Qualification of Employees for GXP Compliance

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The US Food and Drug Administration requires all employees who work in controlled areas to be trained. FDA provides latitude for organizations in regulated industry to develop their own training systems to ensure that employees are appropriately trained for GXP compliance. This article focuses on the topic of employee qualification, a critical kind of training in regulated industry. It further provides a comprehensive framework for an organizational approach to employee qualification. A typology of training is presented. Specific employee qualification considerations, including employee qualification as process, qualification status, and measures to demonstrate qualification are discussed. Employee qualification should be based on a complexity and criticality assessment. These concepts demonstrate an organized approach to employee qualification, compliant with regulatory requirements and expectations, and consistent with modern principles of risk analysis.

This is the third of a series of articles on the development of a GXP training system. The first was "Developing a New Employee Orientation Program for GXP Compliance," *Journal of GXP Compliance*, Vol. 13, No. 3 (Summer 2009), pp. 82-92. The second was "Developing a Continuing CGMP Training Program," *Journal of GXP Compliance*, Vol. 13, No. 4 (Autumn 2009), pp. 86-96.

INTRODUCTION AND OBJECTIVE

This paper discusses qualification of specific categories of employees in a GXP environment. Employee categories addressed include production operators and technical subject matter experts (SMEs). These personnel are designated for specific critical tasks in an organization. Concepts discussed herein are also applicable to laboratory analysts.

This paper follows previous published work that discussed new employee orientation programs, associated GXP training, and a continuing current good manufacturing practice (CGMP) training program. The present paper is useful to anyone working in regulated industry with an interest in, and responsibility for, training programs. It also is useful to quality assurance personnel who evaluate training and its relationship to deviations, out-of-specification (OOS) findings, and associated excursions as part of investigations.

The first part of this article discusses types of employee training, including awareness training, training *per se* (which includes a paper-and-pencil assessment), employee qualification (i.e., training that includes a skill demonstration), and qualification of SMEs. The second part addresses types of qualification, including employee qualification as process and as status, as well as the use of skill demonstration assessments (SDAs) in employee qualification.

The third part focuses on the rationale for qualification, highlighting the role the qualification process plays in deviation investigations and root cause analyses. The fourth part considers the criteria for deciding what kind of training is appropriate for a specific procedure; this depends on the complexity and criticality of the procedure and the associated process. The final part delin-

eates two other aspects of the qualification process, employee disqualification and employee requalification.

REGULATORY BASIS FOR TRAINING

FDA requires employees in all regulated areas to be trained. For example, 21 CFR 58.29 states "Each individual engaged in […] a nonclinical laboratory study shall have education, training, and experience, or combination thereof, to enable that individual to perform the assigned functions" (1). This requirement is repeated, with slight variation in phrasing, for other regulated areas (see Table I). FDA regulations say little more about training requirements. According to FDA's John Levchuk, "The FDA has not published a guideline establishing acceptable procedures for personnel training, nor is a guideline being planned." This point was reiterated by FDA's Vasilios Frankos, who stated, "At this time we have no plans to provide companies with training materials for their employees" (2).

Several FDA guidance for industry provide more direction for training. In the *Quality Systems Approach to Pharmaceutical cGMP Regulations*, for example, FDA indicates, "Under a quality system, managers are expected to establish training programs that include the following:

- Evaluation of training needs
- Provision of training to satisfy these needs
- Evaluation of effectiveness of training
- Documentation of training and/or re-training

"When operating in a robust quality system environment, it is important that managers verify that skills gained from training are implemented in day-to-day performance" (3).

FDA has thereby provided an opening for each organization in regulated industry to develop its own training system that will ensure that its employees are appropriately trained for GXP compliance.

TABLE I: FDA regulations for employee training.

Regulation	Regulated personnel
21 CFR 58.29	Non-clinical lab personnel
21 CFR 110.10	Human food handlers personnel
21 CFR 113.10	Thermally processed food handlers
21 CFR 114.83	Acidified food-processing handlers
21 CFR 120.13	HACCP systems managers
21 CFR 123.10	HACCP systems managers
21 CFR 211.25	Pharmaceutical personnel
21 CFR 225.10	Medicated feed personnel
21 CFR 600.10	Biological products personnel
21 CFR 606.20	Blood component personnel
21 CFR 820.25	Medical device personnel
21 CFR 1271.170	Human tissue recovery personnel

CATEGORIES OF TRAINING

Before discussing qualification of employees for GXP compliance, let us first describe the respective categories and/or levels of training in the organization. It is possible to identify several levels of training in an organization. They make up a series, ordered by the complexity of training activities. From lowest level of complexity to highest, they include awareness training, training *per se*, qualification, and qualification of subject matter experts (SMEs) (see Figure 1).

Awareness Training

Awareness training, or familiarization training, is an activity that involves conveying subject matter to an audience, with the goal of making the audience aware of the content of the communication. This activity can barely be called training. The subject matter being communicated can be informational or actionable. An example of informational content is an organization's announcement that layoffs will begin on a specific date. An example of actionable content is an announcement that the South Corridor will be closed for renovation beginning next week, and pedestrians should use the North Corridor until further notice.

Awareness training can take the form of a mass meeting in an auditorium, a "read-and-sign" document that is circulated to all affected personnel, an e-mail message, etc. Awareness training is typically documented by having the audience members sign attendance sheets, the buck sheet on a "read-and-sign" document, etc. (4).

Figure 1:
Complexity of training.

Kind of training	Awareness training	Training *per se*	Employee Qualification	Qualification of SMEs
Characteristics	No assessment	Training plus KTA	Training plus SDA	Qualification across relevant SOPs
Level:	Low →			High

KTA: Knowledge Transfer Assessment
SDA: Skill Demonstration Assessment

In many organizations, "read-and-sign training" constitutes the bulk of training conducted. Organizations are now evaluating the appropriateness of "read-and-sign training" for certain types of procedures. Many times, implicit in this type of training is the organization's need to exhibit due diligence to reduce its liability. The trainee signature is evidence of the organization's due diligence (5). Procedures for which "read-and-sign training" is not appropriate should be transitioned into the next higher level of training.

Training per se

The next higher level is training *per se*, sometimes called facilitation. This is an act of communication that intends to improve the workplace proficiency of members of the audience. Training *per se* includes the trainer (facilitator) or trainers, trainee(s) with various skill set(s) and disposition(s), training materials (including the training script) and assessment materials, training organization (i.e., supervisory factors, business case), facilities (i.e., allocated space, allotted time, utilities), and auxiliary materials (i.e., instruments and equipment, raw and in-process materials used in the training), etc. Training *per se* includes several delivery modalities, such as e-learning, mentoring, and classroom delivery (6). The organization and its environment, within which the training activities, training organization, and training facilities are located, are also important for situating employees and their tasks. These categories can have a profound impact on the conduct and effectiveness of training *per se*.

Finally, training *per se* is complemented by an assessment that allows the trainer to assess whether the training intervention had or did not have the desired impact on the job, in the workplace (7). That typically takes the form of a knowledge transfer assessment (KTA), a paper-and-pencil quiz that predicts performance on-the-job. If trainee proficiency or non-proficiency has been correlated with a quiz score, so that high scores correlate with task proficiency and low scores correlate with non-proficiency, then the KTA is validated, and performance on the job can be predicted from trainee performance on the KTA (8).

Employee Qualification

At the third level, employee qualification is a kind of training augmented by a skill demonstration assessment (SDA). Employee qualification on a procedure or process is performed by a qualified trainer who is also a SME, or by a team consisting of a qualified trainer and a SME. The SME must have expertise in the procedure or process on which the trainee is qualifying. The qualified trainer is responsible for the documentation of the qualification event. The training is often conducted under structured on-the-job training (SOJT) programs. In the case of the team training, the trainer and the SME are jointly responsible for the documentation.

Employee qualification differs in several ways from training *per se*. Perhaps most importantly, training *per se* and qualification involve different systems within the brain of the trainee. Training *per se* tends to involve the declarative memory system, while employee qualification tends to involve the procedural memory system (see Figure 2).

Both declarative and procedural memory systems are elements of long-term memory, as contrasted to short-term or working memory. Declarative (including semantic and episodic) memory is an explicit form of memory, where facts are stored and can be recalled and

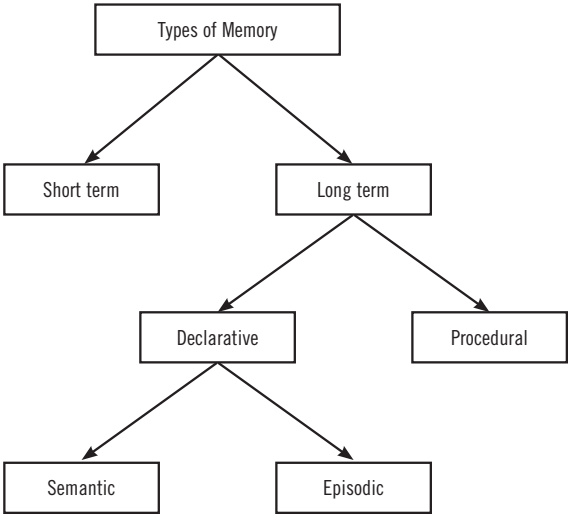
"declared." Procedural memory, by contrast, is an implicit form of memory, whereby performances can be elicited without conscious thought.

The episodic memory system is related to the location or time of a personally experienced event; an example would be the content of a particular training event that this trainee attended. The semantic memory system is related to facts that are not based on any personal recollection of episodic memory. An example would be identifying the pharmaceutical company with the highest global sales figures. The procedural memory system is related to a skill, such as motor or cognitive performance; an example would be operating a forklift truck (9).

How do these memory systems relate to kinds of training? Training *per se* includes a paper-and-pencil assessment (KTA), which consists of recalling information provided in a particular training event, or else general knowledge such as the name of the book that Upton Sinclair published in 1906. Thus training *per se* engages the declarative memory system, either episodic or semantic.

Employee qualification involves a skill demonstration assessment (SDA) that consists of the trainee independently performing the requisite workplace tasks, while being monitored and assessed by the trainer. Thus qualifications engage the procedural memory system. During the actual performance, the trainee may or may not be able to provide a declarative account of the task performance. If the trainee's performance is indeed independent, it would not be recommended that the trainer engage in dialogue or ask questions. Instead, the "tell, show, do, and follow-up" cycle of SOJT can be augmented by a debriefing, wherein the trainee can give a declarative account should the trainer so desire.

Figure 2:
Types of memory.



Qualification of SMEs

The final kind of training is the qualification of SMEs. Employees are designated as subject matter experts in two ways. One is an experiential approach, based on management's designation that an employee is a SME; the other is a formal approach, such as successfully completing a qualification program. Thus the process for qualifying SMEs is homologous to the process for qualifying trainers.

While the experiential approach may involve training of management to utilize specific criteria, to exercise good judgment, and to complete relevant documentation when designating the employee an SME, it does not involve employee training.

The formal approach to the qualification of SMEs does involve training. This kind of qualification is typically instituted by organizations that need to document that their SMEs are qualified, for instance if the organization is operating under a consent decree. Under such conditions, not only will the process of designating SMEs be formalized, but the role of SMEs in the writing of standard operating procedures (SOPs) will be proceduralized as well.

Under these conditions, SMEs become qualified when they have successfully qualified on a number of SOPs that address the competences of their subject matter. The business owner usually identifies the particular SOPs that characterize the subject matter. The ensuing employee qualification process has two elements: overview training on the one hand and skills training on the other. Overview training (i.e., training *per se* that provides an overview of the subject matter) tends to be more conceptually focused, while skills training tends to be more performance oriented. Concepts tell what a thing is; tasks describe how to do something. Concepts provide the "science" for task performance. For example, the process of sanitizing equipment might

be conceptualized as "reducing the levels of microorganisms and particulates to acceptable limits," thereby minimizing the risk of product contamination from the equipment.

Overview training may be delivered by a qualified trainer in a classroom. There will be a SOP that will be the basis of this overview training, as well as a KTA. The event is documented in a training record where the facilitator and trainee concur that the trainee has successfully concluded the training (or not). Should the trainee be unsuccessful in the overview training, by procedure the trainee will have options such as repeating the training event at a later date, etc.

Once the overview training is successfully concluded, the trainee goes on to the SOJT events. The qualification event will usually be conducted one-on-one by a SME who is also a qualified trainer, as a SOJT event. There will be a SOP for each of the SOJTs in the module, as well as SDA for each. The completed SDA form is then entered into the training tracking system.

Consider the typical SME qualification process for the use of vaporized hydrogen peroxide (HPV) for sterilizing controlled areas (10). That SME's individual training plan (i.e., curriculum) might include the following three modules and associated training events.

Figure 3 displays the initial module, which would include an introduction to cleaning, sanitization, and sterilization, followed by a SOJT session on facility cleaning. The training content would reflect 21 CFR 211.56(b) and (c), and the written procedures mandated there.

Figure 4 displays the next module, where the overview session might include further discussion on cleaning, sanitization, and sterilization. This is followed by one SOJT session on clean-in-place and another on sterilize-in-place.

Figure 5 displays the final module in the training curriculum, which might include an overview of sterilizing with vaporized hydrogen peroxide, followed by one SOJT session on storage, handling, and preparation of hydrogen peroxide and another SOJT session on introducing HPV to a room, managing the sterilization cycle, and assessing the outcomes of the process.

If the trainee's performance is assessed as less than successful, by procedure this would be recorded in the training tracking system, and the trainee would be advised of the various options, including repeating the training process, etc.

After the trainee has been successfully trained to the relevant SOPs, and the three training records and the five SDAs have been entered into the training tracking system, the trainee is fully qualified. This means the trainee is ready to function independently as an SME in the use of HPV for sterilizing controlled facilities.

QUALIFICATION CONSIDERATIONS

Qualification, in general, means fitness for some purpose, demonstrated by meeting necessary conditions or qualifying criteria. In regulated industry, "qualification" is used on the one hand in a process sense and, on the other hand, in a status sense. "Qualification" can mean the process of becoming qualified. This is "qualification" as a process, for instance "the qualification of the equipment on Line 28 is complete." Closely associated with that usage is "qualification" as a status, as in "the hiring manager said that the candidate had all the qualifications for the position."

Qualification Process

Qualification as process can be applied to anything (e.g., equipment, instruments, facilities, and computer systems). As Steven Ostrove states, "equipment, or systems, actually used as part of the production process for the production or manufacturing of a pharmaceutical or medical device product must be qualified prior to its use" (11). It can also be applied to personnel. Ostrove also acknowledges that "the term 'Qualification' appears twice in Title 21 of the CFR: 21 CFR 211.25—Personnel qualifications (and) 21 CFR 211.34 – Consultants" (11). According to the well-accepted approach to equipment qualification, there are three main phases to the qualification process: Installation qualification (IQ), operational qualification (OQ) (12), and performance qualification (PQ) (13).

These three phases can also usefully be applied to the process of qualification of personnel, as follows:

- Personnel IQ may be likened to providing objective evidence that the prospective trainee has the requisite education and background for the relevant SOP. If the SOP lists several prerequisites, documented evidence must indicate that the prospec-

Figure 3:
Initial module.

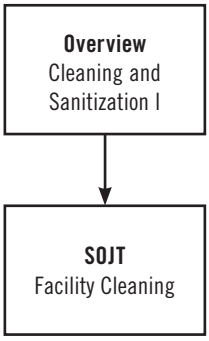


Figure 4:
Second module.

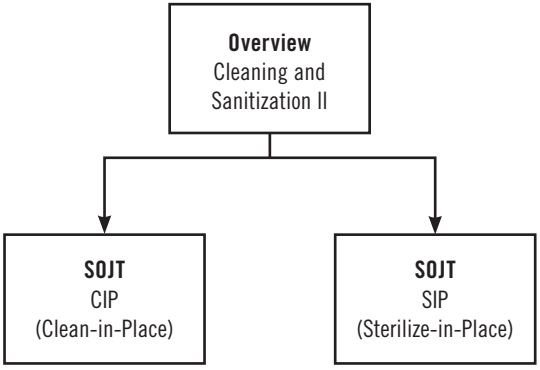
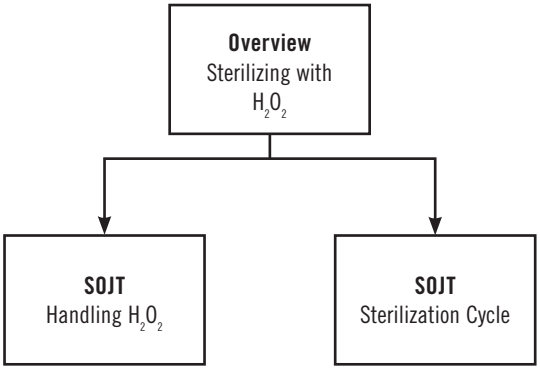


Figure 5:
Last module.



tive trainee has completed training on each of these (14).

- Personnel OQ may be likened to providing objective evidence that the trainee can function in the training situation (event) in an appropriate fashion. In a structured SOJT event, for example, this means the trainee performance is within the "control limits" set by the SOP. In the last analysis, this means that the trainee can perform the task correctly and independently (15).
- Personnel PQ may be likened to the demonstration of acceptable performance during representative operational conditions. The trainee's activities (e.g., on the shop floor or at the lab bench at the close of the training) consistently produce a product that meets the standards set by the SOP or manufacturing order. In the good manufacturing practice (GMP) framework, the performances are directly related to the quality attributes (i.e., the SISPQ) of the drug product (16).

Once the process of employee qualification is successfully completed, employees are qualified, and remain so unless and until they become disqualified.

Qualification Status

Qualification as status, sometimes called certification, characteristically applies to persons. For instance, employees are sometimes designated SME because they are the originator of a new SOP. The reasoning for this practice is the following. An SME on a given SOP, who is a qualified trainer (17), can train another employee on that SOP. But who will provide the training to a new SOP? Who is to be the first mover? For a new SOP, there must be at least one SME, or compliant training will never occur. Those SMEs must be designated by management (in this case, the business owner), not because they have been through a qualification process, there isn't any, but because they are the originator of the SOP, which is a status.

Occasionally an organization will develop a procedure that indicates employees are qualified when they have successfully executed the procedure three times. To be distinguished from various certified fellow employee (CFE) approaches to training, this approach requires neither a SME nor a qualified trainer. However,

it appears to violate the predicate rule, personnel qualifications, which stipulates that "Each person engaged in the manufacture, processing, packing, or holding of a drug product shall have the education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions" (18). This means that employees must be capable of performing assigned tasks prior to touching the regulated product. They already have the educational, training, and experiential status—they are not "learning as they go."

Qualification Measures

Qualification measures consist of skill demonstration assessments (SDAs). A training procedure for employee qualification stipulates how, when, and where the trainee can independently perform the task on relevant equipment.

The training procedure will also stipulate that the trainer use a controlled form that is the SDA checklist. The SDA checklist has fields for entering the number and version of the relevant operational SOP. The checklist also includes a number of items that describe the identified critical or representative tasks to be assessed on the SDA. These are the items assessing the trainee's performance (see Figure 6). The trainee performs and the trainer (or some other SME) monitors the performance and checks each item in turn: "yes" if the performance was successful, "no" if not. When the performance is complete (whether successful or not), the trainee and the trainer sign and date the SDA. Area management may sign as well. The completed checklist is submitted to the data entry personnel of the validated training tracking system, or, in case of manual data processing, to the staff of the document repository.

THE RATIONALE FOR QUALIFICATION

Why should an organization qualify something or someone, be it equipment, computer system, facilities, or personnel? Faced with a problem (call it "P")—a manufacturing deviation or out-of-spec lab result—the organization conducts an investigation to find the root cause. This investigation identifies a number of elements of the manufacturing or lab system, where the variation in at least one of the elements causes variation (deviation) in P.

Elements of the manufacturing system that are identified as potential causes of the deviation typically include equipment, facilities, utilities, raw material, procedure, employee performance, etc. Consider the Ishikawa diagram displayed in Figure 7 (19). The investigation proceeds by eliminating the various elements of the system that might have been the cause of the deviation. Each of the elements is reviewed in turn.

Figure 6:
Illustrative SDA for sanitization program for controlled area.

Name of SOP: _____	SOP #: _____	Version #: _____
TRAINER: Monitor the trainee's performance and check each of the following items: "yes" if the performance was successful, "no" if not.	Yes	No
Demonstrate correct mopping technique for cleaning and sanitizing tasks.		
Demonstrate correct techniques for using wipes on horizontal and vertical surfaces during cleaning and sanitizing tasks.		
Perform the daily and weekly cleaning and sanitizing tasks for the controlled area.		
Perform the monthly and quarterly sanitizing tasks for the controlled area.		
Document cleaning and sanitizing data on the Cleaning and Sanitization Log for the controlled area.		
Trainee signature: _____	Date: _____	
Trainer signature: _____	Date: _____	

By a process of elimination, elements are considered and eliminated from consideration, until only one remains. That remaining element is labeled the "root cause." An element is removed from consideration once it is determined that it could not have been the root cause of the deviation. That is where the process of qualification becomes important. An excellent way to eliminate an element from further consideration as a root cause of a problem is by qualifying that element in advance.

Take equipment, for example. Installation qualification ensures that a piece of equipment, say an autoclave, has been installed within design specifications. Operational qualification ensures that the autoclave operates as designed and as required by the user. Performance qualification ensures that the autoclave displays continued suitability for its intended use. The IQ, OQ, and PQ of elements are critical for pharmaceutical, biotech, and medical device manufacturing and lab systems. Pharmaceutical, biotech, and medical device companies all must install, operate, and maintain equipment to be used in the manufacturing and laboratory system within design specifications, ensuring their operations are reliable and the quality of the output or product is consistent. In this case, the output of the autoclave is sterilized instruments.

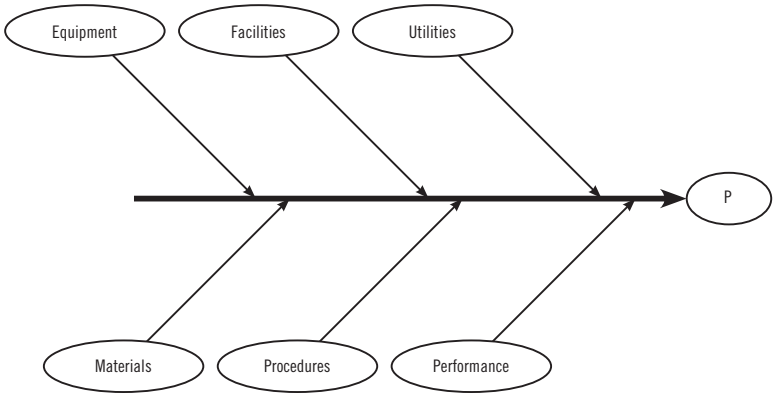
When an autoclave is qualified, it is ensured that it has been installed according to design specifications, it operates in a reliable fashion, and that its output or product has a uniform (and high) quality. Thus the autoclave will not vary from design specifications upon installation. The autoclave will not vary from its specified range during the operation of the system. And its output, sterilized instruments, will not vary from the desired level of quality. Because there has been no variation of the autoclave that has been qualified, it cannot be the cause of the manufacturing deviation or out-of-specification (OOS) lab result. Through the qualification process, that element can be eliminated from consideration in an investigation.

As the various elements are eliminated, the set of candidates for "root cause" decreases. Suppose the only elements remaining are raw materials and employee performance (see Figure 8). The same approach can be applied to the performance element (i.e., employee performance). At some point the employees working on the process that generated the deviation had been trained on the relevant SOPs (or not). The constituents of the performance element include employees (who were the trainees), their trainer(s), the training materials and assessment materials, the training organization, facilities, and auxiliary materials utilized in training (see Figure 9).

Each constituent element is considered and eliminated from consideration when it is determined that it could not have been the root cause of the deviation. The process of employee qualification provides an important way to eliminate a constituent element in advance (20). Was the trainer qualified? Were the employees (trainees) qualified?

Remaining constituent elements can be analyzed in further detail. Thus if the training organization remains, it can be further analyzed into supervisory factors and business case. If the employees (who were the trainees) remain, they can be further analyzed in terms of skill set(s) and disposition(s). Was their morale low? If the category training facilities remains, it can be further analyzed into allocated space, allotted time, and utilities. Were the location and time adequate and appropriate? If the constituent element auxiliary materials remains, it can be analyzed into instruments and equipment, raw and in-process ma-

Figure 7:
Main elements.



terials, etc. (21). These further analyses would make up a more fine-grained version of the Ishikawa diagram.

This discussion has considered the rationale for qualification, highlighting on the role the qualification process plays in deviation investigations and root cause analyses. Employee qualification proves to be a relatively expensive kind of training, when compared to training *per se*. The one-on-one character of this kind of training, the adding of a qualification event to the training process, and other factors contribute to this expense. How does an organization determine which procedures require employee qualification, and which require only training *per se*? This raises the issue of the criticality of a procedure.

CRITICAL COMPLEX PROCEDURES REQUIRE EMPLOYEE QUALIFICATION

An important consideration in determining whether the training will consist of training *per se* or employee qualification is the criticality of the procedure and the process it represents. A procedure is considered to be critical, if the following:

- The procedure requires a complex or highly skilled activity or a job for which a high skill level must be demonstrated to perform a task in the direct manufacturing of a drug product
- The procedure addresses employee safety, or may result in a business compliance risk to the company if not properly performed.

These criteria clearly reflect aspects of criticality and complexity that go into risk assessment.

Whether or not a procedure is deemed to be critical should be guided by three basic questions. What might go wrong with the associated process? What is the likelihood that this will happen? What and how severe are the consequences if this goes wrong (22)?

The first of these three questions raises the issue of the *complexity* of the associated process. The more complex the process, the greater the likelihood that something will go wrong in the process. The third question raises the issue of the *criticality* of the process. The more critical the process, the more severe the consequences should something go wrong. In brief, a procedure for environmental monitoring is more complex and more critical than an SOP for signature cards. As the FDA's guidance for industry, *Q9 Quality Risk Management*, has put it, "the level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk" (23). Thus the dimensions of complexity and criticality of the associated process must be taken into account in determining whether a procedure is critical.

The dimensions that characterize risk are usually characterized as high (direct impact), medium (indirect but significant impact) or low (insignificant impact) (24). The dimensions of criticality and complexity can be displayed as seen in Table II.

When the Complexity x Criticality of a process is Low/Low

Figure 8:
Qualified elements eliminated from diagram.

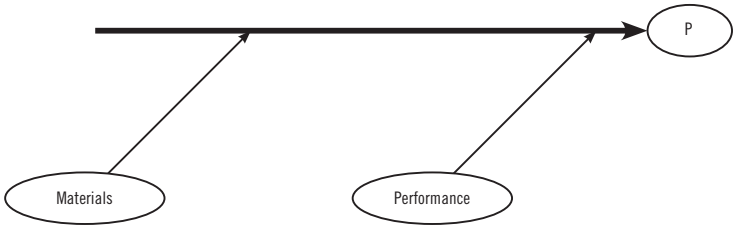
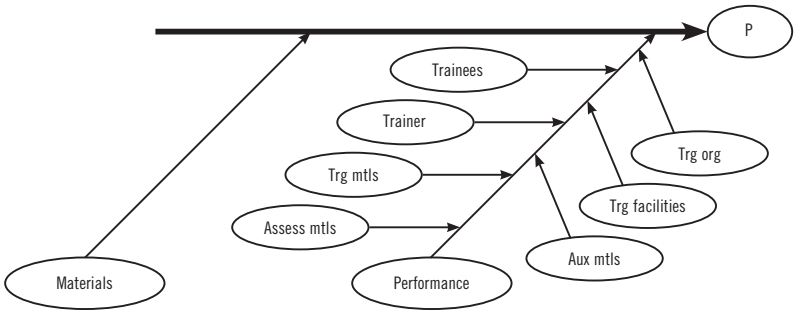


Figure 9:
Constituent elements of employee performance.



(Scenario A in Table II), training *per se* including a KTA may be the appropriate kind of training. Training to a procedure for weight checks of cartons might be an illustration of Scenario A. When the Complexity x Criticality of a process is High/High (Scenario C in Table II), qualification including an SDA may be the appropriate kind of training. In the intermediate situation, when the Complexity x Criticality is Med/Med (Scenario B in Table II), management must decide, perhaps on a case-by-case basis, which kind of training is appropriate. Of course, the criteria and decision process for selecting the kind of training for each SOP should be incorporated in a written procedure.

DISQUALIFICATION AND REQUALIFICATION

Qualified employees can be disqualified for multiple reasons. These include time-based expiration of training, extended absences, job changes, and other understandable reasons. Disqualification can also occur should performance on the job fail to meet qualification standards. This disqualification process can be the result of a management or quality assurance (QA) department observation of non-compliant performance.

Disqualification can also be the result of a pattern of exceptions that can be attributed to the employee, such as the following:

- Serious deviations
- Retraining history
- Repeated deviation
- Investigation reports
- Out-of-specification results.

Management initiates the disqualification process. The QA department should review and approve any particular disqualification, as well as review and approve requalification standards and process. The training department is responsible for monitoring disqualification and requalification events, as well as ensuring that the disqualification and requalification documents are submitted to the data entry personnel of the validated training tracking system, or, in case of manual data processing, to the staff of the document repository.

CONCLUSION

While FDA requires employees who work in controlled areas to be trained, it also provides latitude for organizations to develop their own training systems to make sure their employees are appropriately trained for GXP compliance. This discussion addressed key considerations in the topic of employee qualification, a critical kind of training in regulated industry. It further provided a comprehensive framework for an organizational approach to employee qualification.

A typology of training, ranging from the least complex kind, awareness training, through training *per se* (which includes a KTA), employee qualification (training that includes an SDA), and finally up to the qualification of SMEs was presented. Specific groups emphasized in this discussion include employee qualification and SME qualification. Next addressed were specific employee qualification considerations, including employee qualification as process, qualification status, and measures to demonstrate qualification. Qualification may be demonstrated by use of a skills demonstration assessment checklist. We then focused on the rationale for qualification; highlighting the role the qualification process plays in deviation investigations and root cause analyses.

Employee qualification proves to be a relatively expensive kind of training compared to training *per se*. How does management decide which procedures require employee qualification, and which require only training *per se*? We discussed the criteria for deciding what kind of training is appropriate for a specific procedure; this depends on the complexity and criticality of the procedure and the associated process. The final part delineated two other aspects of the qualifica-

TABLE II: Complexity and criticality of process.

		Complexity		
		Low	Med	High
	Low	A		
Criticality	Med		B	
	High			C

tion process, employee disqualification and employee requalification.

Concepts described in the presented framework should be documented in the organization's training policy and procedures addressing employee qualification. These concepts demonstrate an organized approach to employee qualification, compliant with regulatory requirements and expectations, and consistent with modern principles of risk analysis.

REFERENCES

1. See 21CFR58.29(a), Personnel.
2. See John Levchuk, "Training for GMPs—A Commentary," Presented at the Pharmaceutical Manufacturers Association program, Training for the 90s (Arlington, VA: Sept. 1990), now available as "Training for GMPs," *Journal of Parenteral Science and Technology*, Vol. 45, No. 6 (Nov-Dec 1991), pp. 270-5; also Vasilios Frankos, *Overview of the Implementation of the Current Good Manufacturing Practices for Dietary Supplements Guidance for Industry*, Rockville, MD: Center for Food Safety and Applied Nutrition (24 Oct 2007).
3. See FDA, *Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations* (27 Sept 2006), p. 13. For other instances, see the following FDA Guidance for Industry: *DRAFT: Current Good Manufacturing Practice for Medical Gases* (06 May 2003), p. 4; and *Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice*, September 29, 2004, p. 13.
4. An example of such awareness training is FDA's ALERT Training initiative: "The ALERT initiative is intended to raise the awareness of state and local government agency and industry representatives regarding food defense issues and preparedness." See www.fda.gov/Food/FoodDefense/Training/ALERT/default.htm There are no assessments.
5. For the business risk assessment (as contrasted to the quality risk assessment) that is involved in an organization's determination of due diligence, see Gordon Welty, "Developing a Continuing CGMP Training Program," *Journal of GXP Compliance*, Vol. 13, No. 4 (Autumn 2009), pp. 86-87.
6. See Edward E. Scannell, "Facilitation; all but unknown a decade ago, 'facilitating' has become the 'in' thing for trainers. Many trainers, in fact, have abandoned their 'trainer' hats and term themselves 'facilitators' instead." See his "We've Got To Stop Meeting Like This," *Training & Development*, Vol. 46 Issue 1 (Jan 1992), p. 71. An example is FDA's FIRST initiative, which is closely related to the ALERT initiative. "Employees FIRST educates front-line food industry workers from farm to table about the risk of intentional food contamination and the actions they can take to identify and reduce these risks." See www.fda.gov/Food/FoodDefense/Training/ucm135038.htm Ten "Knowledge Check Questions" are included at the end of the FIRST training materials.
7. E-learning is a special case of a communication or a training event. If the e-learning module lacks an assessment, it is a "page turner," hence awareness training on a par with a "read and sign" document. If the e-learning module includes an assessment, it is a training event, albeit special in the sense that it incorporates a virtual trainer.
8. On KTAs, see Welty, "Developing Assessments of Trainee Proficiency," *Journal of GXP Compliance*, Vol. 12, No. 1 (Oct 2007), reprinted in *The ADDIE Model*, Duluth, MN: Advanstar (2009), pp. 24-27. There is a substantial legal exposure to the use of unvalidated KTAs (short quizzes), and there are serious costs to validating KTAs; see Welty, op. cit. p. 29, esp. note 23. See Christopher Smalley, "Validation of Training," *Validation of Pharmaceutical Processes*, 3rd ed. (ed. James P. Agalloco and Frederick J. Carleton), NY Informa Healthcare (2008), p. 523-528 for further discussion of KTAs.
9. See, for example, Andrew Budson and Bruce Price "Memory Dysfunction," *New England Journal of Medicine*, Vol. 352, Issue 7 (2005), pp. 692-699. They point out that the inferolateral temporal lobes are critical for the semantic memory system, the medial temporal lobes, including the hippocampus and parahippocampus, form the core of the episodic memory system, while the basal ganglia, cerebellum, and supplementary motor area are critical for procedural memory.
10. See Gerald McDonnell, *Antisepsis, Disinfection, and Sterilization: Types, Actions, and Resistance*, NY: Wiley (2007), pp. 119-122, 201-206. Also International Organization for Standardization (ISO), *ISO 14937: Sterilization of health care products —General requirements for characterization of a sterilizing agent and the development, validation and routine control of a sterilization process for medical devices*, Geneva: ISO (2000).
11. Steven Ostrove, "Qualification and Change Control," *Validation of Pharmaceutical Processes*, 3rd ed. (ed. James P. Agalloco and Frederick J. Carleton), NY: Informa Healthcare (2008), p. 130.
12. Bohdan Ferenc, "Qualification and Change Control," *Validation of Pharmaceutical Processes*, 2nd ed. (ed. Frederick J. Carleton and James P. Agalloco), NY: Marcel Dekker (1999), p. 132; p. 139.

13. See the FDA's Guidance for Industry, *Process Validation: General Principles and Practices*, Rockville, MD: CDER/ CBER (Nov. 2008), "Performance Qualification Approach."
14. As Christopher Smalley has put it, "How does a new employee become educated in the skills needed to perform their job safely and effectively? Imagine for a moment that we are performing an IQ similar to that for a new piece of equipment. Are your specifications adequate? That is, are the job description and other documentation that describe the job to be performed adequate? What are the minimum requirements for the employee being 'installed'?" See his "Validation of Training," op. cit., p. 519.
15. On the closely related notion of trainability testing, see Dominic Cooper et al, *Recruitment and Selection*, Andover, UK: Cengage Learning EMEA, (2003), pp. 111-113; also Sylvia Downs, *Testing Trainability*, Philadelphia: Nelson (1985).
16. In a non-GMP framework, say OSHA, the performances are related elsewhere – say to the industrial safety of the employee.
17. As Smalley has expressed it, "One of the best approaches to training on this content is to use the SME responsible for writing the procedures." See his "Validation of Training," op. cit., p. 520.
18. See 21 CFR 211.25(a), Personnel qualifications.
19. See Gary McLean, *Organizational Development*, San Francisco, CA: Berrett-Koehler (2005), pp. 104-106. See also Kaoru Ishikawa, *Introduction to Quality Control*, trans. J. H. Loftus, Tokyo : 3A Corporation (1990). Another useful set of categories might incorporate the quality system and the five manufacturing systems of the FDA's guidance *Quality Systems Approach to Pharmaceutical Current Good Manufacturing Practice Regulations*, op. cit., page 7.
20. As Smalley has expressed it, "Let us recap some of the topics raised in implementing the 'IQ.' They are training requirements, training design, training execution, and evaluation of training. Embedded in these topics is the requirement to document," op. cit., p. 520.
21. The elements of auxiliary materials, for instance instruments and equipment, can be subjected to the same qualification process as the Equipment element already discussed, even if they are used for training purposes only.
22. International Conference on Harmonisation (ICH), *Quality Risk Management Q9* (09 Nov. 2005), p. 3.
23. See the FDA's Guidance for Industry, *Q9 Quality Risk Management*, Rockville, MD: CDER/ CBER (June 2006), p. 3. See also Kevin O'Donnell and Anne Greene, "A Risk Management Solution Designed to Facilitate Risk-Based Qualification, Validation, and Change Control Activities within GMP and Pharmaceutical Regulatory Compliance Environments in the EU, Part I," *Journal of GXP Compliance*, Vol. 10, No. 4 (July 2006), p. 16.
24. See, for instance, Sandy Weinberg and Ron Fuqua "A Stochastic Model of 'Quality by Design' for the Pharmaceutical Industry," to be presented at the *Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy*, Orlando, FL: PittCon (Feb/Mar 2010), p. 5. See also Kevin O'Donnell and Anne Greene, "A Risk Management Solution Designed to Facilitate Risk-Based Qualification, Validation, and Change Control Activities within GMP and Pharmaceutical Regulatory Compliance Environments in the EU, Part II," *Journal of GXP Compliance*, Vol. 10, No. 4 (July 2006), p. 29 on Complexity and Criticality Considerations. **GXP**

ARTICLE ACRONYM LISTING

CFE	Certified Fellow Employee
CGMP	Current Good Manufacturing Practice
FDA	US Food and Drug Administration
GMP	Good Manufacturing Practice
HPV	Vaporized Hydrogen Peroxide
IQ	Installation Qualification
KTA	Knowledge Transfer Assessment
OQ	Operational Qualification
PQ	Performance Qualification
QA	Quality Assurance
SDAs	Skill Demonstration Assessments
SOJT	Structured On-The-Job Training
SMEs	Subject Matter Experts
SOPs	Standard Operating Procedures

ABOUT THE AUTHOR

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