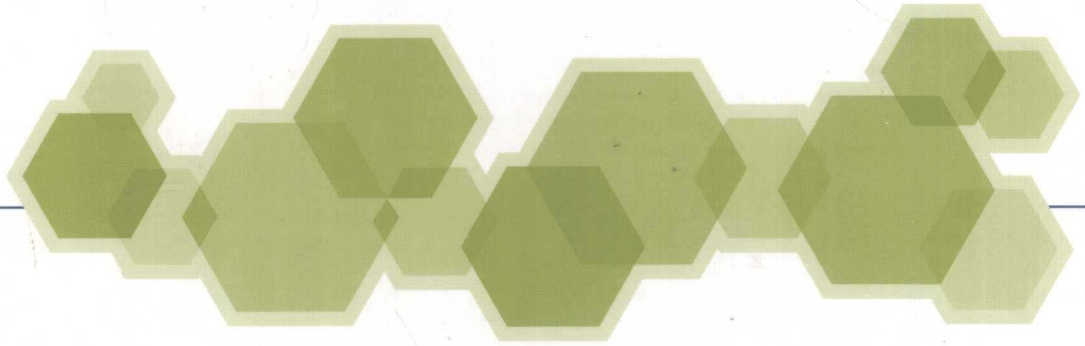
PHARMACEUTICAL QUALITY



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PDA
Bethesda, MD, USA
DHI Publishing, LLC
River Grove, IL, USA

10 9 8 7 6 5 4 3 2 1

ISBN: 1-930114-61-3

PDA
3 Bethesda Metro Center
Suite 1500
Bethesda, MD 20814
United States
301-986-0293

Davis Healthcare International Publishing, LLC
2636 West Street
River Grove
IL 60171
United States
www.DHIBooks..com

INTRODUCTION

RICHARD PRINCE

This is a book devoted to the ideal and the pursuit of quality. The term 'quality', a noun, describes the inherent characteristics or properties of things. It can also be equated with the conscious desire to attain and maintain something of value. Time can both add to and steal from it. For the purposes of this book, the concept of quality rests on three observations about us. Firstly, that we are internally driven to understand how the natural world works. Secondly, that we try to influence and improve our condition and our environment, even if it is for relatively short periods of time. Thirdly, that there is a worthy rationale, whether philosophical, religious or scientific, behind our yearning to understand and manipulate our world, however minutely that might be. If quality is an ideal worth pursuing, it can be, like a vessel at sea, swept away by the vicissitudes of human behavior, the structure of social and work organizations and the waves of random change. Consciously or not, we seek nothing less than the equilibrium of quality in our lives.

So, what is quality? In cultures with open, modern societies, it means personal freedom, thus the embrace of change and dissent. In cultures with closed, traditional societies, it means strict conformity to established precedent, thus the embrace of orthodoxy. Science finds its home in open societies. Quality may also be expressed in terms of personal values or attributes such as integrity, courage, and tolerance; in terms of business values such as economy, effectiveness and efficiency; in terms of process values such as reliability and sterility assurance; and in terms of product values such as uniformity, specificity, and safety.

The flow of people and the collision of their ideas add great meaning to our lives. We are an intensely social species. Good things, or preferred outcomes, do not occur in a vacuum. What are the human forces that motivate us to create, build, or to improve something? I maintain that humankind's common instinct for goodness (at least in

principle if not in practice) fuels our notions of what quality is. Most of us embrace the concepts of social justice and harmony. This suggests to me that there is an underlying ethical dimension to quality. This may be described as an abiding gesture to create good. Let's look at some of these forces, both intangible and tangible.

The intangible forces center on our knowing our history as a species. We have now been a direct witness and chronicler of human history for several millennia. History is instructive if anything else. It tells us something about the causes of human behavior and institutions, for example the development of organized religion, but it also reminds us of those things, or qualities, that we most cherish as a species. What are these qualities? They include our desire to be social creatures, bound together in societies, or civilizations, which self-regulate themselves much like the biochemical interplay at work in the simplest microorganism. Indeed, there is much to be said for simplicity as a virtuous quality. Even complex things, like people, can be more easily understood if the simpler needs of their nature are first understood. These core human needs include the desire to be secure, to be respected (and loved), and to be productive. It is not possible to succeed as an organization if the people that compose it do not perceive, themselves, to be successful. The art of quality requires us, therefore, to understand the very human dimension at stake in any organizational arrangement.

There are also tangible forces at work in producing a state of quality. These tangible forces tug at us daily and are found in our need for the protection of ourselves, our families, and those causes we care about. It is simply true that quality, as an attribute, is something desired by everyone. There is an imperative for us all to behave or to perform work in a 'quality way.' Failure to behave as expected can lead to loss of life. Failure to work as expected can lead to loss of career. The ideals, or perhaps meaning, of quality is inextricably bound with the concept of preferred or predicted outcomes. Thus, quality has a causal relationship to positive outcomes, not negative outcomes. Can it be said that a given system or process is operating with the characteristics of quality if it is operating consistently wrong (as measured against predefined acceptance criteria)? Of course not!

Can it further be said that a given system or process is operating with the characteristics of quality if it is operating inconsistently wrong (as measured against predefined acceptance criteria)? Well, maybe. Exactly knowing where to draw the plane as to where quality begins and ends is inexact at best. For example, what confidence do we have in the quality of a parenteral drug batch that was shown to be correctly manufactured yet failed to meet one of its (test) acceptance criteria? Not much, and such a batch should be denied entry into commerce. Further, what confidence do we have in the quality of a second parenteral drug batch that was plagued by process deviations yet met all of its test requirements? The answer is not automatic. How critical are the effects of the process deviations thought to be upon final product quality? How accurate and precise are the test systems used to measure the assorted quality attributes? Does the absence of required verification checks at

critical process points doom a batch even if meets all of its test requirements. If not, why not? Is quality defined by a complex interplay of multiple variables involving people, process, product and practice? All of this is tied up in our notion of quality. This book challenges us to think more deeply about the meaning of quality.

A book devoted to quality has the rather sanguine consequence of meaning that this is not a book about 'regulatory compliance,' a professional field of endeavor often blurred with the field of quality. A quality deficit can, if detected, lead to a compliance issue. For example, the absence of a Quality System itself, or its non-alignment with governing regulations, places a company in compliance jeopardy. Conversely, a quality deficit may not lead to a detectable compliance hit. For example, the absence of documented scientific rationale to support a given specification may go undetected by an auditor or investigator. A Quality System should in theory drive both quality and compliance, whether seen through the lens of the regulated or the regulator.

In the healthcare industry, quality means research innovation, speed-to-market, regulatory compliance, manufacturing reliability, product stability and, of course, business performance. There are the terms we all know: quality assurance, quality control, quality unit, quality system, quality management system, quality attributes, among others. There are also the definitions: for example, consistent conformance to requirements, meeting (or exceeding) customer expectations, and documented evidence of following rules and requirements. Is there something transcendent in meaning beyond these terms and definitions, something that aptly depicts or is representative of what quality is? And concerning quality, how should we build and measure it? The immodest goal of this book is for us all to think anew about quality.

In this book, the reader will find examinations of quality that are written from international, governmental, industrial, and individual perspectives. Collectively, these Chapters seek to enrich our recognition of what quality is, or what we think it is. The governing principle surrounding the structure of this book is its assertion that quality is a complex subject, one that is somewhat of a riddle. So, how again should we think of quality? Is there a model, or approach, that social scientists can take for examining the role of quality in history? Is quality an indivisible ethic? If so, are there universal indicators for perceiving and/or recognizing quality? Is quality, like love, timeless, ethereal, essential, universal, but equally unfathomable? Here is my answer: Quality is something we unconsciously provide and something we consciously want. Quality is about our priorities, and it is luminous. The spine of quality is now offered.

The first section of the book, encompassing ten Chapters, presents international and national systems (and perspectives) of quality. The opening Chapter, contributed by the World Health Organization, discusses the global disequilibrium of quality, and the 'divide' between perceptions and needs of quality that people have depending on where they live. The second Chapter written by a leading industry consultant takes a truly international perspective of the current state of Good Manufacturing Practices.

The third Chapter is written by a leading policy maker within the Food and Drug Administration and it articulates points to consider for the attainment of quality management practices in the American drug industry. What follows are Chapters describing quality in seven countries from four continents. The reader will therefore have the opportunity to review case studies from Australia, Britain, Canada, Germany, Israel, Japan and Singapore. These Chapters all essentially followed a common 'algorithm'. Namely, they define the government system (structure) responsible for regulating quality in the respective country; describe the associated regulations that cover quality; discuss (if applicable) how the "national system of quality" in a given country is related, juxtaposed, or affiliated with other so-called systems of quality within that country or with other countries; describe the dominant values (and underlying ethical criteria) associated with the given national system of quality; and finally describe the respective country's vision of quality.

The second section of the book, encompassing six Chapters, focuses on industrial quality systematics, the interplay of quality systems in commercial pharmaceutical manufacturing. This is offered as a practicum for the pharmaceutical industry. Quality systematics is defined herein as an organizational strategy that enables and supports good manufacturing practices and desired quality performance. A myriad of quality systems (e.g., facility qualification, contamination control, equipment qualification, method validation/verification, change control, training, and the like) are duly described and are applicable for properly operating a manufacturing plant, whether internal or external (i.e., contract service provider) to the company. The first Chapter offers a high-level, cross-linked analysis of quality systems resident in the pharmaceutical and allied industries. These component quality systems themselves organically form the Quality System. A second Chapter similarly describes a Quality System for contract service users. The third Chapter in this section succinctly describes quality in relation to computerization and automation, critical components of any modern manufacturing facility. The fourth Chapter details the quality systems required in Quality Control biopharmaceutical test departments. The fifth Chapter discusses the use of statistics to measure and improve manufacturing performance. The sixth Chapter provides an overview of pharmaceutical quality auditing methodologies.

The third and final section of the book, encompassing four Chapters, provides perspectives on quality from industry thought leaders. The first Chapter describes the pursuit of quality for biopharmaceuticals, paying homage to and building upon the quality principles given us by seminal thinkers like Deming, Juran, among others. The second Chapter discusses the dual perspectives of quality, from the prism of a former FDA investigator and, now, industry consultant. The third Chapter discusses the causal relationship between training and learning. The final Chapter of the book discusses the need to build quality into legal operations.

Language gives form to our experience of the world. It is the assessment of our experience that gives form to quality. There is nothing easy about achieving quality. It is a relentless pursuit of innovation, of fitness, of conformance, and of good. It is a conscious choice we make individually and collectively. Quality is prized, but one must know what quality is before its attainment can be justifiably claimed. In the final analysis, quality is a natural behavioral norm, characterized by a yearning to honor commitments, to improve conditions, and to seek relevance and a proper place in our large universe. Quality is nothing less than a philosophical calling, and the pursuit of quality is its own reward. If quality, like love and beauty, is a truly universal aspiration, it follows that the instinctive perception and conception of quality resides within us all. Enlightened leaders understand and heed this calling.

Richard Prince

Short Hills,
June 2004

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