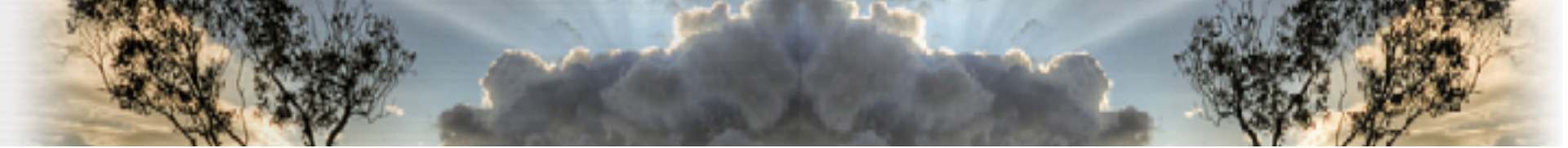


EBF Cyberconnect Events

Focus Workshop: Spotlight on (LBA/CBA and Automation) TECHNOLOGY

20-21 May 2021

Automation and the Data Integrity challenges

Cecilia Arfvidsson, on behalf of the EBF

Data Integrity (DI) definitions

- **FDA CGMP Definition**: data integrity refers to the completeness, consistency, and accuracy of data. Complete, consistent, and accurate data should be **attributable, legible, contemporaneously** recorded, **original** or a true copy, and **accurate** (**ALCOA**).

- **WHO** (World Health Organization): is the degree to which data are **complete, consistent, accurate, trustworthy and reliable** and that these characteristics of the data are maintained throughout the data life cycle

- **PIC/S** (Pharmaceutical Inspection Co-Operation Scheme): Key concepts are summarised by the acronym **ALCOA**: Attributable, Legible, Contemporaneous, Original, Accurate. To this list can be added the following: **Complete, Consistent, Enduring and Available (ALCOA+5).**

Recently Updated DI guidance

- **MHRA** Guidance (issued in 2018) and **WHO/OECD** Draft Guidelines highlight the DI additional challenges with evolving **new technologies and automation**


Working document QAS/19.819
October 2019
Draft for comments

World Health Organization

GUIDELINE ON DATA INTEGRITY

(October 2019)

DRAFT FOR COMMENTS

*In recent years, **the number of observations** made regarding the integrity of data, documentation and record management practices during inspections … **has been increasing**. Possible causes for this may include (i) too much reliance on human practices; (ii) **the use of computerized systems that are not appropriately managed and validated**; and (iii) failure to adequately review and manage original data and records."*

WHO guideline on Data Integrity (draft)


MHRA

Medicines & Healthcare products Regulatory Agency

Medicines & Healthcare products Regulatory Agency (MHRA)

'GXP' Data Integrity Guidance and Definiti

March 2018

*The way regulatory data is generated has **continued to evolve** in line with the ongoing development of supporting technologies such as the **increasing use of electronic data capture, automation of systems and use of remote technologies**….Systems to support these ways of working can range from manual processes with paper records to the **use of fully computerised systems**. The main purpose of the regulatory **requirements remains the same**, i.e. having confidence in the **quality** and the **integrity** of the data generated (to ensure patient safety and quality of products) and being **able to reconstruct** activities.*

MHRA GXP Data Integrity guidance (2018)

E-data in an automated environment

- What are the **key drivers** for **automation**?
  - **cost** reduction
  - free up lab **resources**
  - reduce monotonous activities
  - improve **efficiency**
  - improve assay **accuracy**
  - …..

The **validation** and **management** activities will likely also focus on these items….

- Likely consequences and **possible risks**
  - **data integrity** is not enough considered
  - an **overreliance** on an automated **system's validated state**
  - data integrity gaps not identified in a timely manner due **lack of system knowledge and awareness**

Data integrity and automation

The data integrity risk assessment (or equivalent) should consider factors required to follow a process or perform a function. It is expected to consider not only a computerised system but also the supporting people, guidance, training and quality systems. Therefore, ***automation or the use of a 'validated system' (e.g. e-CRF; analytical equipment) may lower but not eliminate data integrity risk****. Where there is human intervention, particularly influencing how or what data is recorded, reported or retained, an* ***increased risk may exist from poor organisational controls or data verification due to an overreliance on the system's validated state***

MHRA GXP Data Integrity guidance

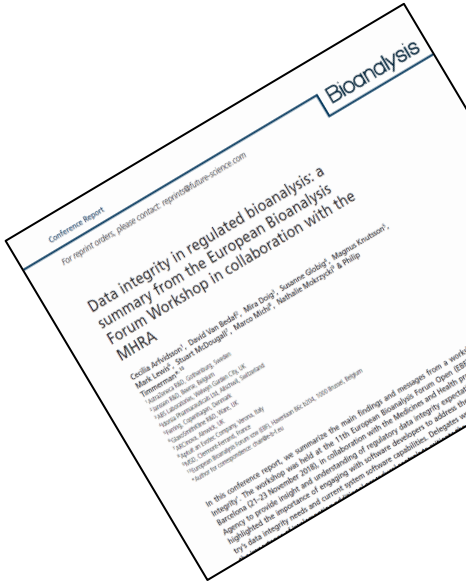
- Main **computerized systems** are still **human driven** (data exported, imported and accepted following a human initiation) with humans as the **final decision makers**.
- Soon we will likely see more **fully automated laboratories/autonomous laboratory** systems whereby **decisions** are **performed by the software**. It is still important to have **each step recorded** in a way that it can be reconstructed or re-created if needed.

EBF and the e-Environment theme

- e-Environment discussions at previous EBF Open Symposiums:
  - 2012 ELN workshop
  - 2013 Workshop: defining raw data in regulated bioanalysis
  - 2014 Workshop on e-Data: towards a common standard
  - 2015 Workshop: generic data transfer agreement
  - 2015 Session: Going paperless
  - 2016 Discussion forum: Harmonised implementation of OECD17
  - 2016 Session: e-Environment
  - 2017 Workshop: Approaches on implementing OECD17
  - 2018 Session: e-Environment
  - 2018 Workshop: Data integrity with contributions from the MHRA
  - 2019 Workshop: Building Common Understanding for Future System Solutions
  - 2020 Workshop: Towards a vendor neutral secure bi-directional data transfer process

Key take home messages from 2018 e-Environment WS

EBF e-environment workshop[1] arranged in **collaboration with the MHRA** to provide insight and understanding of **regulatory data integrity expectations** – just as applicable to **automated workflows** as to **manual workflows**.

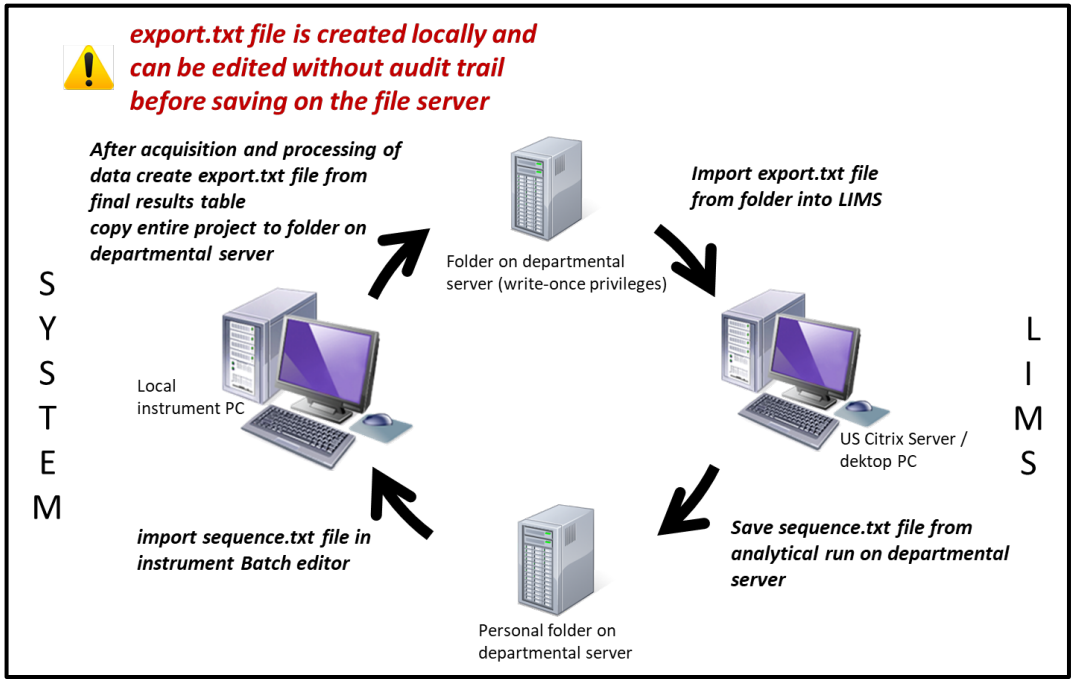


- **Know your software** system data and processes
- **Map your processes** to identify the potential risks and weaknesses
- Reduce the risk by implementing solutions that have been identified as a result of **improved software awareness** and knowledge
- Open up the dialogue for **enhanced interaction between system vendors, pharma/CROs and regulatory authorities** to understand current, and define future, system data integrity capabilities.

[1]Arfvidsson C, Van Bedaf D, Doig M *et al*. *Bioanalysis* 11(13), 1227–1231 (2019).

2019 e-Environment WS - Building Common Understanding for Future System Solutions

EBF arranged a workshop with the purpose to create a **new opportunity for dialogue** and to bring software developers, Pharma/CRO labs and regulatory authorities together



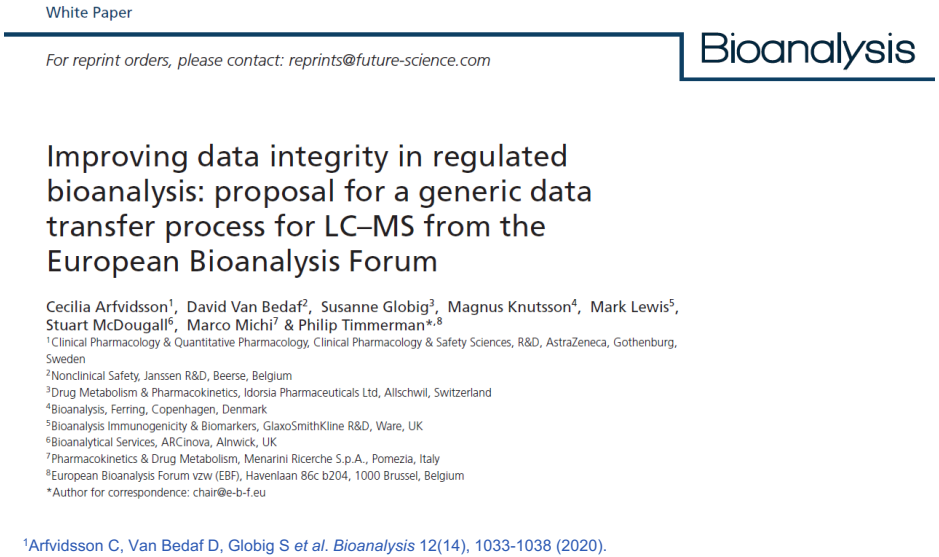
- Highlight **current key DI challenges**, focusing on the data transfers in the **LC/MS workflows**
- What are the **missing functionalities** in today's process?
- What can the **software developers** do to **help improve** the current situation?

Key take home messages from 2019 e-Environment WS

- The “**interface landscape**” is often the key issue for most bioanalytical labs and workflows when it comes to Data Integrity
- EBF focus - a **joint mission** to resolve the current interface and secure data transfer issues
- The workshop a successful **first step** towards a **consensus** and an **increased dialogue** between the software developers and the bioanalytical community
- A **concrete message** from the **software developers** - the BioA community needs to **agree on a joint request** for the software developers to focus their efforts.

2020 focus - Improved Data Integrity in the LC/MS workflows

Following the e-environment workshop at the EBF OS 2019 the **EBF proposal** for a **generic data transfer specification** was published in Bioanalysis[1]



White Paper

For reprint orders, please contact: reprints@future-science.com

Bioanalysis

Improving data integrity in regulated bioanalysis: proposal for a generic data transfer process for LC–MS from the European Bioanalysis Forum

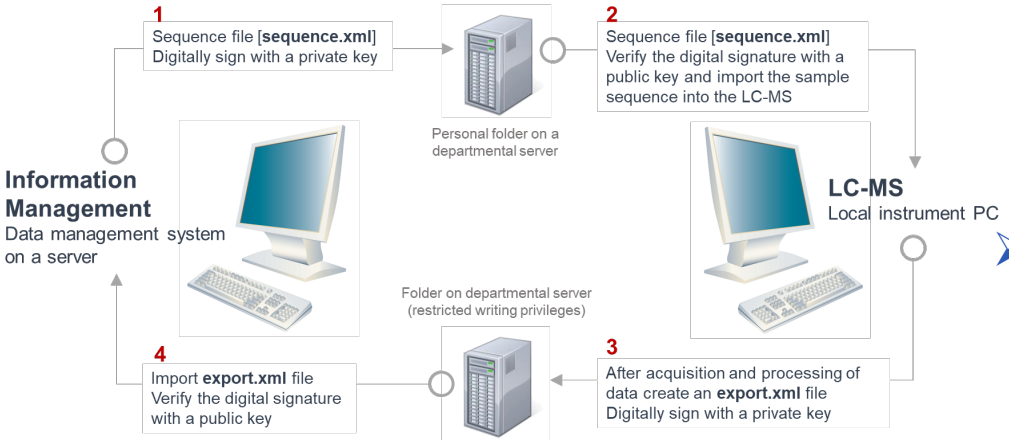
Cecilia Arfvidsson[1], David Van Bedaf[2], Susanne Globig[3], Magnus Knutsson[4], Mark Lewis[5], Stuart McDougall[6], Marco Michi[7] & Philip Timmerman*,[8]
[1]Clinical Pharmacology & Quantitative Pharmacology, Clinical Pharmacology & Safety Sciences, R&D, AstraZeneca, Gothenburg, Sweden
[2]Nonclinical Safety, Janssen R&D, Beerse, Belgium
[3]Drug Metabolism & Pharmacokinetics, Idorsia Pharmaceuticals Ltd, Allschwil, Switzerland
[4]Bioanalysis, Ferring, Copenhagen, Denmark
[5]Bioanalysis Immunogenicity & Biomarkers, GlaxoSmithKline R&D, Ware, UK
[6]Bioanalytical Services, ARCinova, Alnwick, UK
[7]Pharmacokinetics & Drug Metabolism, Menarini Ricerche S.p.A., Pomezia, Italy
[8]European Bioanalysis Forum vzw (EBF), Havenlaan 86c b204, 1000 Brussel, Belgium
*Author for correspondence: chair@e-b-f.eu

[1]Arfvidsson C, Van Bedaf D, Globig S *et al*. *Bioanalysis* 12(14), 1033-1038 (2020).

- Highlighting the **need for improved data integrity compliance** in today's LC/MS workflow
- **Progress** can be made if/when all agree on a **common standard**.
- Focus on the bi-directional **data transfers** between information management (IM) system and LC/MS, using only a **minimum data set**, strictly required to **safeguard DI**

2020 e-Environment WS - Towards a vendor neutral bi-directional data transfer process

At last year's workshop a **vendor neutral data transfer model** was presented by a **joint software developer / instrument vendor team** as a response to EBF paper.



- Replacing current use of .txt files with **digitally signed vendor neutral .xml files** to significantly increase data security
- **Remove** manual and time-consuming **quality-control steps** to mitigate the DI risks
- Data transfers more **secure**, but also **easier to audit** and with a near zero impact for any **user experience**

In 2021 EBF continues the collaborations to facilitate in an implementation of the prototype

Key learnings for future DI challenges

- The EBF data transfer proposal was an attempt to **move away from the current status quo** and to showcase that **progress can be made** when
  - all **relevant parties** are **present** round the table
  - a **limited scope** is agreed
  - BioA come together with **one voice** and **one request**

- We think that this could be used as an **inspiration** to facilitate in **additional DI challenges**
  - considering additional platforms/systems
  - looking at the complete data set
  - long-term storage and archiving
  - file-less interface solution

A continuous engagement and dialogue between all relevant parties is critical to mitigate future DI challenges

Acknowledgements

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  - David Van Bedaf (Janssen)
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  - Jens Sigh (NovoNordisk)
  - Yvan Verlinden (Janssen R&D)
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  - Dave Abramowitz (Sciex)
  - Arjan Timmerman (Waters)
  - Burkhard Schaefer (BSSN-software)

- EBF core community

Thank you for your attention!

- Any questions?

Contact Information

Questions: info@e-b-f.eu

European Bioanalysis Forum vzw

www.e-b-f.eu