software upgrade INC4214	Date: 2/10/13
Risk and COSSH assessments reviewed /performed by : No COSHH assessment required as similar analyser using same reagents in use already RA-300-019 updated	Date: 12/9/13
All relevant staff trained and competency log completed: N/A see	Date: 2/10/13

06:20
24/02/2014

Non GMP Compliant Record



Training record /competency log produced /amended by: Staff passwords set up but training will take place as part of software upgrade INC4214	Date: 2/10/13
Risk and COSSH assessments reviewed /performed by : No COSHH assessment required as similar analyser using same reagents in use already RA-300-019 updated	Date: 12/9/13
All relevant staff trained and competency log completed: N/A see INC 4214	Date: 2/10/13

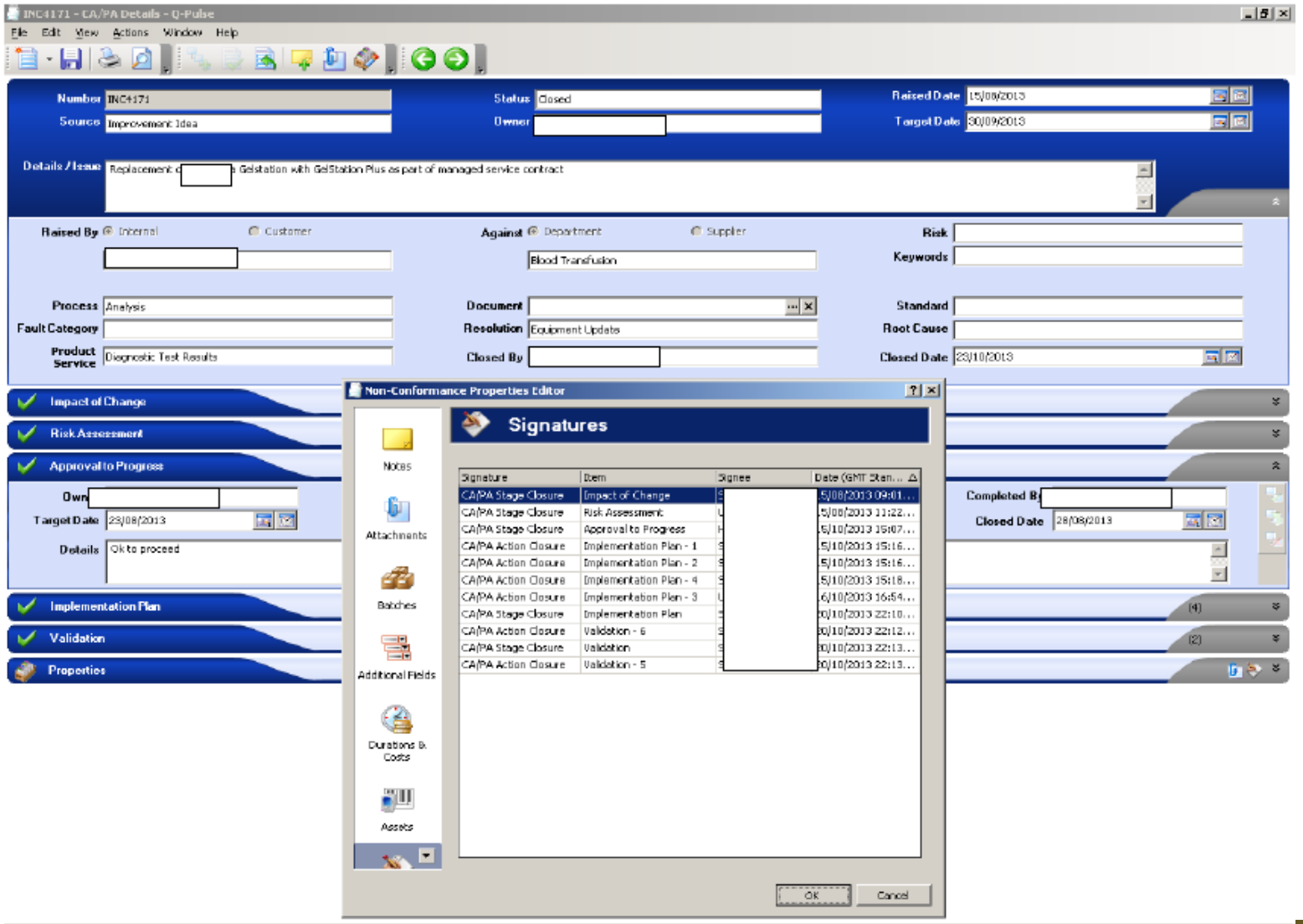
Target Date: 26/7/2013	Actual Date:7/10/2013	Close Date: 7/10/2013	Closed By: [redacted]

[redacted] Hospital Services NHS [redacted] Trust Pathology Directorate	Implemented: 11/04/07	Page 1 of 1
Departments: All	Title: Pathology Change Control Proforma for Improvement Ideas	Authorised by: [redacted]
Version: 1.02 Issued: 12/02/09	Doc No: [redacted]000-012	Author: [redacted]

Agenda

- Example Deficiency 2014
- Result Of Poor Record Creation
- Data Integrity
- EU GMP Chapter 4 Requirements
- Non GMP Compliant Record
- **Date Stamped Entry In QPulse**
- Example Policy

Date stamped entries



Agenda

- Example Deficiency 2014
- Result Of Poor Record Creation
- Data Integrity
- EU GMP Chapter 4 Requirements
- Non GMP Compliant Record
- Date Stamped Entry In QPulse
- **Example Policy**

Example Policy

1.0 Entering Data

1.1 Handwritten entries on documents must be made using permanent (indelible) blue or black ink. Erasable ink, non-waterproof ink, and pencil are not permitted

1.2 Correction fluid and correction tape are not allowed on documents.

1.3 The date and time hand written on a document will be the current date and time at the location where the handwritten entry is made

1.4 The preferred format for the handwritten date on documents is the format: 2 digit day, three character month, 4 digit year.

1.5 Document entries must be made at the time of completing a task.

Example Policy

1.6 Signature entries shall be consistent with the signature recorded in the site signature log.

1.7 Initial entries shall be consistent with the initials recorded in the site signature log

1.8 No one shall enter a signature or initials for someone else.

1.9 All entries must be made directly onto the official record or document. The use of scratch paper, post-it notes, or unofficial notes to record data is not permitted.

1.10 All documents requiring review and approval signatures shall contain the original handwritten signature and date signed. Signatures made by rubber stamps, pre-printed labels, photocopy, or fax are not permitted.

Example Policy

2.0 Editing Data

2.1 When a correction is needed, draw a single line through the entire incorrect entry, enter the correct information and initial and date the correction. When the reason for the correction is not obvious, place an asterisk or number next to the incorrect entry and explain the correction at the bottom of the page, identified by the asterisk or corresponding number.

Note: Over writing is not permitted.

2.2 All missing entries must be explained. If an entry is not completed at the time the function is performed, place an asterisk or number at the point of the missing entry and at the bottom of the page explaining the missing entry. Initial and date the entry

Example Policy

2.3 To ensure that inappropriate entries are not made at a later date, a line shall be drawn on all blank spaces if the reason for that blank space is not apparent. If the blank space is left because an entry is not applicable, “NA” may be entered.

2.4 Backdating (entering a date on a day after the entry was made or the task was performed) is not permitted

2.5 Postdating (entering a date in the future) is not permitted

2.6 When a document requires an entry upon completion of an activity and the activity was performed but not documented, an explanation (by the performer of the activity) of why there was an omission must be included, signed, and dated

Example Policy

3.0 Computer based records

3.1 Primary (raw data) records such as:
- Approval of Policies / Procedures
- Pre approval and post approval of Change Controls
- Approval of Non conformances

shall be completed using a “date stamped” entry

3.2 Typed dates and names entered in the system to record completion of actions for which the primary record (raw data) is elsewhere (for example recording completion dates of actions) shall reference the primary data source and match the date entries in that raw data

© Crown copyright 2014

About copyright
All material created by the Medicines and Healthcare Products Regulatory Agency, including materials featured within these Medicines and Healthcare Products Regulatory Agency presentation notes and delegate pack, is subject to Crown copyright protection. We control the copyright to our work (which includes all information, database rights, logos and visual images), under a delegation of authority from the Controller of Her Majesty's Stationery Office (HMSO).

The Medicines and Healthcare Products Regulatory Agency authorises you to make one free copy, by downloading to printer or to electronic, magnetic or optical storage media, of these presentations for the purposes of private research, study and reference. Any other copy or use of Crown copyright materials featured on this site, in any form or medium is subject to the prior approval of the Medicines and Healthcare Products Regulatory Agency.

Further information, including an application form for requests to reproduce our material can be found at **www.mhra.gov.uk/crowncopyright**

Material from other organisations
The permission to reproduce Crown copyright protected material does not extend to any material in this pack which is subject to a separate licence or is the copyright of a third party. Authorisation to reproduce such material must be obtained from the copyright holders concerned.