Upsizing Compliance in a Downsizing Environment: Strategies for Ensuring GXP Compliance in the Face of Cost Reductions

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“Effective GMP” discusses specific good manufacturing practice topics useful to practitioners in compliance and validation. We intend that this column will be a useful resource for daily work applications. The primary objective for this column is to provide useful information.

Reader comments, questions, and suggestions are needed to help us fulfill our objective for this column. Suggestions for future discussion topics or questions to be addressed are requested. We need your help to make “Effective GMP” a useful resource. Please send your comments and suggestions to column coordinator Eldon Henson at eldon.henson@ovidien.com or journal coordinating editor Susan Haigney at shaigney@advanstar.com.

KEY POINTS

The following key points are discussed:

• The healthcare industry is currently in a period of seemingly opposing objectives—cost cutting during a period of increasing US Food and Drug Administration enforcement of compliance deficiencies.
• This discussion addresses the identification of areas in which we cannot minimize compliance focus while providing thoughts and approaches that might represent opportunities.
• Principles of quality risk management may be applied to identify compliance improvement opportunities. A seven-step approach is proposed.
• Industry cannot take risks with “black or white” GXP elements. Opportunities may exist within gray areas—activities that are not explicitly defined in GXP or guidance documents.
INTRODUCTION
You cannot pick up a newspaper or turn on the news these days without seeing or hearing that more cutbacks are occurring in the healthcare industry. In what was once considered one of the most secure industries, healthcare has endured more than its share of cost reduction initiatives and consolidations in the past few years. Concurrently, the pendulum at the US Food and Drug Administration has shifted to an era of enforcement, prosecution, penalties, and publicity toward compliance to GXPs. Without question, we have entered one of the most significant periods of enforcement in history. So, how do those of us in FDA-regulated healthcare companies reconcile these two seemingly opposing objectives—cost cutting during a period of high enforcement?

This discussion aims to help identify those areas in which we cannot minimize compliance focus, while providing thoughts and approaches that might represent opportunities. The following three issues are addressed:

- What are those areas of GXP compliance considered “untouchable” that we must protect and preserve?
- How can we use risk management principles to identify opportunities for efficiency gains?
- What are some specific areas of opportunity that might be considered for efficiency gains?

CURRENT REALITIES IN HEALTHCARE INDUSTRIES
Every day, it seems, another healthcare firm announces downsizing, layoffs, consolidation, or “right sizing.” It was only a few years ago that healthcare was the darling of Wall Street and given a free hand for growth. In fact, many healthcare firms considered it simply a cost of doing business to overstaff in some key GXP areas. These same firms were known for their expansive and beautiful campus-like plants and corporate headquarters. Many of the positions originally justified on the basis of meeting GXP requirements have become the victim of one of the big “Rs”—redundancies, restructuring, rationalization, or reduction in force.

Times have changed. Most healthcare firms have announced cuts, layoffs, and reductions in staff during the past two years. In September 2010 alone, 6,000 layoffs occurred in the pharmaceutical industry contributing to more than 43,000 total for the year. In what was once the most secure of all industries, healthcare accounted for more than 16% of all layoffs in 2010 (1).

At the same time, FDA has entered into one of its most significant eras of enforcement in history. Commissioner Margaret Hamburg announced in August 2009 that FDA would “ensure swift, aggressive, and effective enforcement of FDA laws and regulations” (2) including current good manufacturing practices (CGMPs). FDA has significantly added resources, increased inspections, increased frequency and speed for issuing warning letters, and expanded the use of prosecution to ensure compliance. In fact, FDA has publicly stated that they will use extraordinary means to prosecute senior management when violations occur whether management was aware or not if they were in a position that they should have known (e.g., FDA will utilize the Park Doctrine to prosecute individuals).

Given the current enforcement approach by FDA, how can we ensure that we do not adversely impact GXP compliance during a time of downsizing? How can we possibly stay abreast or ahead of ever-expanding FDA requirements, yet fulfill our corporate responsibility to reduce costs? To make matters even more challenging, the drive to reduce costs also makes needed healthcare products more affordable to those consumers in need. So, how can we balance these seemingly divergent objectives?

FDA’S VIEW OF DOWNSIZING AND COST CUTTING
FDA’s primary concern is compliance. GXPs are clear in stating that firms must provide adequate resources to fulfill requirements established in the regulations. A high percentage of warning letters issued by FDA refer to a failure of the quality control unit to fulfill its responsibilities.

Another way of gauging FDA’s views regarding resources is to examine the impact of consent decrees issued for violation of GXPs. In most of these cases, firms significantly increase resources to bolster compliance to the required levels. The author is aware of
one example in which more than 100 quality employees were added to a single 1,800-employee facility to fulfill requirements resulting from a consent decree. In short, lack of resources is no excuse for failing to meet GXP requirements.

FDA and Congress have expressed concerns about cost reductions in the face of increased enforcement. In a recent hearing of the US Representatives Committee on Oversight and Government Reform, concerns were expressed about industry placing “profits first” and “costing down QC” at the expense of product safety (3). During this hearing which occurred in September 2010, one US Congressman questioned whether “cost cutting contributed to a culture” in which product safety issues could occur. Such concerns have clearly contributed to FDA’s emphasis on enforcement.

**IDENTIFYING AND PRIORITIZING COMPLIANCE “UNTOUCHABLES”**

No one would advocate that any element of GXP compliance is negotiable. We must comply with every requirement of GXP every time and all the time. However, much of what we consider the “c” in CGMPs is not black or white. Anyone can determine what to do for those black and white items. However, the real value of quality and compliance professionals is to reach a level of comfort operating in the “gray.” In other words, many aspects of GXP compliance are open to interpretation, and there are many alternative ways to comply. For example, GXP clearly indicate that procedures must be written and approved by the quality unit. GXP require that these documents or standard operating procedures (SOPs) must be controlled in a manner to ensure they are available, that the current version is the only version active, and that a change control process be in place to manage changes to procedures. GXP do not require that document systems use hard copies. Many firms use only electronic systems to manage and maintain their SOP systems.

Another example is the GXP requirement to manage change. There are many different change control systems in place in the healthcare industry. For the most part, GXP direct what to do or the required outcome, but provide flexibility on the “how” to comply.

In a downsizing environment, it is essential that we draw lines in the sand on GXP activities that cannot be compromised. These “untouchables” must be clear, communicated, and consistently maintained. Examples of untouchables are those elements clearly specified in GXP. One way to clearly identify those untouchables is to identify those items frequently cited as deficient by FDA. For instance, the following are the top nine drug CGMP citations for calendar year 2009 (4):

- Failing to fulfill responsibilities of the quality unit
- Laboratory controls deficiencies
- Production and process controls (failure to follow written procedures)
- Production record and review issues
- Production and process controls (deficiencies in written procedures and approval)
- Batch production and control records deficiencies
- Equipment cleaning and maintenance
- Deficiencies with written procedures for equipment cleaning and maintenance
- Inadequate personnel qualifications.

**USE OF RISK MANAGEMENT APPROACHES FOR IDENTIFYING COMPLIANCE IMPROVEMENT**

Despite the lack of ambiguity regarding many aspects of GXP, there are some opportunities for efficiencies (e.g., reduced costs). It is also possible to improve compliance and reduce costs simultaneously, if done properly. There are probably several approaches for identifying opportunities via risk assessment. The approach outlined as follows will require some allocation of time by a number of individuals. However, the potential benefits in compliance or cost reduction are significant.

One possible approach for identifying improvement opportunities is to utilize principles of quality risk management. This approach involves systematically reviewing all elements of GXP while applying an assessment of potential efficiency or cost gains when gaps are identified. The best approach for accomplishing this assessment requires that you dedicate a cross-
functional group of individuals for a number of days. The time requirements will vary depending upon the size and complexity of the operations. By providing clear focus on this task using a dedicated group, you will likely get a better outcome faster. This approach involves the following seven steps.

**What is Required by GXPs?**
This step is actually combined with Step 2. In preparation for this assessment, a spreadsheet, checklist, or other tool should be developed that lists all required elements of the GMP document and guidance you will assess. The more you break down the specific elements of the GMP requirements; the better will be the assessment. The best tool will include all steps in a table (see Figure 1) to allow the team to populate the tool as the effort progresses.

**What Do We Do?**
In this step, the team will provide a very critical assessment of your actual practice for each GXP requirement. In short, you will conduct a gap assessment of current practice against requirements. However, instead of merely highlighting areas in which you fall short of requirements, you will also list areas in which you do more than GXPs require. We certainly want to identify deficiencies in GXP compliance, but we also need to identify those areas in which your practices might be above and beyond current FDA expectations. This step is the most important to the success of this activity and will likely consume the most time for the team.

### Identify Gaps for Each GXP Element Assessed

The gap assessment should include both activities that do not fulfill the GXP requirement and any activities occurring that are above and beyond the basic GXP expectations. Probably in every firm, there are activities that have been accumulated over the years in response to issues, concerns, management decrees, etc. that are not necessarily required by GXPs. Some of these must be continued, but you should identify those that do not represent commitments made to FDA via responses to FDA-483 forms or through corrective action and preventive action (CAPA) activities. Use the spreadsheet tool to record all of these gaps whether they represent a GXP deficiency or extraordinary activity.

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**Figure 1:** Example spreadsheet tool for identifying compliance and efficiency improvements.

<table>
<thead>
<tr>
<th>GXP Item</th>
<th>What we do currently</th>
<th>Is there a gap? If so, what?</th>
<th>For gaps, compliance risk?*</th>
<th>For gaps, cost or efficiency benefit?*</th>
<th>Improvement Opportunity (Yes or No)</th>
<th>Action Plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>211.84(d)(2) – Reduced testing allowed (e.g. obtain results from Certificate of analysis (COA) if COA analyses validated at appropriate)</td>
<td>Reduced testing after full testing for 30 batches (if results acceptable) full testing every 5th lot thereafter</td>
<td>Possibly – some firms conduct full testing at extended intervals, such as every 10th lot or longer, if Justified</td>
<td>Should consider – it appears there is clear precedence for extending our interval</td>
<td>Benefits will be considered high if we extend to every 20th lot or medium if every 10th lot</td>
<td>Yes</td>
<td>Review historical results for key raw materials – unless issues arise, extend intervals for full testing to every 10th lot for APIs and every 20th lot for excipients and components (QA/QC by 3/31/11)</td>
</tr>
</tbody>
</table>

* Determine if compliance risk or cost/efficiency benefit is high, medium, or low.
Determine the Compliance Risk if a Change to That Activity is Made for Each Item Where a Gap is Identified

Once you identify gaps between the regulatory requirements and what you do, simply determine what the risk would be if you changed that practice. One way to quantify compliance risk is to assign a rating of must do, should consider, or do not do, as follows:

- **Must do.** A must do compliance rating would be an item that might result in an FDA-483 observation if you are not currently in compliance or an item that is clearly and completely beyond GXP expectation. Therefore, in essence, must do means you must correct the compliance deficiency or the current practice could be overkill. In other words, an item assigned this classification would require some type of action.

- **Should consider.** A should consider compliance rating might be a possible FDA concern or an item that could be managed via an alternative process. In other words, these items could represent opportunities for improvement.

- **Do not do.** A do not do compliance rating would mean there is no compliance gap either way (i.e., you are complying with requirements). Doing anything else might pose a risk.

Determine the Cost or Efficiency Benefit for Each Item Where a Gap is Identified

For each gap, you would also determine the potential efficiency or cost reduction gain should you implement a change. Items that might yield significant savings would be rated high potential, lesser benefits might be rated medium, and others low.

Identify Improvement Opportunities and Priorities

After you have assessed the potential risks and benefits from each GXP gap, you need to determine which might represent reasonable opportunities. One approach to evaluate the balance between compliance risk and benefits is to place each item in a nine-block chart (see Figure 2).

Thus, items that fall into the shaded blocks of this diagram would be activities that might represent opportunities for improvement that would both improve compliance (or at least be compliance neutral) and provide an efficiency or cost benefit.

Develop an Action Plan and Management System to Monitor Activities

Finally, develop a plan to address any gaps considered must do or those beneficial should consider items. As for any action plan item, you need to assign responsibility for completing the item and a target date for completion. Any must do compliance items possibly should be entered into your formal CAPA program.

**REDEPLOYMENT STRATEGIES FOR SHIFTING PEOPLE TO ACHIEVE COST-CUTTING GOALS**

The approach for identifying compliance or efficiency gaps using a risk management tool may not fully address opportunities for redeploying people resources.
The following are two primary approaches for identifying potential people redeployment opportunities:
• Utilize the risk-based assessment described above
• Utilize zero-based people budgeting.

Simply employing an across-the-board reduction in key compliance resources is not a formula for success. In most cases where unfocused reductions occur, compliance activities suffer. Clearly, this is one concern noted by FDA speakers during this age of enforcement. Investigators have been instructed to examine significant workforce reductions to ascertain whether key compliance activities have been impacted. The author is aware of one investigation suggesting that workforce reductions should be included in the firm’s change control program to ensure proper review and approval.

The use of a risk-based or zero-based (e.g., determining from scratch what resources are needed to accomplish compliance tasks—assuming that you begin with zero and justifying resources by work output required) approaches can both yield efficiency or cost benefits without negatively impacting compliance if done properly. However, the approach should be thoroughly considered and the risks comprehensively considered.

CONCLUSIONS
The concept of improving GXP compliance in the face of downsizing may seem contradictory or simply impossible. If you approach downsizing and compliance in the same way as the past with the same objectives in mind, it probably is impossible. However, it is possible to improve both compliance and the bottom line simultaneously if you employ a comprehensive, risk-based approach to assessing opportunities. Reducing your workforce without considering compliance impact will certainly result in the possibility of FDA inspection concerns, if not potential enforcement activities. One approach for identifying opportunities is presented in this article. In essence, we cannot take risks with those GXP elements considered black or white. We can, however, look for opportunities within the gray areas—those areas whose activities are not explicitly spelled out in GXP or guidance regulations.

The bottom line in this age of downsizing is that FDA is intolerant of violations of GXPs. Some would argue that we should increase resources and activities to ensure compliance during this era. However, both our customers and our shareholders demand that we at least consider assessing our systems for opportunities to improve compliance while embracing efficiency or cost improvements.

REFERENCES

ARTICLE ACRONYM LISTING
CAPA Corrective Action and Preventive Action
CGMPs Current Good Manufacturing Practice
COA Certificate of Analysis
FDA US Food and Drug Administration
SOPs Standard Operating Procedures

ABOUT THE AUTHOR
Eldon Henson is currently Director, API and R&D Quality at Mallinckrodt (A Covidien Company) in St. Louis, MO and serves on the board of the Missouri Valley Chapter of PDA. He has written numerous other articles on topics, such as laboratory operations, annual product reviews, document control, training, re-establishing a culture of compliance, integrity in GXP environments, and validation topics. Henson has written many GMP training modules for Eduneering (see www.eduneering.com), a web-based training content provider. He holds B.A. and M.A. degrees in microbiology from Southern Illinois University-Carbondale and has worked in various quality and manufacturing roles at Abbott Laboratories, Novartis, Boehringer-Ingelheim, Sigma-Aldrich, and KV Pharmaceutical. Henson can be reached by e-mail at eldon.henson@coviden.com or henson333@hotmail.com.