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Training and the FDA Draft Guidance on Quality Systems

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FDA's 1978 CGMPs included training as part of Quality Control. A draft guidance from the agency now clarifies what is necessary to ensure that your company's training efforts are adequate.

Developing personnel—incorporating management's role in the training efforts—is one of the elements discussed in the U.S. Food and Drug Administration's (FDA's) draft guidance, "Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations."[1] For companies with an established, well-functioning training system, the guidance confirms good training practice; for companies that have yet to develop a comprehensive, performance-based training system, the document "explains how implementing quality systems"—including training—"can help manufacturers achieve compliance with 21 CFR 210 and 211."

Although the FDA's 1978 CGMP regulations were forward-thinking in identifying "performance" as the intended goal of "education, training, experience, or combination thereof," the regulations did not go into detail about what a good training system included. Other articles have provided information, but not with the imprimatur of the FDA that is found with the draft guidance.[2-4]

Beyond the specific quality system element "develop personnel," which includes training, the draft guidance also discusses quality agreements in the section Control Outsourced Operations, which is very applicable to working with vendors or consultants providing courseware or training services to a pharma/biopharma company.

The training-related aspects of a quality system that are found in the draft guidance and their relationship to best practices in the field of training and performance are worth serious consideration. They need to be considered, as well, in light of the regulatory requirements of some other international agencies and how they compare with the expectations in this draft guidance.

In general, the FDA's expectations for training are more holistic and view training as a true system, that is, the organizational structure, responsibilities, elements, procedures, and resources that are integrated to meet the quality and business goals of the company and its customers. This would include having defined requirements or specifications, procedures, actions, and monitoring/feedback that are used for improvement.

Quality Terms

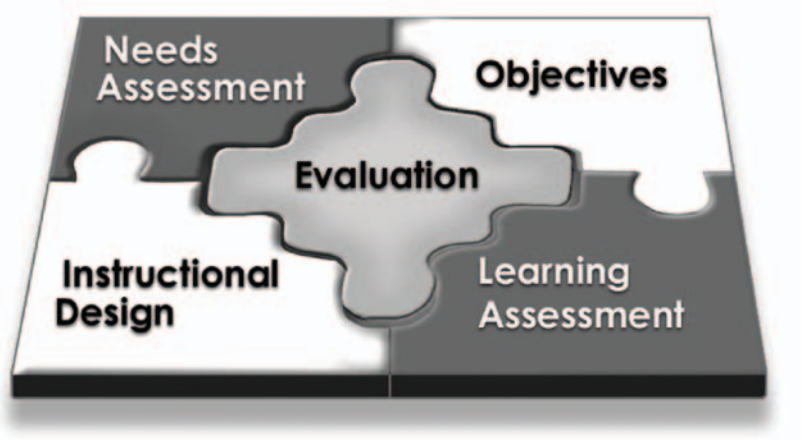
There are, unfortunately, frequent inconsistencies in how the terms *system, system elements*, and *programs* are used in the pharmaceutical industry. For our purposes (as in practice at several large pharmaceutical companies) we will consider the GMPs to be a *quality system* made up of quality *system elements* such as change control, validation, and training. These quality system elements are usually integrated with other elements. The training system element (or more simply, the

training system) includes all the training programs plus the resources and tools used in administering and managing the training activities.

A training program includes the specific resources, curricula, training courses, staff, and other tools needed in equipping personnel with the knowledge and skills they need to perform their assigned tasks effectively and safely. For example, there may be a safety training program, a GMP training program, a program dealing with ethics and business behavior, and others focused on procedures and job skills.

A training course is the instructional methods, media, and content arranged to meet specific goals and objectives.

The term *system* may also be used to refer to some of the electronic tools used to track and manage training called learning management systems (LMSs).



The draft guidance calls for quality agreements "that clearly describe the materials or service, quality specifications, responsibilities and communication mechanisms."

FDA Expectations

One of the reasons FDA gives for issuing this draft guidance is "to address the harmonization of the [U.S.] CGMP regulations and other non-U.S pharmaceutical regulatory systems as well as the FDA's own medical device quality system regulation." "Comparison of International Regulatory Expectations on Training" lists some of the expectations found in the FDA's draft guidance and comparable language found in the Canadian and European drug GMPs, in addition to the GMP requirements for Active Pharmaceutical Ingredients (APIs) found in the International Conference on Harmonization (ICH) "Q7A" document and the FDA's Quality System Regulation for Medical Devices, 21 CFR 820.[5-8] As can be seen in the comparison, the draft guidance goes considerably beyond any one set of GMPs. In fact, it incorporates most of the requirements in addition to addressing organizational culture that contributes to effective communication and continual improvement. In sum, the FDA created a comprehensive set of items that, if addressed, will allow a company to satisfy the training requirements of other regulatory agencies around the world.

Controlled Outsourcing

FDA's draft guidance also discusses work conducted by "second parties," such as contractors and consultants. It is interesting to note that second parties "performing CGMP regulation training" are specifically mentioned.

The draft guidance calls for quality agreements "that clearly describe the materials or service, quality specifications, responsibilities and communication mechanisms." Additionally, the company must ensure that the contractor or consultant is qualified and that the company's Quality Unit "is responsible for approving or rejecting products or services provided under contract."

Items that may be part of a quality agreement (or found in other parts of a contract) provided by a vendor of web-based training courses could include:

- Design documents that are available
- Qualification protocols available for client use
- Audit report availability
- When changes/updates are available
- Client reviews, approvals, and sign-offs
- Change management procedures

Vision of Training

In the draft guidance, FDA states that the company's managers "are expected to establish training programs that include the following:

- Evaluation of training needs,
- Provision of training to satisfy these needs,
- Evaluation of the effectiveness of training, [and]
- Documentation of training and/or retraining."

In practical terms, what does that mean? In short, the FDA is identifying certain activities that are to be included in a training program. FDA's list is in accord with what training professionals see as critical components of a training program. These components, as shown in "Critical Components of a Training Program," include the following.

Needs Assessment. The procedures used to reveal the gaps between the desired level of performance quality in the pharmaceutical workplace and existing quality indicators[9]

Objectives. The specification of the knowledge, skills, and attitudes (KSAs) that personnel working in the industry must possess to maintain the highest standards for the safety, identity, strength, purity, and quality (SISPQ) of pharmaceutical products[10]

Instructional Design. The blend of effective interactive learning activities that have been designed to ensure that personnel acquire the appropriate KSAs[11]

Comparison of International Regulatory Expectations on Training

FDA QSA draft guidance	Canadian GMPs
"Managers are expected to encourage communication by creating an environment that values employee suggestions..." (1)	"People are the most important element in any pharmaceutical operation, for without the proper personnel with the right attitude and the right training, it is almost impossible to [produce and distribute] good quality drugs." Personnel: Rationale (5)
"Management is also expected to develop cross-cutting groups to share ideas to improve procedures and processes." (1)	
"Personnel be qualified to do the operations that are assigned to them..." (1)	"An adequate number of personnel with the necessary qualifications and practical experience appropriate to their responsibilities are available on site. Personnel: Interpretation 4. (5) "Personnel working in areas where highly active, toxic, infectious or sensitizing materials are handled, are given specific training." Personnel: Interpretation 5.5 (5)
...in accordance with the nature of, and potential risk to quality presented by their operational activities." (1)	"Personnel working in areas where highly active, toxic, infectious or sensitizing materials are handled, are given specific training." Personnel: Interpretation 5.5 (5)
"Under a quality system managers are expected to define appropriate qualifications for each position..." (1)	"An adequate number of personnel with the necessary qualifications and practical experience appropriate to their responsibilities are available on site." Personnel: Interpretation, 4. (5)
"Personnel should also understand the impact of their activities on the product and the customer..." (1)	
"...continued training is critical to ensure that employees remain proficient in their operational functions and in their understanding of GMP regulations." (1)	"All personnel...receive initial and continuing training relevant to their job responsibilities" Personnel: Interpretation 5. (5)
"Typical quality system training would address the policies, processes, procedures, and written instructions..." (1)	"Training is provided prior to implementation of new or revised SOPs." Personnel: Interpretation 5.3 (5)
"...training is expected to focus on both the employees' specific job functions and the related CGMP regulatory requirements." (1)	"All personnel are aware of the principles of GMP that affect them..." Personnel: Interpretation 5. "Personnel working in areas where highly active, toxic, infectious or sensitizing materials are handled, are given specific training." Personnel: Interpretation 5.5 (5)
"...managers are expected to establish training programs that include the following: Evaluation of training needs" (1)	
"Provision of training to satisfy these needs" (1)	"Training is provided by qualified personnel having regard to the function and in accordance with a written technical programme for all personnel involved..." Personnel: Interpretation 5.1 "Personnel working in areas where highly active, toxic, infectious or sensitizing materials are handled, are given specific training." Personnel: Interpretation 5.5 (5)
"Evaluation of the effectiveness of training" (1)	"The effectiveness of continuing training is periodically assessed." Personnel: Interpretation 5.2 (5)
"Documentation of training and/or retraining" (1)	"Records of training are maintained." Personnel: Interpretation 5.4 (5)
"...it is important that supervisory managers ensure that skills gained from training be incorporated into day-to-day performance." (1)	"Performance of personnel is periodically reviewed." Personnel: Interpretation 5.6 (5)

EU GMPs	Q7A API GMPs	US Device Regs
"The concept of Quality Assurance and all the measures capable of improving its understanding and implementation should be fully discussed during the training sessions." Personnel: Training 2.12 (6)	"Each manufacturer should establish, document, and implement an effective system for managing quality that involves the active participation of management and appropriate manufacturing personnel." Quality Management: Principles 2.1 (7)	
"The manufacturer should provide training for all the personnel whose duties take them into production areas or into control laboratories (including the technical, maintenance and cleaning personnel), and for other personnel whose activities could affect the quality of the product." Personnel: Training 2.8 (6)	"There should be an adequate number of personnel qualified by appropriate education, training, and/or experience to perform and supervise the manufacture of intermediates and APIs." Personnel: Personnel Qualifications 3.1 (7)	General. Each manufacturer shall have sufficient personnel with the necessary education, background, training, and experience to assure that all activities required by this part are correctly performed. 820.25(a) (8)
"The manufacturer should provide training for all the personnel whose duties take them into production areas or into control laboratories (including the technical, maintenance and cleaning personnel), and for other personnel whose activities could affect the quality of the product." Personnel: Training 2.8 (6)		
	"The responsibilities of all personnel...should be in writing." Personnel: Personnel Qualifications 3.1 (7)	
		"As part of their training, personnel shall be made aware of device defects which may occur from the improper performance of their specific jobs." 820.25(b)(1) "Personnel who perform verification and validation activities shall be made aware of defects and errors that may be encountered as part of their job functions." 820.25(b)2 (8)
"All personnel should...receive initial and continuing training, including hygiene instructions, relevant to their needs." Personnel: Principle (6)	"Training should be regularly conducted..." Personnel: Personnel Qualifications 3.1 (7)	
"Besides the basic training on the theory and practice of Good Manufacturing Practice, newly recruited personnel should receive training appropriate to the duties assigned to them." Personnel: Training 2.9 (6)		
"Personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitising materials are handled, should be given specific training." Personnel: Training 2.10 (6)	"Training...should cover at a minimum, the particular operations that the employee performs and GMP as it relates to the employee's functions." Personnel: Personnel Qualifications 3.1 (7)	"Personnel who perform verification and validation activities shall be made aware of defects and errors that may be encountered as part of their job functions."820.25(b)2 (8)
		"Each manufacturer shall establish procedures for identifying training needs..." 820.25(a) (8)
"The manufacturer should provide training for all the personnel whose duties take them into production areas or into control laboratories (including the technical, maintenance and cleaning personnel), and for other personnel whose activities could affect the quality of the product." Personnel: Training 2.9 (6) "Personnel working in areas where contamination is a hazard, e.g. clean areas or areas where highly active, toxic, infectious or sensitising materials are handled, should be given specific training." Personnel: Training 2.10 (6)	"Training should be regularly conducted by trained individuals..." Personnel: Personnel Qualifications 3.1	
"...Continuing training should also be given, and its practical effectiveness should be periodically assessed." Personnel: Training 2.9 (6)	"Training should be periodically assessed." Personnel: Personnel Qualifications 3.1 (7)	
"...Training records should be kept." Personnel: Training 2.9 (6)		Training shall be documented. 820.25(b) (8)

A company can use the best training courses ever developed, but if it cannot provide detailed records of who was trained, when training was conducted, and what was achieved (such as level of performance), the effort is insufficient.

Assessment. The measures used to reliably and validly determine that personnel possess the appropriate KSAs[12]

Evaluation. The rigorous data collection and analysis required to demonstrate that a given instructional design has effectively enabled personnel to attain the appropriate KSAs and closed any previously identified performance gaps.[13]

Critical Components

For a training program to be effective and successful—that is, effectively and efficiently shape attitudes and provide personnel with the knowledge and skills to enable them to perform their work—those five components must not only be present, but must be aligned. In other words, they must be designed and executed to function in an integrated, balanced, and synergistic way.

Misalignment in one or more of these components with any of the others could seriously undermine the quality of the products produced by a pharmaceutical company and fail to fulfill the vision of the FDA for developing personnel. For example, consider a company that has a training program in place with training courses built on well-specified objectives with clear evidence from both internal assessment and external evaluations that the training is effective, but the objectives of the training courses are not aligned with the specific requirements important to the company. The training program could even be award-winning, but if it is not designed to close performance gaps detected through on-going and targeted needs assessments, it would not meet the FDA's expectation of "Provision of training to satisfy these [identified] needs."

Similarly, suppose that a sound needs assessment has been done, unambiguous objectives have been appropriately derived from the identified needs, and state-of-the-art instructional and assessment procedures have been aligned with the objectives. That sounds fine. But if the effectiveness of the training has not been demonstrated through rigorous evaluation, or if exacting documentation of the training implementation has not been maintained, then the FDA's expectations of "evaluation of the effectiveness of training, [and] documentation of training and/or retraining" have not been met.[13,14] A company can use the best training courses ever developed, but if it cannot provide detailed records of who was trained, when training was conducted, and what was achieved (such as level of performance), the effort is insufficient.

On-going needs assessment procedures integrated with formative (intended to improve the effectiveness and impact of a course or training program that is being developed) and summative (intended to determine the effectiveness and impact of a course or training program that has been implemented) evaluation activities woven throughout the training development and implementation process are essential to realizing the expectations of the FDA specified in the draft guidance. In addition, training that directly addresses the learning objectives derived from the needs assessment must use state-of-the-art instructional models that have been developed using well-established instructional systems design (ISD) methods.[11] Finally, a robust documentation program must be wrapped around the whole training enterprise so that the training development process, its implementation, and its results have procedures and records that allow transparency of the training efforts to the pharmaceutical company as well as FDA regulators.[14]

Implications of the Draft Guidance

The type of training that has come to be known as e-learning interactive courseware is especially well-suited to meeting the expectations of the FDA specified in the draft guidance, Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations. [15-18] Some of the reasons follow.

1) Interactive courseware can be integrated with an online learning management system (LMS) that enables the level of record keeping expected by the FDA.
2) Interactive courseware can be developed, qualified, and validated using the accepted "life-cycle approach" for software applications and subsequently implemented with confidence that each and every employee in a pharmaceutical company has received the specific training that enables them to learn the KSAs required to safely and effectively perform their job.
3) Interactive courseware can be subjected to rigorous evaluation strategies that have been specifically designed for this type of training.[19]
4) The needs assessment and instructional systems design procedures used to develop interactive courseware can be as carefully documented as the implementation of the training.[20]

Although e-learning is not a solution to all training needs, it can and does provide a useful tool in helping to achieve performance. And, it can be done in a way that is consistent with FDA's expectations.

A High-Level Map

FDA's draft guidance is neither a checklist nor a blueprint for developing quality systems within a pharmaceutical or biopharma company. Rather, it is a high-level map of features that need to be present in a well-functioning, integrated quality

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system. Many of these features, including those related to training, have been used by leading companies (inside and outside of the pharma industry) for years. FDA's expectations for training as presented in the draft guidance document harmonize with how training is viewed by other regulatory agencies around the world and by other centers (such as the Center for Devices and Radiation Health) within the FDA.

FDA's listing of what needs to be included in a training system doesn't specifically match instructional system models or use language in the same manner as training professionals, but FDA's expectations are consistent with features and results found in comprehensive, effective training programs and well-designed courses.

Although other training approaches may be warranted in certain situations, properly developed e-learning solutions may well be the most viable tools in helping to achieve the level of performance and compliance sought by regulatory agencies. The advantages of e-learning include the relative ease with which its design, use, and results can be documented and evaluated as well as its coherence with widely accepted development and validation procedures.

Clearly, FDA's draft guidance is a useful tool for those interested in training. It emphasizes that training is an important element of a quality system and that management has a critical role in assuring that a company's personnel have the knowledge, skills, and attitudes that are essential in creating products that have safety, identity, strength, purity, and quality.

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