Ensuring the Integrity of Electronic Health Records

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The Best Practices for E-records Compliance

Orlando López

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For Lizette, Mikhail Sr., István, Christian, and Mikhail Jr.
who continue making the journey of life worthwhile.

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Foreword

Orlando López is a well-recognized name in the realm of computer system e-compliance and validation.

Regulatory agencies have published many new or revised regulations and guidance relating to electronic/automated systems and any data created or managed within these. It can be quite a task following these regulatory documents and, even more so, to interpret them. At the same time, the regulated healthcare industry continues to increase their use of automated systems, for reasons of efficiency, cost, business need, and finally compliance. As a consequence, the integrity of electronic data/records is of paramount importance to industry, or else consequences can be dire.

This book is, therefore, a useful tool for those working in the field and those with just an academic interest. Orlando covers the subject from a variety of viewpoints: regulators, industry, suppliers, and technology in the 24 chapters of this book. It therefore definitely has something of interest for everyone.

Given that in the experience of regulatory agencies and many an auditor, the industry is still a long way from having full and commendable controls over electronic records integrity, this book should be an excellent aide to advance the state of compliance. I wish it all the success it deserves.

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Vice President Technical, Parexel
March 2020

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Preface

> Because the data have broad public health significance, they are expected to be of high quality and integrity.
>
> **US FDA, Pharmaceutical CGMP for the 21st Century – A Risk-Based Approach, Final Report," September 2004.**

Data integrity (1) (DI) has been one of the foundations of the Current Good Manufacturing Practice (2) (CGMP) principles for years.

As an example, the European Union (EU) Commission Directives 91/412/EEC (1991) and 003/94/EC (1994) in Article 9 item 2, and the 21 Code of Federal Regulation (CFR) Part 211.68 (1976) contain the requirements associated with DI in the EU and United States (US), respectively.

Falsification of data is considered by the regulatory agencies and competent authorities a critical deficiency to the regulated entity (3).

On the other hand, the information properly recorded is the basis for manufacturers to assure product identity, strengths, purity, and safety (4). The collected electronic records (e-records (5)) also demonstrate that the manufacturing process adheres to the CGMP, including instructions.

All data (paper and electronic) generated throughout a product's lifecycle must be accurate, auditable, in conformance with data definitions, complete, consistent, with integrity, provenance, and valid. This includes data generated during clinical or pre/post-approval stages.

Multiple DI citations during the last years have been reported by the US Food and Drugs Administration (FDA) investigators and European inspectors. A sample of EU Non-Compliance Reports referencing DI issues can be found in Appendix VI. Many US FDA Warning Letters (WL) and EU Non-Compliance Reports deal with serious DI violations.

DI questions have been and will continue to be the focus of many CGMP inspections. Consequently, the main international authorities and

organizations – CEFIC, CFDA, EMA, EU Annex 11, EU OMLC, Health Canada, ICH E6, MHRA, PIC/S, SIDGP, TGA, US FDA, and WHO – published documents describing the regulatory expectations with DI.

Although all guidelines are not intended to impose an additional regulatory burden to the regulated companies, a lot of hesitation predominates the pharmaceutical industry on how to implement these requirements into the daily business and how to integrate suppliers' involvement.

The objective of this book is to provide solutions to the regulated user pertinent to the e-records integrity situations. Some chapters update the information provided in my first book about e-records integrity (6).

Data integrity refers to whether data is trustworthy. Just because data is trustworthy does not mean it is also useful (7). The usefulness of data is achieved by implementing data quality into the practices of data handling (8).

Each chapter in this book provides practical information to enable compliance with e-records integrity while highlighting and efficiently integrating worldwide regulation into the subject. The ideas presented in this book are based on many years of experience in the regulated industries in various computer systems development, maintenance, and quality functions. Based on risk assessment principles, a practical approach is presented to guide the readers around the technical, design, and testing aspects of the e-records integrity controls recommended in worldwide regulations and guidelines.

As in my first book about e-records integrity, out of the scope of this one is the behavioral aspects of regulated life science industries that knowingly employ unreliable or unlawful activities.

Enjoy the reading. If you have any suggestion for improvement or any question, send it to olopez6102@gmail.com.

Orlando López
SME – E-records Quality

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1. Data integrity - The property that data has not been altered in an unauthorized manner since it was created, while in transit, during processing or stored. (NIST SP 800–57 Part 1).
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4. Wechsler, J., "Data Integrity Key to GMP Compliance," *BioPharma International*, 27(9), September 2014, pp 40–45.
5. An e-record is a collection of related data treated as a unit initially recorded in an electronic format that requires a computer system to access or process (SAG, *"A Guide to Archiving of Electronic Records*," February 2014).
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Chapter 1

Introduction

DI is a critical aspect to the design, implementation, and usage of any system which stores, processes, or retrieves data. The overall intent of any DI technique described in this book is the same: ensure data is recorded exactly as intended and upon later retrieval, ensure the data is the same as it was when it was originally recorded. Any alteration to the data is traced to the person who performed the modification.

> Records should be maintained to demonstrate that the quality system has operated effectively and that the specified requirements have been met.
>
> **Australian Code of Good Manufacturing Practice for human blood and blood components, human tissues and human cellular therapy products, April 2013.**

Any possible concern related to the reliability of data must be identified and understood for appropriate controls to be put in place.

The responsibility regarding accurately handling electronic records (e-records) and the integrity of such e-records lies with the manufacturer or distributor undergoing inspection. These entities have full responsibility to assess their data handling systems for potential vulnerabilities and take steps to design and implement good e-records governance practices to ensure that e-records integrity is maintained (1).

Since the publication of my first book about DI (2) in 2017, the information about DI in the regulated industry has increased by the multiple publications drafted and finalized.

The new/updated publications since 2017 are:

- Health Canada Good Manufacturing Practices (GMP) Guidelines, Version 3 (GUI-0001), February 2018
- MHRA, GxP Data Integrity Guidance and Definitions, March 2018
- Russia Federal State Institute of Drugs and Good Practices (SIMGP), Data integrity and validation of computerized systems, August 2018
- PICS, Good Practices for Management and Integrity in Regulated GMP/GDP Environments (PI 041–1 (Draft 3)), November 2018
- US FDA, Data Integrity and Compliance with Drug CGMP. December 2018
- CEFIC, Practical risk-based guide for managing data integrity, March 2019
- WHO, Guideline on Data Integrity (Draft), October 2019
- US FDA and MHRA, Data Integrity in Global Clinical Trials, December 2019
- IPEC, Data Integrity for Pharmaceutical Grade Excipients, April 2020
- OECD, Advisory Document on GLP Data Integrity (Draft), August 2020
- NMPA (former CFDA), "Drug Data Management Practices Guidance," December 2020

All guidance documents can be found at https://drive.google.com/drive/folders/1pB9XE29MuFpCBmNpQq0iG8RubmOCPe-u?usp=sharing

The industry has paid more attention to DI as a result of the regulatory agencies' publications. In addition, the amount of materials published by regulated users is massive.

DI continues to be globally a major concern to all regulatory agencies.

This book is divided into 24 chapters and 5 appendices relevant to production systems and quality control systems and pertinent to medicine manufacturers.

This book updates previous written practical information to enable a better understanding of the controls applicable to e-records. It highlights the e-records suitability implementation and associated risk-assessed controls, and e-records handling (3).

Chapter 2, "E-records Lifecycle Revisited," updates the electronic e-records lifecycle by adding two new phases to the typical lifecycle covered in the regulatory guidelines. These two new phases are related to the design of the e-records set. These two new phases are implemented before starting to collect e-records.

Chapter 3, "Data and E-records Lifecycles – A Comparison," discusses the correlation between data and e-records lifecycle.

Chapter 4, "MHRA Guidance – Revisited," is an analysis of the most recent revision (March 2018) guidance document of the Medicines and Healthcare Products Regulatory Agency (MHRA, United Kingdom (UK) medicines and medical devices regulatory agency).

The key expectations of EU CGMPs inspectors in the area of e-records integrity can be found in Chapter 5, "E-records Integrity Expectations of EU GMP Inspectors."

Based on a presentation I did in August 2018 (4), Chapter 6, "Comparison of Health Authority E-records Integrity Expectations," highlights the e-records integrity-related guidance documents published by Health Authorities only.

Chapter 7, "Maxims of E-records Integrity," discusses the e-records integrity principles applicable to medicine manufacturing operations. The lifecycle, the validity and fidelity, and the reliability of e-records integrity depend on maxims or fundamental rules for the effective handling of e-records integrity.

The vulnerabilities of e-records may be used to undermine the quality of records and may ultimately undermine the quality of medicinal products (1). Chapter 8 examines the typical vulnerabilities of e-records. The risk assessment performed at the beginning of a records handling implementation uncovers these vulnerabilities. Based on Chapter 8, Chapters 9 and 10 discuss the risk assessment and the handling, respectively, of e-records vulnerabilities.

Chapter 11, "Security Service," focuses on the security controls expected by worldwide regulatory agencies and competent authorities. Focal items include access control, password policy, and audit trails.

The required controls on computer-generated raw data in medicine manufacturing operations are discussed in Chapter 12, "Defining and Managing Manufacturing Data."

Transient data controls are discussed in Chapter 13.

Chapter 14 considers the critical issue of date and timestamping in digital environments.

E-records migration is the process of transferring e-records and related metadata between one durable storage location, format, or computer system to another. This subject is addressed in Chapter 15.

Chapter 16, "Ensuring E-records Integrity of Cloud Service Providers," provides the activities which the regulated entity and the cloud service provider must implement to safeguard the integrity of e-records.

Hybrid situations include combinations of paper records (or other non-electronic media) and e-records, paper records and electronic signatures,

or handwritten signatures executed to e-records. Chapter 17 addresses the issues associated with records of hybrid systems.

Centered on information security, Chapter 18, "Technologies Supporting E-records Integrity," provides a broad overview of the cryptographic technologies that can keep e-records integrity for any CGMP-regulated activity.

Chapter 19 describes the integration of the computer system and e-records lifecycles.

Chapter 20 covers miscellaneous e-records integrity issues such as BaaS, audit trails reviews, testing audit trails, database integrity, testing the retention of e-records, and e-records integrity in wireless environments.

A manufacturing-related e-records remediation project is re-examined in Chapter 21.

My advice on how to design e-records integrity into your practices is offered in Chapter 22.

Data integrity refers to the trustworthiness of data. Evidently, just because data is trustworthy, it does not mean it is also useful. The usefulness of data is achieved by implementing data quality into practices of data handling. Elements to consider in data quality are presented in Chapter 23. The objective of this chapter is to modify the mind frame in our industry and establish data quality in our practices.

The emphasis in this book is e-records integrity in medicine manufacturing practices regulations.

To bring up to the reader additional information, this book refers to relevant regulations/guidance. Some descriptions are based on listed guidance, but judicious editing was necessary to fit the context of this book.

It is not the intention of this book to develop a standard for the regulated industry. This book intends to guide how the industry can effectively manage e-records integrity vulnerabilities and raise basic compliance in this area.

Except for the definition of DI, this book is consistent with the UK MHRA (5) and the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) (6) DI guidance documents.

The recommendations to implement e-records controls, as described in this book, are purely from the standpoint and opinion of the author and should serve as a suggestion only. They are not intended to serve as the regulators' official implementation process.

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3. Committee on National Security Systems Instruction (CNSSI), "Glossary," CNSSI 4009, April 2015.
4. NIST, *Managing Information Security Risk* (Special Publication 800–39, National Institute of Standards and Technology, March 2011).
5. Health Canada, "GMP Guide for Drug Products (GUI-0001-ENG)," February 2018.
6. NIST, *An Introduction to Computer Security: The NIST Handbook*, Chapter 6, Computer Security Risk Management (Special Publication 800-12 Rev. 1, National Institute of Standards and Technology, June 2017).
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1. Health Canada, "Good Manufacturing Practices Guide for Drug Products, GUI-0001," February 2018. https://lnkd.in/dU8N7PB.
2. E-records Handling – The process of ensuring that data is stored, archived or disposed of safely and securely during and after the decommissioning of the computer system.
3. WHO, "Guideline on Data Integrity," QAS/19.819, October 2019 (Draft).
4. Critical e-records – Critical e-records is interpreted as meaning e-records with high risk to product quality or patient safety. (ISPE GAMP COP Annex 11 – Interpretation, July/August 2011).
5. EU, "Questions and Answers: Good Manufacturing Practice and Good Distribution Practice, Data Integrity," August 2016. https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/guidance-good-manufacturing-practice-good-distribution-practice-questions-answers#data-integrity-(new-august-2016)-section.
6. Russia Federal State Institute of Drugs and Good Practices (SIDGP), "Data Integrity & Computer System Validation Guideline," September 2018 (Draft).
7. ISPE GAMP Forum, "Risk Assessment for Use of Automated Systems Supporting Manufacturing Processes – Part 2 – Risk to Records," *Pharmaceutical Engineering*, 23(6), November/December 2003.

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1. Security – The protection of computer hardware and software from accidental or malicious access, use, modification, destruction, or disclosure. Security also pertains to personnel, data, communications, and the physical protection of computer installations. (IEEE)
2. EU Annex 11, "Glossary – System Owner."
3. MHRA, "MHRA GxP Data Integrity Guidance and Definitions," March 2018.
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2. Raw data is defined as the original record (data) which can be described as the first capture of information, whether recorded on paper or electronically (MHRA).
3. ISO 9001:2015, "Quality Management Systems – Requirements," 4.2.4 Control of Records.
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15. A DMZ is a physical or logical subnetwork that contains and exposes an organization's external-facing services to a larger and untrusted network, usually the Internet. The purpose of a DMZ is to add a layer of security to an organization's local area network (LAN); an external network node only has direct access to equipment in the DMZ, rather than any other part of the network.
16. 21 CFR Part 211.160; EU Chapter 4 Section 4.8; ICH Q7 Section 6.14.
17. López, O., *Computer Infrastructure Qualification for FDA Regulated Industries*. (PDA and DHI Publishing, LLC, River Grove, IL, 2006).
18. EU, "Questions and Answers: Good Manufacturing Practice and Good Distribution Practice, Data Integrity," August 2016. https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/guidance-good-manufacturing-practice-good-distribution-practice-questions-answers#data-integrity-(new-august-2016)-section
19. US FDA, "CPG Section 425.400 – Computerized Drug Processing; Input/Output Checking," September 1987.
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2. Reliable data – A reliable data is one whose content can be trusted as a full and accurate representation of the transaction, activities, or facts to which they attest and can be depended upon during subsequent transaction or activities. (NARA).
3. US FDA, "Data Integrity and Compliance with Drug CGMP, Q&A," December 2018.
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5. López, O., *Computer Infrastructure Qualification for FDA Regulated Industries*. (PDA and DHI Publishing, LLC, River Grove, IL, 2006).

6. Interface – In this chapter interface means that data is received from a sending system and forwarded to a receiving system without permanent storage of data in this interfacing system. (CEFIC, "*Practical Risk-based Guide for Managing Data Integrity*," March 2019 (Rev 1)).
7. EU Annex 11 p5.
8. MHRA, "GxP Data Integrity and Definitions," March 2018.
9. López, O., "Digital Date and Time Stamps," In: *Pharmaceutical and Medical Devices Manufacturing Computer Systems Validation*. (CRC Press, Boca Raton, FL, 1st ed., 2018). pp 201–205.
10. López, O. "Overview of Technologies Supporting Security Requirements in 21 CFR Part 11 – Part II," Pharmaceutical Technology, March 2002.
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3. US FDA, "21 CFR Part 11 - Electronic Records; Electronic Signatures; Final Rule – Preamble," Comment 74, March 1997.
4. Time drift is when two or more servers do not have identical times. The discrepancy can vary from seconds to minutes and can become extensive if left unchecked.
5. Kerberos (http://www.isi.edu/gost/info/Kerberos/) is an industry-standard authentication system suitable for distributed computing using a public network.

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2. Service provider – An organization supplying services to one or more internal or external customers. (ITIL Service Design, 2011 Edition).
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7. "Article 579 Item 2 in the Resolution of the Executive Board No. 17, Brazilian GMPs," April 2010.
8. ISO 9001, Quality Management Systems – Requirements (Section 4.1).
9. European Union Agency for Network and Information Security (ENISA), "Cloud Security Guide for SMEs," April 2015.
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1. López, O., "EU Annex 11 and Data Integrity: Designing Data Integrity into your Practices," In: *Paper Presented at the 2014 ISPE Annual Meeting*, Las Vegas, NV, 12–15 October 2014.
2. Integrity – the degree to which a system or component prevents unauthorized access to, or modified of, computer programs or data. (IEEE).
3. Electronic record – information recorded in electronic form that requires a computer system to access or process. (SAG, "A Guide to Archiving of Electronic Records," February 2014).
4. Wechsler, J., "Data Integrity Key to GMP Compliance, Pharmaceutical Technology," September 2014.
5. NIST, *Recommendation for Key Management, Part 1: General*. (Special Publication 800–57 Part 1 Rev 4, July 2015).
6. López, O., "Trustworthy Computer Systems," In: *Data Integrity in Pharmaceutical and Medical Devices Regulation Operations*. (CRC Press, Boca Raton, FL, 1st ed., 2017). pp 101–119.
7. Vibbert, J.M., "The Internet of Things: Data Protection and Data Security," *Global Environment Information Law Journal*, 7(3), Spring 2016.
8. Davis, L., "MHRA: Data Integrity defined?" *PharmOut*. https://www.pharmout.net/mhra-data-integrity-defined/.
9. Information security – is a set of strategies for managing the processes, tools and policies necessary to prevent, detect, document and counter threats to digital and non-digital information. Infosec responsibilities include establishing a set of business processes that will protect information assets regardless of how the information is formatted or whether it is in transit, is being processed or is at rest in storage. (http://searchsecurity.techtarget.com/definition/information-security-infosec).

10. Cryptographic – It is the practice and study of techniques for secure communication in the presence of third parties. (http://searchsoftwarequality.techtarget.com/definition/cryptography).
11. In this chapter "CGMP regulated activities" is defined as the manufacturing-related activities established in the basic legislation compiled in Volume 1 and Volume 5 of the publication "The Rules governing medicinal products in the European Union" http://ec.europa.eu/health/documents/eudralex/index_en.htm, US FDA 21 CFR Part 211, "Current Good Manufacturing Practice In Manufacturing, Processing, Packing or Holding of Drugs; General and Current Good Manufacturing Practice For Finished Pharmaceuticals" or any predicate rule applicable to medicinal products for the referenced country.
12. Digital signature – Digital signature means an electronic signature based upon cryptographic methods of originator authentication, computed by using a set of rules and a set of parameters such that the identity of the signer and the integrity of the data can be verified. (US FDA 21 CFR Part 11.3(5)).
13. Virtual Private Network – Describes the use of encryption to provide a secure telecommunications route between parties over an insecure or public network, such as the internet.
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15. IT Infrastructure Library (ITIL), "The Official Introduction to the ITIL Service Lifecycle," 2007.
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17. "NIST SP 800–57P1 – Recommendation for Key Management," (Gaithersburg, MD, January 2016).
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19. Symmetric-key Algorithm – It is a cryptographic algorithm that uses the same key to encrypt and decrypt data.
20. Alanazi, H., Zaidan, B., Zaidan, A., Jalab, H., Shabbir, M. Al-Nabhani, Y., "New Comparative Study Between DES, 3DES and AES within Nine Factors," *Journal of Computing*, 2(3), March 2010, 152–157. ISSN 2151-9617.
21. A public-key certificate (also known as a digital certificate or identity certificate) is an electronic representation of identification or passport, issued by a certification authority (CA) to a PKI user, stating identification information, validity period, the holder's public key, the identity and digital signature of the issuer, and the purpose for which it is issued.
22. https://searchsecurity.techtarget.com/definition/X509-certificate.
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24. MHRA, "MHRA GxP Data Integrity Guidance and Definitions," March 2018.

25. EudraLex, The Rules Governing Medicinal Products in the European Union, Volume 4, "EU Guidelines to Good Manufacturing Practice, Medicinal Products for Human and Veterinary Use Part 1, Annex 11 – Computerized Systems," June 2011.
26. MHRA, "MHRA GxP Data Integrity Guidance and Definitions," March 2018.
27. A trustee is the user account, group account, or logon session to which an access control entry (ACE) applies. Each ACE in access (ACL) has one security identifier (SID) that identifies a trustee.
28. PI 041–1, "Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments," *Pharmaceutical Inspection Co-operation Scheme (PIC/S)*, November 2018, (Draft 3).
29. Private key – a cryptographic key that can be obtained and used by anyone to encrypt messages intended for a recipient, such that the encrypted messages can be deciphered only by using a second key that is known only to the recipient.
30. A keyed-hash message authentication code (HMAC) is a specific type of message authentication code (MAC) involving a cryptographic hash function (hence the "H") in combination with a secret cryptographic key.

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2. PI 011–3, "Good Practices for Computerised Systems in Regulated "GXP" Environments," *Pharmaceutical Inspection Cooperation Scheme (PIC/S)*, September 2007.
3. EudraLex, "The Rules Governing Medicinal Products in the European Union, Volume 4, EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use, Annex 20 – Quality Risk Management," February 2008.
4. MHRA, "MHRA Expectation Regarding Self-Inspection and Data Integrity," September 2014.
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3. López, O., *Computer Infrastructure Qualification for FDA Regulated Industries*. (PDA and DHI Publishing, LLC, River Grove, IL, 2006).
4. US FDA, "Guidance for Industry: Electronic Records; Electronic Signatures — Scope and Application," August 2003.
5. PI 041–1, "Good Practices for Data Management and Integrity in Regulated GMP/GDP Environment," *Pharmaceutical Inspection Co-operation Scheme (PIC/S)*, November 2018 (Draft 3).
6. "US Federal Register vol 43 no 45013," September 1978.

7. Conseil Européen des Fédérations de l'Industrie Chimique (CEFIC), "Practical Risk-based Guide for Managing Data Integrity," March 2019 (Rev 1).
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12. US FDA CPG 7132a.11, "Computerized Drug Processing; CGMP Applicability To Hardware and Software," September 1987.

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2. Conseil Européen des Fédérations de l'Industrie Chimique (CEFIC), "Practical Risk-Based Guide for Managing Data Integrity,". March 2019 (Rev 1).
3. EU, "Questions and Answers: Good Manufacturing Practice and Good Distribution Practice, Data Integrity," August 2016. https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice/guidance-good-manufacturing-practice-good-distribution-practice-questions-answers#data-integrity-(new-august-2016)-section.
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2. A model to describe, assess, and/or predict quality.
3. The term "GMP regulated activities" in the EU context is defined as the manufacturing related activities established in the basic legislation compiled in Volume 1 and Volume 5 of the publication "The Rules governing medicinal products in the European Union," http://ec.europa.eu/health/documents/eudralex/index_en.htm.
4. Commission Directive 2003/94/EC laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use, October 1994.
5. Commission Directive 91/412/EEC laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products, July 1991.
6. A directive is a legal act of the European Union, which requires member states to achieve a particular result without dictating the means of achieving that result. It can be distinguished from regulations which are self-executing and do not require any implementing measures. Directives normally leave member

states with a certain amount of leeway as to the exact rules to be adopted. Directives can be adopted using a variety of legislative procedures depending on their subject matter.
7. EC, "Volume 4 – EU Guidelines to Good Manufacturing Practice: Medicinal Products for Human and Veterinary Use – Annex 11: Computerized Systems," (European Commission, Brussels, June 2011). pp 1–4.
8. Health Canada, "Good Manufacturing Practices (GMP) Guidelines – GUI-0001," February 2018.
9. "Annex 11 to PIC/S Guide to Good Manufacturing Practice for Medicinal Products, Document PE 009–10, PIC/S Secretariat, 14 rue du Roveray, CH-1207 Geneva," January 2013.
10. System owner – The person is responsible for the availability, and maintenance of a computerized system and for the security of the data residing on that system. (EU Annex 11).
11. Non-conformance – A departure from minimum requirements specified in a contract, specification, drawing, or other approved product description or service.
12. EudraLex, "The Rules Governing Medicinal Products in the European Union Volume 4, EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use Chapter 1, Pharmaceutical Quality System, Section 1.4A (xiv)," January 2013.
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5. Syncsort Editors, "Data Integrity vs. Data Quality: How Are They Different?" January 2019. https://blog.syncsort.com/2019/01/data-quality/data-integrity-vs-data-quality-different/.
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8. US NARA, "Records Management Guidance for Agencies Implementing Electronic Signature Technologies," October 2000.
9. EU GMP Annex 11 p5, "Computerised Systems," June 2011.
10. PI 041–1, "Good Practices for Data Management and Integrity in Regulated GMP/GDP Environment," *Pharmaceutical Inspection Co-operation Scheme (PIC/S)*, November 2018 (Draft 3).
11. US FDA, "21 Code of Federal Regulations Part 211.68(b)," December 2008.
12. EU GMP Annex 11 p9, "Computerised Systems," June 2011.
13. EU GMP Annex 11 p6, "Computerised Systems," June 2011.
14. US FDA, "Guide to Inspection of Computerized Systems in the Food Processing Industry," April 2003.
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1. Canadian Health Care GMPs C.02.024.1 – 6.
2. TGA, "Australian Code of Good Manufacturing Practice for Human Blood and Blood Components, Human Tissues and Human Cellular Therapy Products,". Version 1.0 April 2013.
1. López, O., "Electronic Records Integrity in a Data Warehouse and Business Intelligence," *Journal of Validation Technology Compliance*, 22(2), April 2016.
2. Raw Data – Raw data is defined as the original record (data) which can be described as the first capture of information, whether recorded on paper or electronically. Information that is originally captured in a dynamic state should remain available in that state. (MHRA)
3. Data – Facts, figures and statistics collected for reference or analysis. All original records and true copies of original records, including source data and metadata and all subsequent transformations and reports of these data, that are generated or recorded at the time of the GXP activity and allow complete reconstruction and evaluation of the GXP activity. (MHRA)
4. http://www.pharmtech.com/ema-creates-taskforce-big-data-0 and http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2017/03/news_detail_002718.jsp&mid=WC0b01ac058004d5c1.
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6. Data Process Mapping – It is a generation of a visual representation of the creation and movement of data through the business process including documentation of the systems used. (CEFIC, "*Practical Risk-based Guide for Managing Data Integrity*," March 2019 (Rev 1)).
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