

Guidance for Industry Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations

DRAFT GUIDANCE

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Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Veterinary Medicine (CVM)
Office of Regulatory Affairs (ORA)**

**September 2004
Pharmaceutical CGMPs**

Guidance for Industry

Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations

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43 fact that since 1978, when the last major revision of the CGMP regulations was published, there
44 have been many advances in manufacturing technologies and in our understanding of quality
45 systems. Many pharmaceutical manufacturers are implementing comprehensive, modern quality
46 systems and risk management approaches. The Agency also saw a need to address the
47 harmonization of the CGMPs and other non-U.S. pharmaceutical regulatory systems as well as
48 FDA's own medical device quality systems regulations.

49
50 The CGMP initiative steering committee created a Quality System Guidance Development
51 working group (QS working group) to compare the current CGMP regulations, which call for
52 specific quality management elements, to other existing quality management systems. The QS
53 working group mapped the relationship between CGMP regulations (parts 210 and 211 and the
54 1978 Preamble to the CGMP regulations²) and various quality system models, such as the Drug
55 Manufacturing Inspections Program (i.e., systems-based inspectional program),³ the
56 Environmental Protection Agency's Guidance for Developing Quality Systems for
57 Environmental Programs, ISO Quality Standards, other quality publications, and experience
58 from regulatory cases. The QS working group determined that, although the regulations do
59 provide great flexibility, the CGMP regulations do not consider all of the elements that today
60 constitute most quality management systems. The CGMP regulations and other systems differ
61 somewhat in organization and in certain constituent elements; however, they are very similar and
62 share underlying principles. For example, the CGMP regulations stress quality control. More
63 recently developed quality systems stress quality management, quality assurance, and the use of
64 risk management tools, in addition to quality control. The QS working group decided that it
65 would be very useful to examine exactly how the CGMP regulations and the elements of a
66 modern, comprehensive quality system fit together in today's manufacturing world. This
67 guidance is the result of that examination.

68 **B. Goal of the Guidance**

69
70
71 This guidance describes a comprehensive quality systems model, which, if implemented, will
72 allow manufacturers to operate robust, modern quality systems that are fully compliant with
73 CGMP regulations. The guidance demonstrates how and where the requirements of the CGMP
74 regulations fit within this comprehensive model. The inherent flexibility of the CGMP
75 regulations should enable manufacturers to implement a quality system in a form that is
76 appropriate for their specific operations.

77
78 The overarching philosophy articulated in both the CGMP regulations *and* in robust modern
79 quality systems is:

80
81 ***Quality should be built into the product, and***
82 ***testing alone cannot be relied on to ensure product quality.***
83

² See Reference #1.

³ See Reference #2.

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84 This guidance is intended to serve as a bridge between the 1978 regulations and our current
85 understanding of quality systems. In addition to being part of the FDA's CGMP initiative, this
86 guidance is being issued for a number of reasons:
87

- 88 • A quality system addresses the public and private sectors' mutual goal of providing a high-
89 quality drug product to patients and prescribers. A well-built quality system should prevent
90 or reduce the number of recalls, returned or salvaged products, and defective products
91 entering the marketplace.
- 92 • It is important that we harmonize the CGMPs to the extent possible with other widely used
93 quality management systems including ISO 9000, non-U.S. pharmaceutical quality management
94 requirements, and FDA's own medical device quality system regulations. With the globalization
95 of pharmaceutical manufacturing and the increasing prevalence of drug- and biologic-device
96 combination products, the convergence of quality management principles across different regions
97 and among various product types is very desirable.
- 98 • The FDA has concluded that modern quality systems, when coupled with manufacturing process
99 and product knowledge, can handle many types of changes to facilities, equipment, and processes
100 without the need for a regulatory submission. Manufacturers with appropriate process knowledge
101 and a robust quality system should be able to implement many types of improvements without the
102 need for a prior regulatory filing. In addition, an effective quality system, by lowering the risk of
103 manufacturing problems, may result in shorter and fewer FDA inspections.
- 104 • A quality system can provide the necessary framework for implementing *quality by design*⁴
105 (building in quality from the development phase and throughout a product's life-cycle),
106 continuous improvement, and risk management in the drug manufacturing process. A quality
107 system adopted by a manufacturer can be tailored to fit the specific environment, taking into
108 account factors such as scope of operations, complexity of processes, and appropriate use of finite
109 resources.
110

111 C. Scope of the Guidance

112
113 This guidance applies to manufacturers of drug products (finished pharmaceuticals), including
114 products regulated by the Center for Biologics Evaluation and Research (CBER), the Center for
115 Drug Evaluation and Research (CDER), and the Center for Veterinary Medicine (CVM). It may
116 also be useful to manufacturers of components used in the manufacture of these products.
117

118 This document is *not* intended to create new expectations for pharmaceutical manufacturing that
119 go beyond the requirements laid out in the current regulations nor is the guidance intended to be
120 a guide for the conduct of FDA inspections. Rather, the document explains how implementing
121 comprehensive quality systems can help manufacturers achieve compliance with 21 CFR parts
122 210 and 211. Although the QS working group found that many of the quality system elements
123 correlate with specific CGMP requirements, some do not. In the end, the Agency expects
124 compliance with the CGMP regulations, and FDA's inspection program remains geared to
125 compliance with those regulations.
126

⁴ This concept is being developed under the ICH Q8 Pharmaceutical Development Expert Working Group.

127 **D. Organization of this Draft Guidance**
128

129 To provide a reference familiar to industry, the quality systems model described in this guidance
130 is organized — in its major sections — according to the structure of international quality
131 standards. Major sections of the model include the following:
132

- 133 • Management Responsibilities
 - 134 • Resources
 - 135 • Manufacturing Operations
 - 136 • Evaluation Activities
- 137

138 Under each of these sections the key elements found in modern quality systems are discussed.
139 When an element correlates with a CGMP regulatory requirement, we note that correlation. In
140 some cases, a specific CGMP regulation is discussed in more detail as it relates to a quality
141 system element. At the end of each section, a table is included listing the quality system
142 elements of that section and the specific CGMP regulations with which they correlate. A
143 glossary is included at the end of the document.
144
145

146 **III. CGMPs AND THE CONCEPTS OF MODERN QUALITY SYSTEMS**
147

148 Several key concepts are critical for any discussion of modern quality systems. The following
149 concepts are used throughout this guidance as they relate to the manufacture of pharmaceutical
150 products.
151

152 **A. Quality**
153

154 Every pharmaceutical product has established identity, strength, purity, and other quality
155 characteristics designed to ensure the required levels of safety and effectiveness. For the
156 purposes of this draft guidance document, the phrase *achieving quality* means achieving these
157 characteristics for the product.
158

159 **B. Quality by Design and Product Development**
160

161 *Quality by design* means designing and developing manufacturing processes *during the product*
162 *development* stage to consistently ensure a predefined quality at the end of the manufacturing
163 process.⁵ A quality system provides a sound framework for the transfer of process knowledge
164 from development to the commercial manufacturing processes and for postdevelopment changes
165 and optimization
166

167 **C. Risk Management and Risk Assessment**
168

169 The concept *risk management* is a major focus of the Pharmaceutical CGMPs for the 21st
170 Century Initiative. Risk management can guide the setting of specifications and process

⁵ These concepts are being developed under the ICH-Q8 Pharmaceutical Development Expert Working Group.

171 parameters. Risk assessment is also used in determining the need for discrepancy investigations
172 and corrective action. As risk assessment⁶ is used more formally by manufacturers, it can be
173 implemented within the quality system framework.

174

175 **D. CAPA (Corrective and Preventive Action)**

176

177 *CAPA* is a well-known CGMP regulatory concept that focuses on investigating and correcting
178 discrepancies and attempting to prevent recurrence. Quality system models discuss *CAPA* as
179 three concepts, all of which are used in this guidance.

180

- 181 • Remedial corrections
- 182 • Root cause analysis with corrective action to prevent recurrence
- 183 • Preventive action to prevent initial occurrence

184

185 **E. Change Control**

186

187 *Change control* is another well-known CGMP regulatory concept that focuses on managing
188 change to prevent unintended consequences. The major implementation of change control in the
189 CGMP regulations is through the assigned responsibilities of the quality control unit. Certain
190 manufacturing changes (e.g., changes that alter specifications, a critical product attribute or
191 bioavailability) require regulatory filings and prior regulatory approval (601.12 and 314.70).

192

193 A quality system also contains change control activities, including quality planning and control
194 of revisions to specifications, process parameters, and procedures. In this guidance, *change* is
195 discussed in terms of creating a regulatory environment that encourages change towards
196 continuous improvement. This means a manufacturer is empowered to make changes based on
197 the variability of materials used in manufacturing and optimization of the process from learning
198 over time.

199

200 **F. The Quality Unit**

201

202 Many of the modern quality systems ideas described in this section correlate very closely with
203 the CGMP regulations (refer to the charts later in the document). Current industry practice
204 generally divides the responsibilities of the Quality Control Unit (QCU), as defined in the CGMP
205 regulations, between quality control (QC) and quality assurance (QA) functions.

206

- 207 • QC usually consists of testing of selected in-process materials and finished products to
208 evaluate the performance of the manufacturing process, and to ensure adherence to
209 proper specifications and limits.
- 210 • QA primarily includes the review and approval of all procedures related to production,
211 maintenance, and review of associated records, and auditing, and performing trend
212 analyses.

⁶ This concept is being developed under the ICH Q9 Risk Analysis Expert Working Group.

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213 This guidance uses the term *quality unit*⁷ (QU) to reflect modern practice while remaining
214 consistent with the CGMP definition in 21 CFR 210.3(b)(15). The concept *quality unit* is also
215 consistent with modern quality systems in ensuring that the various operations associated with all
216 systems are appropriately conducted, approved, and monitored. The CGMP regulations
217 specifically assign the quality unit the authority to create, monitor, and implement the quality
218 system. However, the quality unit is not meant to take on the responsibilities of other units of a
219 manufacturer's organization, such as the responsibilities handled by manufacturing personnel,
220 engineers, and development scientists.⁸

221
222 Other CGMP assigned responsibilities of the quality unit are consistent with a modern quality
223 system approaches (see § 211.22):

- 224
225 • Ensuring that controls are implemented and completed satisfactorily during
226 manufacturing operations
- 227 • Ensuring that developed procedures and specifications are appropriate and followed,
228 including those used by a firm under contract to the manufacturer
- 229 • Approving or rejecting in-process materials and drug products — although such activities
230 do not substitute for, or preclude, the daily responsibility of manufacturing personnel to
231 build quality into the product
- 232 • Reviewing production records and investigating any unexplained discrepancies
233

234 Under a robust quality system, the manufacturing units and the quality unit can remain
235 independent, but still be included in the total concept of producing quality products. In very
236 small operations, a single individual can function as the quality unit. That person is still
237 accountable for implementing all the controls and reviewing results of manufacture to ensure that
238 product quality standards have been met.

239 **G. Six-system Inspection Model**

240
241 The FDA's Drug Manufacturing Inspection Compliance Program, which constitutes instructions
242 to FDA personnel for conducting inspections, is a systems-based approach for inspections and is
243 very consistent with the robust quality systems model presented in this guidance.⁹ The diagram
244 below shows the relationship among the six systems: the quality system and the five
245 manufacturing systems. The quality system provides the foundation for the manufacturing
246 systems that are linked and function within it. The quality systems model described in this
247 guidance does not treat the five manufacturing systems as discrete entities, but instead integrates
248 them into appropriate sections of the model. Those familiar with the six-system inspection
249 approach will see organizational differences in this guidance; however, the inter-relationship

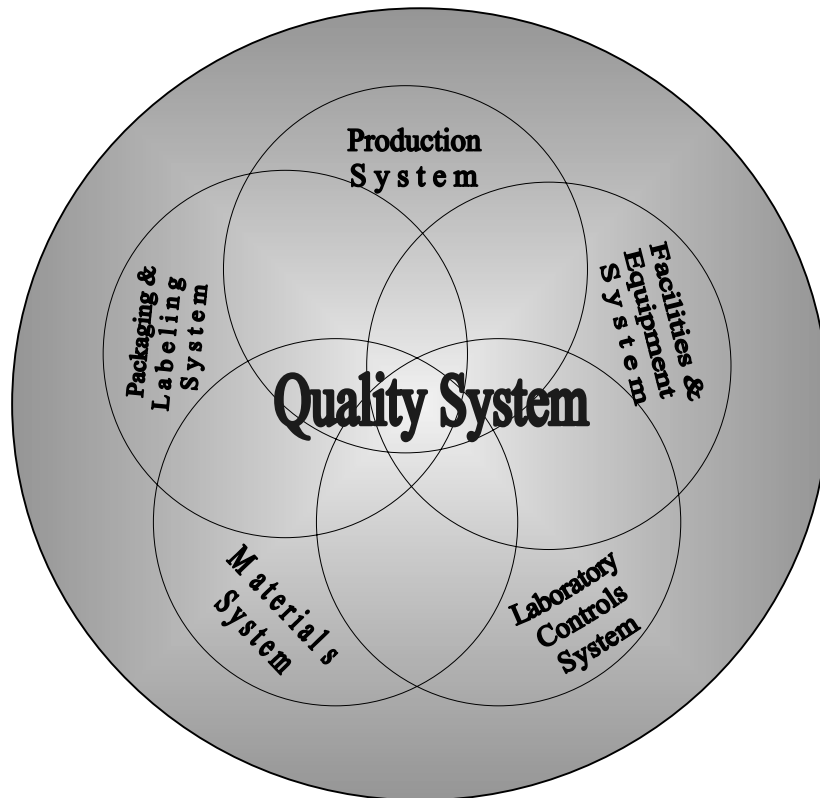
⁷ Generally, the term *quality unit* is used in this guidance. However, *quality control unit* is used when directly quoting parts 210 and 211.

⁸ See Reference #1, comment 91.

⁹ See Reference #2; This inspectional approach is currently in use by CDER and CBER for blood and blood product inspections. CBER and CVM are developing a similar approach for drug product inspections.

250 should be readily apparent. One of the important themes of the systems based inspection
251 compliance program is to be able to assess whether each of the systems is in a state of control.
252 The quality system model presented in this guidance will also serve to help firms achieve the
253 desired state of control.
254

255 **FIG. 1 - SIX-SYSTEM INSPECTION APPROACH**
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IV. THE QUALITY SYSTEMS MODEL

The goal of this section is to describe a model for use in pharmaceutical manufacturing that can help achieve compliance with CGMP regulations. It should be noted that implementing an effective quality system in a manufacturing organization will require significant costs in time and resources. However, the long-term benefits of implementing a quality system will outweigh the costs.¹⁰

This section describes a robust quality systems model, which, if implemented, can provide the controls needed to consistently produce a product of acceptable quality. Where applicable, the relationship between elements of this model and CGMP regulations is noted. At the end of each section, a table shows how the specific CGMP regulations correlate to the elements in the quality systems model. As already explained, many of the quality systems elements correlate closely with the CGMP regulations. It is important to emphasize that this guidance is not recommending new regulatory requirements. The guidance is intended to provide recommendations to manufacturers who are implementing, or plan to implement, a quality systems model to help them comply with CGMP regulations. FDA regulatory and inspectional coverage will remain focused on the specific CGMP regulations.

The model is organized into four major sections:

- Management Responsibilities
- Resources
- Manufacturing Operations
- Evaluation Activities

Under each of these sections, the specific elements of a robust modern quality systems model are described. When elements of the quality systems model correlate with specific CGMP regulations, this correlation is noted.

A. Management Responsibilities

Modern robust quality systems models call for management to play a key role in the design, implementation, and management of the quality system. For example, management is responsible for establishing the quality systems structure appropriate for the specific organization. Management has ultimate responsibility to provide the leadership needed for the successful functioning of the quality system. This section describes management's role in developing, implementing, and managing a robust quality system. There is little overlap with the CGMP regulations in this section (see the table at the end of the section).

1. Provide Leadership

In a robust, modern quality system, senior management demonstrates commitment to developing and maintaining their quality system. Leadership is demonstrated by aligning quality system

¹⁰ See Reference #3

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318 plans with the manufacturer's strategic plans to ensure that the quality system supports the
319 manufacturer's mission and strategies. Senior managers set implementation priorities and
320 develop action plans. Managers can provide support of the quality system by:

- 321
- 322 • Actively participating in system design, implementation, and monitoring, including
323 system review (see IV.A.5.)
 - 324 • Advocating continual improvement of operations and the quality system
 - 325 • Committing necessary resources
- 326

327 In a robust quality systems environment, managers should demonstrate strong and visible
328 support for the quality system and ensure its global implementation throughout the organization
329 (e.g., across multiple sites).

330

331 Managers should also encourage internal communication on quality issues at all levels in the
332 organization. Communication should be ongoing among research and development, regulatory
333 affairs, manufacturing, and quality unit personnel on issues that affect quality, with management
334 included whenever appropriate.

335

336 2. *Structure the Organization*

337

338 When designing a robust quality system, management has the responsibility to determine the
339 structure of the organization and ensure that assigned authorities and responsibilities support the
340 production, quality, and management activities needed to produce quality products. Senior
341 managers have the responsibility to ensure that the organization's structure is documented.

342

343 Managers have the responsibility to communicate employee roles, responsibilities, and
344 authorities within the system and ensure that interactions are defined and understood.

345

346 An organization also has the responsibility to give the individual who is appointed to manage the
347 quality system the authority to detect problems and effect solutions. Usually, a senior manager
348 administers the quality system and can, thus, ensure that the organization receives prompt
349 feedback on quality issues.

350

351 3. *Build Your Quality System to Meet Requirements*

352

353 Implementing a robust quality system can help ensure compliance with regulations related to
354 safety, identity, strength, quality, and purity as long as the quality system addresses the minimum
355 requirements of CGMP regulations as well as the needs of the manufacturer. Under the quality
356 systems model, the Agency recommends that senior managers ensure that the quality system they
357 design and implement provides clear organizational guidance and facilitates systematic
358 evaluation of issues. For example, according to the model, when documenting a quality system,
359 the following should be included.

360

- 361 • The scope of the quality system, including any outsourcing (see IV.B.4.)
- 362 • The standard of quality that will be used

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- 363 • The manufacturer's policies to implement the quality systems criteria, and the
364 supporting objectives (see IV.A.4.)
- 365 • The procedures needed to establish and maintain the quality system

366 It is recommended under a modern quality systems approach that a formal process be established
367 to submit change requests to directives. It is also recommended that, when operating under a
368 quality system, manufacturers develop and document record control procedures to complete,
369 secure, protect, and archive records, including data, which act as evidence of operational and
370 quality system activities. This approach is consistent with the CGMP regulations, which require
371 manufacturers to develop and document controls for specifications, plans, and procedures that
372 direct operational and quality system activities and to ensure that these directives are accurate,
373 appropriately reviewed and approved, and available for use (see the CGMPs at §§ 211.22 (c) and
374 (d)).

375
376 4. *Establish Policies, Objectives, and Plans*

377
378 Under a modern quality system, policies, objectives, and plans provide the means by which
379 senior managers articulate their vision of quality to all levels of the organization.

380
381 It is expected that under a quality system senior management would incorporate a strong
382 commitment to quality into the organizational mission. Senior managers are expected to develop
383 an organizational quality policy that aligns with this mission; commit to meeting requirements
384 and improving the quality system; and propose objectives to fulfill the quality policy. Under a
385 quality system, to make the policy relevant, it must be communicated to, and understood by,
386 personnel and contractors (as applicable), and revised as needed.

387
388 Managers operating within a quality system are expected to define the quality objectives needed
389 to implement the quality policy. Senior management is expected to ensure that the quality
390 objectives are created at the top level of the organization (and other levels as needed) through a
391 formal quality planning process. Objectives are typically aligned with the manufacturer's
392 strategic plans. A quality system seeks to ensure that managers support the objectives with
393 necessary resources and have measurable goals that are monitored regularly.

394
395 Under a quality system, managers would be expected to use quality planning to identify
396 resources and define methods to achieve the quality objectives. It is recommended that quality
397 plans be documented and communicated to personnel to ensure awareness of how their
398 operational activities are aligned with strategic and quality goals.

399
400 5. *Review the System*

401
402 System review is a key component in any robust quality system to ensure its continuing
403 suitability, adequacy, and effectiveness. Under a quality system, senior managers are expected
404 to conduct reviews of the whole quality system according to a planned schedule. Such a review
405 typically includes both an assessment of the product as well as customer needs (in this section,
406 *customer* is defined as the recipient of the product and the product is the goods or services being
407 provided). Under a quality system, the review should consider at least the following:

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- 409 • The appropriateness of the quality policy and objectives
- 410 • The results of audits and other assessments
- 411 • Customer feedback, including complaints
- 412 • The analysis of data trending results
- 413 • The status of actions to prevent a potential problem or a recurrence
- 414 • Any follow-up actions from previous management reviews
- 415 • Any changes in business practices or environment that may affect the quality system
- 416 (such as the volume or type of operations)
- 417 • Product characteristics meet the customer's needs

418 When developing and implementing new quality systems, reviews should take place more
419 frequently than when the system has matured. Outside of scheduled reviews, the quality system
420 is typically included as a standing agenda item in general management meetings.

421
422 Review outcomes typically include:

- 423 • Improvements to the quality system and related quality processes
- 424 • Improvements to manufacturing processes and products
- 425 • Realignment of resources

426
427
428 Under a quality system, the results of a management review are expected to be recorded.
429 Planned actions should be implemented using effective corrective and preventive action and
430 change control procedures.

431
432 The following table shows how the CGMP regulations correlate to specific elements in the
433 quality systems model for this section. Manufacturers should always refer to the specific
434 regulations to ensure that they are complying with all regulations.

435

21 CFR CGMP Regulations Related to Management Responsibilities	
Quality System Element	Regulatory Citations
1. Leadership	—
2. Structure	Establish quality function: § 211.22 (a) (see definition § 210.3(b)(15))
	Notification: § 211.180(f)
3. Build QS	QU procedures: § 211.22(d)
	QU procedures, specifications: § 211.22(c), with reinforcement in: §§ 211.100(a), 211.160(a)

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	QU control steps: § 211.22(a), with reinforcement in §§: 211.42(c), 211.84(a), 211.87, 211.101(c)(1), 211.110(c), 211.115(b), 211.142, 211.165(d), 211.192
	QU quality assurance; review/investigate: § 211.22(a), 211.100(a-b) 211.180(f), 211.192, 211.198(a)
	Record control: § 211.180(a-d), 211.180(c), 211.180(d), 211.180(e), 211.186, 211.192, 211.194, 211.198(b)
4. Establish Policies, Objectives and Plans	Procedures: § 211.22(c-d), 211.100(a)
5. System Review	Record review: § 211.180(e), 211.192, 211.198(b)(2)

436

437

438

B. Resources

439

440 Appropriate allocation of resources is key to creating a robust quality system and to complying
441 with the CGMP regulations. This section discusses the role of resources in developing,
442 implementing, and managing a robust quality system that fully complies with the CGMP
443 regulations.

444

445 *1. General Arrangements*

446

447 Under a robust quality system, there should be sufficient allocation of resources for quality
448 system and operational activities. Under the model, senior management, or a designee, is
449 responsible for providing adequate resources for the following:

450

- 451 • To supply and maintain the appropriate facilities and equipment to consistently
452 manufacture a quality product
- 453 • To acquire and receive materials that are suitable for their intended purpose
- 454 • For processing the materials to produce the finished drug product
- 455 • For laboratory analysis of the finished drug product, including collection, storage, and
456 examination of in-process, stability, and reserve samples

457 *2. Develop Personnel*

458

459 Under a quality system, senior management is expected to support a problem-solving and
460 communicative organizational culture. Managers are expected to encourage communication by
461 creating an environment that values employee suggestions and acts on suggestions for
462 improvement. Management is also expected to develop cross-cutting groups to share ideas to
463 improve procedures and processes.

464

465 In the quality system, it is recommended that personnel be qualified to do the operations that are
466 assigned to them in accordance with the nature of, and potential risk to quality presented by, their
467 operational activities. Under a quality system, managers are expected to define appropriate
468 qualifications for each position to help ensure individuals are assigned appropriate

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469 responsibilities. Personnel should also understand the impact of their activities on the product
470 and the customer (this quality systems parameter is also found in the CGMP regulations, which
471 identify specific qualifications (i.e., education, training, and experience or any combination
472 thereof; see §§ 211.25(a) & (b)).

473
474 Under a quality system, continued training is critical to ensure that the employees remain
475 proficient in their operational functions and in their understanding of CGMP regulations.
476 Typical quality systems training would address the policies, processes, procedures, and written
477 instructions related to operational activities, the product/service, the quality system, and the
478 desired work culture (e.g., team building, communication, change, behavior). Under a quality
479 system (and the CGMP regulations), training is expected to focus on both the employees’
480 specific job functions and the related CGMP regulatory requirements.

481
482 Under a quality system, managers are expected to establish training programs that include the
483 following:

- 484
- 485 • Evaluation of training needs
 - 486 • Provision of training to satisfy these needs
 - 487 • Evaluation of effectiveness of training
 - 488 • Documentation of training and/or re-training

489 When operating in a robust quality system environment, it is important that supervisory
490 managers ensure that skills gained from training be incorporated into day-to-day performance.

491 *3. Facilities and Equipment*

492
493 Under a quality system, the technical experts (e.g., engineers, development scientists), who have
494 an understanding of pharmaceutical science, risk factors, and manufacturing processes related to
495 the product, are responsible for specific facility and equipment requirements.

496
497 According to CGMP regulations, the QCU has the responsibility of reviewing and approving all
498 initial design criteria and procedures pertaining to facilities and equipment and any subsequent
499 changes (see § 211.22(c)). FDA can, as resources permit, provide a preoperational review of
500 manufacturing facilities.¹¹

501
502 According to the CGMP regulations, equipment must be qualified, calibrated, cleaned, and
503 maintained to prevent contamination and mix-ups (§§ 211.63, 211.67, 211.68). Note that the
504 CGMP regulations require a higher standard for calibration and maintenance than most generic
505 quality system models. The CGMP regulations place as much emphasis on process equipment as
506 on testing equipment (§ 211.42(b)), while most quality systems focus only on testing
507 equipment.¹²

508
509

¹¹ See Reference #4.

¹² See Reference #5.

510 4. Control Outsourced Operations

511
512 When outsourcing, a second party is hired under a contract to perform the operational processes
513 that are part of a manufacturer's inherent responsibilities. For example, a manufacturer may hire
514 another firm to package and label or perform CGMP regulation training. Quality systems call for
515 contracts (quality agreements) that clearly describe the materials or service, quality specifications
516 responsibilities, and communication mechanisms.

517
518 Under a quality system, the manufacturer ensures that the contract firm is qualified. The firm's
519 personnel should be adequately trained and monitored for performance according to their quality
520 system, and the contract firm's and contracting manufacturer's quality standards should not
521 conflict. It is critical in a quality system to ensure that the contracting manufacturer's officers
522 are familiar with the specific requirements of the contract. However, under the CGMP
523 requirements, the QCU is responsible for approving or rejecting products or services provided
524 under contract (see § 211.22(a)).

525
526 As the following table illustrates, the CGMP regulations are consistent with the elements of a
527 quality system in many areas in this section. However, manufacturers should always refer to the
528 specific regulations to ensure that they are complying with all regulations.

529

21 CFR CGMP Regulations Related to Resources	
Quality System Element	Regulatory Citation
1. General Arrangements	—
2. Develop Personnel	Qualifications: § 211.25(a)
	Staff number: § 211.25(c)
	Staff training: § 211.25(a-b)
3. Facilities and Equipment	Buildings and facilities: §§ 211.22(b), 211.28(c), 211.42 – 211.58, 211.173
	Equipment: § 211.63 – 211.72, 211.105, 211.160(b)(4), 211.182
	Lab facilities: § 211.22(b)
4. Control Outsourced Operations	Consultants: § 211.34
	Outsourcing: § 211.22(a)

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532

533

C. Manufacturing Operations

534 There is significant overlap between the elements of a quality system and the CGMP regulation
535 requirements for manufacturing operations. It is important to emphasize again that FDA's
536 enforcement programs and inspectional coverage remain based on the CGMP regulations. When
537 quality system elements in this section do not correlate to the CGMP regulations, the guidance

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538 makes recommendations to help facilitate compliance with the CGMP regulations. The language
539 in this section has been tailored to the pharmaceutical manufacturing environment.

540

541 *1. Design and Develop Product and Processes*

542

543 In a modern quality systems manufacturing environment, the significant characteristics of the
544 product being manufactured should be defined, from design to delivery, and control should be
545 exercised over all changes. Quality and manufacturing processes and procedures — and changes
546 to them — should be defined, approved, and controlled (CGMP also requires this; see §
547 211.100). It is important to establish responsibility for designing or changing products.

548 Documenting associated processes will ensure that critical variables are identified.

549 This documentation includes:

550

551 • Resources and facilities needed

552 • Procedures to carry out the process

553 • Identification of the process owner who will maintain and update the process as
554 needed

555 • Identification and control of critical variables

556 • Quality control measures, necessary data collection, monitoring, and appropriate
557 controls for the product and process

558 • Any validation activities, including operating ranges and acceptance criteria

559 • Effects on related process, functions, or personnel

560 As discussed under section IV.A. Management, above, the model calls for managers to ensure
561 that product specifications and process parameters are determined by the appropriate technical
562 experts (e.g., engineers, development scientists). In the pharmaceutical environment, experts
563 would have an understanding of pharmaceutical science, risk factors, and manufacturing
564 processes as well as how variations in materials and processes can ultimately affect the finished
565 product.

566

567 *2. Monitor Packaging and Labeling Processes*

568

569 Packaging and labeling controls, critical stages in the pharmaceutical manufacturing process, are
570 not specifically addressed in quality systems models. Therefore, the Agency recommends that
571 manufacturers always refer to the packaging and labeling control regulations at 21 CFR 211
572 Subpart G. In addition — and this *is* consistent with modern quality systems — FDA
573 recommends that, as part of the design process, before commercial production, the controls for
574 all processes within the packaging and labeling system be planned and documented in written
575 procedures. The procedures should outline quality control activities and the responsible
576 positions. Specifications and controls for the packaging and labeling materials should also be
577 determined before commercial production. Distinct labels with discriminating features for
578 different products, such as a product marketed with different strengths, should be included to
579 prevent mislabeling and resulting recalls.

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581 In modern quality systems environments, when new or reengineered processes are developed, it
582 is expected that they will be designed in a controlled manner. A design plan would include
583 authorities and responsibilities; design and development stages; and appropriate review,
584 verification, and validation. If different groups are involved in design and development, the
585 model recommends that responsibilities of the different groups be documented to avoid omission
586 of key duties and ensure that the groups communicate effectively. Plans should be updated when
587 needed during the design process. Prior to implementation of processes (or shipment of a
588 product), a robust quality system will ensure that the process and product will perform as
589 intended. Change controls should be maintained throughout the design process.

590

591 *3. Examine Inputs*

592

593 In modern quality systems models, the term *input* refers to any material that goes into a final
594 product, no matter whether the material is purchased by the manufacturer or produced by the
595 manufacturer for the purpose of processing. *Materials* can include items such as components
596 (e.g., ingredients, process water, and gas), containers, and closures. A robust quality system will
597 ensure that all inputs to the manufacturing process are reliable because quality controls will have
598 been established for the receipt, production, storage, and use of all inputs.

599

600 The quality systems model calls for the verification of the components and services provided by
601 suppliers and contractors; however, the model offers a method for implementing verification that
602 is different from those in the CGMP regulations.

603

604 The CGMP regulations require either testing or use of a certificate of analysis (COA) plus an
605 identity analysis (see §§ 211.22 and 211.84). In the preamble to the CGMP regulations (see
606 comment 239 in the preamble), these requirements were explicitly interpreted. The preamble
607 states that reliability can be validated by conducting tests or examinations and comparing the
608 results to the supplier's COA. Sufficient initial tests must be done to establish reliability and to
609 determine a schedule for periodic rechecking. As an essential element of purchasing controls, it
610 is recommended that data for acceptance and rejection of materials be analyzed for information
611 on supplier performance.¹³

612

613 The quality systems approach also calls for the auditing of suppliers on a periodic basis. During
614 the audit, the manufacturer can observe the testing or examinations conducted by the supplier to
615 help determine the reliability of the supplier's COA. An audit should also include a systematic
616 examination of the supplier's quality system to ensure that reliability is maintained. The FDA
617 recommends that a combination approach be used (i.e., verifying the suppliers' COA through
618 analysis and audits of the supplier). If full analytical testing is not done, the audit should cover
619 the supplier's analysis. (A specific identity test is still required in § 211.84(d)(1).)

620

621 Under a quality systems approach, there should be procedures to verify that materials are from
622 approved sources (for application and licensed products, certain sources are specified in the

¹³ The Agency recommends that manufacturers have a measure of the variability of materials that could affect their process controls. For example, certain changes in physical properties may affect the process, which may affect a finished product's dissolution characteristics.

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623 submissions). Procedures should also be established to encompass the acceptance, use, or the
624 rejection and disposition of materials produced by the facility (e.g., purified water). Systems that
625 produce these in-house materials should be designed, maintained, qualified, and validated where
626 appropriate to ensure the materials meet their acceptance criteria.

627
628 In addition, we recommend that changes to materials (e.g., specification, supplier, or materials
629 handling) be implemented through a change control system (certain changes require review and
630 approval by the quality control unit (see § 211.100(a)). It is also important to have a system in
631 place to respond to changes in materials from suppliers so that necessary adjustments to the
632 process can be made and unintended consequences prevented.

633
634 *4. Perform and Monitor Operations*

635
636 The core purpose of implementing a quality systems approach is to enable a manufacturer to
637 more efficiently and effectively perform and monitor operations. The goal of establishing,
638 adhering to, measuring, and documenting specifications and process parameters is to objectively
639 assess whether an operation is meeting its design (and product performance) objectives. In a
640 robust quality system, production and process controls should be designed to ensure that the
641 finished products have the identity, strength, quality and purity they purport or are represented to
642 possess (CGMP also requires this; see § 211.100(a)).

643
644 In a modern quality system, a design concept established during product development typically
645 matures into a commercial design after process experimentation and progressive modification.
646 Areas of process weakness should be identified, and factors that are influential on critical quality
647 attributes should receive increased scrutiny. (The FDA recommends that scale-up studies be
648 used to help demonstrate that a fundamentally sound *design* has been fully realized.) A
649 sufficiently robust manufacturing process should be in place prior to commercial production.
650 With proper design (see section IV.C.1), and reliable mechanisms to transfer process knowledge
651 from development to commercial production, a manufacturer should be able to validate the
652 manufacturing process.¹⁴ In a quality system, process validation provides initial proof, through
653 commercial batch manufacture, that the design of the process produces the intended product
654 quality. Sufficient testing data will provide essential information on performance of the new
655 process, as well as a mechanism for continuous improvement. Modern equipment with the
656 potential for continuous monitoring and control can further enhance this knowledge base.
657 Although initial commercial batches can provide evidence to support the validity and consistency
658 of the process,¹⁵ the *entire life-cycle* should be addressed by the establishment of continuous
659 improvement mechanisms in the quality system.¹⁶ Thus, in accordance with the quality systems
660 approach, process validation is not a one time event, but an activity that continues.

661

¹⁴ See Reference #6.

¹⁵ Even with good design and development work, initial *conformance batches* only provide confidence that future batches will meet specifications if the process is repeated within defined operating parameters, equipment tolerances, personnel practices, environmental attributes, and material quality.

¹⁶ See Reference #7.

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662 As experience is gained in commercial production, opportunities for process improvements may
663 become evident. (CGMP regulations at § 211.180 require the review and evaluation of records
664 to determine the need for any change. These records contain data and information from
665 production that provide insights into the product's state of control. Change control systems
666 should provide for a dependable mechanism for prompt implementation of technically sound
667 manufacturing improvements.)
668

669 Under a quality system, written procedures are followed and deviations from them are justified
670 and documented (CGMP requires this; see § 211.100(b)) to ensure that the manufacturer can
671 trace the history of the product, as appropriate, concerning personnel, materials, equipment, and
672 chronology and that processes for product release are complete and recorded.
673

674 Both the CGMP regulations (see § 211.110) and quality systems models call for the monitoring
675 of critical process parameters during production.
676

- 677 • Process steps should be verified using a validated computer system or a second person.
678 Batch production records should be prepared contemporaneously with each phase of
679 production. Although time limits can be established when they are important to the
680 quality of the finished product (CGMP addresses this; see § 211.111), this does not
681 preclude the ability to establish production controls based on in-process parameters that
682 can be based on desired process endpoints measured using real time testing or monitoring
683 apparatus (e.g., blend until mixed vs. blend for 10 minutes).
- 684 • Procedures should be in place to prevent objectionable microorganisms in finished
685 product that is not required to be sterile and to prevent microbial contamination of
686 finished products purported to be sterile (CGMP also requires this; see § 211.113)
687 Sterilization processes should be validated (CGMP also requires this; see § 211.113(b))
688 for sterile drugs.¹⁷

689 Pharmaceutical products must meet their specifications and manufacturing processes must
690 consistently meet their parameters. Under a quality system, selected data are used to evaluate the
691 quality of a process or product. In addition, data collection can provide a means to encourage
692 and analyze potential suggestions for improvement. A quality systems approach calls for the
693 manufacturer to develop procedures that monitor, measure, and analyze the operations (including
694 analytical methods and/or statistical techniques). Knowledge continues to accumulate from
695 development through the entire commercial life of the product. Significant unanticipated
696 variables should be detected by a well-managed quality system and adjustments implemented.
697 Procedures should be revisited as needed to refine operational design based on new knowledge.
698 Process understanding increases with experience and helps identify the need for change towards
699 continuous improvement. When implementing data collection procedures, consider the
700 following:

- 701 — Are collection methods documented?
- 702 — When in the product life-cycle will the data be collected?
- 703 — How and to whom will measurement and monitoring activities be assigned?
- 704

¹⁷ See Reference #8

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705 — When should analysis and evaluation (e.g. trending) of laboratory data be performed
706 (see V.E.1.)?

707 — What records are needed?

708 A modern quality system approach indicates that change control is warranted when data analysis
709 or other information reveals an area needing improvement. Changes to an established process
710 should be controlled and documented to ensure that desired attributes for the finished product
711 will be met (CGMP also requires this; see § 211.100(a)).

712
713 Change control with regard to pharmaceuticals is addressed in more detail in the CGMPs. When
714 developing a process change, it is important to keep the process design and scientific knowledge
715 of the product in mind. When major design issues are encountered through process experience, a
716 firm may need to revisit the adequacy of the design of the manufacturing facility (§ 211.42), the
717 design of the manufacturing equipment (§ 211.63), the design of the production and control
718 procedures (§ 211.100), or the design of laboratory controls (§ 211.160). When implementing a
719 change, determining its effect should be based on monitoring and evaluating those specific
720 elements that may be affected based on understanding of the process. This allows the steps taken
721 to implement a change and the effects of the change on the process to be considered
722 systematically. Evaluating the effects of a change can entail additional tests or examinations of
723 subsequent batches (e.g., additional in-process testing or additional stability studies).

724
725 The quality system elements identified in this guidance, if implemented, will help a manufacturer
726 manage change and implement continuous improvement in manufacturing.

727
728 Under a quality system, procedures should be in place to ensure the accuracy of test results. Test
729 results that are out of specification may be due to testing problems or manufacturing problems
730 and should be investigated.¹⁸ Invalidation of test results should be scientifically and statistically
731 sound and justified.

732
733 The Agency recommends that, upon the completion of manufacturing and to maintain quality,
734 the manufacturer should consider shipment requirements to meet special handling needs (in the
735 case of pharmaceuticals, one example might be refrigeration).

736
737 Under a quality system, trends should be continually identified and evaluated. One way of
738 accomplishing this is the use of statistical process control. The information from trend analyses
739 can be used to continually monitor quality, identify potential variances before they become
740 problems, bolster data already collected for the annual review, and facilitate improvement
741 throughout the product life-cycle. Process capability assessment can serve as a basis for
742 determining the need for changes that can result in process improvements and efficiency (see
743 IV.D.1.).

744
745 5. *Address Nonconformities*

746
747 A key component in any quality system is handling nonconformities and/or deviations. The
748 investigation, conclusion, and follow-up should be documented (CGMP also requires this; see 21

¹⁸ See Reference #9

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749 CFR 211.192). To ensure that a product conforms to requirements and expectations, it is
750 important to measure process and the product attributes (e.g., specified control parameters
751 strength) as planned. Discrepancies may be detected during any stage of the process by an
752 employee or during quality control activities. Not all discrepancies will result in product defects;
753 however, it is important to document and handle them appropriately. A discrepancy investigation
754 process is critical when a discrepancy is found that affects product quality (CGMP also requires
755 this; see § 211.192).

756
757 In a quality system, it is critical to develop and document procedures to define responsibilities
758 for halting and resuming operations, recording the nonconformity, investigating the discrepancy,
759 and taking remedial action. The corrected product or process should also be re-examined for
760 conformance and assessed for the significance of the nonconformity (CGMP also requires this;
761 see § 211.115). If the nonconformity is significant, based on consequences to process efficiency,
762 product quality, safety, and availability, it is important to evaluate how to prevent recurrence.

763
764 Under a quality system, if a product or process does not meet requirements and has not been
765 released for use, it is essential to identify or segregate it so that it is not distributed to the
766 customer by accident. Remedial action may include correcting the nonconformity; or, with
767 proper authorization, allowing the product to proceed with proper authorization and the problem
768 documented, or using the product for another application; or rejecting the product. If an
769 individual product that does not meet requirements has been released, the product can be
770 recalled.¹⁹ Customer complaints should be handled as discrepancies and be investigated (CGMP
771 addresses this; see § 211.198).

772
773 The following table shows how the CGMP regulations correlate to specific elements in the
774 quality systems model. Manufacturers should always refer to the specific regulations to ensure
775 that they are complying with all regulations.

776

21 CFR CGMP Regulations Related to Manufacturing Operations	
Quality System Element	Regulatory Citation
1. Design and Develop Product and Processes	Production: § 211.100(a)
2. Examine Inputs	Materials: §§ 210.3(b), 211.80 – 211.94, 211.101, 211.122, 211.125
3. Perform and Monitor Operations	Production: §§ 211.100, 211.103, 211.110, 211.111, 211.113
	QC criteria: §§ 211.22(a-c), 211.115(b), 211.160(a), 211.165(d)
	QC checkpoints: §§ 211.22 (a), 211.84(a), 211.87, 211.110(c)
4. Address Nonconformities	Discrepancy investigation: §§ 211.22(a), 211.115, 211.192, 211.198 Recalls: 21 CFR Part 7

¹⁹ See 21 CFR Part 7

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D. Evaluation Activities

As in the previous section, the elements of a quality system correlate closely with the requirements in the CGMP regulations. See the table at the end of the section for the specifics.

1. Analyze Data for Trends

Quality systems call for continually monitoring trends and improving systems. This can be achieved by monitoring data and information, identifying and resolving problems, and anticipating and preventing problems.

Quality systems procedures involve collecting data from monitoring, measurement, complaint handling, or other activities, and tracking this data over time, as appropriate. Analysis of data can provide indications that controls are losing effectiveness. The information generated will be essential to achieving problem resolution or problem prevention (see IV.D.3.).

Although the annual review required in the CGMP regulations (§ 211.180(e)) call for review of representative batches on an annual basis; quality systems calls for trending on a regular basis. Trending enables the detection of potential problems as early as possible to plan corrective and preventive actions. Another important concept of modern quality systems is the use of trending to examine processes as a whole; this is consistent with the annual review approach. These trending analyses can help focus internal audits (see IV.D.2.).

2. Conduct Internal Audit

A quality systems approach calls for audits to be conducted at planned intervals to evaluate effective implementation and maintenance of the quality system and to determine if processes and products meet established parameters and specifications. As with other procedures, audit procedures should be developed and documented to ensure that the planned audit schedule takes into account the relative risks of the various quality system activities, the results of previous audits and corrective actions, and the need to audit the entire system at least annually. Quality systems recommend that procedures describe how auditors are trained in objective evidence gathering, their responsibilities, and auditing procedures. Procedures should also define auditing activities such as the scope and methodology of the audit, selection of auditors, and audit conduct (audit plans, opening meetings, interviews, closing meeting and reports). It is critical to maintain records of audit findings and assign responsibility for follow-up to prevent problems from recurring (see IV.D.3.).

The quality systems model calls for managers who are responsible for the areas audited to take timely action to resolve audit findings and ensure that follow-up actions are completed, verified, and recorded. (FDA’s policy is to not routinely review or copy reports and records that result from internal audits per Compliance Policy Guide 130.300.²⁰)

²⁰ See Reference #10.

821 3. *Risk Assessment*

822
823 Effective decision-making in a quality systems environment is based on an informed
824 understanding of quality issues. Elements of risk should be considered relative to intended use,
825 and in the case of pharmaceuticals, patient safety and ensuring availability of medically
826 necessary drug products. Management should assign priorities to activities or actions based on
827 the consequences of action or inaction — otherwise known as *risk assessment*. It is important to
828 engage appropriate parties in assessing the consequences. Such parties include customers,
829 appropriate manufacturing personnel, and other stakeholders. Assessing consequences includes
830 using the manufacturer's risk assessment model to address risks, developing a strategy by
831 deciding which options to implement, taking actions to implement the strategy, and evaluating
832 the results. Since risk assessment is a reiterative process, the assessment should be repeated if
833 new information is developed that changes the need for, or nature of, risk management.

834
835 In a manufacturing quality systems environment, risk assessment is used as a tool in the
836 development of product specifications and critical process parameters. Used in conjunction with
837 process understanding, risk assessment helps manage and control change.

838
839 4. *Corrective Action*

840
841 Corrective action is a reactive tool for system improvement to ensure that significant problems
842 do not recur. Both quality systems and the CGMP regulations emphasize corrective actions.
843 Quality systems approaches call for procedures to be developed and documented to ensure that
844 the need for action is evaluated relevant to the possible consequences, the root cause of the
845 problem is investigated, possible actions are determined, a selected action is taken within a
846 defined timeframe, and the effectiveness of the action taken is evaluated. It is essential to
847 maintain records of corrective actions taken (CGMP also requires this; see § 211.192).

848
849 It is essential to determine what actions are needed to prevent problem recurrence using
850 information from sources such as:

- 851
- 852 • Nonconformance reports and rejections
 - 853 • Complaints
 - 854 • Internal and external audits
 - 855 • Data and risk analyses related to operations and quality system processes
 - 856 • Management review decisions
- 857

858 5. *Preventive Action*

859
860 Being proactive is an essential tool in quality systems management. Tasks can include
861 succession planning, training, capturing institutional knowledge, and planning for personnel,
862 policy, and process changes.

863
864 A preventive action procedure will help ensure that potential problems and root causes are
865 identified, possible consequences assessed, and actions considered. The selected preventative
866 action should be evaluated and recorded, and the system should be monitored for the

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867 effectiveness of the action. Problems can be anticipated and their occurrence prevented using
868 information from reviews of data and risk analyses associated with operational and quality
869 system processes, and by keeping abreast of changes in scientific and regulatory requirements.

870

871 **6. Promote Improvement**

872

873 The effectiveness and efficiency of the quality system can be improved through the quality
874 activities described in this guidance. Management may choose to use other improvement
875 activities as appropriate. It is critical that senior management be involved in the evaluation of
876 this improvement process (section IV.D.3.).

877

878 The following table shows how the CGMP regulations correlate to specific elements in the
879 quality systems model for this section. Manufacturers should always refer to the specific
880 regulations to ensure that they are complying with all regulations.

881

21 CFR CGMP Regulations Related to Evaluation Activities	
Quality System Element	Regulatory Citation
1. Analyze Data for Trends	Annual Review: § 211.180(e)
2. Conduct Internal Audits	Annual Review: § 211.180(e)
3. Risk Assessment	—
4. Corrective Action	Discrepancy investigation: § 211.22(a), 211.192
5. Preventive Action	—
6. Promote Improvement	—

882

883

884 **V. CONCLUSION**

885

886 Implementation of a *comprehensive quality systems model for human and veterinary*
887 *pharmaceutical products, including biological products, will facilitate compliance with 21 CFR*
888 *parts 210 and 211. The central goal of a quality system is to ensure consistent production of safe*
889 *and effective products and that these activities are sustainable. Quality professionals are aware*
890 *that good intentions alone will not ensure good products. A robust quality system will promote*
891 *process consistency by integrating effective knowledge-building mechanisms into daily*
892 *operational decisions. Specifically, successful quality systems share the following*
893 *characteristics, each of which have been discussed in detail above:*

894

895

- Science-based approaches

896

- Decisions based on an understanding of the intended use of a product

897

- Proper identification and control of areas of potential process weakness

898

- Responsive deviation and investigation systems that lead to timely remediation

899

- Sound methods for assessing risk

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- 900 • Well-defined processes and products, starting from development and extending
901 throughout the product life cycle
- 902 • Systems for careful analyses of product quality
- 903 • Supportive management (philosophically and financially)

904

905 Both good manufacturing practice and good business practice require a robust quality system.
906 When fully developed and effectively managed, a quality system will lead to consistent,
907 predictable processes that ensure that pharmaceuticals are safe, effective, and available for the
908 consumer.

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GLOSSARY

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To gain a common understanding of a quality system as a whole, the following terms are used throughout the guidance.

Annual Review - An evaluation, conducted at least annually, which assesses the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures.

CAPA – “Corrective and preventive action”: A systematic approach which includes actions needed to: correct (“correction”); prevent recurrence (“corrective action”); and eliminate the cause of potential (“preventive action”) nonconforming product and other quality problems. [21CFR 820.100]

Continuous Improvement – ongoing activities to evaluate and positively change products, processes, and the quality system to increase effectiveness.

Correction - Repair, rework, or adjustment and relates to the disposition of an existing discrepancy

Corrective Action - Action taken to eliminate the causes of an existing non-conformity, defect or other undesirable situation to prevent recurrence.

Customer – a person or organization (internal or external) that receives a product or service anywhere along the product’s life-cycle.

Discrepancy - Datum or result outside of the expected range, an unfulfilled requirement; may be called non-conformity, defect, deviation, out-of-specification, out-of-limit, out-of-trend, etc.

Metrics - measurements taken over time that monitor, assess, and communicate vital information about the results of a process or activity. Metrics are generally quantitative, but can be qualitative.

Nonconformity – a deficiency in a characteristic, product specification, process parameter, record, or procedure that renders the quality of a product unacceptable, indeterminate or not according to specified requirements.

Packaging Materials – as used in the Packaging and Labeling System, excludes container and closures which are covered by 21 CFR 211 Subpart E (preamble comment # 312).

Pre-production – drug development phase prior to pilot production.

Preventive Action - Action taken to eliminate the cause of a potential non-conformity, defect, or other undesirable situation to prevent occurrence

Product/Service – the intended results of activities or processes; products/services can be tangible or intangible.

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Quality – a measure of a product’s or service’s ability to satisfy the customer’s stated or implied needs.

Quality Assurance – proactive and retrospective activities that provide confidence that requirements are fulfilled.

Quality Control – the steps taken during the generation of a product or service to ensure that it meets requirements and that the product or service is reproducible.

Quality Management – accountability for the successful implementation of the quality system.

Quality Objectives – specific measurable activities or processes to meet the intentions and directions as defined in the quality policy.

Quality Plan – the documented result of quality planning that is disseminated to all relevant levels of the organization.

Quality Planning – a management activity that sets quality objectives and defines the operational and/or quality system processes and the resources needed to fulfill the objectives.

Quality Policy – a statement of intentions and direction issued by the highest level of the organization related to satisfying customers’ needs. It is similar to a strategic direction that communicates quality expectations that the organization is striving to achieve.

Quality System – formalized business practices that define management responsibilities for organizational structure, processes, procedures and resources needed to fulfill product/service requirements, customer satisfaction, and continual improvement. In the CGMP regulatory context, the quality system establishes the foundation to promote the effective functioning of the five other major systems.

Quality Unit – A group organized within an organization to promote quality in general practice.

Risk Assessment - A systematic evaluation of the risk of a process by determining what can go wrong (risk identification), how likely is it to occur (risk estimation), and what the consequences are.

Senior Management – top management officials in a firm who have the authority and responsibility to mobilize resources

Stakeholders – an individual or organization having an ownership or interest in the delivery, results and metrics of the quality system framework or business process improvements.