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CCS #18: Culture vs. Compliance

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"Compliance Case Studies" (CCS) provides a forum for compliance practitioners to share information about actual compliance experiences. Previous discussions addressed a wide range of compliance activities. Previous case study titles discussed in this series include the following:

1. Equipment Cleaning and Visual Evaluation, Journal of GXP Compliance (JGXP), V13, #1, Winter, 2009.
2. Questionable Equipment Qualification, JGXP, V14, #1, Winter, 2010.
3. Manual Processes – Performance, Responsibilities, and Training, JGXP, V14, #1, Winter, 2010.
4. Cleaning Validation Unknown HPLC Peaks, JGXP, V14, #1, Winter, 2010.
5. Secondary Packages with Defective Glue Joints, JGXP, V14, #2, Spring, 2010.
6. Identical Mixing Tanks, JGXP, V14, #3, Summer, 2010.
7. Broken Punches, JGXP, V14, #3, Summer, 2010.
8. White Spots on Tablets, JGXP, V14, #4, Autumn, 2010.
9. Substandard Data and Documentation Practices, JGXP, V15, #2, Spring, 2011.
10. Change Control for "Like-For-Like" Changes, JGXP, V16, #2, Spring, 2012.
11. "Glass" Fragments in a Parenteral Product, JGXP, V18, #3, Autumn 2014.
12. Yellow Discoloration on White Coated Tablets After Commercial Distribution, JGXP, V18, #4, Winter 2014.
13. Consistent Sampling, Results, and Original Data. JGXP, V18, #4, Winter 2014.
14. "Like-for-Like" Changes – What, if Anything, should be Done? JGXP, V19, #1, Spring, 2015.
15. Manufacturing Support Audit Observations. JGXP, V19, #2, July 2015.
16. Microbial Contamination from Food. JGXP, V24, #6, November 2020.
17. Spots on Tablets – An Investigation. JGXP, V25, #2, March 2021.

Readers are invited to participate and contribute manuscripts for this series – please share your successful practices with others. Please contact journal editor-in-chief Paul Pluta et or journal managing editor Stacey Bruzzese through the comments section with questions, comments, or submissions for publication.

ABSTRACT

This discussion describes compliance events caused by non-technical root causes – attitudes, misunderstandings, resistance to change, conflicting circumstances, and other personal traits in employees in a GMP environment, i.e., elements of culture in the pharma workplace. In these events, organizational culture had strong influence in causing compliance problems. Case studies presented should foster awareness of such problems. Inadequate training is often contributory; other factors, however, occurring with experienced and knowledgeable employees are also involved. Problems described were reported by managers from multiple companies; each manager believed their work environment to be highly compliant with a quality orientation. These examples demonstrate the need for compliance professionals to be continually vigilant for potential compliance problems – and especially less obvious culture problems -- in daily work activities.

INTRODUCTION

There are numerous articles, white papers, webinars, and other scholarly offerings on GMP compliance issues. Each of these have value; they reflect the experiences and perspectives of the authors. Fundamental in these are annual reviews of regulatory observations and identification of non-compliance trends (1,2). Other reports focus on more general discussions (3,4). Still others may specialize in compliance problems in specific technical functions (5,6). See Tables below.

1. Lack of Written Procedures or Failure to Follow Written Procedures
2. Failures in Laboratory Controls
3. Faulty Production Record Reviews
4. Absence of Written Procedures
5. Improper Cleaning/Sanitizing/Maintenance

Table 1. Five Notorious Compliance Issues in the Pharmaceutical Industry (3)

1. Failure to employ properly qualified, experienced, and trained people
2. Failure to maintain adequate funds for GMP infrastructure
3. Lack of knowledge and vigilance
4. Failure to solicit support from consultants and regulatory bodies
5. Errors in sourcing raw materials
6. Missing useful associations
7. Failure in time management
8. Failure in designing and maintenance of facilities

Table 2. Eight Common Mistakes in GMP Compliance Failure (4)

1. A risk-based approach to maintenance is not used
2. Computerized Maintenance Management Systems (CMMS) are not utilized, are under-utilized, or are not validated
3. Maintenance plans are not updated as part of new equipment introduction
4. Maintenance staff and contractors are not trained properly
5. The GMP impact of lubricants is not considered
6. Maintenance of utilities and supplies falls between department cracks
7. Maintenance activities are undocumented
8. Modern maintenance management techniques are not used
9. Equipment documentation is not readily accessible
10. Maintenance is not considered during equipment purchases

Table 3. Ten Common GMP Challenges Facing Maintenance Departments in Pharmaceutical Plants (5)

Compliance Case Studies

Compliance Case Studies has previously described compliance events and problem-solving for an extensive range of occurrences. Each of these events from pharma managers were interesting occurrences with unexpected technical root causes. For example, a problem with white spots on tablets was caused by incorrect machine assembly (7); false negative cleaning validation data were caused by overly cautious sampling technique (8); faulty carton sealing was caused by inexact equipment operational procedures (9). Another well-publicized and highly unexpected event involved the presence of yellow discoloration on white coated tablet caused by product contact with drug residue on pharmacy counting trays during prescription dispensing in community pharmacies (10).

Several additional problem examples have been subsequently communicated to IVT. These involved people issues – a cause not addressed in usual compliance discussions. Examples in several cases occurred with new employees and new situations; inadequate training is usually blamed for these events. Others, however, were caused by experienced, knowledgeable, and trusted employees who are well-versed in compliance. All compliance events were unexpected; every manager believes their organizations to be highly compliant -- “Quality is job #1.”

Discussion Topics

This discussion describes several compliance events involving personnel in pharma manufacturing facilities. Examples were provided to the*Journal of GXP Compliance* by multiple managers from multiple companies. Events described demonstrated several culture issues affecting GMP compliance. Topics include:

- Friendship vs. compliance
- “We do whatever it takes” vs. compliance
- Productivity vs. compliance.

Readers are invited to submit other examples of compliance events to be included in*Compliance Case Studies* , in the IVT blog, or in*Voices in Validation* podcasts. Subscribers appreciate these examples; they serve as reminders of possible compliance issues at their sites for future investigation.

FRIENDSHIP VS. COMPLIANCE

Two examples demonstrate the power of friendship and co-worker loyalty vs. compliance.

Case Study #1.Extra Cleaning of Cleaning Validation Sampling Locations

A validation manager visited the production area to observe equipment cleaning by manufacturing operators prior to cleaning validation sampling. The operators performed cleaning according to written procedures. After cleaning was completed, the operators used cleaning validation sampling documents to perform additional cleaning on equipment sampling locations. These documents were used in cleaning validation protocols and should not have been available for equipment cleaning. Documents had been copied by the manufacturing area personnel from previous cleaning validation protocols. In effect, cleaning personnel had “answers” to cleaning validation testing before the test was given.

This case study demonstrates misunderstanding of validation principles on the part of cleaning personnel. Additional cleaning of the validation sampling locations in anticipation of cleaning validation testing could be construed as a fraudulent cleaning validation.

When the additional cleaning of sampling location was observed, the validation manager stopped the cleaning process; the planned sampling would not have addressed the objective of the cleaning validation – clean equipment after one cleaning process as directed in an approved procedure.

Validation technicians were also present during cleaning by the manufacturing operators. The validation technicians were questioned: "Were they aware of the multiple cleaning practice by manufacturing operators?" They responded that this practice had been in place for several months. When asked why they did not report this practice to cleaning validation management, they responded "We have to work with these people."

Compliance Issues. Multiple problems were identified in the above event. Manufacturing operators were deliberately cleaning identified cleaning validation sampling locations multiple times to increase assurance of passing cleaning validation. Their supervisors were also aware of this practice. Whomever initiated this practice was likely very proud of his action; reality, however, was that the integrity of the site cleaning validation program was significantly damaged.

Most disturbing to the Validation Manager relating this event was that his sampling technicians were aware of this practice for some time and did not divulge its use. Their collegial loyalty to co-workers -- "We have to work with these people" -- rather than to their work responsibility and department management was highly disappointing.

Case Study #2. Backdating Manufacturing Records

Another Quality Manager described a similar incident in which a QC document reviewer modified manufacturing records when document data was absent.

Product manufacturing records submitted for QC release would occasionally contain pages that were incomplete. The QC document reviewer would complete missing fields without consulting production personnel. The QC reviewer would add missing information, sign, and date entries as if they were done at the intended time of performance. Sign/date were thus backdated by the QC reviewer.

Fraudulent documents prepared by the QC Review person were inadvertently discovered. The QC Review person admitted to her practice and rationalized that she didn't want her co-workers to get in trouble for incomplete documentation and delaying release of product lots.

Compliance Issues. Backdating is a fraudulent compliance issue. When information is added to GMP documentation, the exact date of entry must always be written. The QC Reviewer was an experienced person with significant site responsibilities. HR became involved and punitive action was severe. The integrity of site documentation became questionable due to this incident.

"WE DO WHATEVER IT TAKES" VS. COMPLIANCE

The following examples occurred at a manufacturing site that was initiating several new procedures involving cleaning validation. Personnel at the site were trained in the new procedures; examples indicate that training was not completely successful.

Case Study #3 – Extra Soap

A manager described an event in which a newly trained technician was manually cleaning a mixing tank. The manager noticed an unusually large volume of soap foam in the tank spilling over the sides of the tank. The manager asked the technician, "Why so many soap suds?" The technician responded that the tank was unusually dirty with residue, so he thought he would add an extra scoopful of detergent to help with the cleaning. When the manager reminded the technician about the recent training and the need to use exact amounts of detergent per procedure, the technician responded that he did not think the soap amount was part of the discussion. He thought that adding soap was completely up to him. He exemplified the thinking of "we do whatever it takes to get the job done." Even though training was just conducted explaining the importance of following the exact directions in the cleaning method, the technician followed his usual method of cleaning – "doing whatever it takes."

Compliance Issues. Additional training of site personnel was scheduled to discuss transition from "doing whatever it takes" to following procedures.

Case Study #4 – "The New Cleaning Procedure Doesn't Work."

The small parts of equipment used in a filling process for an individual site product were cleaned by a manual cleaning process using alcohol. Cleaning was performed in an explosion-proof (XP) room. Parts were submersed in a tub of alcohol and agitated for a prescribed time. Equipment was then rinsed with water. Additional steps were then performed to complete cleaning. This process was validated and performed routinely for several years without any problems.

A construction project at the site eliminated the cleaning XP room. The project was thought to have minimal impact since only one product was cleaned in the room. A new aqueous cleaning method (no alcohol) was developed and validated.

A periodic cleaning validation was being done on the aqueous cleaning process. Cleaning sampling technicians entered the cleaning room expecting to sample equipment. They noted that alcohol was being used for cleaning – the previous approved cleaning method -- even though the most recent approved cleaning method specified aqueous cleaning without alcohol. The manufacturing operators were questioned as to why they were using the alcohol method especially in a non-XP room. They responded that the aqueous method was ineffective. When asked why they did not communicate this to management, they responded they did not have time to do this, they couldn't wait for cleaning development work, and it was easier to go back to the old method. Documentation on previous lots was reviewed. All procedures required the use of the aqueous cleaning method but were actually cleaned using alcohol. Operators claimed they were told that either method was acceptable for use since both had been validated.

Compliance Issues. Multiple compliance problems were identified in the above event -- cGMP, documentation practices, and solvent safety. Ultimately an XP room was located, and small-parts cleaning was modified to use alcohol.

Case Study #5--Wash Equipment Multiple Times

Another example of "doing what it takes" occurred with a cleaning validation on a new product. The production operators washed manufacturing equipment three time per directions from management. They proudly stated "We are doing everything we can to pass the cleaning validation. Three different people cleaned the equipment before sampling. With three different washings, they equipment should be clean."

Compliance Issues. This event demonstrates gross misunderstanding of validation principles. Cleaning equipment three times and getting acceptable test results, and then contending that results support single cleaning of equipment is obviously incorrect and a serious misunderstanding of cleaning validation. Doing whatever it takes to pass is folly in a GMP procedure environment.

PRODUCTIVITY VS. COMPLIANCE

All business must be productive and financially sound for survival. An excessive productivity culture diminishing compliance performance is dangerous.

Case Study #6. Unnecessary Testing

An engineering technician was assigned to complete five IQ and PQ protocols on new identical metal detection equipment. The first machine was successfully completed; a thorough ad complete qualification summary report had been prepared. Testing for machines #2 and #3 were submitted a few weeks later. When requested to present the data for machines #2 and #3, the technician submitted pages of machine #1 data. His response: "The machines are all the same; there is no need to repeat same testing on all machines." When confronted about not testing all machines, the technician responded that he was doing as instructed by his engineering manager; he was told that no one in the Validation Approval Committee would notice the duplicate of data.

The technician was also asked to present original data used in the original machine qualification (not typewritten data in report). The technician responded that he discarded the original data since data were now in the report. The report was the only record of data – there were no original data.

Compliance Issues. Multiple problems were identified in the above event. Falsifying data, fraudulently violating protocols, and destroying original data were significant compliance problems. Function management directing these activities is even worse.

Case Study #7. Engineering Validation Approval Committee (VAC) Representation

A new Validation Manager at a manufacturing site was becoming acquainted with the site Validation Approval Committee (VAC). He observed the Engineering representative to be relatively inexperienced in technical engineering issues at the plant. The new person rarely contributed to discussions evaluating submitted validation documents. When the site manager was confronted about the Engineering representative assignment to the VAC, the manager stated that he always assigned new people to the VAC because it was an excellent training ground for new personnel. A new Engineering representative was requested with greater expertise and experience in engineering validation.

The new VAC representative was appropriately critical on documents submitted by non-engineering functions but was a "rubber stamp" on engineering documents. Engineering documents that were poorly written, not sufficiently supported by data, or with other deficiencies were argued to be acceptable -- "documents were good enough" -- by the VAC engineering rep. When confronted about his attitude, the engineering rep stated this his boss told him

that his job was to “get docs through the system” – an extreme focus on productivity at the expense of compliance. Another new Engineering representative was requested.

Compliance Issues. The Validation manager developed a procedural document identifying responsibilities of the VAC. These include three primary responsibilities regarding validation documents including technical scientific excellence, compliance with regulations and policies, and document quality. Finally – a key responsibility -- the VAC must function as an internal regulatory agency and review documents through the eyes of a regulatory auditor. The must feel responsibility for the quality of the documents they approve. If a regulatory auditor finds deficiencies in a validation document, the VAC has not done its job. All VAC members approved these requirements.

SUMMARY AND FINAL THOUGHTS

This discussion described a variety of compliance problems caused by the strong influence of site culture. Three dominant culture characteristics were identified:

- Friendship. Personal relationships between co-workers caused compliance problems to be concealed. Recall Watergate: “The cover-up is worse than the crime.”
- “We do whatever it takes.” Conversion to a GMP-procedure approach to manufacturing and associated activities must eliminate all remnants of a “do whatever it takes” attitude in employees.
- Productivity. A focus on productivity at the expense of compliance may be dangerous.

The compliance problem examples described above should remind compliance professionals that they must be continually vigilant for potential human compliance problems in daily work activities – especially less obvious culture problems. Elements of site culture may be a strong deterrent to GMP compliance.

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