BEC GLOBAL 2023 Services Catalog

Passion for Quality

BUSINESS EXCELLENCE CONSULTING

ACCREDITED IACET PROVIDER

Contact Information

www.bec-global.com info@bec-global.com
www.calidadpr.com info@calidadpr.com
Ph: +1.787.705.7272

Table of Contents

Welcome	3
About Us—History of BEC/BEC-GLOBAL	4
Our People	5
Remediation and Quality System Compliance Services	6-7
Training and Educational Services	8
Training and Education Courses	9-11
Audit and Assessment Services	12-14
Regulatory Affairs Services	14-15
FDA Inspection Support	16
Quality Culture	17
Data Integrity	18
Investigation and CAPA Systems Support	19
Human Error Investigation and Reduction	20
Outsourcing Activities	21
Publications: Books	22 - 24
Publications: Technical Articles	25 - 27
Accreditations	28

Welcome to the BEC-GLOBAL Services Catalog

Founded in 2005, Business Excellence Consulting Inc. (BEC) offers consulting, remediation, auditing, regulatory affairs, and training services for the FDA-regulated industry. As a worldwide leading company, BEC covers all your compliance and regulatory needs for the pharmaceutical, biotech, medical device, combination product, API, cosmetic, and food industries.

In these pages you will find what is needed to improve your compliance and quality system in a way that is cost-effective and tailored to your specific needs.

Our team of experienced FDA industry professionals (more than 70 resources, averaging 20+ years of experience) will assist you with the implementation of risk-based, robust and sustainable solutions. We will support your efforts to achieve and maintain a compliant quality system as well as educate and develop your staff to maximize their contribution to the business.

BEC provides the following:

Industries we assist

Pharma – Biotech – OTC
Medical Devices
Combination Products
Food and Dietary Supplements
APIs
Excipients
Cosmetics

Type of Services

FDA Inspection Support (PAI, surveillance, for cause)
Training and Regulatory Education
Auditing and Assessment
Remediation and Quality Systems Compliance
Data Integrity
Quality Systems Implementation for FDA industries
Risk Management
Investigation and CAPA System Support
Human Error Prevention and Reduction
Supplier Control Programs
U.S. Agent
Submissions: DMF, ANDA, NADA, 510K
U.S. Registration and Listing processes
ISO Certification Consulting and Support
Validation Life-Cycle
Temporary Support: backlog reduction of Investigations, CAPAs, Complaints, and Change Controls

Our value proposition is based on four elements:

- U.S. FDA regulated market is our focus
- Experience, Knowledge, and Expertise
- Proven Results
- Cost-effective and Affordable Services

About Us—History of BEC-GLOBAL

Passion for quality, sharing our knowledge, and working as partners with our clients in their pursuit of excellence best describes **Business Excellence Consulting, Inc. (BEC)** and our global trademark, **BEC GLOBAL**.

Since May 2005, our company has grown to provide a wide array of regulatory remediation and support services, including the placement of highly qualified professionals at client sites. Our people are our most important asset. Their average hands-on experience working in the FDA-regulated environment exceeds 20 years. Currently, we have more than 70 highly skilled and experienced professionals including engineers, chemists, biochemists, and biologists, serving clients worldwide.

Accreditations and Certifications

Since May 2015, our company has been accredited under the *ANSI/ IACET Standard for Continuing Education and Training* which is recognized internationally as a standard of excellence in instructional practices. The ANSI/IACET Standard for Continuing Education and Training is a universal model for learning process excellence. It defines a *proven model* for developing effective and valuable continuing education and training (CE/T) programs by measuring a CE/T provider's training program from procedure to process to result. As a result of this accreditation, BEC is authorized to issue the IACET CEU.

Our Clients

Major pharmaceutical, medical device, biotech, API, cosmetic, and food companies are part of our broad client portfolio in four continents. In addition to Puerto Rico and the continental USA, we provide services in Argentina, Bahamas, Belgium, Canada, Chile, China, Colombia, Costa Rica, Czech Republic, Dominican Republic, Ecuador, France, Germany, Japan, Malaysia, Mexico, India, Indonesia, Ireland, Italy, Peru, Singapore, Spain, Switzerland, and the UK.

About Us—Our People

Our founders



José (Pepe) Rodríguez-Pérez, President and founder holds a bachelor's degree in biology and a PhD in immunology, both from the University of Granada, Spain, with post-graduate studies in medical sciences. During his 25+ year of career, he spent over 15 years working in a manufacturing plant (Abbott Laboratories). He also was a Science Advisor for the U.S. FDA from 2009 to 2012. He founded Business Excellence Consulting in May 2005 and since then has been leading its operation and expansion to a global consulting firm. He served as a senior member of the American Society of Quality and Chair of the Puerto Rico section during the period 2003-05. He was secretary from 2005 to 2012. Pepe holds seven American Society of Quality (ASQ) certifications: Certified Six Sigma Black Belt, Manager of Quality & Organizational Excellence, Quality Engineer, Quality Auditor, HACCP Auditor, Pharmaceutical GMP Professional, and Biomedical Auditor. He is also a member of RAPS, ISPE, AAMI, and PDA.

He is the author of eight best-selling books (published by ASQ-Quality Press) covering FDA topics:

- ⇒ CAPA for the FDA - Regulated Industry (2010),
- ⇒ Quality Risk Management in the FDA-Regulated Industry (2012),
- ⇒ The FDA & Worldwide Current Good Manufacturing Practices and Quality System Requirements Guidebook for Finished Pharmaceuticals (2014)
- ⇒ Handbook of Investigation and Effective CAPA Systems 2nd edition (2016)
- ⇒ Quality Risk Management in the FDA-Regulated Industry 2nd edition (2017)
- ⇒ Human Error reduction in Manufacturing (2018. second edition scheduled for early 2023)
- ⇒ Data Integrity and Compliance (2019)
- ⇒ Handbook of Investigation and Effective CAPA Systems 3rd edition (2022)

Another recent titles published by BEC Press are:

- ⇒ Quality Culture in the Pharmaceutical Industry (2021)
- ⇒ Cultura de Calidad y Cumplimiento en la Industria Alimentaria (2021)
- ⇒ Handbook of U.S. Cosmetic Products Regulations (2022)
- ⇒ La Gestión de Riesgos en las Industrias Alimentarias (2022

He is also the author of peer-review articles covering topics such as risk management, CAPA system, and data integrity.



Norma L. Copeland , Vice-President and co-owner of BEC Inc. She has a bachelor's degree in business administration, major in accounting from the University of Puerto Rico. Prior of founding BEC Inc. she worked in the advertisement industry. She oversees human resources and all administrative aspects of the company.

Remediation and Quality System Compliance

BEC provides an affordable and comprehensive range of quality system remediation services for the FDA regulated industry. Our core expertise allows us to assist you in implementing risk-based, robust and sustainable solutions for your quality system. Regulatory inspections and compliance assessments frequently require regulated companies to respond to specific enforcement actions. We have comprehensive experience in developing, implementing, reviewing, and remediating all aspects of cGMP and quality systems for the FDA regulated sectors. Making your quality system compliant and sustainable while maximizing your investment is our main goal.

We provide expert compliance solutions to regulated companies including remediation strategy, planning and execution. Our expertise covers fixing your CAPA system (we wrote the best-selling book on this topic), validations, reviewing and writing technical documentation, SOPs, conducting failure investigations and preparing effective CAPAs. We also prepare our clients for successful FDA pre-approval and surveillance inspections (including mock inspections), providing support during inspections, in 483s and warning letter responses.

We also specialize in supporting foreign companies willing to market their regulated products in the U.S. We have a proven track record of assisting companies in introducing generic and OTC drugs, APIs, dietary supplements, food, medical devices and combination products into the U.S. In addition we also provide regulatory support to those companies, and we also prepare their quality systems to meet the FDA specific requirements.

We offer the following services:

Implementation of FDA cGMP/compliant quality system
FDA Inspections
- Pre-inspection readiness
- War-room handling/support during inspections
- Form 483 and warning letter response support
- Regulatory meeting preparation and support

FDA Pre-Approval Inspections (PAI)
Mock Inspections and cGMP assessments
Investigation and CAPA System
- Laboratory, manufacturing and complaint (including FAR) support and backlog reduction
- Retrospective/prospective review
- Investigations/complaints handling outsourcing

Human Error Reduction and Prevention Programs
Implementation and enhancement of Quality Risk Management programs
Quality by Design and Pharmaceutical Development Support
Annual Product Review/Product Quality Review Support and Outsourcing
Computer System Validation and 21 CFR Part 11
Data Integrity audit and assessment, remediation and training
Operational support
- QC laboratory analysts
- QA documentation and change control
- Documentation simplification and enhancement
- Batch record enhancement

Remediation and Quality System Compliance *cont.*

Validation Life-cycle Services

- Risk-based validation master plan development and management
- Equipment commissioning/qualification: manufacturing, packaging, laboratory, facilities/ utilities
- Cleaning validations
- Sterilization method validations
- Computer system validation for cGMP applications: SCADA, LIMS, BMS, ERP, TRACK-WISE, MES, Laboratory electronic notebook
- Computerized system validation life cycle: concept, requirements, design, vendor management, procurement, commissioning, qualification/validation, operation/maintenance, retirement
- 21 CFR 11 assessment and remediation
- Quality control laboratory: analytical test method validation, computer system validation, qualification of analytical equipment
- Qualification/validation package assessments
- Development of continuous process verification programs aligned with the new FDA guidance
- Full statistical support (SPC, DOE, data analysis, sampling assessment)

Training and Education Services

With more than 80 courses and workshops, BEC is well known for the high quality of our regulatory and compliance training and education. Since 2005, we have been leaders in providing education and training to thousands of professionals every year. Since May 2015, BEC's educational program has been accredited under the *ANSI/IACET Standard for Continuing Education and Training* which is recognized internationally as a standard of excellence in instructional practices. The ANSI/IACET Standard for Continuing Education and Training is a universal model for learning process excellence. It defines a *proven model* for developing effective and valuable continuing education and training (CE/T) programs by measuring a CE/T provider's training program from procedure to process to result. As a result of this accreditation, BEC is authorized to issue the IACET CEU.

We believe in providing education, not just training. As Albert Einstein once said: "Education is that which remains, if one has forgotten everything he learned". Our courses focus not only on the "what" and the "how", but also on the "WHY". FDA-regulated companies must make sure that their employees, at all levels, receive comprehensive regulatory and compliance training and education. With BEC's effective training and educational programs, you will see immediate returns. And, as a bonus, all our IACET accredited courses include an evaluation of the training's effectiveness.

We offer comprehensive training and educational programs designed to develop the knowledge and skills needed to meet the many challenges of the FDA-regulated industry. A robust and sustainable regulatory educational program is one of the best preventive actions a regulated company can take. Also, it is the perfect complement to any remediation efforts.

Our instructors are experts in their field and they are supported through a strong Train the Trainer program. Our IACET accreditation demonstrates the excellence of our educational process.

We offer a wide range of courses covering all areas of pharmaceutical, medical devices, combination, food and dietary supplements and API's cGMP. All our courses can be offered in the following formats:

- Public courses
- On-site courses with on-site instructors
- On-site courses with remote instructors (via Teams, ZOOM, Webex, Skype, etc.)
- Online courses (under development)

The following three pages contain a list of our courses for 2023.

2023 Training and Education Courses Catalog

ASQ Certification Academias

1) ASQ Certified Quality Auditor
2) ASQ Certified Quality Engineer
3) ASQ Certified Six Sigma Green
4) ASQ Certified Six Sigma Black Belt
5) ASQ Certified Manager of Quality & Organizational Excellence
6) ASQ Certified Quality Improvement Associate
7) ASQ Certified Medical Device Auditor
8) ASQ Certified Pharmaceutical GMP Professional
9) ASQ Certified Food Safety & Quality Auditor
10) ASQ Certified Quality Technician
11) ASQ Certified Quality Inspector
12) ASQ Certified Supplier Quality Professional

Investigations and Effective CAPA Systems

13) Investigation/CAPA System and Human Errors Reduction Certification
14) Investigation and Effective CAPA Systems Certification
15) Root Cause Analysis
16) Effective CAPA Systems Management Overview
17) Effective OOS/OOT Investigations for QC Analytical Laboratory Certification
18) Microbiology Investigations and Environmental Monitoring Program
19) Implementing a Mature and Sustainable Investigations/CAPA Program

Regulations and Standards

20) Medical Device Quality System Expert Certification
21) 21 CFR 111: cGMP for Dietary Supplements
22) 21 CFR 117: cGMP for Food
23) 21 CFR 210/211: cGMP for Finished Drugs
24) 21 CFR 820: QSR for Medical Devices
25) Understanding Combination Products
26) ISO 9001:2015
27) ISO 13485:2016
28) ISO 14001:2015
29) ISO 17025:2017
30) ISO 22000:2018
31) Comparison of ISO 13485:2016 to FDA's 21 CFR 820
32) Good Distribution Practices for Medical Products

Food Industry

33) Preventive Controls for Human Food Certification as per FSPCA
34) FSVP Foreign Supplier Verification Program
35) Food Safety Requirements under FSSC 22000 v.5

Technical and Compliance Writing

36) Effective Compliance and Regulatory Writing

Training and Education Courses Catalog cont.

Auditing

37) Internal Auditing Certification
38) FDA Inspection Readiness for FSMA
39) ISO 9001:2015 Lead Auditor (36-hour Exemplar Global Certified)
40) ISO 13485:2016 Lead Auditor (36-hour Exemplar Global Certified)

Risk Management

41) Quality Risk Management Certification
42) ISO 14971:2019

Statistics

43) Data Trending Analysis
44) Basic Applied Statistics
45) Sampling Best Practices for the FDA-Regulated Industry

Validations

46) Computer System Validation for the FDA-Regulated Industry
47) Validation Overview
48) Cleaning Validation Lifecycle
49) Essential Elements for the Manufacture for Aseptically Produced Sterile Products
50) Facilities and Critical Utilities Systems Qualification
51) Laboratory Equipment Qualification
52) General Concepts of Thermal, Radiation, Chemical and Filtration Sterilization Validation
53) Test Method Validation
54) Process Validation for Medical Devices
55) Cleaning validation for medical Devices
56) Process Validation for Pharmaceutical

Compliance

57) How to Write Procedures to Reduce Human Errors
58) Overview of Stability Programs for Drug, Biotech, and Combination Products
59) Best Practices for Complaint Handling in the FDA regulated products
60) Trending analysis for the stability program

Training Program

61) Train the Trainer
62) How to Measure Training Effectiveness

Training and Education Courses Catalog cont.

Organizational Behavior

63) Decision Making
64) Critical Thinking
65) Negotiation Skills
66) Hiring Strategies/ Interviewing Skills
67) Generation Gaps
68) Leadership Skills
69) Supervisory Skills
70) Safety in the Workplace
71) Assertiveness and Self Confidence
72) Conflict Management

Data Integrity

73) Data Integrity Certification
74) Data Integrity module for QC laboratory personnel
75) Data Integrity module for manufacturing and operation personnel
76) Data Integrity module for management

Management Controls

77) Pharmaceutical cGMP for Leaders and Managers – Managerial Responsibilities
78) How to Implement an Effective Change Management Control Program
79) FDA Quality Management Maturity Model and **Quality Culture**
80) Quality Unit and QA – Managerial Responsibilities
81) Quality Control Management Responsibilities
82) Pharmaceutical Inspection Readiness Certification

Audit and Assessment

If your company needs an in-depth, expert assessment of a specific issue, to outsource your entire internal or supplier audit program or anything in between, BEC can support you through our team of experts covering all FDA-regulated areas.

We are servicing several major global companies auditing their critical suppliers worldwide. During the past 7 years, we performed more than one hundred audits in 19 countries, covering Asia, North America, Central and South America and Europe.

We offer the following services:

Preparation for FDA Regulatory Inspection

BEC has provided FDA inspection readiness services for the last 12 years with an excellent success rate. Our expert service includes the following activities:

* Initial gap assessment to identify opportunity areas, including comprehensive data integrity assessment
* Development of a detailed and comprehensive remediation plan to address weak or noncompliance areas
* Training your staff to prepare for an FDA inspection and to interact with the inspector
* Formal mock inspection to practice and to challenge staff and quality systems prior to the inspection
* War-room handling/support during the inspection, with both onsite and remote expert support
* Post-inspection support preparing formal responses and managing interactions with the FDA, including regulatory meeting preparation and support

We have extensive experience helping companies to address critical agency findings, as well as untitled and warning letters. We have a proven, demonstrable track record addressing complex regulatory problems and compliance issues.

Preparation for FDA Pre-Approval Inspection (PAI)

The inspection focus and methodologies used by FDA inspectors during pre-approval inspections (PAI) are different to those used for regular, surveillance, postmarket inspections. Before approval, the FDA typically evaluates the manufacturer by on-site inspections when the company is named in the Chemistry, Manufacturing, and Controls (CMC) section of a New Drug Application (NDA), Abbreviated New Drug Application (ANDA) or Biologic License Application (BLA). The pre-approval inspection (PAI) is performed to contribute to the FDA's assurance that a manufacturing establishment named in a drug application is capable of manufacturing a drug, and that submitted data is accurate and complete.

Our company has extensive experience helping companies with NDA and ANDA preapproval inspections. In this case, in addition to all preparation activities mentioned for regular FDA inspections, our experts will perform an intensive assessment of the following three elements:

Readiness for Commercial Manufacturing
Conformance to Application
Data Integrity Audit

Audit and Assessment *cont.*

Mock FDA Regulatory Inspections / FDA Readiness

We assist your company with the best possible preparation for your next FDA inspection. After hundreds of FDA inspections, we know very well how inspections are performed, and what inspectors look for. We can even mimic the FDA inspection atmosphere when more than one inspector is expected. Our mock inspections can include one-day education on FDA readiness and how to interact with the FDA inspector. We will advise your company on which documentation needs to be ready, how to establish an effective war-room to attend the inspection and how to effectively manage all aspect of the inspection, from logistics to record-keeping.

Quality System Assessment/GMP Compliance

Our team of experienced professionals can perform a thorough, in-depth assessment of your quality system against regulatory requirements and guidances, industry best practices and other standards such as USP and ICH. Our detailed risk-based audit report will include recommendations to enhance your weaknesses and can be used as the basis for a remediation/corrective action plan.

Often our clients request us to audit specific elements of their quality system. Some examples of recently performed audits are:

Data Integrity
Pest control
Incoming Process Control
Manufacturing Processes
Packaging Processes
Warehouse and Distribution Centers
Sterilization Process
QC Analytical laboratory
LIMS
QC Microbiology laboratory
CAPA Systems
Change Control
Internal Audit Program
Supplier Certification Program
Training Program and Learning Verification
Facilities and Critical Utility Systems
Validation Program

Internal Audit/Self Inspection

The internal audit program is a regulatory requirement of the FDA and worldwide regulators. This program, when well executed, is your primary line of defense against regulatory inspection findings. However, many FDA regulated companies have weak internal audit programs. This is due to:

- Internal auditors are inherently non-independent
- Internal auditors often lack the education and experience necessary in many areas such as data integrity, computer system validation, laboratory test methods, equipment validation, etc
- Many internal audit programs are not risk-based

We established a very successful internal audit outsourcing model where we perform, twice a year, an in-depth assessment of the different elements of the applicable quality system, with a team of experts covering all the critical areas and elements. This model guarantees you a much more robust internal audit program that saves your company money. Typically, you can save up to 50% of your current investment in the internal audit program.

Audit and Assessment *cont.*

Supplier Control Programs

We can design, implement and/or support a risk-based efficient supplier control program. Each year, our experts perform more than one hundred third party audits worldwide. We are servicing several major global companies auditing their critical suppliers worldwide. During 2017, we performed audits in 18 countries, covering Asia, North America, Central and South America and Europe. To learn how you can implement a compliant, risk-based supplier control program at a very reasonable cost, contact us.

Regulatory Affairs

We offer expert regulatory support and consulting services related to U.S. FDA regulated products. We prepare and/or review regulatory documentation and dossiers (eCTD compliant), or we can act as your U.S. Agent representative for regulatory purposes. We can recognize simple, frequently overlooked standardization and process changes, which can bring significant benefit in efficiencies, cost savings and can expedite your regulatory submission. When direct communication with FDA is needed related to your eCTD plans, Business Excellence Consulting, Inc. can be present as your eCTD expert partner. Our company also provides advice on product manufacturing, product specification development, and training on U.S. regulatory processes.

Submissions

- **U.S. Agent:** FDA requires that any foreign establishment engaged in the manufacture, preparation, propagation, compounding, or processing of a device imported into the United States identifies a United States agent (U.S. agent) for that establishment. The U.S. agent must either reside in the U.S. or maintain a place of business in the U.S. We can serve as your company's U.S. Agent. We are located in the city of Guaynabo, Puerto (USA) and our offices are located at a few minutes driving distance from the FDA's San Juan District Office. We have direct access/communication with the San Juan Office and are also located in the same time zone than the FDA Headquarters in Maryland, USA which facilitates constant and timely communication with the Agency. Moreover, all our industry experts are bilingual, fluent both in Spanish and English.

- eCTD preparation: We specialize in writing, formatting and publishing high quality documentation for submission of your Investigational New Drug (IND) application, New Drug Application (NDA), Abbreviated New Drug Application (ANDA), Biologics License Application (BLA) and Drug Master File (DMF) as well as subsequent amendments and supplements (Changes Being Effected (CBE or CBE-30), Prior Approval Supplements (PAS)). Our team of experts has extensive experience in different areas within the pharmaceutical, medical devices and food industries, assuring that not only documents formatting and functionality are correct but also that technical contents is complete and accurate. As a result, we can expedite your regulatory submission and FDA review and approval times can be reduced drastically.

- Medical Devices dossiers: Preparation, review and submission of 510K and PMA dossiers.

Regulatory Affairs *cont.*

Submissions (cont.)

- **Submission via the FDA's Electronic Submission Gateway (ESG):** The FDA Electronic Submissions Gateway (ESG) is an Agency-wide solution for accepting electronic regulatory submissions. The FDA ESG enables the secure submission of premarket and postmarket regulatory information for review. As an authorized U.S. agent, we can submit your IND, NDA, ANDA, BLA, DMF, 510(k), PMA and SPL files as well as subsequent amendments and supplements, where applicable, via the FDA's ESG on your behalf.

- **Drug Establishment Registration and Drug Listing:** Domestic and foreign establishments that manufacture, repack, or re-label drug products in the United States are required to register with the FDA and to list all of their commercially marketed drug products. This information helps the FDA maintain a catalog of all drugs in commercial distribution in the United States and is submitted in the form of extensible markup language (XML) files in a standard Structured Product Labeling (SPL) format. Business Excellence Consulting, Inc. can assist your company with SPL files creation/updates, renewals (annual registration for each Fiscal Year must be completed between October 1 and December 31) and submission through the FDA's Electronic Submission Gateway (ESG).

- **Establishment Registration and Device Listing:** Owners or operators of places of business (also called establishments or facilities) that are involved in the production and distribution of medical devices intended for use in the U.S. are required to register annually with the FDA. All device establishments must complete their annual registration for each Fiscal Year between October 1 and December 31. This process (registration and listing) can be completed by a designated Official Correspondent on your company's behalf. At Business Excellence Consulting, Inc. we have the experience to act as your designated Official Correspondent and assume responsibilities for your Initial Registration, Annual Registration and any required updates to your Registration and Listing Information.

- **Registration of Food Facilities:** FDA requires that facilities engaged in manufacturing, processing, packing, or holding food for consumption in the United States are registered and that such registrations are renewed every other year. Our team of experts can assist you in registering your products and mainting your registration up to date.

Training on U.S. Regulatory Processes: We can develop and offer training courses focused on U.S. regulations and/or regulatory process that can fit your learning needs. Additionally, we offer more than 80 regulatory and compliance courses and workshops (refer to the Training and Education Services section for a list of courses offered).

FDA Inspection Support

Preparation for FDA Regulatory Inspection

BEC has provided FDA inspection support services for the last seventeen years with an excellent success rate. Our expert service includes the following activities:

- Initial gap assessment to identify opportunities areas, including comprehensive data integrity assessment
- Development of a detailed and comprehensive remediation plan to address weak or non-compliance areas
- Training your staff to prepare for an FDA inspection and how to interact with the inspector
- Formal mock inspection to practice and to challenge staff and quality systems prior to the inspection
- War-room handling/support during the inspection, with both onsite and remote expert support
- Post-inspection support preparing formal responses and managing interactions with the FDA, including regulatory meeting preparation and support

We have extensive experience helping companies to address critical agency findings, as well as untitled and warning letters. We have a proven, demonstrable track record addressing complex regulatory problems and compliance issues.

Preparation for FDA Pre-Approval Inspection (PAI)

The inspection focus and methodologies used by FDA inspectors during pre-approval inspections (PAI) are different to those used for regular, surveillance, postmarket inspections. Before approval, FDA typically evaluates the manufacturer by on-site inspections when the company is named in the Chemistry, Manufacturing, and Controls (CMC) section of a New Drug Application (NDA), Abbreviated New Drug Application (ANDA) or Biologic License Application (BLA). The pre-approval inspection (PAI) is performed to contribute to FDA's assurance that a manufacturing establishment named in a drug application is capable of manufacturing a drug, and that submitted data is accurate and complete.

Our company has extensive experience helping companies with NDA and ANDA preapproval inspections. In this case, in addition to all preparation activities mentioned for regular FDA inspections, our experts will perform an intensive assessment of the following three elements:

Readiness for Commercial Manufacturing
Conformance to Application
Data Integrity Audit

Mock FDA Regulatory Inspections / FDA Readiness

We will assist your company with the best possible preparation for your next FDA inspection. After hundreds of FDA inspections, we know very well how inspections are performed, and what inspectors are looking for. We can even mimic the FDA inspection atmosphere when more than one inspector is expected. Our mock inspections can include one-day education on FDA readiness and how to interact with the FDA inspector. We will advise your company on which documentation needs to be ready, how to establish an effective war-room to attend the inspection and how to effectively manage all aspects of the inspection, from logistics to record-keeping.

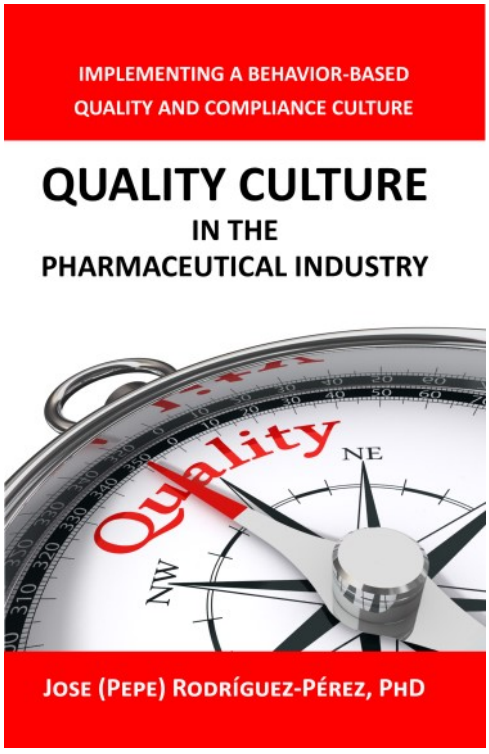
Quality Culture

Why so many pharmaceutical companies are struggling to meet GMP and other regulatory requirements?. The reason is clear: because they are trying to improve their quality management systems by fixing symptoms rather than by attacking the fundamental and primary root cause of their problems which is the lack of an adequate quality and compliance culture.

The purpose of this book is to provide those leaders and senior managers with a clear roadmap to solve their regulatory problems and to return to the route of compliance by implementing a strong and positive quality and compliance culture. The recipe is simple: all you need is good people (including good leaders and senior managers), good procedures and good training programs sailing into a strong and positive culture of quality and compliance.

When a company implements a ***behavior-based quality and culture compliance***, they look into their problems as a whole, and they understand that there are multiple factors (including the soft ones related to personal and organizational behaviors) that affect performance. A very positive consequence of this systematic thinking is the shift from CAPA programs that are mostly correctives to ones where the systemic preventive actions are predominant.

Quality is everyone's responsibility, but when it comes to creating, strengthening, or maintaining a culture within an organization, there is one group who really owns it: the leaders and senior managers. The good news is that creating or strengthening a positive and sustainable quality culture is an achievable task although not an easy or quick one. In this book you will find ten foundational principles of a strong and positive quality culture, their associated desired behaviors and a set of leading indicators that can be used to monitor and enhance leadership engagement, people engagement, and culture and maturity.



To learn more about our quality and compliance culture program and how implement it at your company, contact us for a free, no obligation quote.

Data Integrity

Data Integrity is a global mandatory requirement for the regulated healthcare industry. Developing a medical product and bringing it to market involves many different players and activities. A fundamental step is linked to the robustness and accuracy of the data submitted by manufacturers to regulatory authorities. That data must be comprehensive, complete, accurate, and true to ensure the quality of studies supporting applications for medical products to be placed on the market. Complete, consistent, and accurate data should be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA). It also must comply with good manufacturing practices (GMP), good clinical practices (GCP), and good laboratory practices (GLP).

Data Integrity is a basic element of good documentation practices, one of the most fundamental pillars of any quality management system, including current good manufacturing practices. There has been a dramatic increase in the number of U.S. FDA warning letters, World Health Organization (WHO) notices of concern, and EU statements of noncompliance in which false or misleading information has been identified during inspections. Failure to properly manage data integrity applies equally to paper and electronic data. It can arise either from poor systematic control of the data management systems due to a lack of knowledge, human error or from intentionally hidden, falsified or misleading data. Recently, a string of FDA-issued warning letters for data integrity violations has been published on the agency's website. Between 2015 and 2016, major regulatory bodies, such as the European Medicines Agency (EMA), the FDA, the WHO, and the Pharmaceutical Inspection Co-operation Scheme (PIC/S), published guidance documents on the topic of data integrity/data management.

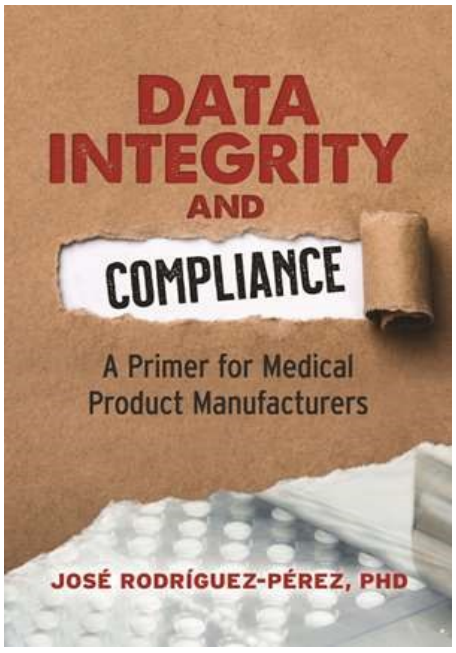
Our company can offer you the following services related to data integrity:

- **Comprehensive Audits and Assessments** to identify system weaknesses regarding your manual, electronic and hybrid data feed. We cover all aspects of your records and data recording practices specially laboratory systems and electronic storage.

- **FDA inspection preparedness** for Data Integrity including mock inspection.

- **Remediation Consulting** focused on FDA recommended best practices.

- **Training** for your personnel at all levels including a very comprehensive 3-day certification for managers and subject matter experts. Participants learn how to lead the detection and remediation of data integrity problems. For company-wide solutions we offer the following courses:
    - **Data Integrity Certification**
    - Data Integrity module for QC Laboratory Personnel
    - Data Integrity Module for Manufacturing and Operation Personnel
    - Data Integrity Module for Management
    - Data Integrity Module for the General Population



Investigation and CAPA System Support

Root causes identification and effective corrective and preventive actions is a critical expectation of the FDA and other regulatory agencies worldwide. Indeed, this area represents one of the most frequently cited problems during regulatory inspections. As an example, almost 90% of medical device's warning letters issued by U.S. FDA include CAPA citations. Weak investigations and ineffective CAPAs are at the center of most regulatory enforcement actions.

Requirements for compliant deviation and CAPA systems are well established by regulatory agencies. Each organization must conduct focused investigations, identify true root causes, and implement effective corrective action and preventive action in a timely manner, including measuring their effectiveness. BEC has provided investigations and CAPA system support since 2005 to major pharmaceutical, medical device, and food companies located worldwide. Among the services that our company can provide are:

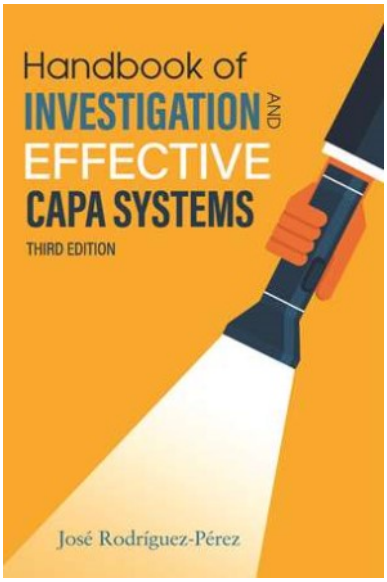
TRAINING – To improve the capability of your personnel to make better investigations and to implement effective corrective and preventive actions. We have different courses and certifications that can be tailored to your specific needs. Our trainings explore the deviation and CAPA processes and best practices for both. Your participants learn how to avoid pitfalls and minimize regulatory scrutiny by having thorough investigations and a robust and a compliant deviation/CAPA system. Among our courses are:

- Five-day Investigator and CAPA Expert Certification for investigators, CAPA owners and approvers
- One-day CAPA System Management Overview for managers and directors

TEMPORARY SUPPORT – We can assist your company with temporary expert support to:

- Reduce backlog of laboratory, production or customer complaint investigations
- Fix and enhance your deviation/CAPA system. Our expert resources will design a compliant and sustainable deviation/NCR and CAPA system. After all, we wrote the best-selling book in this topic.

MONITOR – BEC can provide your company with affordable ways to monitor the effectiveness of your deviation/CAPA system. Our service of independent reviews of deviation and CAPA documents will provide you peace of mind about this critical system. Dozens of companies that went through a CAPA warning letter hired us to provide an independent verification of their deviations and CAPA documents.

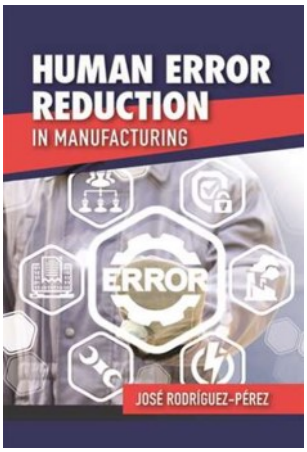


OUTSOURCING – Our company offers full outsourcing possibilities for the above mentioned activities related to deviation and CAPA system activities.

Our best-selling books on this topic are used by companies around the globe to enhance their investigation and CAPA systems.

Human Error Investigation and Reduction

The cost of human errors to the manufacturing industry is estimated to be in the billions of US dollars. Recent statistics show that human error is the cause of nearly 80% of failures and deviations in the manufacturing sector. This poses a tremendous challenge to regulated companies as it translates to a significant loss of time, money, and consumer confidence each year, including regulatory enforcement activities.



Global regulators have increased their focus on deviations and root cause analysis (RCA), and this process is one of the largest sources of inspection observations. Frequently identifying "human error" as a root cause and "retraining" as a CAPA is a clear indication to the regulatory authorities that you're not solving the problems that exist in your organization. Worse, it can give regulators the impression that your staff is ill-prepared, error prone, and you don't have a handle on the real causes of your deviations. Human failure (voluntary and involuntary) is more a symptom than a cause. Current theories see human failures as the symptoms of deeper causes. In other words, human failures are consequences, not causes.

BEC has provided human error reduction expertise support since 2005 to major pharmaceutical, medical device, and food companies located worldwide. Our new book HUMAN ERROR REDUCTION IN MANUFACTURING was published September 2018 by ASQ-Quality Press (a second edition of this book will be available first quarter 2023).

Among the services that our company provides are:

ERROR REDUCTION PROGRAM - We can assist you with human reliability experts who can help with procedures and process simplification to reduce human errors and mistakes by:

- Evaluating your current situation (human error deviations and CAPAs)
- Investigating the *real* root causes of the above
- Suggesting comprehensive, sustainable and affordable actions to minimize the occurrence of human error(s) at your facilities

HUMAN RELIABILITY TRAINING – We can help your company to better understand why human errors occur, and this will enable your staff at all levels to move the organization from "error prone" to "error free" resulting in fewer enforcement observations/actions from global regulatory agencies. We have a comprehensive three day certification for quality assurance, production, regulatory affairs, supplier quality and quality control personnel. Participants will learn and practice how to:

- Investigate error incidents properly
- Evaluate the CAPA investigation process to identify all the root cause(s)
- Identify the root causes that lead to human error
- Identify the controls that could avoid human error

MONITOR – BEC can help your company with affordable ways to monitor the effectiveness of your human error reduction program. After implementation of the program, we can independently review your human error deviation and CAPA documents to ensure they are adequate in terms of root cause investigation and appropriate CAPA plans.

Outsourcing Activities

BEC is providing support in the form of outsourced programs to regulated companies for the following elements of their quality system:

- Training Program
- Internal Audit
- Supplier Audit Program
- Complaint Investigation
- Investigation of Deviations/NCR/CAPA
- APR/PQR
- Function of "Remote Quality Unit"

Every day more companies are discovering the value and benefit derived from outsourcing specific critical activities to specialized providers such as our company. We provide our outsourcing clients with real and proven expertise in the FDA-regulated industry, 24/7 support, very affordable and cost-effective fees.

As an example, our outsourcing value model for the self-inspection program of a typical pharmaceutical plant includes the following elements:

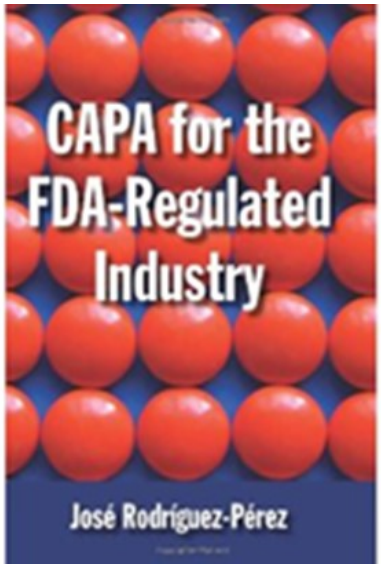
- Developing and maintaining a risk-based and compliant internal audit program for the site
- Subject matter expert auditors with an average of 25+ year in the FDA-regulated industry
- Full support during external audits/inspections regarding internal audit function
- Follow-up of CAPAs generated after internal audit findings
- In total, we provide 50 days of audit during a calendar year covering all the elements of the quality system:
    - Data Integrity (manual, electronic, and hybrid systems)
    - CSV
    - QC analytical lab
    - QC microbiological lab
    - Critical systems and utilities
    - Calibration and PM program
    - Stability program
    - Master validation program
    - Quality system
    - Production system
    - Investigation and CAPA system
    - Complaint handling
    - Management controls

To learn how your company can benefit with our expertise, certified auditors and our affordable fees, contact us at info@bec-global.com

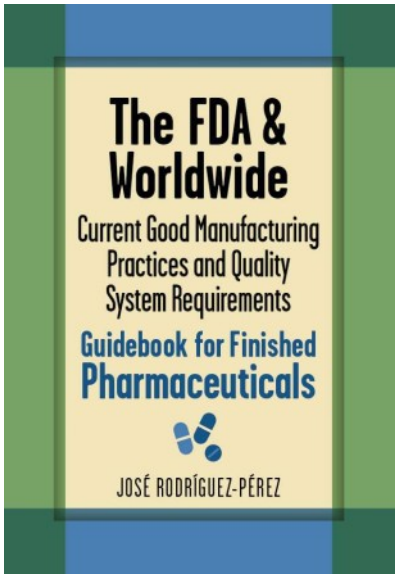
Books

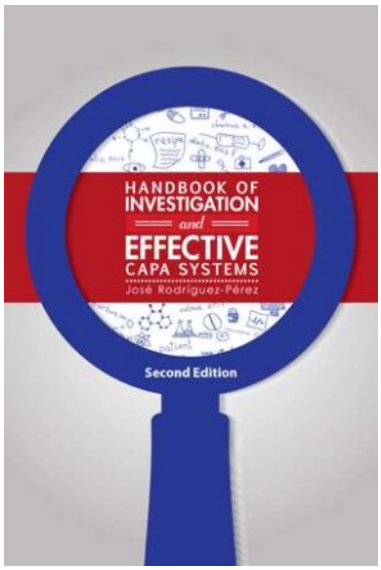
The authors of these books, published by the American Society of Quality, are part of our staff. Our first book, CAPA for the FDA-Regulated Industry became a best-seller since its publication in 2010 and was updated with a second edition in 2016 under the title of *Handbook of Investigation and Effective CAPA System*., and its 3rd edition will be published 2022. Our second book, *Quality Risk Management in the FDA-Regulated Industry* was published in 2012 and also became a best seller with an updated second edition published in February 2017.

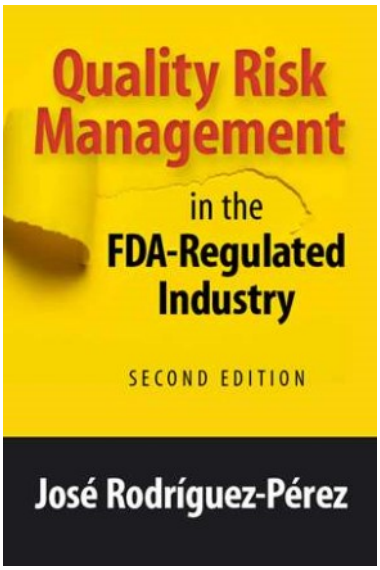
Our focus on the FDA regulated industry is also shown by the title of other two books: Statistical *Process Control for the FDA-Regulated Industry* (2013) and *The FDA and Worldwide GMP for Finished Pharmaceuticals* published in 2014.

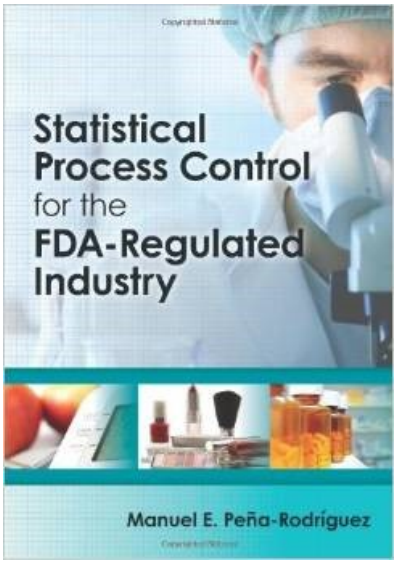






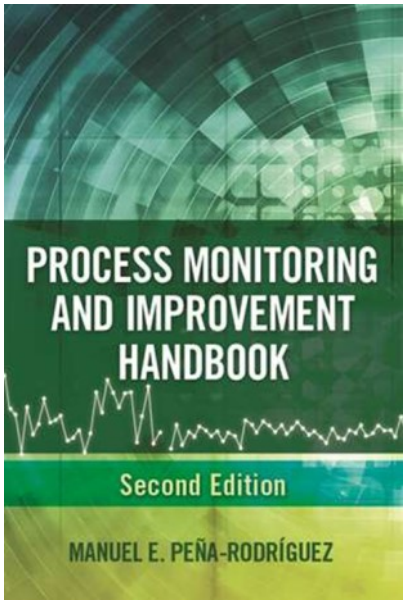


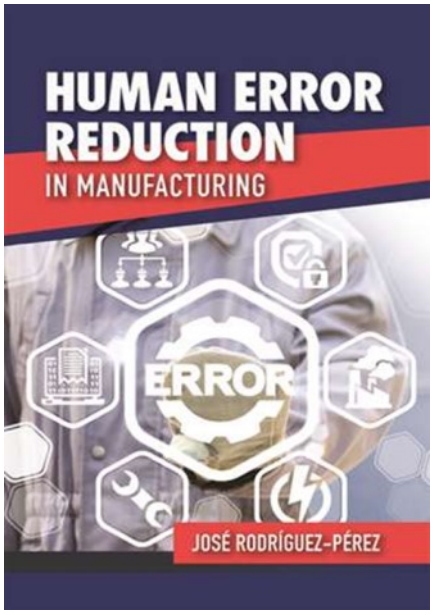


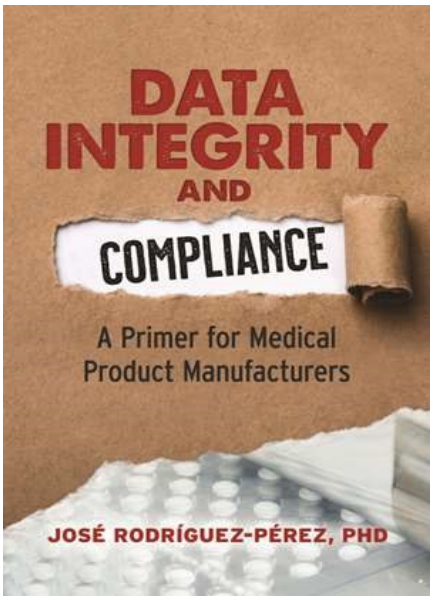


Books

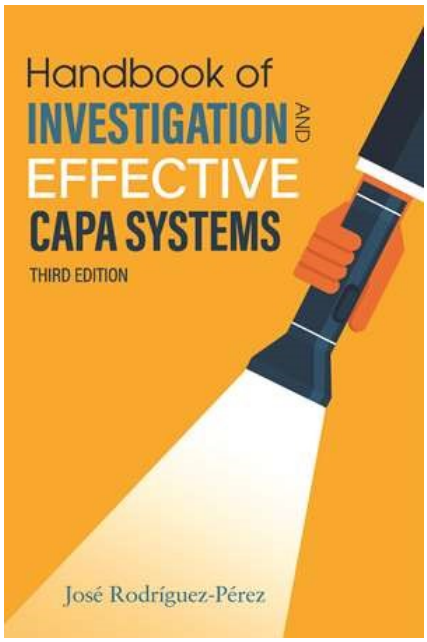
In September 2018, ASQ Quality Progress published the second edition of the process monitoring/statistical analysis book of Manuel Peña and the long-awaited book on human error reduction from our president and founder, José (Pepe) Rodríguez. In June 2019 it was published a new book covering the topic of Data Integrity and Compliance. All our books can be purchased directly from www.asq.org or from www.amazon.com.







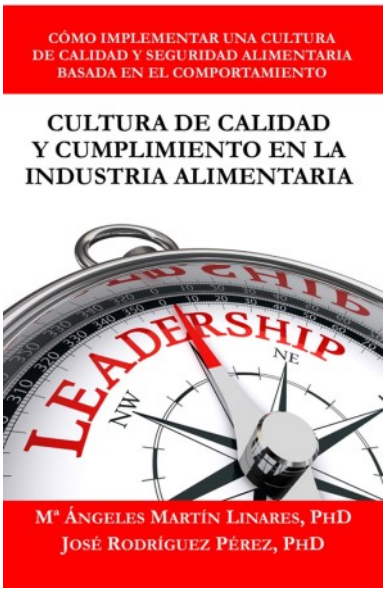
In February 2022—ASQ Quality Press published the third edition of our best selling book HANDBOOK OF INVESTIGATION AD EFFECTIVE CAPA SYSTEMS

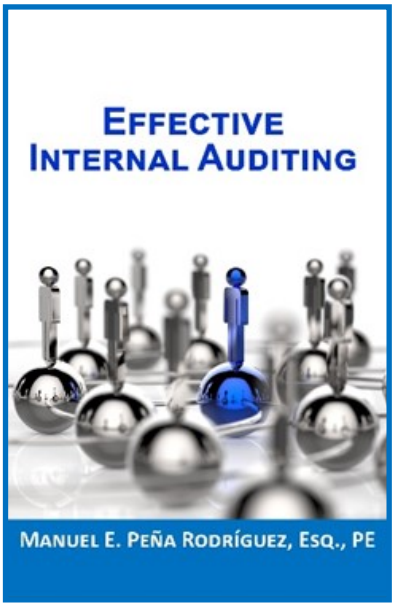


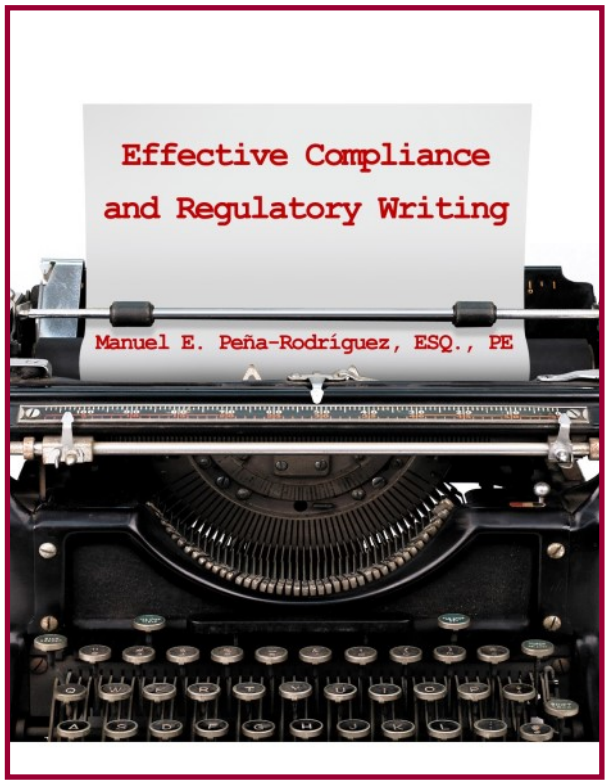
Books

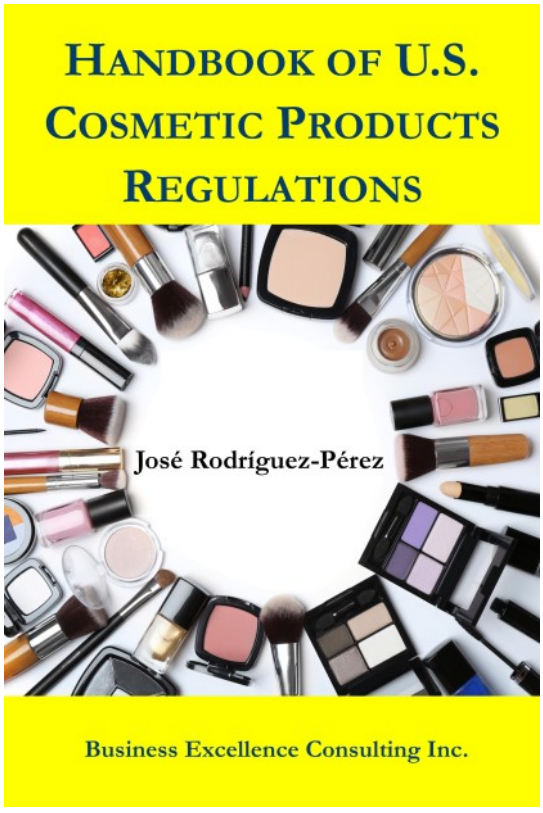
In 2021 we began to publish some new titles directly in www.amazon.com. Four titles have been published so far in English and one in Spanish.











Technical Articles published by our staff

To receive a pdf copy of our articles published by Quality Progress you can send an email request to info@bec-global.com. Recent articles can be downloaded from www.bec-global.com


FEATURE
CAPA

Pitfalls and Pratfalls

12 missteps that can trip up your CAPA and ways to sidestep them

by José Rodríguez-Pérez and Manuel E. Peña-Rodríguez

A corrective and preventive action (CAPA) system can be most powerful when you need to improve a quality management system (QMS). However, there can be flaws in the way CAPAs are conducted, which can weaken and disrupt your investigation.

The concept of CAPA is not restricted to any particular industry or sector. It is a widely accepted concept, basic to any QMS. Because quality systems strive to continuously improve systems, processes, and products and services, there must be mechanisms in place to recognize existing or potential quality issues, take the appropriate steps necessary to investigate and resolve those issues, and, finally, ensure the same issues do not recur.

Specifically, the life sciences regulated industries (the manufacturing of medical devices, biopharmaceuticals and traditional drugs) are plagued with deviations and nonconformities. Worldwide regulatory agencies perform thousands of inspections every year. Too often, investigation and CAPA system violations are at the top of the list. Here are 12 CAPA missteps and suggestions to overcome them.

1 Lack of an investigation plan

Having a plan is probably the most important element of the investigation. However, you rarely find this critical piece in the investigation report. Most of the time, the investigation is an anarchic process full of back and forth, trial and error, or going-around-in-circles situations. A good investigation plan is essential to

Just the Facts

A corrective and preventive action (CAPA) system can be powerful in improving your organization's quality management system.

To make your CAPA more effective, watch for these 12 common mistakes and address them before your investigation is weakened or disrupted.

42 QP September 2019


FEATURE
SAMPLING

Serious About Samples

Understanding different approaches for process monitoring and when to use them | by Manuel E. Peña-Rodríguez

Sampling is one of the most-used methods in quality systems to control the output of any given process. Specifically, sampling allows organizations to distinguish between good product and defective product. In this way, defective product is rejected, while good product continues through the production stream.

One of the most-discussed topics in sampling is sample size. There are many methods used to determine the size of the sample. There is, however, another important aspect of sample selection: representativeness of the samples.

To be representative, a sample must have the same chance of being collected as the other samples do. Suppose that a sample size is calculated as 32, for example. Obtaining a representative sample would mean collecting four samples every hour during an eight-hour shift.

A non-representative sample would be obtained if you collected the first 32 samples of the shift or the last 32 samples of the shift. Using the first approach (four samples every hour), it would be easier to detect defects if they occur randomly throughout the shift. Sampling only at the beginning or end of the shift, however, makes it difficult to detect defects if they happen randomly throughout the shift.

An example would be sampling labels in a continuous


CAPA SYSTEM

ESSEN

JUST THE FACTS

Don't overlook assessing the effectiveness of your CAPA system and your solutions

by José Rodríguez-Pérez and Manuel E. Peña-Rodríguez

Corrective and preventive action (CAPA) systems are widely used in many industries to assess how a quality management system is performing.

Often, organizations don't thoroughly evaluate the effectiveness of the CAPA plan, as well as the actions being taken to eliminate the problems.

The authors offer advice on evaluating the system and verifying the solutions implemented are effective and working.

EVALU

ATION

40 QP June 2021

Technical Articles published by our staff



Zooming in on Industry-specific Issues

Field Notes

FDA REGULATION

Maintaining Data Integrity

Avoiding regulator scrutiny in the medical products industry

by José Rodríguez Pérez

In August 2015, the European Union (EU) banned the marketing of about 700 Indian-made generic drugs for alleged manipulation of clinical trials data. The largest-ever EU-wide suspension of sales and distribution of generic drugs ordered by the European Commission was applicable to all 28 member nations.[1]

Recently, there has been a dramatic escalation in the number of U.S. Food and Drug Administration (FDA) warning letters, World Health Organization (WHO) notices of concern, and EU statements of noncompliance in which false or misleading information has been identified during inspections. Failure to properly manage data integrity applies equally to paper and electronic data. It can arise either from poor systematic control of the data management systems due to a lack of knowledge, human error or from intentionally hidden, falsified or misleading data.

What is data integrity?

Data integrity is a global mandatory requirement for the regulated healthcare industry. Developing and bringing a medical product to market involves different players and activities; therefore, robustness and accuracy of the data submitted by manufacturers to regulatory authorities is crucial. The data must be comprehensive, complete, accurate and true to ensure the quality of studies supporting applications for medical products to be placed on the market. Complete, consistent, and accurate data must be attributable, legible, contemporaneously recorded, original or a true copy, and accurate (ALCOA).[2] See Table 1.

Data integrity also must comply with good manufacturing practices (GMP), good clinical practices (GCP), and good laboratory practices (GLP). In recent years, however, data integrity issues are jeopardizing the regulatory compliance status of organizations. In many instances, data integrity problems are created by sloppy documentation practices or incidents that cause the loss of data, but regulators tend to label those situations as fraud. Moreover, it demonstrates a lack of commitment

TABLE 1

Complete, consistent and accurate data

Characteristics	Meaning
Attributable	Establishes who performed an action and when. Traceable to an individual.
Legible	Data must be recorded permanently in a durable medium and be readable by others. Traceable changes.
Contemporaneous	Activities must be recorded at the time they occur (when activity is performed or the information is obtained).
Original	The information must be the original record (first capture of the data) or a certified true copy. Not the transcribed data.
Accurate	Data reflect true information.

14 QP March 2017 | qualityprogress.com



Field Notes

chromatography [HPLC] testing sequence versus recording only at the end of the day).

Commitment from all

Data integrity enables good decision-making by manufacturers and regulatory authorities. It is a fundamental mandatory requirement of the medical products quality system, applying equally to manual (paper) and electronic systems. To ensure data integrity, senior management must engage in the promotion of a quality culture along with the implementation of appropriate organizational and technical controls. It requires participation and commitment by staff at all levels within the organization, by the organization's suppliers and by its distributors.

Data integrity is a basic element of good documentation practices, one of the most fundamental pillars of any quality management system, including current good manufacturing practices.

Data integrity is a basic element of good documentation practices, one of the most fundamental pillars of any quality management system, including CGMP. Upper management, and especially quality leaders at every regulated organization must ensure that everyone is accountable for their actions, including having proper documentation of activities performed. Unfortunately, most regulated organizations only react to data integrity issues after regulators discover them.

An outrageous example of this can be found in a warning letter[3] issued in July 2014 in which the FDA required an organization to "identify the specific managers in place who participated in, facilitated, encouraged or failed to stop subordinates from falsifying data in CGMP records, and determine the extent of top and middle management's involvement in or awareness of data manipulation." In the same inspection, the FDA also discovered that "your firm falsified documents designed to demonstrate the effectiveness of CGMP training ... That a senior manager was engaged in the falsification of documents is troubling and raises questions about validity of documents generated by your firm."

Senior management, especially those with quality management responsibilities, should ensure that data integrity risk is assessed, mitigated and communicated in accordance with the principles of quality risk management. The effort and resources assigned to data integrity measures should be commensurate with the risk to product quality, and balanced with other QA resource demands. Where long-term measures are identified to achieve the desired state of control, interim measures should be implemented to mitigate risk and should be monitored for effectiveness.

Data integrity and human error

Finally, remember that regulators do not distinguish between human error or sloppiness, and data falsifications and fraud when assessing the impact of data integrity failures, as demonstrated in the following excerpt from a 2015 FDA warning letter:[4]

"In correspondence with the agency, you indicate that no malicious data integrity patterns and practices were found. Also, you state that no intentional activity to disguise, misrepresent or replace failing data with passing data was identified and no evidence of file deletion or manipulation was found. Your response and comments focus primarily on the issue of intent, and do not adequately address the seriousness of the CGMP violations found during the inspection." QP

REFERENCES

1. "India: EU Bans 700 Generic Drugs Alleging Manipulation of Trials by GVK Biosciences, Company Denies Claim," Business and Human Rights Resource Center, http://tinyurl.com/qp-eu-hr-center.
2. U.S. Food and Drug Administration (FDA), Draft Guidance for Industry "Data Integrity and Compliance With CGMP—Guidance for Industry," draft guidance, April 2016, http://tinyurl.com/qp-fda-draft-guide.
3. Sarah Barlow, "Current Expectations and Guidance, Including Data Integrity and Compliance With CGMP," FDA presentation at the International Society for Pharmaceutical Engineering's Data Integrity Workshop, Bethesda, MD, June 5, 2016, http://tinyurl.com/qp-barlow-present.
4. FDA, "Inspectional Observations—Form FDA 483" Ranbaxy Laboratories Ltd. examples, January 2014, http://tinyurl.com/qp-fda-form.
5. Alexander Gaffney, "India's Data Integrity Problems," Regulatory Affairs Professional Society, Feb. 3, 2015, http://tinyurl.com/qp-raps-data-integrity.
6. Pharmaceutical Inspection Convention, "Draft PIC/S Guidance: Good Practices for Data Management and Integrity in Regulated GMP/GDP Environments," Aug. 10, 2016, www.picscheme.org/layout/document.php?id=714.
7. FDA, "Merck Biosciences Ltd. Warning Letter," July 8, 2014, http://tinyurl.com/qp-fda-warn-letter.
8. FDA, "Apotex Research Private Ltd. Warning Letter," Jan. 30, 2015, http://tinyurl.com/qp-fda-warn-letter2.

FOR MORE INFORMATION

Parenteral Drug Association (PDA), *PDA Letter* April 2015.

International Society for Pharmaceutical Engineering, "Special Report: Data Integrity," *Pharmaceutical Engineering*, March/April 2016, Vol. 36, No. 2, pp. 40-66.

José Rodríguez Pérez is president of Business Excellence Consulting Inc. in Guaynabo, Puerto Rico. He has a doctorate in biology from the University of Granada in Spain. A senior ASQ member, he has many ASQ certifications: auditor, biomedical auditor, hazard analysis and critical control points auditor, engineer, manager of quality/organizational excellence, pharmaceutical good manufacturing practices professional and Six Sigma Black Belt. His most recent book is *Handbook of Investigation and Effective CAPA Systems* (ASQ Quality Press, 2016).

16 QP March 2017 | qualityprogress.com



RISK MANAGEMENT

Fail-Safe FMEA

Combination of quality tools keeps risk in check

by José Rodríguez-Pérez and Manuel E. Peña-Rodríguez

In 50 Words Or Less

- Failing to manage risk puts consumers and entire organizations in jeopardy.
- Using failure mode and effects analysis (FMEA) can help identify risk but isn't enough to avoid potential disaster.
- By combining FMEA with other tools, organizations can ensure their products won't harm the people they're supposed to help.

QUALITY RISK MANAGEMENT principles are used effectively in many areas of business and government—including finance, insurance, occupational safety and public health—and by the agencies regulating these industries.

Risk management's widespread use isn't a surprise because every product and every process has an associated risk. But while there are some examples of the use of quality risk management in the medical product manufacturing industry, they are limited and do not take full advantage of what risk management has to offer. After all, inadequate or ineffective quality risk management can harm patients, product users and company value.

January 2012 • QP 31

Technical Articles published by our staff



IACET—Certificate of Accreditation



ACCREDITED IACET PROVIDER

Certificate of Accreditation

The *International Association for Continuing Education and Training* certifies that

Business Excellence Consulting Inc.

City View Plaza Suite 802

has complied with the ANSI/IACET Standard, which is recognized internationally as a standard of excellence in instructional practices and is authorized to issue the IACET CEU.

Accreditation Begins: 5/1/2020

Accreditation Ends: 4/30/2025

Accreditation Number: 5579680-2

IACET ACCREDITED

BEC-GLOBAL Services Worldwide Presence

BUSINESS
EXCELLENCE
CONSULTING



BEC-GLOBAL
www.bec-global.com **info@bec-global.com**
www.calidadpr.com **info@calidadpr.com**
Ph: +1.787.705.7272

Main Office
City View Plaza, Suite 802
Guaynabo, Puerto Rico, 00968 (USA)

Postal Address
P.O Box 8326, Bayamón, PR, 00960-8326, (USA)