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This article is the seventh in a series on training and the ADDIE Model. The first article, "Strategy and Tactics of Task Analysis," appeared in the *Journal of GXP Compliance (JGXP)*, Volume 11, Number 3, April 2007; the second appeared as "The 'Design' Phase of the ADDIE Model," Volume 11, Number 4, July 2007; the third, "Developing Assessments of Trainee Proficiency," appeared in Volume 12, Number 1, October 2007; the fourth appeared as "Strategy and Tactics for Pilot Implementation in the ADDIE Model," in Volume 12, Number 2, January 2008; the fifth, "Strategy and Tactics of Training Recordkeeping," appeared in Volume 12, Number 3, Spring 2008; the sixth, "Formative Evaluation in the ADDIE Model," was printed in the Summer 2008 issue of JGXP.

INTRODUCTION

The ADDIE model provides high-level guidance for the development and revision of programs of all sorts, including GXP training programs. The phases of the ADDIE Model are analyze, design, develop, implement, and evaluate. These phases are sequential; each depends upon the successful completion of the preceding phase.

The final implementation of a training module comes among the last phases of the ADDIE model. A performance gap or a training gap initiated the process, and a carefully planned approach to address the performance gap has been prepared during the design phase. If management approves the design, the training program, including training materials and assessment materials, has been created in the development phase. These training materials and assessment materials are rolled out in a pilot implementation; a proof of concept study highlighting the iterative feature of the ADDIE model. In the case of a pilot implementation, the results of the program evaluation are fed back, closing the loop, facilitating further refinement of the training program. In the evaluation phase this is called a "formative evaluation" (1). Further design and development efforts follow, until the module meets organizational needs. Then comes the final implementation of the training module. When the module has finally been implemented, it can be the object of a "summative evaluation" that will estimate the relative cost and benefit of the finalized program in terms of organizational goals.

In this age of technological change, much attention has focused on the timing of training. On the one hand, training is optimally delivered close enough to task performance to ensure that the skill enhancement is still relevant but not yet forgotten. These requirements have led to just-in-time training (JITT), which has benefited from e-learning and other developments (2). On the other hand, in the pharmaceutical, biopharmaceutical, medical device, blood product, and other US Food and Drug Administration regulated industries, the need for optimal delivery of the training is constrained by the requirement that employees be trained before they are assigned to "touch" the product.

At first glance, that requirement might seem to be trivial—just ensure that the training has been delivered "before," and be done with it. But the very dynamic of change that has driven manufacturing technologies as well as e-learning can create a climate of turbulence in process and procedure that makes ensuring "before" quite risky, and raises the prospect of serious compliance consequences if it turns out to be "after." The requirement that employees must be trained before they touch

the product becomes especially acute in the case of final implementation of a training module, when it is no longer a matter of selecting the trainees as it is in the case of a pilot. Each and every employee impacted by a new or revised procedure must be trained. This article examines that problem and considers several approaches to addressing it.

First, we will review the scope and impact of the FDA regulations for pharmaceutical manufacturing in general, and about training in particular. The case for other regulated industries mentioned previously is the same. Next, we will critically examine several approaches to ensuring that employees are trained before they touch the drug product, and find that each has shortcomings. Third, we will propose an alternative approach that facilitates the communication necessary to ensure the requisite training has taken place in a timely fashion.

SCOPE AND IMPACT OF THE FDA REGULATIONS

The FDA regulations for pharmaceutical manufacturing, set out in 21 CFR 211, are comprehensive in both scope and impact. Regarding scope, these regulations provide guidance for each person engaged in the manufacture, processing, packing, and holding of a drug product. The phrase "each person" includes both employees and supervisors.

The phrase "manufacture, processing, packing, and holding" is also comprehensive. It includes packing and labeling operations, testing, and quality control of drug products. In sum we can say the scope of the regulations includes any person who is touching the drug product or supervising the persons who are directly touching the drug product.

How do these FDA regulations impact on these persons? The regulations require that the pharmaceutical manufacturer develop written standard operating procedures (SOPs) that provide guidance for a broad range of activities, including the following:

- Equipment and facility cleaning
- Equipment calibration and maintenance
- Handling of drug components and containers
- Production and process controls
- Batch records
- In process sampling and controls
- Quality lab controls
- Reprocessing of batches
- Packaging and labeling operations
- Warehousing
- Distribution
- Returned drugs, among other activities.

Moreover, these must be written procedures (3).

So a set of SOPs is required that will provide comprehensive guidance for dealing with the inputs, processes, and outputs of drug manufacturing, as well as quality control over this manufacturing. Not only are written SOPs required; the regulations insist the quality unit approves them—they are controlled documents—and the procedures be followed (4).

Moving from the general to the particular, the FDA regulations stipulate that all employees and supervisors be trained. 21 CFR 211.25(a) states that each person engaged in the manufacture of a drug product shall be trained in the following (5):

- In the particular operations that the employee performs
- In current good manufacturing practices (CGMPs)
- Including the CGMP regulations in chapter 211
- The dozen or so written procedures required by these regulations.

The scope of this training will "relate to the employee's functions;" the objective of this training will be "to enable that person to perform the assigned functions."

Moreover, 21 CFR 211.25(b) goes on to say that the supervisors of these persons shall be trained so as "to provide assurance that the drug product has the safety, identity, strength, quality and purity (SISPQ) that it purports or is represented to possess." In particular, these supervisors will make the task assignments to the employees who will actually touch the product.

Three points follow from these stipulations. First, employees must have technical (or skill) training in their particular assignments. Second, the employees must have training in CGMPS that constrain the exercise of skills. Third, supervisors are responsible for the SISPQ of the drug product, and must be trained to fulfill that responsibility. All this training must take place in a timely fashion.

Training Or The Lack Thereof

How well have companies within the scope of 21 CFR 211 responded to these requirements? In a review of a sample of the FDA's GMP warning letters sent during the five-year period between January 2003 and Dec 2007 (6), there were 25 warning letters that mentioned deviations regarding aspects of 21 CFR 211 during that time period. They listed a number of observations that the FDA investigator had made during site visits to companies within the scope, including such issues as cleaning, contamination, sampling, etc. Seven of these warning letters (over 25%) also cited inadequacy of training or inadequacy of the documentation of training, including inadequacy of skills training, training in GMPs, and supervisory training.

This pattern is not a historical anomaly; FDA has been concerned about the adequacy of training in the pharmaceutical industry for some time. For example, regarding a somewhat earlier time period, FDA senior compliance officer Philip Campbell asked, "Are the employees trained?" He further inquired, "Are the supervisors trained?" Finally, he asked "Are there records of that training, and is it ongoing?" (7).

The fact that more than a quarter of these FDA findings point to problems in training should come as no surprise. On the one hand, whenever there is a remediation (corrective action and preventive action [CAPA]) for any deviation investigation or audit observation, that remediation will usually involve a revision of procedure or other controlled document, which in turn almost invariably involves training to the revised SOP. As Carl Draper, Director of the FDA's Office of Enforcement, has stated, "The implementation of revised SOPs should include employee training" (8). So training will be the indirect outcome of a remediation and will be the focus of some attention in the follow-up of the CAPA. Thus we expect that any warning letter directly addressing issues of cleaning, contamination, lab work, sampling, testing, utilities, whatever may also include a call for training, or for better training.

On the other hand, it seems that FDA has come to expect ineffective training (9), or inadequate documentation of training (10). These expectations, along with the relative ease of assessing the occurrence and documentation of training via the ubiquitous tracking systems and learning management systems (LMSs), make the investigator's focus on these areas understandable.

Training Versus Retraining

Recognizing the inadequacy of training does not amount to a call for "retraining," by which the employees that were originally trained are retrained to the same training materials, by the same trainer, in the same fashion. There is a substantial difference between training as an indirect outcome of a CAPA, and retraining as a direct outcome of an investigation, as a CAPA itself. Investigators quickly recognize the fallacy of retraining as a solitary or even major remediation (11). For an example of such a fallacy, consider the FDA's Adverse Determination Letter regarding the Baltimore manufacturing facility of the American Red Cross, dated 27 July 2006. A Red Cross employee was not trained before touching the whole blood product. When this problem was discovered two months after the event, the Red Cross conducted an investigation and concluded that this was a training problem. "The corrective action was to fully retrain all employees" (12). FDA responded that "as a result of the incomplete investigation, [the Red Cross] failed to determine all root causes of the problem" (12). The Red Cross was then fined more than $700,000.

A manufacturing unit is strongly inclined to release an impounded batch by declaring that the catchall category "human error" was the root cause of the deviation or failure, and suggest retraining of the employee(s) as the corrective action. This is goal displacement (13); it places the unit's goal, releasing the batch, above the organization's goal, which is identifying the root cause and implementing a remediation that will ensure the deviation will not recur. This goal displacement results in a false alarm, where retraining is the direct outcome of an investigation. The fallaciousness of re-training is amply demonstrated— retraining, retraining, retraining of the same employee(s), ad infinitum. As Philip Lindemann points out, "Not identifying the cause of failure may lead to additional failures" (14). The investigator will recognize this, as will upper management, if there are metrics tracking CAPAs. The investigator and upper management will thereupon question the adequacy of the organization's investigations.

Moreover, if "human error" were proposed as the root cause of the deviation requiring retraining, then the actual root cause would be the following:

- Unreceptive trainee(s)
- Inadequate training materials
- An unprepared or incompetent trainer

• Ineffective interaction of trainee(s) and trainer
• Some combination thereof (15).

For none of these cases would remediation be as simple as retraining, because the trainee would need to be motivated, the training materials would need to be revised, the trainer would need to be qualified, or the interaction would need to be enhanced before the remediation could go forward.

When John Levchuk calls for reinforcement training as a remediation for "future skills deficiencies" (16), he indicates that refined or redefined training materials may be indicated, because "usually, only those skills most likely to be forgotten or suffer compliance erosion over time would be targeted for inclusion in a periodic reinforcement program" (17). Moreover, when he goes on to call for remedial training as a remediation for "acquired skills deficiency," he states that it would be "more appropriate and efficient if it were targeted to an incumbent's specific skills deficiencies." Thus Levchuk is not calling for retraining in either case.

In this part we have reviewed the scope and impact of FDA regulations of pharmaceutical manufacturing in general, and of training in particular, and found them to be comprehensive. Any person who touches the drug product, or who supervises someone who directly touches the drug product, falls within the scope of the regulations. These regulations impact on these persons via written SOPs that provide comprehensive guidance for dealing with the inputs, processes, outputs, and the quality control of drug manufacturing. These employees must be trained on these procedures insofar as they relate to the employees' functions, so as to enable those persons to perform the assigned functions. As the process and procedures change, the impacted employees must be trained in a timely fashion, hence, the critical issues attending the rollout of a finalized training module.

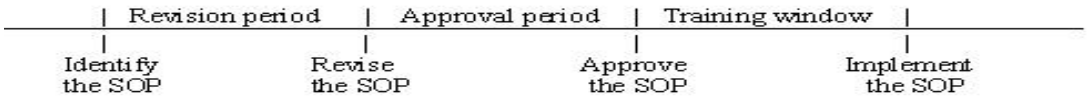
The issue can be summarized as follows. An SOP is identified as subject to revision. The SOP is revised and routed for approval. At the point of approval, a "training window" is opened (typically two weeks in length) before the SOP is implemented. Within this training window, all impacted employees (i.e., those who will be assigned to touch the product while executing the tasks controlled by the SOP) must be trained. This is schematized in Figure 1, where the four critical points are indicated on the timeline, delineating the three periods: Revision, approval, and training window.

There are two major logistical complications that follow. First, all training and assessment materials must be prepared before the SOP is approved; if not, they won't be available for the training that must be conducted within the training window. Second, the participants in the training must be identified and scheduled for training, again before the SOP is approved. This includes both the trainer(s) and the impacted employees who will be the trainees. In particular, the employees must be those who will be assigned to touch the product under the guidance of the SOP. These two complications suggest that the timing of the requisite training is critical, especially with reference to the points in time where the revision of the SOP is initiated and the employees will touch the product.

THREE TYPICAL RESPONSES

This section reviews three typical organizational responses to the necessity that all required training on the finalized module has occurred before the employee is assigned to touch the drug product. Organizations tend to move through these three responses in turn; when one is found to be inadequate, the next is tried. The first proposal is typically the notion that there is a "training burden" and suggestions are advanced to alleviate this burden. The second proposal is to create a procedure for the supervisor's checking of the employee's training

Figure 1: Three periods of SOP revision including training window.



status. Last, various "technological solutions" to the issue are proposed. None of these proposals are adequate to the problem. They address the logistical complications in part, but fail to take into account the lead-time and communication process that is necessary.

Reduce the Training Burden

Many organizations within the scope of 21 CFR 211 respond to the requirements listed therein by focusing attention on reducing the "training burden." The organization's management believes that employees are spending too much time in training—time removed from more productive activities. Furthermore, the more time spent in training, or the more training events that are attended, the greater the likelihood that a mistake will occur, and the untrained employee will end up touching the product. The proposed solution is to reduce the number of SOPs required for any given position's curriculum and reduce the training burden (18).

This is no solution at all. The number of procedures required for a position depends upon the technological sophistication (complexity) and proximity to the product (criticality) of the tasks associated with that position (19). If the person is a janitor, there may be a few SOPs required. If the person is a supervisor or SME of an aseptic filling line, the number of SOPs may be very large. It is not a training burden. It is a "technology burden," and it is necessary to face the implications of the fact that FDA regulates science-based industries. These are tech operations issues, not training issues.

Managers are the only ones who can reduce the technology burden. Line management must review each and every SOP that goes into a position's curriculum. Essentially, the line manager must make a business case for each SOP versus each job. Certain SOPs (e.g., one controlling the employee's maintenance of his or her locker) may well be eliminated. This is where the following four elements would clear up these misunderstandings and mistaken senses of responsibility:

- Proceduralization of the training process
- Initiating an annual training plan
- Instituting an explicit risk analysis for every procedure
- The development of a training council (of line management).

The only training issue is how to bring the employee up to task proficiency once an SOP is included in a given curriculum, and ensure that the level of proficiency (and documentation thereof) is "audit proof" (i.e., will stand a regulatory inspection). This means that line management, from the VP of Tech Ops on down, must factor in the time and money (resources) to allow the training to take place. Via the training council, the line managers who have identified the training needs will also approve the training resources, for example, less training for janitors and more training for supervisors of aseptic filling operations. No amount of talk about a "training burden" will help ensure that the employee is trained before being assigned to touch the product.

Creating A Procedure For The Checking Of The Training Status

In many cases, an organization will realize that it must take further steps to ensure that employees are trained on the relevant SOPs before they are assigned to touch the drug product. Sometimes this is a result of a deviation investigation or an audit observation. Other times it may be the result of cost considerations, seeking to reduce rework and reprocessing, or because of compliance concerns. In any case, a typical organizational response is to develop a new SOP that calls upon supervision to check the employee's training status. Such a controlled document can be called a task assignment procedure.

Such a procedure might require that the supervisor ensure all necessary training and qualification requirements have been completed and documented prior to assigning an employee to touch the product. This check is typically performed by looking at the employee's training record in the validated tracking system or LMS during task scheduling. If employees have been trained on all the procedures listed in their curricula, the supervisor makes the task assignments.

What if the supervisor makes a mistake in checking the training records? What if the supervisor is not diligent, or overlooks a particular employee, or misses a page of the training record? Referring again to the Red Cross example, where the employee was not trained before touching the product, the Red Cross concluded that, "the Education Coordinator failed to compare the employee's previous training transcript with the training requirements" (20).

Thereupon an organization might develop an even further SOP that requires periodic checks by the quality unit of a random sample of employees found in GMP areas at a given time, to ascertain if they are in fact qualified for their assigned job functions. Such a controlled document can be referred to as an "assignment monitoring procedure." Should discrepancies be found, the assignment monitoring procedure would require the generation of a notice of event (NOE) to inform management that a deviation has occurred. That NOE would need to address both the impact on the batch, to the extent the untrained employee had touched the drug product, and the supervisory error itself (21).

There are several major problems with this organizational approach. It presupposes that employees' training curricula, listed in the tracking system, correctly and currently include the procedures that are relevant to the tasks to which the employees may be assigned. On the one hand, the curricula may not correctly reflect the procedures. How does a supervisor ensure that every single procedure that relates to this task, or this process—regardless of who the originator of the SOP may be—has been included in this curriculum? On the other hand, the curriculum may not currently reflect the procedures. How does the supervisor ensure that the versioning up of each procedure has been the occasion for an update of the employee's curriculum?

These are hardly trivial questions. Change control and change management are substantial problems in a regulated industry subject to pervasive and persistent technological development. As if that weren't enough, procedures are versioned up to change a single word. Procedures are versioned up and then found to be misaligned with higher corporate policies and standards; then they are versioned up still further to restore the status quo ante and alignment. Procedures are versioned up, omitting key paragraphs; they are subsequently versioned up to reinsert the omitted paragraphs. Multiple procedures coexist for similar functions (e.g., gowning); these procedures are versioned up, one by one, by their disparate business owners independent of each other.

The remedy for the constant revision of procedures is a combination of making better business cases for proposed changes, and having critical review of the documents in process (22). But that remedy will not resolve the supervisor's dilemma of task assignment. If the curriculum is either incorrect or not current, the supervisor cannot ensure the employee is adequately trained, no matter how diligently the training record is checked, no matter how carefully the task assignment procedure is executed. And the assignment monitoring procedure will most likely identify non-compliant task assignments after the fact. The only way to ensure compliance in this case is by over-training (i.e., by providing training to employees for whom the SOP may not be relevant). Of course that is not cost effective training (23).

Moreover, over-training may result in employee resistance to training. Many times this occurs among high-performing individuals, say in a research and development institute, and presents special problems for organizational morale and productivity.

It is crucial to recognize the misspecification of task responsibilities in the proposed task assignment procedure. This procedure places the key responsibility on the supervisor for ensuring that employee training and qualification requirements are completed and documented prior to task assignment, while not giving that supervisor necessary information about the accuracy and currency of the curricula, the status of procedure initiation, the status of procedure revision.

Instead, the task assignment procedure should stipulate that the originator (or business owner) of any new or revised SOP should communicate with each and every impacted functional area to determine who the impacted employees are (i.e., the training audience for the forthcoming SOP). In terms of the timeline given in Figure 1, the originator of the new or revised procedure must indicate to the management of each impacted functional area, the precise location on the document management timeline of that SOP. In particular, the originator must indicate the SOP that has been identified as subject to revision, and is in the process of being revised.

Implement A Technological Solution

Many organizations recognize that the proceduralization of task assignment is inadequate and believe that a technological solution, usually in the form of a learning management system, will address the problem. For instance, Ed Cohen has recently identified three LMS "innovations"

that might jointly suffice to "effectively manage organizational compliance requirements." The first innovation is where "LMSs can automatically cascade all [procedural] changes through the system; incorporate information and training assignments tied to the change into development plans for every employee impacted; and monitor employee records to determine whether system-assigned [training] tasks have been completed" (24). This innovation is clearly the technological counterpart to the task assignment procedure; the technological solution similarly begs the question by assuming that the employees' training curricula correctly and currently include the SOPs that are relevant to the tasks that may be assigned.

The second innovation discussed by Cohen is where an LMS protects the integrity of compliance related data. "LMSs also are capable of safeguarding compliance-related data through audit-trail functionality that allows any action impacting compliance data to be tracked and recorded" (25). This innovation simply prevents an unauthorized intervention into the functioning of the LMS, so doesn't bear on the issue of the supervisor's task assignment.

The third innovation is the integration of the LMS with other business systems to ensure compliance. "For example, a pharmaceutical industry employee who has not completed the necessary training required to operate a specific drug dispensing machine cannot use his credentials to access and operate that machine until required training is completed" (26). This innovation provides controls over the execution of tasks by untrained employees. It does not facilitate task assignment. It is a matter of timing; the supervisor must ensure that training has occurred for revised procedures prior to making the task assignments, not prior to the employee's executing the tasks. It is very late in the game when an employee is prevented from using credentials to enter a GMP area or to operate a specific machine. The employee may have been assigned a task for which the requisite training has been completed, yet would be denied access to the area or machine because other training has not been completed. Such an innovation might limit the number of employees available, resulting in the shutdown of the entire production line. The supervisor still does not have the necessary lead time and information to make task assignments.

It is critical that none of the LMS innovations that Cohen discusses address the supervisor's real-world problem of task assignment. Like the preceding proposal for a task assignment procedure, this "technological solution" makes the supervisor responsible for employee training and qualification requirements, while not giving that supervisor timely information about the status of procedure initiation and the status of procedure revision.

Instead, we must ensure that the originator of a new or revised SOP has communicated with each impacted functional area to determine the training audience for that forthcoming SOP. And this bring us to the final part of this paper, where we propose an alternative approach to ensuring that the requisite training on the finalized module has occurred before the employee is assigned to touch the drug product.

THE ROLE OF THE TRAINING OUTLINE

This section addresses four topics. First we will compare and contrast the purpose of an SOP with the purpose of training to a procedure. Next we will delineate the role of a training outline as a brief summary of the training implications of a new or revised SOP. Third, we will present a process map of the development and utilization of a training outline, and the associated training audience list. Fourth, we will discuss the use of the training audience list as the alternate approach to ensuring the requisite training occurs. To anticipate, the training outline will be recommended as best practice to ensure that all requisite training on the finalized module has occurred before employees are assigned to touch the drug product.

The Purpose Of An SOP

A procedure lists the necessary steps (tasks) that, taken together, are sufficient to produce the desired process result. It can address several kinds of process: a person-to-machine process, a person-to-paper process, a person-to-person process, or some combination of the three types. An SOP, typically in documentary form, indicates the sequence of tasks, the personnel or positions that are responsible for the tasks, and the standards that define the satisfactory completion of the tasks (27).

The Purpose Of Training To A Procedure

Training is a person-to-person process that prepares each employee (the trainee) to successfully execute the steps (tasks) in a procedure, in the appropriate setting, stipulated order, mandated workgroup, and specified timeframe. Training is the combination of trainee(s), training materials, virtual or actual trainer, and the interaction of these elements.

Thus procedures and training are different. The procedure is a controlled document subject to the quality unit's approval. Training is an interactive process. Of course a procedure can be the object of training, and training can be made into a procedure. But the two are distinct; reading a procedure (a person-to-paper process) is not the same as being trained on that procedure (28); being trained on a procedure is not the same as being a subject matter expert on that process.

How do we align the procedure and its associated training? How do we provide the supervisor with necessary information about changes to relevant procedures so as to ensure that employee training and qualification are completed and documented?

The Role of the Training Outline

The training outline is a controlled document that provides a brief summary of the training implications of a new or revised procedure (29). The following are the typical 12 fields in a training outline:

- Course title
- Course number and version
- Training audience
- Curriculum fit
- Prerequisite courses and required skills
- Trainers
- Behavioral objectives
- Training delivery method
- Course length
- Special instructions
- Measures of effectiveness
- Approval.

The training outline allows any employee to quickly ascertain critical dimensions of training associated with a particular SOP, including the behavioral objectives of the training, the training module's fit in the larger curriculum, the delivery method, assessment materials, and of course the training audience. Figure 2 displays a process map of the development and utilization of a training outline, and the associated training audience list.

Developing And Utilizing The Training Audience List

When a performance gap or training gap is identified, management must decide on the appropriate corrective action and preventive action to respond to the gap. The following are two possibilities:

- It involves a life cycle document or documents
- It involves non-life-cycle or GMP regulatory training (30).

In either case, the associated training will require the development or revision of a training outline. The instructional designer (or originator of the procedure) will ask, "Does a training outline exist?" If one already exists, the training outline will be reviewed and revised as necessary. If not, one will be prepared.

The instructional designer will review the following five points:

- Does the SOP or other document contain background history or perspective of the process that would aid in the training?
- Does the SOP or other document cover all related processes?
- Does the SOP or other document thoroughly identify CGMP aspects?
- Is all relevant training information covered in the training outline?
- Will all facilitators present the training and information consistently?

In the case of non-lifecycle documents and GMP regulatory training, the instructional designer can ask management about the range of the training audience; usually it will straightforwardly be all employees, all managers, etc.

In the case of a lifecycle document, the instructional designer will review the SOP scope statement as well as the task responsibilities, and generate a provisional training audience list. This is the problematic case. These are the employees who must be trained to the new or revised SOP, based on the finalized training module, before they are assigned to touch the drug product.

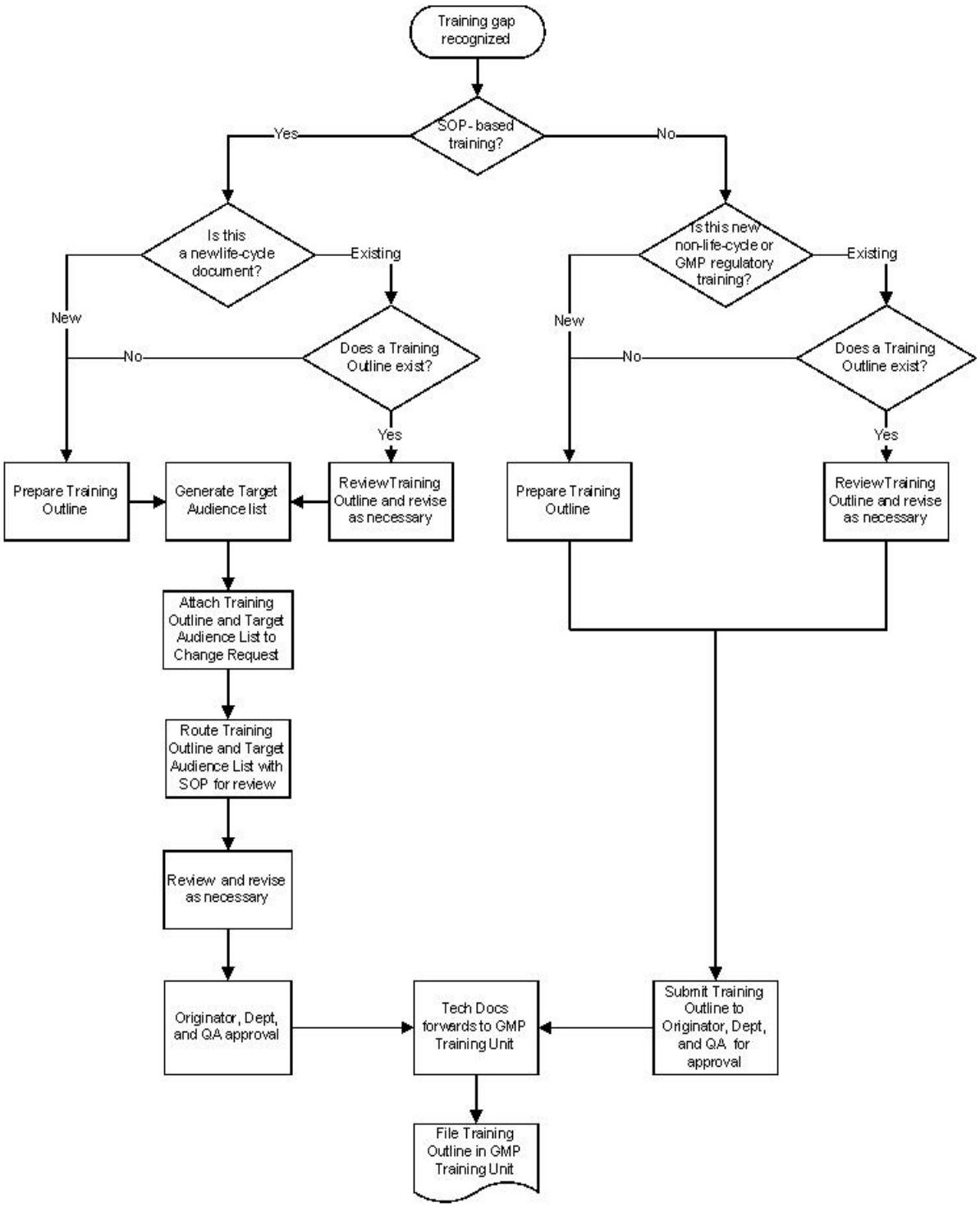


Figure 2: Process map of the development and utilization of the training outline.

The instructional designer will then attach the training outline, and the associated (provisional) training audience list to the procedure's change request. When the procedure and its training outline are circulated for review and approval, the training audience list will be circulated as well. Management of each unit impacted by the procedure will review the list and recommend limiting it or expanding it, based on their direct responsibility for the task assignments of the listed employees.

The instructional designer will then take those recommendations into account as the procedure, training outline, and training audience list are reviewed and approved. Moreover, management in the impacted units are alerted for the approval and implementation dates of the SOP, and can accordingly schedule impacted personnel for necessary training on the finalized module.

After the new or revised procedure has been approved, the training window opens, within which the impacted employees can be trained to the SOP before the procedure goes into effect. It is critical that the training audience be defined before that window opens, hence before the SOP is approved, so that all training on the finalized module will be completed before the implementation date (31). At this point, the other proposals noted above, especially the use of a task assignment procedure and various technological solutions such as a validated training tracking system, will provide further assurance that all requisite training has been completed. Thus, the risk of untrained employees being assigned to touch the regulated product will be minimized.

CONCLUSION

This paper first reviewed the scope and impact of FDA regulations of pharmaceutical manufacturing in general, and of training in particular, and found them to be comprehensive. Any person who touches the drug product, or who supervises that person, falls within the scope of the regulations. These regulations impact on these persons via written SOPs that provide comprehensive guidance for drug manufacturing. These persons must be trained on these procedures insofar as they relate to the employee's functions prior to their being assigned to touch the drug product; hence the importance of ensuring that the final implementation of the training module includes all these employees.

Next we considered several organizational responses to the need to ensure employees are trained before being assigned to touch the drug product. One took the form of trying to reduce the training burden. A second took the form of a procedure requiring that the supervisor ensure all necessary training and qualification requirements in the employee curricula are completed and documented prior to assigning an employee to a task. The third took the form of proposing a technological solution. There are several problems with these approaches, especially the failure to provide the supervisor with timely and necessary information about the accuracy and currency of the employee curricula, and the revision status of the SOPs.

Finally, an alternative response was presented whereby the training outline, a controlled document including a training audience list, is employed by the originator of a new or revised procedure to communicate with each impacted functional area to determine which employees require training. Those employees' curricula are revised to correspond to the new or revised procedure, and supervision is alerted to the opening of the training window before the changes are effective, ensuring the employees are trained on the finalized module before being assigned to touch the drug product.

ENDNOTES

1. This process has been discussed (in thematic order) in Gordon Welty, "Framework for Continuous Improvement," *Journal of GXP Compliance,* Vol. 13, No. 1, January 2009, pp. 79-89; "The Role of Critical Review in the Revision of Procedures," *Journal of GXP Compliance*, Vol. 12, No. 5 (Autumn 2008), pp. 77-89; "The 'Design' Phase of the ADDIE Model," *Journal of GXP Compliance,* Vol. 11, No 4, July 2007, pp. 40-52; "Developing Assessments of Trainee Proficiency," *Journal of GXP Compliance*, Vol. 12, No.1, October 2007, pp. 64-73; "Strategy and Tactics for Program Implementation," *Journal of GXP Compliance*, Vol. 12, No. 2, January 2008, pp. 12-19; "Strategy and Tactics of Training Recordkeeping," *Journal of GXP Compliance*, Vol. 12, No. 3, April 2008), pp. 42-52; and "Formative Evaluation in the ADDIE Model," *Journal of GXP Compliance*, Vol. 12, No. 4, July 2008, pp. 66-73. On the distinction between formative and summative evaluations, see Michael Scriven "The Methodology of Evaluation," in Peter

Taylor and Doris Cowley (eds) *Readings in Curriculum Evaluation*, Dubuque: IA: Wm. C. Brown (1972), pp. 28-48, esp. pp. 29-33.
2. See Carol Watson and Sanford Temkin, "Just-In-Time Teaching:Balancing the Competing Demands of Corporate America and Academe in the Delivery of Management Education," *Journal of Management Education*, Vol. 24, No. 6, December 2000, pp. 763-778; Michael Jones, "Just-in-time Training," *Advances in Developing Human Resources*, Vol. 3, No. 4, 2001, pp. 480-487; and Bob Mosher, "E-Reference: The Real Just-in-Time Training," *Chief Learning Officer Magazine*, Vol. 4, No. 11, November 2005.
3. As an example of the failure to meet the requirement of written procedures, consider the FDA's *Warning Letter* to Greer Laboratories, Inc. dated 24 June 2005: "Your firm failed to establish written procedures applicable to the function of the quality control unit;" available at www.fda.gov/foi/warning_letters/archive/g5395d.pdf.
4. As an example of the failure to follow these written SOPs, see the FDA's *Warning Letter* to Intermax Pharmaceuticals, Inc., dated 13 May 2003: "Although your firm has a written procedure for training; it was found that these procedures are not followed;" available at www.fda.gov/foi/warning_letters/archive/g6159d.pdf.
5. For biopharm personnel, 21 CFR 600.10; for non-clinical lab personnel, 21 CFR 58.29; for medical device personnel, 21 CFR 820.25; for human tissue recovery personnel, 21 CFR 1271.170. For further itemization of the content of training, see FDA, *Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing*, Rockville, MD: CDER (2004), page 13; "Fundamental training topics should include aseptic technique, cleanroom behavior, microbiology, hygiene, gowning, patient safety hazards posed by a nonsterile drug product, and the specific written procedures covering aseptic manufacturing area operations." See also FDA, *Guidance for Industry: Quality Systems Approach to Pharmaceutical CGMP Regulations*, Rockville, MD: CDER (2006), page 13; "Typical quality systems training should address the policies, processes, procedures, and written instructions related to operational activities, the product/service, the quality system, and the desired work culture (e.g., team building, communication, change, behavior)."
6. Available at www.fda.gov/foi/warning.htm
7. Cited in "Production Procedure, QC Unit Citations Top FDA-483 List," *Gold Sheet*, Vol. 38, No. 5 (May 2004), pp. 3-4. For FDA inspections conducted from 2001 to 2003, inadequacy of training was the seventh most cited observation, with 173 observations out of a total of 1933.
8. See the FDA Warning Letter dated 24 June 2005 to Greer Laboratories, Inc., available at www.fda.gov/foi/warning_letters/archive/g5395d.pdf:
9. John Levchuk, "Training for GMPs—A Commentary," Presented at the Pharmaceutical Manufacturers Association program, *Training for the 90s* (Arlington, VA: Sept. 1990)
10. See David Gallup, et al, "Selecting a Training Documentation/ Recordkeeping System in a Pharmaceutical Manufacturing Environment," *PDA Journal of Pharmaceutical Science and Technology*, Vol. 57, No. 1, 2003, pp. 49-55, esp. pp. 49-50 for an insightful discussion of FDA requirements for training documentation; also Vivian Bringslimark, "If Training Is So Easy, Why Isn't Everyone in Compliance?" *Biopharm International*, Vol. 17, No. 1, January 2004, pp. 46-53, esp. pp. 51-52.
11. See James Vesper, "Performance: The Goal of Training—or Why Training Is Not Always the Answer," *BioPharm* [Eugene, OR], Vol. 14, Part 2, 2001, pp. 44-46, esp. p. 44. Also Tony Warchut, "Retraining—Correctly Applied to CAPA," Presented at the *GMP TEA Meeting*, Boehringer Ingelheim, Ridgefield, CT (20 Mar 2009), where retraining as a default CAPA is called a "FDA Red Flag Warning."
12. Available at www.fda.gov/ora/frequent/letters/ARC_20060727_ADLetter.pdf
See also Nicole Fuller "FDA Fines city Red Cross in Training Irregularity," *Baltimore Sun*, August 2, 2006.
13. Robert Merton, *Social Theory and Social Structure*, Glencoe, IL: Free Press, 1957; also John Bohte and Kenneth Meier, "Goal Displacement: Assessing the Motivation for Organizational Cheating," *Public Administration Review*, Vol. 60, No. 2 (March 2000), 173-182.
14. Philip Lindemann, "Maintaining FDA Compliance in Today's Pharmaceutical Manufacturing Facilities," presented at the *PharmTech Annual Event*, Somerset, NJ: 13 June 2006, p. 15.
15. As Levchuk, op. cit. has commented, however, "usually, available information is inadequate to establish a specific reason beyond failure to have a training program, failure to follow the written training program, or failure to ensure that personnel received training."
16. Levchuk, op. cit.
17. See also Vesper, "Performance: The Goal of Training," op. cit., p. 46.
18. The very real, but very different, problem of poorly written and overlapping SOPs has been discussed under the heading "Consolidation of SOPs" in G. Welty, "The 'Design' Phase of the ADDIE Model," op. cit, pp. 44-45.

19. See G. Welty, "The Role of Critical Review in the Revision of Procedures," op. cit., pp. 79-80
20. See www.fda.gov/ora/frequent/letters/ARC_20060727_ADLetter. pdf
21. Assuming for just a moment that each employee's curriculum is correct and current, this proposed approach presupposes that recourse to a notice of event is an adequate organizational response for supervisory error. Regulators typically find this unacceptable, because recourse to a NOE also requires a list of immediate and specific corrective actions that will be taken. As an example of the failure to meet this requirement for NOEs, consider the FDA's *Warning Letter to Pharmaceutical Formulations*, Inc. dated 05 May 2004: "Process failures resulting in the rejection of substantial quantities of drug products were not investigated and there is no documentation to show any corrective actions;" available at www.fda.gov/foi/warning_letters/archive/g4683d.pdf
22. See G. Welty "The Role of Critical Review in the Revision of Procedures," *Journal of GXP Compliance*, op. cit.
23. This is obvious for skill training; as Michael Swartz and Ira Krull, "Training and Compliance," *LCGC North America* [Liquid Chromatography—Gas Chromatography], Vol. 22, No. 9 (2004), pp. 906-912, esp. p. 906, have expressed it for training in CGMP regulations: "It is of little value to train or educate an employee on all of the regulations if there is no impact on the job that person fulfills every day."
24 See Ed Cohen, "Learning Management Systems Mitigate Risk," *Talent Management*, Vol. 4, No. 12, December 2008, pp. 34-35.
25. It is important that the functionality of "electronic signatures" not result in costly overbuilding of the training tracking system; see Tammala Woodrum, "21 CFR Part 11: The role of predicate regulations and associated internal policies," *Drug Information Journal*, Vol. 37, No 2, (2003), pp. 159-164, also G. Welty, "Strategy and Tactics of Training Recordkeeping," *Journal of GXP Compliance*, op. cit, pp. 44-46, and G. Welty, "Training Documentation and Part 11 Compliance," Conference Proceedings, *SALT 2008 Interactive Technologies Conference*, Society for Applied Learning Technology: Arlington, VA (20 Aug 2008).
26. See Cohen, "Learning Management Systems Mitigate Risk," op.cit., p. 35.
27. John DiLollo, "The Use of SOPs in a Pharmaceutical Manufacturing Environment," *Journal of cGMP Compliance*, Vol. 4, No. 3 (2000), pp. 33-35.
28. As Katherine Beauchemin et al., "'Read and Understand' vs 'A Competency-based Approach' to Designing, Evaluating, and Validating SOP Training," *PDA Journal of Pharmaceutical Science and Technology*, Vol. 55, No.1 (2001), pp. 10-15, esp. p. 11 have accurately put it, "Clearly the 'read and understand' method does not meet the criteria set out for validity and reliability;" see also Bringslimark, op. cit., p 46.
29. See also the discussion in Gordon Welty, "The 'Design' Phase of the ADDIE Model," *Journal of GXP Compliance*, op. cit, esp. pp. 49-51.
30. See Welty, "The 'Design' Phase of the ADDIE Model," op. cit., esp. pp. 42-44.
31. James Vesper, "Defining your GMP Training Program with a Training Procedure," *Biopharm* [Eugene, OR], Vol. 13, Part 11 (2000), pp. 28-32, esp. p. 29.

ARTICLE ACRONYM LISTING

CAPA Corrective Action and Preventive Action
CGMPs Current Good Manufacturing Practice
FDA US Food and Drug Administration
JITT Just-In-Time Training
LMS Learning Management System
NOE Notice of Event
SOPs Standard Operating Procedures
SISPQ Safety, Identity, Strength, Quality, and Purity

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