MYTHS AND REALITIES IN VALIDATING BIOTECHNOLOGY FACILITIES

(Derived From Ten Projects)

BY:

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Abstract:

The author discusses myths and realities experienced over 20+ years of validating facilities for biotechnology firms. Five key concepts are then presented which are essential to completing the commissioning and validation of biotechnology facilities right, first time, and on-budget.

Keywords:

Biotechnology facilities, commissioning and validation

Presentation:

Myth or Reality # I: On more than one occasion, those responsible for the design, commissioning, and validation of biotechnology facilities thought they should inform quality and/or validation personnel immediately prior to the initiation of validation. **Be advised that this myth has consistently resulted in significant and costly overruns in time and money** (several examples are provided below):

1. The team did not learn that specific documentation required by validation should be specified with the Purchase Order (PO). This essential documentation should arrive 2 – 4 weeks prior to system/equipment delivery. If the documentation is not specified, some vendor documentation will be delayed, some will not be received at all because it was not specified, or some may be routed to the wrong department upon arrival). This delayed or mis-routed documentation will increase the time required for commissioning and validation efforts.

2. The team did not know to assign someone responsibility for document receipt and organization; the documentation was therefore not organized or lost which slowed commissioning and validation efforts.

3. Quality and validation personnel were not informed of commissioning and installation activities performed by others; therefore, some commissioning and installation documentation was lost, some was inadequately documented, and some was inadvertently repeated.

4. Commissioning and validation did not have the opportunity to meet with vendors during start up to ask key questions. Therefore, protocols had

errors which caused deviations and execution delays or omissions; these errors detracted from the quality of the effort.

5. Validation was not involved in reviewing designs, proposals, and submittals which resulted in design, cleaning, and sterilization issues or misconceptions.

6. Validation was not involved in reviewing vendor's software which resulted in problems with electronic records and signatures, functional specifications, or a mis-understanding of user requirements.

The reality is that once the decision has been made to design and build a GxP biotechnology facility, a team of highly talented people should be assembled. To assemble a team, Senior Management often selects a Project Manager. In some cases, it is possible for a team to be assembled and a Project Manager selected by the team members.

The Project Manager decision should be based on his/her ability to communicate with the team, being knowledgeable about the system/equipment being purchased, having the authority to make operational decisions, and understanding the dynamics of the company's operation. In addition, the PM should be very familiar with the validation and qualification issues related to the system or equipment in question and 'turn-over' packages required during the qualification process.

Members of each discipline should be involved, i.e. Engineering, Production, Purchasing, Quality Assurance, Regulatory Affairs, and Validation. These team members are likely to be employees and consultants.

It is recommended that each team member be highly experienced, with a minimum of 10 years of relevant industry background and multiple relevant previous projects. (If the decision to involve a junior person is made, this person should be involved in addition to the senior person.) It is important that each team member be able to work well with others, and for him/her to be highly skilled in his/her field.

Proper planning should include the following activities:

1. Identifying the project goals, constraints, project phases, and document 'turn-over' packages required at the beginning of the project.

2. Identifying the personnel, responsibilities, and risks involved.

3. Identifying personnel issues (i.e. vacations, team chemistry)

4. Identifying and generating project deliverables.

5. Assembling a team of experts who know what problems to expect, and know how to resolve potential problems before they become problems and affect your project.

Myth or Reality # II: Team Member A (below) provides the better value?

- Team Member A is a mid-level person (@ $75/hr), anticipate 6 months of effort.

- Team Member B is a senior-level person (@ $125/hr), anticipate 4 months of effort.

Who do you choose + how do you decide? Before you answer, ask yourself the following:

1. How long have A and B been working in your industry? If it is less than 5 years, do you want to be their guinea pig? (How long do guinea pigs live?)

2. Will your company remember how much money you saved them or will they remember the number of problems and delays that arose based on your selection?

3. How many letters of recommendation do A and B have? Their letters of recommendation are their commitment to past quality and a good indication of future quality.

4. How many years of relevant experience do these people have? Perhaps you think that you will save money because you use a mid-level person. Will that keep the price down when yours is the first or second facility they've ever worked on?

5. When you interviewed each candidate, what indication did you get that he/she had performed the same task(s) numerous times? What did he/she say that demonstrated that he/she could provide superior value?

6. What do you think will happen when there is a problem with the facility? Which person do you think will know what to do?

7. What will happen when you and your Quality Assurance representative review their work? How will the quality of their work reflect on you? How do you feel about "re-work"? How will re-work make you look? What will happen when your clients and the FDA review the work?

At first glance, these concepts can be difficult to quantify. Therefore, the following answers are suggested.

Answer 1: Less than 5 years is 3 points, 5 – 10 years is 7, over 10 years is 10 points, over 15 years is 15 points.

Answer 2: Rhetorical (N/A)

Answer 3: Assign one point for each letter, maximum of 10 points.

Answer 4: Assign one point for each year of experience, maximum of 25 points

Answer 5: Assign one point for each time that he/she has performed the work you require, maximum of 10 points. Assign 5 points for each explanation that indicated that he/she would do a superior job, maximum of 20 points. Maximum for Answer 5 is 30 points

Answer 6: Assign 3 points if he/she gives you a low level, 7 points for a medium level, or 10 points for a high level of confidence that he/she would know how to handle a problem with the equipment.

Answer 7: Assign 3 points if the firm gives you a low level, 7 points for a medium level, or 10 points for a high level of confidence that the firm will keep the contractor or consultant you select on the job throughout the project

Reality: The average biotechnology facility is constructed to generate sales in excess of $1 million dollars/day. **Reducing the time from 6 months to 4 months is a savings of 60 days. If your product generates over $1,000,000.00/day you've just lost your firm $60,000,000.00!**

From this you may be reminded of the old adage, "you get what you pay for", but there's more to **A senior-level person often accomplishes more in less time while adding more value.** This illustrates the reality of choosing highly talented individuals.

Myth or Reality # III: Is commissioning and validation an "exercise"? Should Senior Management subscribe to the "design/build" concept? For those that share this myth, be advised, projects with clear, concise, quantifiable, and verifiable/testable plans and requirements will result in projects completed sooner than those "exercises". Ask yourself the following questions:

1. How will Purchasing know exactly what to procure without well-defined user requirements?

2. How will the team know how to test systems when the users have not specified what is needed and not defined 'turn-over' packages required by validation?

3. How much testing is enough when the users have not specified what is needed?

4. Moreover, what is the point? (The User, Business, and Functional Requirements provide the foundation for installation, operational, and performance qualification.)

Those that understand the value of validation realize that it adds value by defining facility capabilities and providing a high degree of assurance that the facility can consistently produce a product meeting the desired attributes. Understanding a facility's capabilities is key to maximizing productivity. If you would not buy a bottle of orange juice, take a sip and throw it away, why spend millions of dollars to construct a facility without determining what it is capable of doing?

Myth or Reality # IV: This time, we'll do better job and start "with a clean slate". This is another costly myth. In this Internet age, it is likely that existing information can be leveraged. (Why "re-invent the wheel"). Instead:

1. Obtain vendor information to create SOPs and operational tests.

2. Use commissioning data to support installation, operational and performance testing.

3. Build from your/consultants existing protocols and SOPs.

4. Ask experts for suggestions (i.e. Senior Management, people you've met through ISPE, PDA, BIO, etc)

5. Contact others at your firm from different sites with similar responsibilities (some large firms create validation committees with people from different divisions/sites)

6. Build relationships with other firms. Some firms do this because they know that it is mutually beneficial.

7. Learn from previous projects.

In short, leverage whatever you can!

Myth or Reality # V: Let's just get it done ourselves, we can do it faster and better this way.

Successfully building a biotechnology facility means involving all directly and in-directly affected disciplines. (This doesn't mean that everyone is involved to the same degree, it means that everyone feels that their opinions have been heard and respected). It means sharing with Management and getting their buy-in early and periodically thereafter. Management is likely to be able to provide valuable insights. It also means getting agreement within the team regarding:

1. Definitions
2. Project Scope
3. Timing
4. Test Methodology
5. Applicable Guidelines/Regulations
6. Well defined vendor 'turn-over' packages

By assembling a multi-disciplinary team of highly talented people at the beginning of the project:

- the goals and constraints that comprise the project can be properly developed;
- good documentation and 'turn-over' packages can be well defined;
- Engineering deliverables (i.e. good requirements and design) can be readily evaluated
- existing systems and previous knowledge can be used to 'optimize' the effort
- buy-in from Senior Management can be more easily obtained.

The team can use their knowledge to identify the scope of the project, the documentation deliverables, the project methodology and strategy. For example, involving quality and validation in the design phase of the project allows them to assist the team in identifying a facility design that is "validatable", i.e. designing a facility based on the movement of personnel, raw materials, product, and waste (not merely based on the constraints of the available footprint)

Conclusion:

The five keys to successfully commissioning and validating biotechnology facilities can be summarized as follows:


Proper Planning,


Selecting Highly Talented People,


Good Requirements And Design,


Leverage, and


Buy-In

About The Author:

Jeffrey Gassman has over 20 years of commissioning and validation experience for biotechnology and pharmaceutical clients nationally and internationally. He earned his B.S. in Chemical Engineering from Clarkson University, and his M.S. in Chemical Engineering from Columbia University. In 1995, he became the President of Validation Plus (VPI). His work and leadership has been instrumental in VPI receiving numerous letters of recommendation. In 2004, Mr. Gassman was elected to Who's Who in Science and Engineering in America. In 2009, Mr. Gassman was elected to the Presidential Who's Who in America. He can be reached via email: jeffreygassman@validationplusinc.com