Global Trends, Needs, Issues

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ABSTRACT: Worldwide, Pharmaceutical Plant Management struggles with the competing priorities of lowering costs, rising customer expectations, more demanding government regulations, and the need to reduce cycle times especially in the introduction of new products. All of this takes place in an environment of global competition, regulatory harmonization, mergers and downsizing, and employee insecurity. Employees are expected to do more with less, work with more sophisticated equipment and processes, take on more personal responsibility for quality and productivity, work in teams, etc. In summary, we are talking about CHANGE, the speed of which will accelerate in the years to come. This presentation will discuss how some pharmaceutical plants are addressing these challenges. Examples will be given in the areas of validation, process reengineering, risk analysis, role of the quality function and people. It is my contention that most of the global trends today are insufficient to meet the challenges that we face. I hope that this presentation will generate some ideas on what the global trends should be.

Introduction

This presentation is based on several assumptions. Both the pharmaceutical industry and FDA are under heavy pressure to do more with less, improve quality and lower costs simultaneously. The globalization of our industry is having a dramatic impact on manufacturing and on FDA. Pharmaceutical plants are being closed at an accelerating rate, the remaining plants are supplying the world—not just the local market—and the use of third party contract manufacturers is more and more common. FDA, on the other hand, must rely more on regulatory authorities in other countries. This is driven by costs primarily and secondarily by the globalization of our industry. My last basic assumption is that quality primarily has to do with product and customers and not with regulations and regulators. FDA is not the primary customer. Industry and FDA have the same primary customer—the patient.

In this presentation I will describe some of the positive as well as negative trends. I will also describe some things we have been trying to do to meet the demand of lowering costs and simultaneously improving quality.

Positive Signs

Starting on an optimistic note there are many positive things happening in our industry. I will mention a few. The new Quality System Regulation for Medical Devices, based on ISO-9000 is a significant advance, especially when compared with the drug GMPs. It is based on a much more quality planning. Another positive sign is SUPAC. It is a primary customer—the patient.

It’s conclusions are based on science. It is an attempt to reduce both industry’s and FDA’s costs. And, it uses risk analysis—everything is not equally important. A final positive sign I’d like to mention is the growing dissatisfaction of industry, the growing awareness that something must change: more money being spent, on validation for example, with no apparent benefits for product quality, the customer or the company.

Negative Signs

There are some realities and obstacles that make it difficult to respond to the challenges of quality up, cost down and globalization. I will talk about the four that I consider the most important. I believe our most serious problem is the US’s drug GMPs. The basic philosophy of these GMPs is out of date. It is the philosophy of quality of the ‘50s and ‘60s—control, inspect, don’t trust production, QC/QA department responsible for quality. The proposed revisions to GMPs, May 1996, are a continuation of this non-current philosophy of quality. Contrast the drug GMPs with the Quality System Regulation for Medical Devices mentioned earlier and with what the best industries have learned in the past 50 years as the way to achieve high quality.

• quality built into the product via design and validation
• SPC to measure variation—process capability
• quality is the responsibility of all, especially production
• continuous improvement
• vendor partnership

Another negative sign is the excessive focus on regulation and regulators—what does the FDA say? The reliance on regulatory guidance is growing. We allow the regulators to set quality standards. Standards need to be based on science, commonsense, economic impact and risk/benefit analysis. In this context, I should also mention the Barr case as a negative.
- My third concern is the tremendous waste we have in our quality systems—documentation in excess, validation without process improvement, high and expensive QA/QC departments, etc. Lastly, I'd like to mention the inadequate measures of quality that are frequently used—483 observations, recalls, AQL's (defects in %). These are hardly the measures used by world class industries/companies.

Opportunities

Let us shift back now to a more positive frame of mind. I will present some things we have been trying to do to meet the challenges, what I think the trends should be:

1. Validation
2. Process Optimization
3. Risk Analysis
4. New Role for QC/QA
5. People

This will be only a brief overview of these 5 topics. The references provide more information for those interested.

Validation

The need for obtaining more concrete benefits from our validation efforts/costs has been voiced by many. John Sharp says it well,

"Validation is progressively ceasing to be an important practical study. It has become an abstruse documentary, not the patients who consume the products, but the organizations who run expensive courses on "How to Meet Regulatory Validation Requirements." Perhaps more time could be spent on other things." (1)

Mike Anisfeld in his article on "Validation—How Much Can The World Afford? Are We Getting Value For Money?" reminds us of the tremendous cost of validation (2). He estimates the cost at 20% of the current cost of producing pharmaceuticals.

When I started in the pharmaceutical industry about 30 years ago, I did validation, not because it was a regulatory requirement but because it was good science as I learned it in school and because it was common sense and a business necessity to make sure systems worked correctly. Although the basic concepts of validation have not changed in 30 years, the amount of documentation has increased by orders of magnitude. I doubt the increased documentation has significantly improved the quality of our processes.

The only way to get good value for our validation dollar is to do an effective risk analysis. The consumer risk varies with the type of product—OTC, Ethical; the dosage form—solid dose, injectable; and the criticality of a particular step in the manufacturing process. Logically then, our limited validation funds must be spent where the risks are higher and therefore the benefits greater. We have been using Failure Mode Effect Analysis (FMEA) as a tool to help us perform this risk analysis (3).

Also, we need to do a better job at the design stage—design for manufacturability. There are too many attempts to validate non-validated formulations and manufacturing processes. The variation in these cases is intrinsic to the process. The only solution is to redesign the process and then validate. The transfer of know-how from R&D to manufac-
FMEA in our validation work, in audit preparation, batch record review, change control, trend analysis and master validation plan development.

New Role for QC/QA

The role of QC/QA in our industry must change dramatically. This will require that QC/QA managers acquire new skills (9, 10). They should be:

- improving and optimizing processes
- establishing partnerships with suppliers and customers, especially with their own production department
- benchmarking, particularly other industries where the better quality practices are today
- creating quality awareness—selling quality, recognizing outstanding quality performance
- providing modern quality tools to all employees for continuous improvement
- measuring quality performance and reporting results to management

People

Qualified and motivated people working in an empowering environment has always been a competitive advantage. It will become even more important in our industry in the future (11). We must create the empowering environment (see Table III) which is quite different from the controlling one.

We need to make sure all our people know what is expected of them and why, whether or not they are accomplishing what is expected of them, how to regulate/adjust their process, the total process flow, where they fit in the total process, the total process performance, how to identify and solve problems, how to improve the process.

This will require a tremendous increase in the knowledge and skills of all our people and a paradigm change in the way we think and manage.

As Stoker and Willig (12) remind us, “Only when every employee is fully committed to the achievement of consistent quality and held accountable and rewarded will real progress be made.”

Conclusions

I have presented what I perceive to be some of the positive as well as negative trends in our industry. I have summarized some ways that I have found to be effective in meeting the challenges we face today of higher quality, lower costs and globalization. The details of these techniques I have published in the articles referenced.

We need to develop a holistic, integrated quality system; to use better quality tools, such as FMEA, process capability, process management; increase our understanding and improve control of critical process parameters so that we can move to parametric release. Most important we need to change our mindset from quality control to total quality, to the empowerment of all our people. We have to become more proactive to regulations and regulators. Let us remember that industry and FDA have the same customer—the patient.

At the end, am I optimistic or pessimistic about the future? Optimistic, but the change will be difficult both for the pharmaceutical industry and for its regulators. What do you think?

### References