# Technical Report No. 80

# Data Integrity Management System for Pharmaceutical Laboratories

## PDA Data Integrity Management System for Pharmaceutical Laboratories Technical Report Team

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# Data Integrity Management System for Pharmaceutical Laboratories

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# 1.0   Introduction

A primary responsibility of pharmaceutical manufacturers is to provide safe and efficacious products of appropriate quality to patients and consumers by assuring decisions are based on accurate, reliable, truthful, and complete data. Data integrity is a mandatory requirement and key concern of health authorities. At the time of this writing, data integrity citations, especially those related to computerized systems in laboratory and manufacturing environments, have resulted in a number of significant, well-publicized enforcement actions from the U.S. Food and Drug Administration (FDA) and other regulatory authorities, including the United Kingdom Medicines and Healthcare products Regulatory Agency (MHRA), and European Medicines Agency (EMA). These enforcement actions have taken the form of warning letters, import alerts, statements of GMP noncompliance, notices of concern, and refusals to accept and/or approve applications. Many of these actions involve failing to document or report alterations, deletions, fabrications, and/or misrepresentations of data in quality control laboratories. The range of data integrity findings spans the spectrum from unintentional errors in data reporting and lack of controls necessary to ensure data authenticity to intentional acts involving failure to report data and/or falsification of records.

The spike in enforcement actions, in part, is linked to improved detection capabilities, which have become more prevalent as technological enhancements have extended the level of automation in both pharmaceutical quality control and microbiology laboratories. The extensive use of computer systems and digital media for product testing, as well as in ancillary support systems, provides more visibility to data integrity gaps than was evident with static paper records.

The consequences of failing to uncover data integrity problems through self-discovery or internal audit programs before they are found by regulatory agency inspectors can impact the outcome of the inspection in ways that could be very damaging to a business. Similarly, the business impact on contract manufacturers, contract laboratories, and suppliers can be very serious if they fail to uncover and disclose data integrity problems before regulators or their customers' auditors do. One of the responsibilities of regulatory agency investigators is to verify the accuracy, reliability, and integrity of data submitted in written form or other media prior to, during, or after an inspection, or as part of a drug submission for market authorization, annual report, mandatory quality defect report (e.g., Field Alert), or Adverse Event Report. The regulatory investigators (also referred to as inspectors in some regulatory regions) may detect and document inconsistencies between the information provided and available for review that may suggest data integrity problems that the company will need to correct. Such inconsistencies can be used by the health authority as the basis for a regulatory action or formal written communication. From the regulators' perspective, noncompliance with good data integrity practices is not based solely on the intent to mislead authorities to believe that all laboratory activities are performed according to current good manufacturing practices (CGMP) when they are not. Requirements for appropriate laboratory records and documentation began with the first GMP regulations and expectations have been clarified in other publications such as the FDA Guide to Inspections of Pharmaceutical Quality Control Laboratories published in 1993 *(1)*.

In some instances, a regulatory agency may decide to ban products from entering its jurisdiction and order or recommend that the potentially affected product be removed from the market.[1] Regulatory agencies and organizations that oversee a manufacturing site's adherence to CGMPs have made significant efforts to communicate their expectations to both industry and their inspectorates about managing data and ensuring its integrity. Some of these expectations can be found in the U.S. FDA *Draft Guidance for Industry on Data Integrity and Compliance with CGMP (*April 2016), World Health Organization (WHO) *Guidance on Good Data and Record Management Practices* (May 2016), Draft PIC/S Guidance *Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments* (August 2016), MHRA *GXP Data Integrity Definitions and Guidance* (March 2018), *Guidance for Industry, Part 11, Electronic Records; Electronic Signatures—Scope and Application* (August 2003),

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[1] Some regulatory agencies have the legal authority to order product removal from the market, while others can only recommend such actions.

and *EU Annex 11: Computerised Systems* (June 2011) *(2–8).* Even older health authority publications on traditional audit practices may also be helpful in identifying and preventing data integrity issues in laboratories. Some examples include: FDA Guide to Inspections of Pharmaceutical Quality Control Laboratories *(1)* and the European Medicines Agency (EMA) Questions and Answers: Good Manufacturing Practice–Data Integrity *(9).*

This increased focus on data integrity by health authority investigators has resulted in the need for firms to modify and harmonize strategies to address data integrity gaps in a manner that promotes transparency, accuracy, and reliability of data as well as detection of data integrity breaches.

Industry can use technology shifts, along with the new awareness that stems from recent regulatory sanctions, to enhance their efforts to improve processes and establish mechanisms for detection and mitigation of gaps that impact data integrity in paper, hybrid, and computerized systems. The overall goal of ensuring data reliability is to protect patients as well as provide competitive sustainability.

## 1.1    Purpose

This technical report, developed by subject matter experts from the global pharmaceutical industry and regulatory agencies, summarizes data integrity risks and the best practices, including audit approaches, that can be utilized to develop a robust data integrity management system for laboratory settings with both manual and electronic processes that firms can follow to achieve compliance and mitigate risks. Current regulatory trends indicate breaches in data integrity and a need for additional guidance regarding the regulatory expectations. The intent of this report is to outline regulatory requirements and expectations, along with best industry practices to ensure data integrity, to highlight common gaps in laboratory data management practices, and to recommend methods of remediation.

For the purpose of this report, the term "data integrity" means the degree to which data are complete, consistent, accurate, trustworthy, and reliable and that these characteristics of the data are maintained *(3)* to support the quality of drug products throughout their lifecycle from the point of development through commercialization. The reliability of such data is necessary to support clinical trials, product development, manufacturing, testing, and regulatory reporting requirements, all of which are dependent on the processes and controls in place from the point of data creation to ensure data cannot be altered, deleted, omitted, or in any way modified to misrepresent what actually occurred. Data integrity is the cornerstone of establishing and maintaining confidence in the reliability of data.

## 1.2    Scope

This technical report focuses on the management of data integrity within pharmaceutical quality control analytical and microbiology laboratories and is also applicable to analytical development and R&D laboratories. It provides the framework and tools necessary to establish a robust data integrity management system to ensure data integrity for paper, hybrid, and computerized systems within the laboratory.

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