

# UPDATE

Food and Drug Law, Regulation and Education



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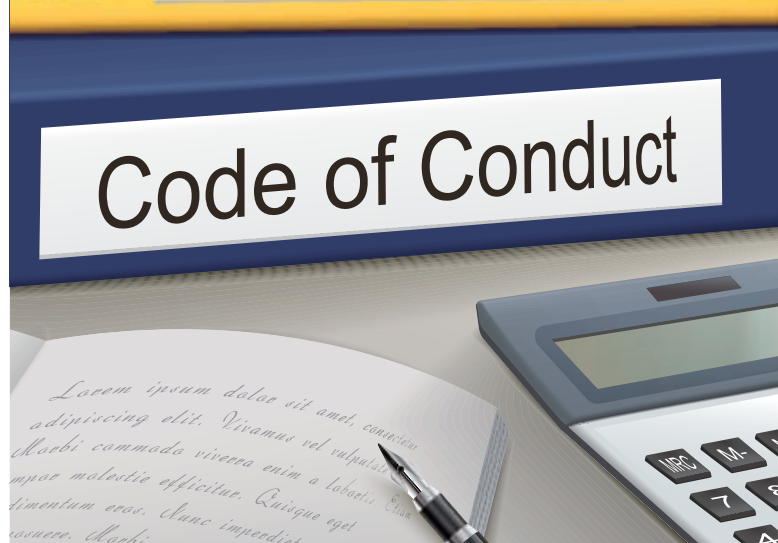
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# Elements of a Code of Conduct for Data Integrity in the Pharmaceutical Industry

By Denyse Baker



**D**ata integrity has been and currently is a major global concern of health authorities and the pharmaceutical industry. Although not a new issue, numerous recent health authority enforcement actions such as Warning Letters, Import Alerts, Product Detentions, and suspension or revocation of Marketing Authorizations has focused renewed attention on data integrity. Data integrity problems can result from lack of awareness of regulatory requirements, employee errors, failure to check accuracy of data, poorly designed processes, software or system malfunction, configuration problems with electronic data handling, or malfeasance by employees.

The Parenteral Drug Association (PDA) has been in dialogue with FDA on possible root causes and countermeasures for data integrity lapses, human error prevention, and means to promote quality culture. It has also conducted several conference sessions on data integrity, which have confirmed the urgency of the need to address this problem in a new way. In response, PDA has formed a Data Integrity Task Force that combines both industry and health authority points of view and is in the process of developing a set of tools to help industry combat data integrity problems including Technical Reports, Training Courses, Data Integrity Workshops, and Points to Consider documents.



**Denyse Baker** is director of Science and Regulatory Affairs for the Parenteral Drug Association (PDA). She has worked in pharmaceutical manufacturing and regulatory affairs for 28 years.

The impacts of employee attitudes and behaviors on quality in manufacturing were identified many years ago thanks to the work of W. Edwards Deming and others. Today, increasingly informed consumers and patients plus reduced margins for errors in manufacturing cost structures have created pressures to find new approaches to creating a culture of quality.<sup>1</sup> One of the foundational concepts identified by PDA members as important to preventing and uncovering data integrity issues is a common understanding of the expectations for employee and management conduct. With this in mind the PDA Data Integrity Task Force set about to create, and is pleased to make available to the pharmaceutical industry, a collection of recommended best practices for employee and management conduct related to data integrity in a ready-to-use format titled *Elements of a Code of Conduct for Data Integrity in the Pharmaceutical Industry*.

While many larger pharmaceutical firms likely already have internal codes of conduct, smaller manufacturing firms or those that supply raw materials, components, or testing services may not have taken this step in quality maturity. The Code of Conduct elements developed by PDA can be used directly by smaller firms or contractors to shore up existing quality systems and as a means of attracting future business. Larger firms or contractees may use these Code elements to assess their current internal codes or in drafting new or revising existing supply and quality agreements. The Code of Conduct for Data Integrity is intended to apply to employees and officers and third party suppliers and others acting on behalf or at the behest of the company, such as persons who develop, test, manufacture, or submit marketing authorizations for pharmaceutical and biological products. The elements can be used collectively

or in part to allow each company to establish its own policies, standards, procedures, code of conduct, or other quality system elements that define its requirements for data integrity. PDA has identified the following types of companies that could benefit from this Code of Conduct:

- Manufacturers of finished drug products for clinical trials, bioequivalence studies, and commercial distribution
- Companies that conduct clinical trials in support of new drug applications including, but not limited to: Investigational New Drug (IND), Clinical Trial Application (CTA), Investigational Medicinal Product Dossier (IMPD), Biologics License Application (BLA), Marketing Authorization Application (MAA), New Drug Application (NDA), and Abbreviated New Drug Application (ANDA)
- Laboratories that develop methods or formulations intended to support new drug applications or laboratories that analyze samples generated from clinical trials
- Manufacturers of excipients, intermediates, or active pharmaceutical ingredients (APIs)
- Contract manufacturing organizations (CMOs)
- Contract research organizations (CROs)
- Contract testing laboratories
- Contractors, consultants, suppliers, and vendors that provide services and data that support the production and control of APIs, drug or biological products

The Code is structured with a preamble containing an introduction to the purpose and scope followed by a listing of the key elements necessary to help ensure the reliability and integrity

of information and data throughout all aspects of a product's lifecycle. The language style for the Code Elements, specifically the use of terms such as "shall" and "must," was chosen to permit the Code to be enforceable by a company once adopted. These elements of a Code of Conduct for Data Integrity are intended to reinforce a culture of quality and trust within the pharmaceutical industry. It is not intended to be a regulatory standard or guidance, nor is it intended to supersede any country-specific or local laws and regulations governing labor, privacy, and/or employee rights.

The document has been developed through the collaboration of PDA members with experience in manufacturing operations, quality, auditing, compliance, and consulting and has been peer reviewed by attorneys with extensive food and drug law experience. It is intended to be used in whole or in part to guide a company's internal practices or in developing agreements with outsourcing partners or other suppliers. In order for the language used in the Code to be as globally applicable as possible, the document scope has been limited to drug and biological medicinal products. The same or similar concepts could be applied for device and combination products manufacturing. PDA is providing this document and these concepts as an example of best practices for the pharmaceutical industry.

The preamble to the PDA Code of Conduct for Data Integrity highlights both the privilege and the responsibility of all those involved in pharmaceutical manufacturing and control to adhere to the highest standards of quality essential for

positive patient outcomes. Senior Management must establish quality standards, requirements, and procedures, and is obligated to maintain and monitor the performance of the quality system that helps to ensure availability of safe and effective drugs. The company must maintain operational management oversight to demonstrate that each product has been developed, manufactured, or tested under conditions that are designed to ensure the reliability and integrity of information and data used to support its quality and fitness for use, and in accordance with applicable laws, regulations, and legislative directives of the regulatory authorities. Ensuring data integrity means collecting, documenting, reporting, and retaining data and information in a manner that accurately, truthfully, and completely represents what actually occurred.

Every employee at each company is responsible for his/her own conduct to maintain a bond of trust between the company and its stakeholders, namely the patients, health care providers, and regulators (i.e., to prevent a broken bond due to data integrity issues). Employees have a duty to perform their GxP functions in an ethical manner that meets company requirements and industry standards as articulated in company requirements, and in accordance with all relevant laws, regulations, or legislative directives of regulatory authorities.

By adopting the voluntary Code of Conduct, senior management is committed, as required by applicable law, to notify applicable licensing/regulatory authority(s) if the company discovers that a pending or approved marketing authorization or other submission to a regulatory authority

contains an untrue statement of material fact or omits material facts (e.g., information is false, misleading, inaccurate, or incomplete). If data, not submitted, but used to determine whether a product batch met specifications, are later found to be false, misleading, inaccurate, or incomplete, a company is committed to filing the appropriate notifications to health authorities (i.e., Field Alert, Biological Product Deviation Report (BPDR), or notification under the Falsified Medicines Directive (FMD)).

The body of the Code includes recommended provisions for employee and company conduct in the areas of Data Collection, Analysis, Reporting and Retention; Electronic Data Acquisition Systems, Electronic Access Security Measures; Auditing of Quality System for Data Integrity; Investigations of and Reporting Wrongful Acts and associated Disciplinary Actions for Employees; Notifying Regulatory Authorities about Data Integrity Issues; Data Integrity of Outsourced Services & Purchased Raw Materials; and Employee Training. It also includes a glossary of terms.

PDA believes these standard elements can also be useful when doing business in different geographical

locations with varying cultural norms. Research into human failures shows that employees do not set out with the intention of creating errors but their behaviors are often driven by unrealistic, unclear, or competing expectations and poorly designed processes.

In addition to the Elements of a Code of Conduct, PDA has developed a separate tool for assessing the maturity of the quality culture at a manufacturing site including the atmosphere for communication from the shop floor to management so that these processes and conditions could be improved, thus reducing risks of data integrity problems and other human errors or accidents. This assessment tool will be in pilot mode during the next few months and more details will be presented at the PDA/FDA Joint Regulatory Conference in September 2016.

PDA believes that by increasing the use of the concepts in the Code, expectations for employee and leadership conduct across the industry will become clearer and standardized allowing firms to uncover and prevent internal data integrity issues in advance of health authority inspections and reduce the number of serious

regulatory findings and resulting warning letters.

The PDA Elements of a Code of Conduct is available for free downloading at the following link: [pda.org/CodeofConduct](http://pda.org/CodeofConduct). We have made this available as a service to the pharmaceutical industry and just ask that you acknowledge PDA as the originator.

*If you have questions regarding the Code or would like more information about PDA's activities related to data integrity, please contact Denyse Baker ([baker@pda.org](mailto:baker@pda.org)). Additionally, the Task Force initially produced two videos that discuss some of the basic concepts and challenges, now available on the PDA website: <https://www.pda.org/pda-letter-portal/multimedia/video>.*

The author acknowledges the PDA Data Integrity Task Force and specifically Dr. Anil Sawant, Merck & Co., Inc., and Mr. Ron Tetzlaff, Paraxel, for their contributions to the Code. ▲

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1. A. Srinivasan, B. Kurey, Creating a Culture of Quality, HARVARD BUSINESS REVIEW, April 2014, available at: <https://hbr.org/2014/04/creating-a-culture-of-quality>.