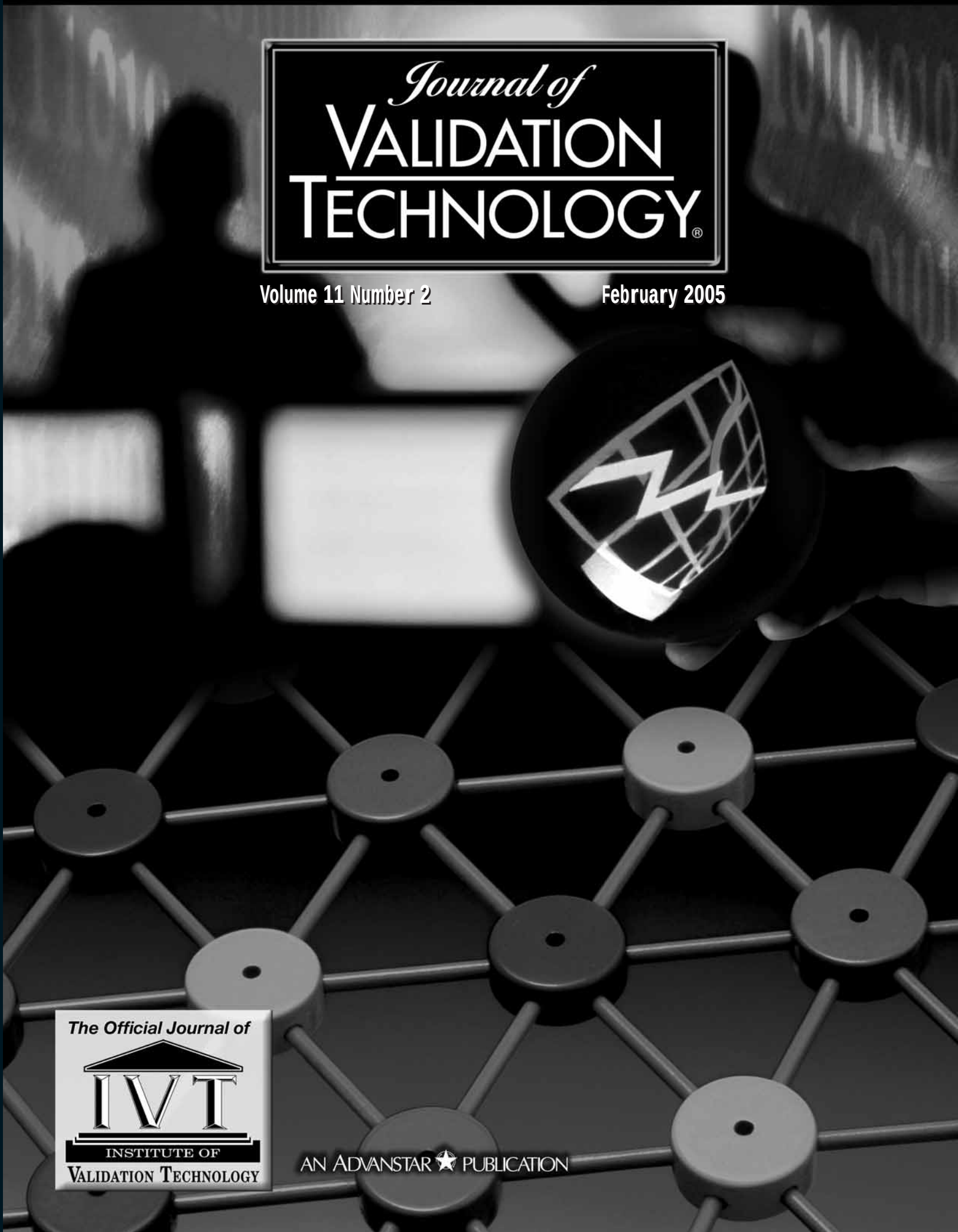

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Lean Six Sigma for Pharmaceutical Projects: How Pharmaceutical Companies Can Minimize Defects and Increase Value

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SCOPE

The Lean Six Sigma approach has been used for years in the chemical, refining, mining, and food industries to improve manufacturing processes. By combining a Lean philosophy with a Six Sigma approach, pharmaceutical companies can improve product and process quality and reduce cost and time to production. Traditionally, automation-development methodologies in pharmaceutical companies push quality verification processes toward the end of the project cycle. In contrast, a Lean Six Sigma approach relies on embedded lean quality processes instead of quality tollgates at every stage of the project life.

By embedding Lean Six Sigma practices as part of the regulatory validation process, pharma companies can benefit from scientific decision-making techniques to optimize implementation and operations. This article reviews the five core phases in the Lean Six Sigma approach, which enable companies to produce the tangible benefits noted above. Intangible benefits created by applying Six Sigma techniques, such as successful teamwork, and indirect benefits including, reductions in cycle time, waste reduction, and the resulting increase in Return on Investment (ROI) are also presented. These and other aspects of Lean Six Sigma are discussed in this paper, which is addressed to all practitioners involved in regulatory compliance, validation, and quality issues in the pharmaceutical and life sciences industry.

Why Lean Six Sigma?

Lean Six Sigma is an innovative methodology that is helping companies across a wide range of industries achieve unprecedented quality gains, cost savings, and revenue growth. At the heart of the Lean Six Sigma philosophy is a team-driven approach that combines team members' experience and know-how with a scientific methodology grounded in metrics and statistics.

The Lean Six Sigma approach is ideally suited to the pharmaceutical industry. By combining Lean production (which focuses on removing waste) with Six Sigma (which reduces variation), pharmaceutical companies can improve their processes and quality. Lean production focuses on improving flow and eliminating everything that does not add value to the process, while Six Sigma focuses on variables that are critical to quality (see "Critical to Quality" *inset*). Lean production provides a way to define value, to set up value-creating activities in the most optimal sequence, and to carry out these activities without interruption. The enhanced flow associated with Lean production results in reduced cycle time and lower costs. Six Sigma produces uniform process outputs as a result of a predictable and reliable process that is more cost-effective to operate since it does away with unnecessary rework, additional scrap, and overtime.

Critical to Quality

Most processes consist of a multitude of input and process variables; monitoring and managing them on a continuous basis would be a time-consuming and prohibitively expensive endeavor. It is also unnecessary. In accordance with the Pareto Principal – which states that a small number or proportion of causes are responsible for a large majority of effects (80/20 rule) – there are often only a very limited number of critical inputs and process variables that drive the process output variables. Therefore, most defects in a process are usually due to a few critical factors. By identifying and correcting the factors that are critical to quality, companies can realize enormous boosts in quality and cost-effectiveness.

Traditional Project Methodologies in the Pharmaceutical Industry

Conventional System Development Lifecycle (SDLC) methodologies are not based on a process view that analyzes and determines process inputs, activities, and outputs. Instead, improvement efforts are carried out late in the testing cycle and are focused on outputs and defects. This can cause major project overruns both in terms of time and cost since the process input variables that are at the root of quality problems have not been identified. A typical example is that quality problems surface at the testing phase causing major revisions to requirement and design specifications as well as to the actual code and/or hardware. Furthermore, due to the "rush to finish," data are not systematically analyzed to better drive the efforts. Instead, solutions are put forward without any true understanding of the problem or its root cause and the efficiency and effectiveness of these solutions can be questionable.

Typically, a "band-aid" solution is put forth, namely, to add more resources to deal with the problem, but this is costly and often counterproductive. To produce a real impact on process performance, it is vital to begin with an understanding of workflows, cycle times, and root causes. In other words, we need an understanding of what is causing the "pain" in the situation under review.

The philosophy behind Lean Six Sigma is that all work can be viewed as a process that can be carried out by following a set of defined and interconnected steps. All processes can be divided into inputs, processing steps, and outputs. This means all processes can be subjected to a consistent methodology for detecting and eliminating errors – and thereby improve the process.

Applying Lean Six Sigma to the Pharmaceutical Industry

Lean Six Sigma introduces a methodology that rectifies the problems associated with "after-the-fact" testing. This disciplined, data-driven methodology for eliminating defects aims for six standard deviations between the mean and the nearest specification limit in any process – from manufacturing to transactions and from products to services – to achieve an error rate of only 3.4 per million opportunities.

Lean Six Sigma can be applied to virtually any function, project, or operation that can be understood as a process with inputs, activities, and outputs – especially relevant for processes in the pharmaceutical industry. Lean Six Sigma is perfectly suited to the validation process, allowing pharmaceutical companies to reap the benefits of an enhanced validation roadmap (due to the tools and templates that ensure successful identification of problems and appropriate resolutions).

The ultimate goal of adopting a Lean Six Sigma approach is to shift from (a) measuring outputs and making process adjustments as the main process control method to (b) measuring and adjusting process inputs to control the process and reach targeted process performance objectives. In the end, by applying Lean Six Sigma, companies can increase profitability by decreasing variability, defects, and waste that drive up production or project costs and undermine customer loyalty.

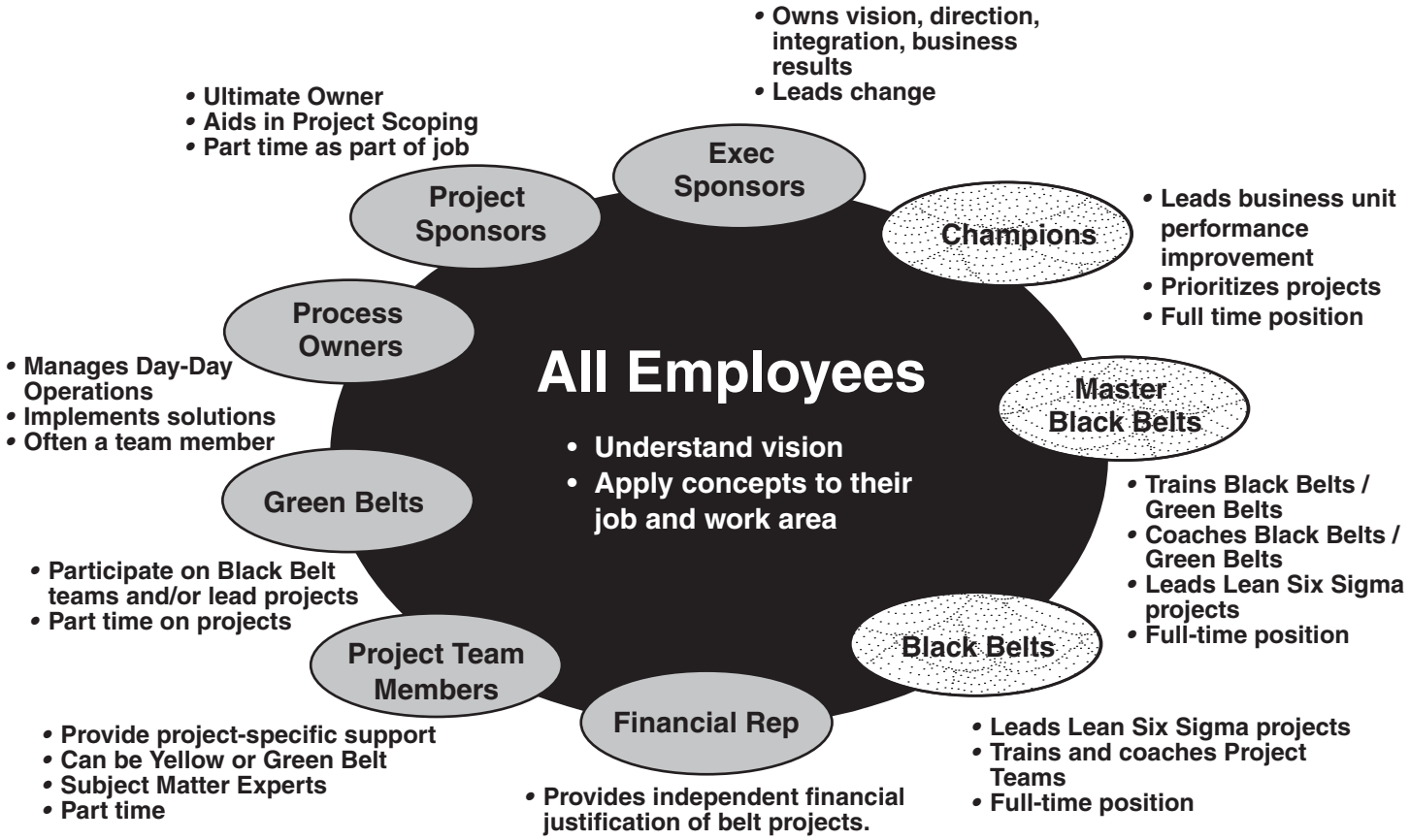
What Lean Six Sigma is Designed to Achieve

The objective of the Lean Six Sigma approach is to implement a metric-based strategy that focuses on process improvement. Currently, opportunities exist in large pharmaceutical projects that require continuous driving to achieve the optimal balance of quality, cost, and time.

As for any business initiative, successful Lean Six Sigma implementation starts with commitment from the key project stakeholders as well as commitment from top management. Stakeholders and management must understand the benefits of Lean Six Sigma to provide the necessary impetus for its implementation. Without this level of involvement, quality initiatives fade away and tasks in the quality process don't get done.

Figure 1

Lean Six Sigma Organization



DMAIC: Removing the "Pain" from the Process

The acronym DMAIC stands for the five phases involved in the Six Sigma process: define; measure; analyze; improve; and control. We start by defining the project goals and boundaries, identifying the issues that must be addressed to improve process and quality, and establishing the project team. We then move to identifying key measures for the process being reviewed and design and execute a plan for data collection. Next comes the analysis phase in which the data collected are examined to determine the root causes responsible for the process not performing as expected. In the next phase, we generate solutions and implement them on a small scale to determine whether they provide the expected performance improvements. In the control phase, we develop, document, and implement a plan to ensure that the performance improvements stay at the desired level.

Building a Winning Lean Six Sigma Team

The importance of management commitment to the Lean Six Sigma process cannot be overemphasized. When management fails to rally personnel and demonstrate an urgent need for improvement, initiatives simply fade away.

Depending on its complexity, a Lean Six Sigma project brings together a team that can consist of some or all of the following participants: Leadership team, Champion, Master Black Belt, Black Belt, and Green Belt.

The Leadership team leads the overall effort. In a manufacturing facility, the Leadership team is usually the plant manager and members of that person's staff. In an IT Department, it may consist of the Chief Information

Officer (CIO) and staff members.

The Champion serves as the project's political and business leader. Champions facilitate the selection of projects, draft the initial project charters, select the personnel needed to complete the project, and eliminate obstacles to the successful achievement of the project.

The Master Black Belt is the technical leader who helps the organization integrate Six Sigma within its operations.

The Black Belt leads the team that carries out the actual hands-on and detailed work. He or she acts as a project manager and assigns tasks, such as data collection and testing, as required. Black Belts act as mentors for Green Belts.

The Green Belt uses basic analytical tools and works on less complex projects. Generally, Green Belts participate in improvement projects in addition to their current job responsibilities.

This team structure can be applied to every aspect of the operational environment as well as the project environment.

DEFINE

A Lean Six Sigma mandate starts with a problem in need of a solution. Lean Six Sigma is used when the source of the problem in a particular process is not obvious. Since the source of the problem is not obvious, the solution to the problem isn't obvious either – and this is due to the wide array of variables that may contribute to the problem.

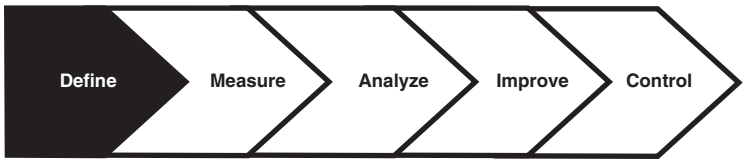
To ferret out the source of the problem and produce effective solutions, we bring together a Lean Six Sigma project team and define its charter (for a more detailed description of a project team, see the "Building a winning Lean Six Sigma Team" *inset*). In addition, all stakeholders and sponsors should be identified, all expectations defined and agreed upon.

Identifying our client's needs and drafting a problem statement lead to a problem objective. We define the measurements that will report the benefits of the improvements. In this particular instance, our objective was to reduce the numbers of errors per unit from an average of 62 to less than 15 within one month during the creation and execution of test cases. We created a map of the process to be improved (see *Figure 2*, Process Map), which was used as a "road map" in deciding on action items. A simple four-step depiction of the process highlights a number of important considerations:

1. Non-value-added activities, for example, reviewing test cases prior to and post execution are illustrated in boxes in the Process Map, *Figure 2*. This allows the team to minimize time and effort spent on these activities since they bring little in the way of improvement in the process.
2. The process flow shows what inputs are required to perform the next activity in the process map.
3. The expected key process input and output variables (KPIV/KPOV) are shown at each step.
4. The chronological order of the process is outlined: create test cases, send, review, execute, and review execution. In this instance, geographical location was not considered, but in other maps this can be a source of information to further map the complexity of the process and areas of opportunity.

By tracking the process flow upstream, inputs and variables may be identified that have an impact later in the process. In the later phases of the project, correcting the variables with the greatest impact will lead to the greatest cost savings by preventing product nonconformity and process variability. Time mapping can be used to illustrate all the waiting time between operations or activities. For example, during the validation of the software, the test protocol must be created, sent for review (a 1- or 2-day wait), and then sent for approval (a 2- or 3-day wait).

Case Study Comment 1



In one of our recent Distributed Control System Software Testing mandates, the problem statement was that 62 errors per PROCESS unit were present in the testing documentation – resulting in increased verification by a team of six people costing $85 per hour per person. This was the "pain" in the process that the client wanted to alleviate.

MEASURE

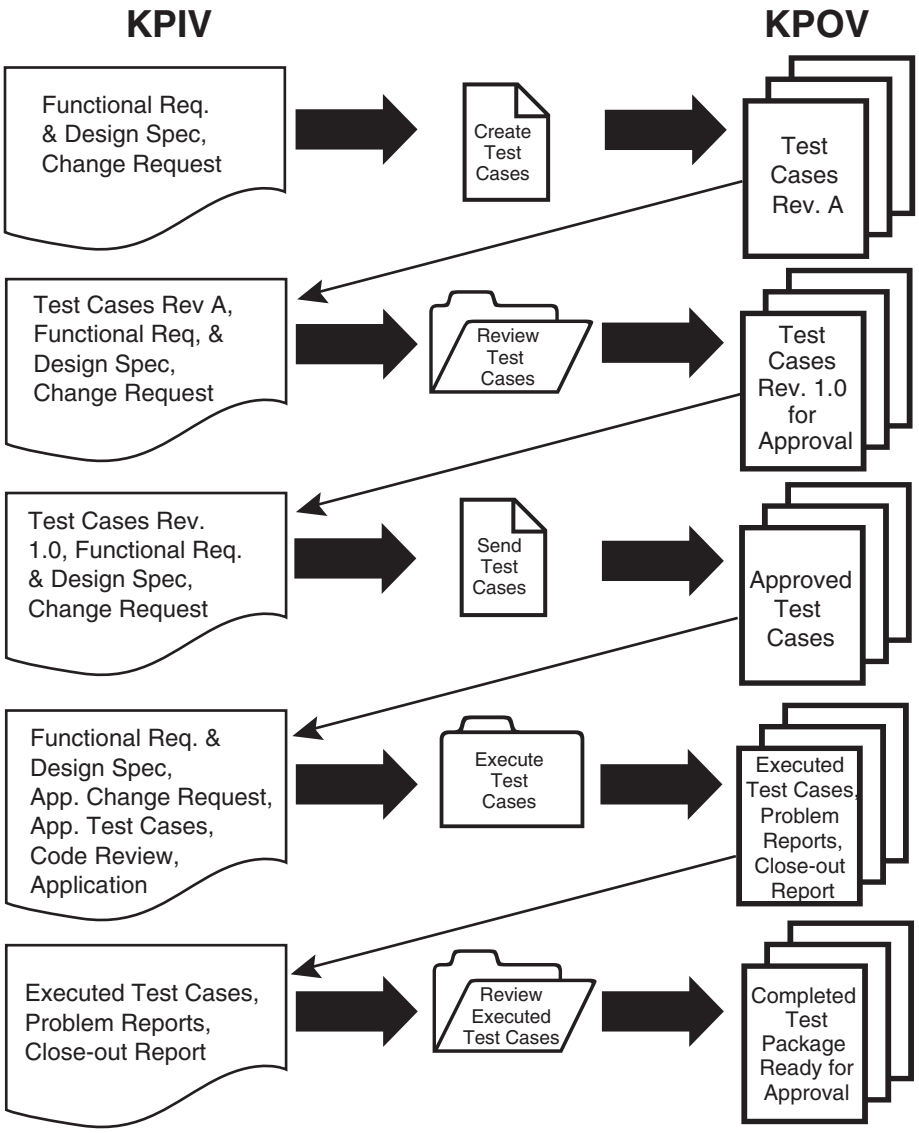
The next phase in the DMAIC methodology is measure. As W. Edwards Deming has stated, "What gets measured gets done." Measurement is critical. When we cannot measure something, we really don't know much about it. When we don't know much about it, we can't control it. Finally, when we can't control it, we are at the mercy of chance.

At the heart of the measurement phase is data collection. Gathering and storing data is an activity that is carried out on a continuous basis at many companies. As a result, data are usually plentiful, and the key to determining the root causes of problems is to find the proper focus. In other words, what data are relevant to the problem and to its solution?

Choosing the right metrics is at the foundation of Lean Six Sigma. The type of improvement sought guides the choice. Every step in a process is an opportunity for error, and multiple steps introduce complexity. The appropriate primary metric in this case is DPMO (Defects per Million Opportunities). Other metrics include: DPU (Defects per Unit, where every quality problem can be described in terms

Figure 2

Process Map

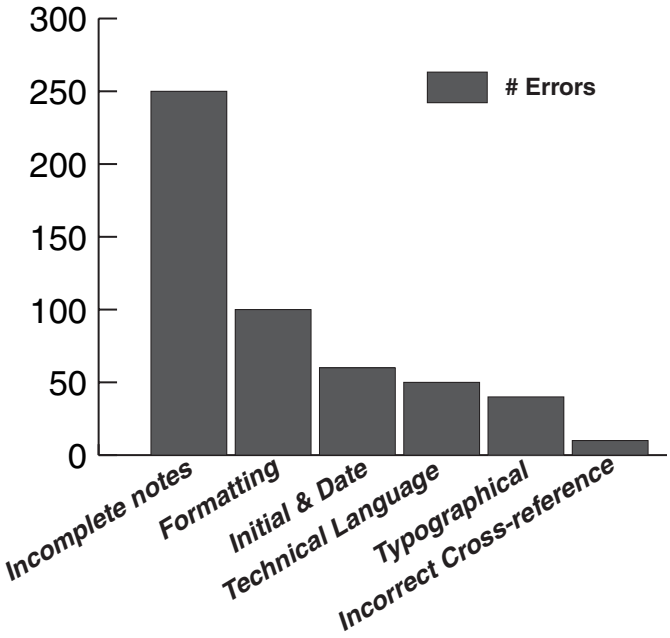


of defects); RTY (Rolled Throughput Yield, which is the net yield following all steps in a process without re-work); and quality costs (the costs of scrap, re-work, and excess inventory or capacity to offset poor yield). There are two general categories of metrics: primary and secondary. Primary metrics are used to monitor progress toward a goal. Secondary metrics are used to identify errors that have migrated downstream in a process due to modification of the process upstream. For example, the primary metric indicates a significant reduction in defects for a temperature sensor; however, field returns (secondary metric) have increased and indicate a problem upstream in the production process.

A Pareto chart (see *Figure 3*, Pareto Analysis) offers a means of finding the proper focus and converting data into information by filtering the data into various categories. Pareto analysis is necessary to: (1) focus the project on the few vital components that have the greatest impact; (2) prevent the risk of spending too much time and effort on the many trivial components that do not have a significant impact on the project; and (3) break the project down into "bite-sized," manageable portions that can be attacked in order of importance.

Figure 3

Pareto Analysis



Case Study Comment 2

In the Distributed Control System Software Testing case mentioned above, we decided to use the Pareto chart. Our Pareto analysis demonstrated that incomplete notes during the execution of the test cases were the main source of error. This category was further assessed to determine root causes and provide opportunities for improvement. The pain in having numerous errors is that each instance of error required a number of people to review, meet, and agree upon a corrective action, approve the corrective action, implement the corrections, and then, re-approve the whole venture. This process finally led to a revision in the closeout report. It is important to keep in mind that all of the aforementioned changes could result in additional errors, hence, compounding the situation.

In this particular case, an increase in training and awareness was determined to be a key factor for improvement. Consequently, training was provided, checklists were implemented, and a clear set of instructions were documented and made available to the execution team. Prior to implementations, these were all reviewed and approved by the quality and review teams to ensure alignment of each step in the process as a whole.

The additional benefit of using the Pareto chart is that it eliminates a dispersed focus; as a result, we did not spread and dilute our efforts on rectifying minor categories such as typographical and cross-reference errors. This information, however, was communicated to the team to increase awareness.

While Pareto charts sometimes show that all categories have equal influence, our Pareto analysis showed a clear influential variable. In cases where all categories are to be equally influential, it is recommended that a new set of categories be selected until an influential factor is clearly visible. In some cases, two influential factors may emerge. The benefit of this intervention is that it stirs the process into control, impacts the main influential variable and affects less influential variables only indirectly.

Essentially, the Pareto chart delineates the influential process input variables from the less influential ones. In cases where new data must be collected, the Pareto chart can guide the project team to determine where and when data should be collected and to develop a plan to collect the data.

As part of the measurement phase, the project team also performs a Gage Reproducibility and Repeatability Study (GR&R) to validate the measurement system used by the testers. The repeatability of a gage is the variability of the measurements obtained by one person while measuring the same item repeatedly. This is also considered the inherent variability of the gage. Reproducibility is the variability introduced into the measurement system by the bias differences of different testers.

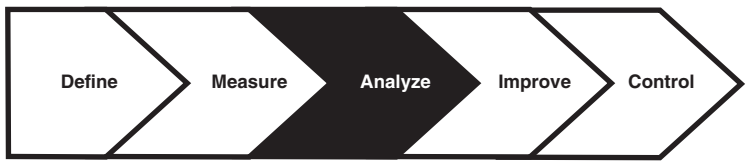
As stated earlier, measurement is critical. The more you measure, the surer you become. By measuring more, there are more data to use to test and evaluate hypotheses.

> ... correcting the variables with the greatest impact will lead to the greatest cost savings by preventing product nonconformity and process variability.

ANALYSIS

In the analysis phase, the project team brainstorms performance objectives, produces a cause-and-effect diagram, identifies value-added and non-value-added functions on the process map, and determines key variables. The Pareto chart marks a transitional point between the measurement and analysis phases. It helps in turning data into useful information by indicating potential correlations between causes and effects. The analysis phase is primarily focused on exploring these correlations. One way to capture these different ideas and stimulate the team's brainstorming on root causes is the cause-and-effect diagram, also known as a fishbone diagram. The fishbone creates a visual display of the many potential causes for a specific problem or effect. It is especially useful in a team setting as it leverages the power of multiple points of view and favors a synergy among the many ideas put forward. (It is also particularly useful for situations in which few quantitative data are available for analysis.) The focus of this brainstorming process is to discover the actual source of the problem rather than pin the blame on one or more individuals, hence

Case Study Comment 3a



In the Distributed Control System Software Testing case mentioned above, we found the root causes for test errors to be related to four major areas: training, documentation, process, and test cases. A brainstorming group of eight people discussed and documented a number of interrelated causes. For example, with respect to training, the team suggested that:

1. More information was required to enhance quality and reduce errors.
2. Some individuals were not reading the information available leading to errors
3. Tools such as templates were not being used properly, which resulted in errors.
4. The resident subject matter expert was not consulted sufficiently which led to guessing as to what was acceptable, resulting in more errors.
5. There was lack of communication on what constituted a complete note. Furthermore, rules were being changed but these updates were not communicated to the team.

In the end, this brainstorming session provided more data for our analysis phase and allowed the entire team to share in an open and frank manner the issues that each person was experiencing.

creating a collaborative environment for conflict resolution.

To build a fishbone diagram, the team starts by stating the problem in the form of a question. Framing it as a "why" question will facilitate the brainstorming, because answers to "why" questions point toward potential root causes. Asking "why?" repeatedly helps eliminate assignable causes and pushes the team to the root. The team should agree on the statement of the problem and then place this question in a box at the "head" of the fishbone.

The rest of the fishbone consists of one line drawn across the page, attached to the problem statement and several lines, or "bones," sprouting vertically from the main line (see *Figure 4*, Fishbone Diagram). These branches are labeled with different categories.

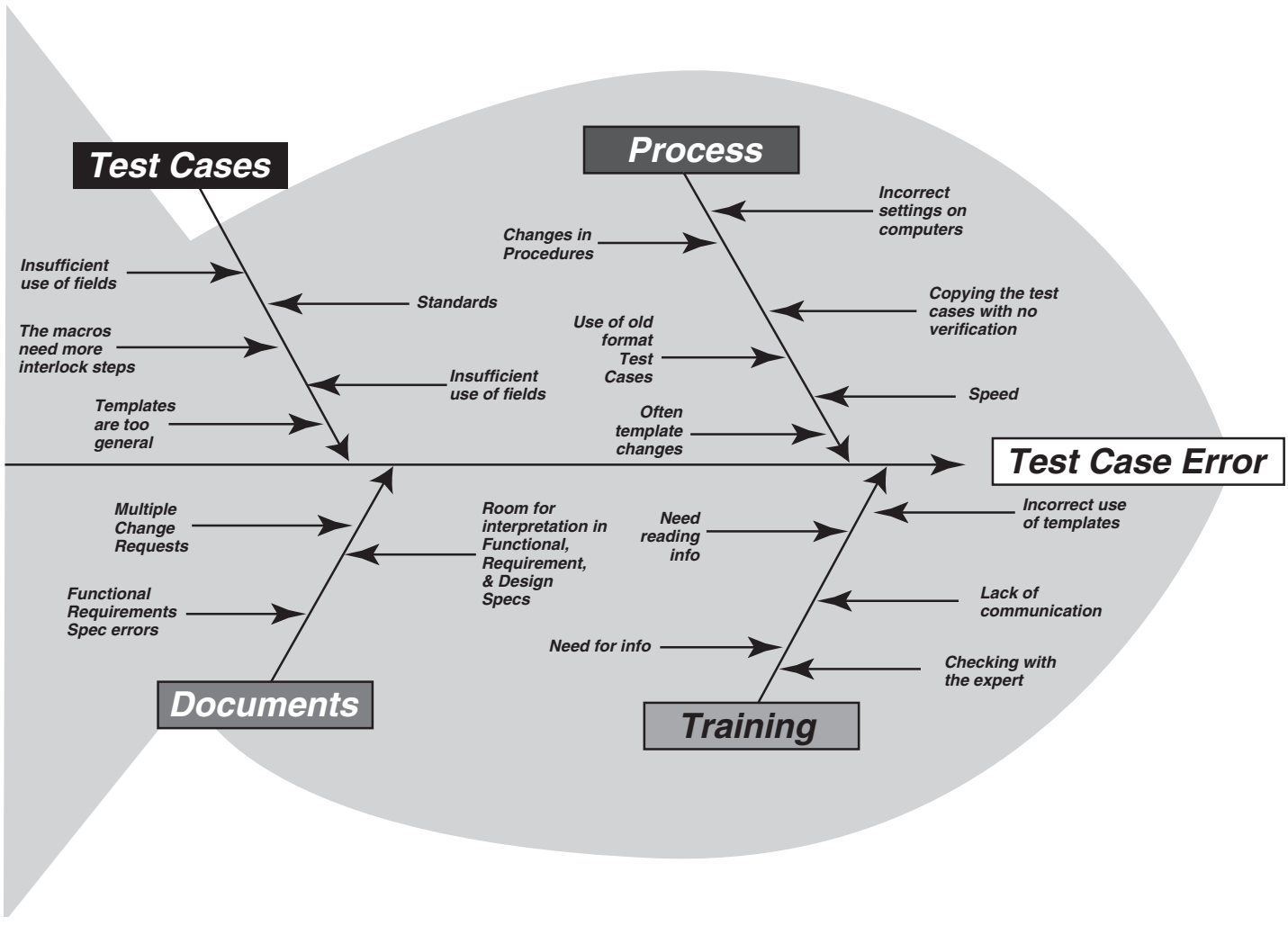
When the branches are labeled, brainstorming on possible causes can begin and be attached to the appropriate branches. For each cause identified, the team continues to ask, "Why does that happen," and to attach that information as another bone of the category branch. The fishbone helps the team get to the true drivers of a problem. It focuses people on the problem rather than focusing on people as the problem.

The keys to success in the analysis phase are to use hypothesis testing to "explore" the data. The team selects the strongest hypothesis from the fishbone diagram and applies hypothesis testing by designing and running experiments.

An important consideration in the analysis phase is the assumption of normality. Many statistical tools and techniques function in accordance with an underlying assumption of normality – that is, normally distributed data sets. Since the probability distribution changes significantly when the distribution is not normal, we may need to compensate by using a

Figure 4

Fishbone Diagram



separate set of tests (non-parametric tests). To make correct choices, we must ascertain that a data set is normally distributed – a normality test will provide the answer.

As part of the analysis phase, we can also determine: (1) process capability and speed; and (2) root source variations and bottlenecks. Tools used in this phase can include FMEA (failure and effects analysis), Cp, and Cpk (short-term process capability indices) as well as statistical tools such as regression and correlation analysis, and design of experiments. Regression testing is necessary to determine the strength with which specific factors influence an outcome. Correlation analysis will tell us the relationship between two variables, setting the stage for teasing out potential cause-and-effect relationships. With design of experiments, the team investigates some of the potential factors that might significantly impact the process output with their variance.

IMPROVE

In the improvement phase, the team brainstorms to determine possible solutions to build consensus around them. The actions that should, in the team's view, reduce or eliminate the impact of the identified root causes are tested. The techniques used to achieve this may include brainstorming, straw models, process flows and maps, and Gantt Charts.

Data are collected for the revised process. Before-and-after data analysis is performed to demonstrate how much of the original quality gap was closed. When the gain in quality is insufficient, document any actual gains, put controls in place to hold on to these gains, closeout the project, and launch a new project. Redefine the problem statement and look again at the data to determine why the problem was not corrected. What must be determined is whether the real root cause was targeted or whether the identified "cause" was only a symptom on which a "band-aid" solution was applied. The outputs of the improvement phase are action items that will bring about the required process improvements.

Case Study Comment 4

In our Distributed Control System Software Testing project, a brainstorming session was held using an affinity diagram (see *Figure 6*, Affinity Diagram). This tool uncovers more information that helps the team reduce review time (a factor closely linked to the number of errors).

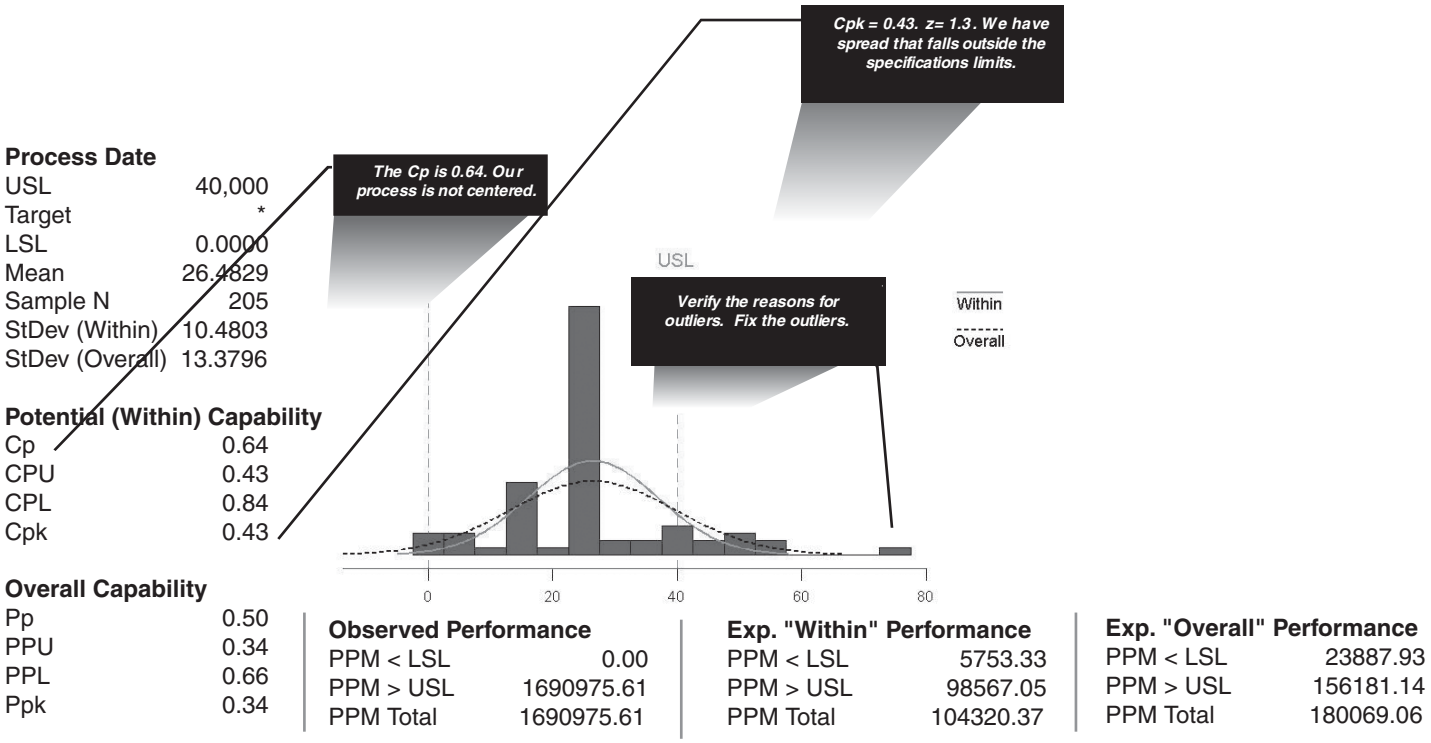
Improvements were made in five categories: (1) communications, (2) test cases, (3) specialization, (4) change requests, and (5) quality process. Improvements included: (1) training and drafting clear employee instructions to enhance communications, (2) use of latest documentation for verification and implementation of test-case templates, (3) designation of specific staff to verify packages, (4) communication of latest change requests to the quality team, and (5) use of a problem-tracking tool and implementation of a formal quality review before the product is delivered to client.

Case Study Comment 3b

In the Distributed Control System Software Testing case mentioned above, we assessed the process capability (see *Figure 5* Process Capability Analysis for Errors) to determine whether we could consistently prepare and execute test cases to a specification that met the customer's tolerance levels. As the graph shows, we were not in control of the process. Initially, we did not have a targeted customer tolerance; consequently, our goal was to establish one. We also discovered that we had agreed on an initial target per process unit. Since each process unit varied significantly in size and complexity, the number of errors correlated to this. It was agreed that a better measure for tolerance would be the number of errors per pages of executed test cases. The targets were reevaluated; the team's objectives became clear, and the process was quickly returned to an acceptable control state.

Figure 5

Process Capability Analysis



Process Date

USL	40,000
Target	*
LSL	0.0000
Mean	26.4829
Sample N	205
StDev (Within)	10.4803
StDev (Overall)	13.3796

Potential (Within) Capability

Cp	0.64
CPU	0.43
CPL	0.84
Cpk	0.43

Overall Capability

Pp	0.50
PPU	0.34
PPL	0.66
Ppk	0.34

Observed Performance

PPM < LSL	0.00
PPM > USL	1690975.61
PPM Total	1690975.61

Exp. "Within" Performance

PPM < LSL	5753.33
PPM > USL	98567.05
PPM Total	104320.37

Exp. "Overall" Performance

PPM < LSL	23887.93
PPM > USL	156181.14
PPM Total	180069.06

CONTROL

The purpose of the control phase is to ensure that quality improvements in the process are durable. At this stage of the project, we lock control measures in place so that project improvements remain effective over the long term.

There is a continuum of control measures available to the team. They range from verbal instructions, which require the greatest effort and provide the least control through written procedures, work instructions, standard procedures, Poka-yoke, and design for manufacturing, which offers more control with less effort required.

In the control phase, the team again collects data to gauge the revised process. It produces control charts for key variables.

The team must also produce documentation of the new method or process and plan training in the new method. By documenting the new process, you help ensure that it is followed. The operators who were directly involved in the project team as Champions ensure that the new controls are maintained. It is important to have buy-in and support from the process owners.

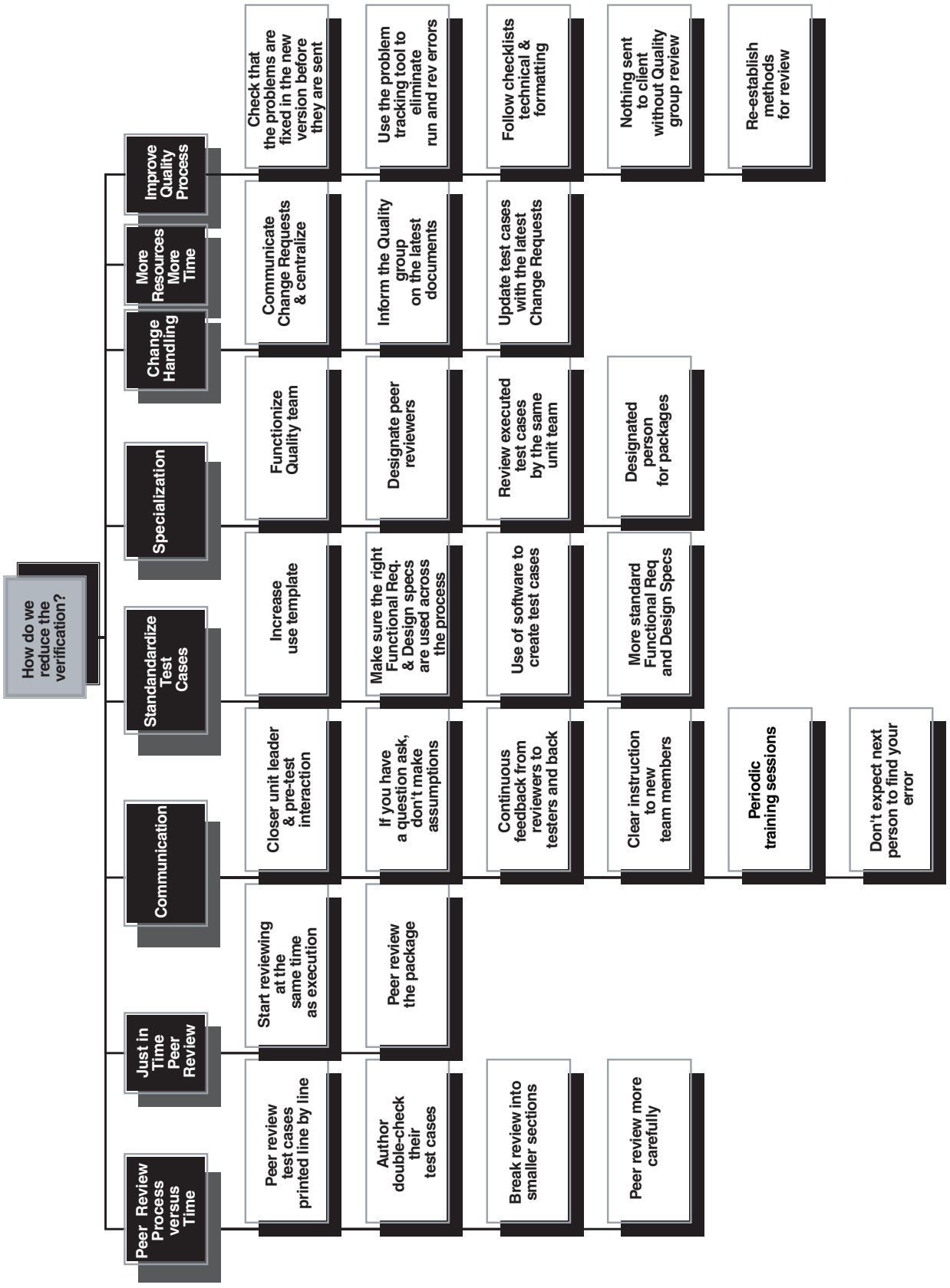
Poka-yoke: Error Proofing

Poka-yoke: Japanese for "error-proofing." It refers to a way of providing a visual or another type of signal to indicate a characteristic state. Error proofing, which can be applied anywhere, is a manufacturing technique for preventing errors by designing the manufacturing process, equipment, and tools in such a way that an operation cannot be performed incorrectly. An example of Poka-yoke is to highlight a tool wall with contours for each tool's location to ensure proper storage positioning.

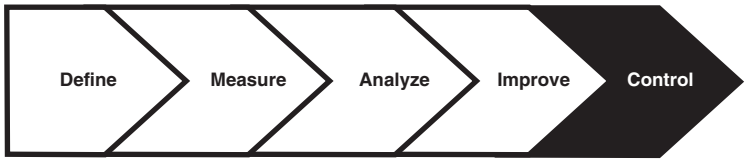
Control measures also help guard against "shift and drift." Practice has shown that most processes experience a shift (due to drift over time) of 1.5 standard deviations; as a result, the mean no longer equals the target. When this happens in a six-sigma process, a larger portion of the distribution now extends beyond the specification limits of 3.4 defects per million units.

Figure 6

Affinity Diagram



Case Study Comment 5



We reached our objectives (see *Figure 7*, Improvement and Control Results), including a 50% increase in productivity. The team was able to process twice the number of pages for test cases without adding new personnel. Along with this considerable increase in productivity, there was an overall reduction in the number of errors per page by an average of about 30%. The team applied a high performance standard and focused on ensuring that all influential variables were kept in control. Finally, customer satisfaction was enhanced and sustained since the goals of the Lean Six Sigma process were well understood and integrated.

In the control phase, the project team may deploy both statistical and non-statistical tools. Statistical tools include control charts and time-series methods; non-statistical controls include procedural adherence, performance management, and preventive activities.

CONCLUSION

Lean Six Sigma has enabled companies in a wide array of industries – from manufacturing to services – to achieve tremendous cost savings and revenue growth. This team-oriented and science-driven methodology can help pharmaceutical companies achieve similar results.

When pharmaceutical companies apply Lean Six Sigma techniques to their processes, they can be confident that the result will be reliable process validations. Lean enterprise and Six Sigma are powerful tools that enable pharmaceutical companies to achieve cost savings through reduced cycle time and lower defect rates. There are many beneficial effects of these outcomes, including enhanced product quality, a lasting positive effect on quality, and improved staff morale due to the effective teamwork mindset that Lean Six Sigma promotes. ❑

A Brief Overview of Six Sigma

In 1987, Motorola launched its "Six Sigma Quality" initiative whose goal was to achieve no more than 3.4 defective parts per million across the whole company. This objective required a four-year, hundredfold improvement in quality.

In 1989, the Six Sigma Research Institute was founded. Funding was provided by a number of Fortune 500 companies.

In 1994, Allied Signal implemented Six Sigma and realized savings of $1.2 billion by 1998.

GE implemented Six Sigma in 1996 and in two years achieved an increase of 11% in revenues and 13% in earnings. In that period, the operating margin rose to a record 16.7%.

Lean Six Sigma-driven organizations include: Ford, John Deere, Johnson & Johnson, and the U.S. Navy.

These techniques can be used in all industries, including the pharmaceutical sector, to improve the capability of business processes.

Invensys has successfully applied these techniques to clients in the pharmaceutical industry.

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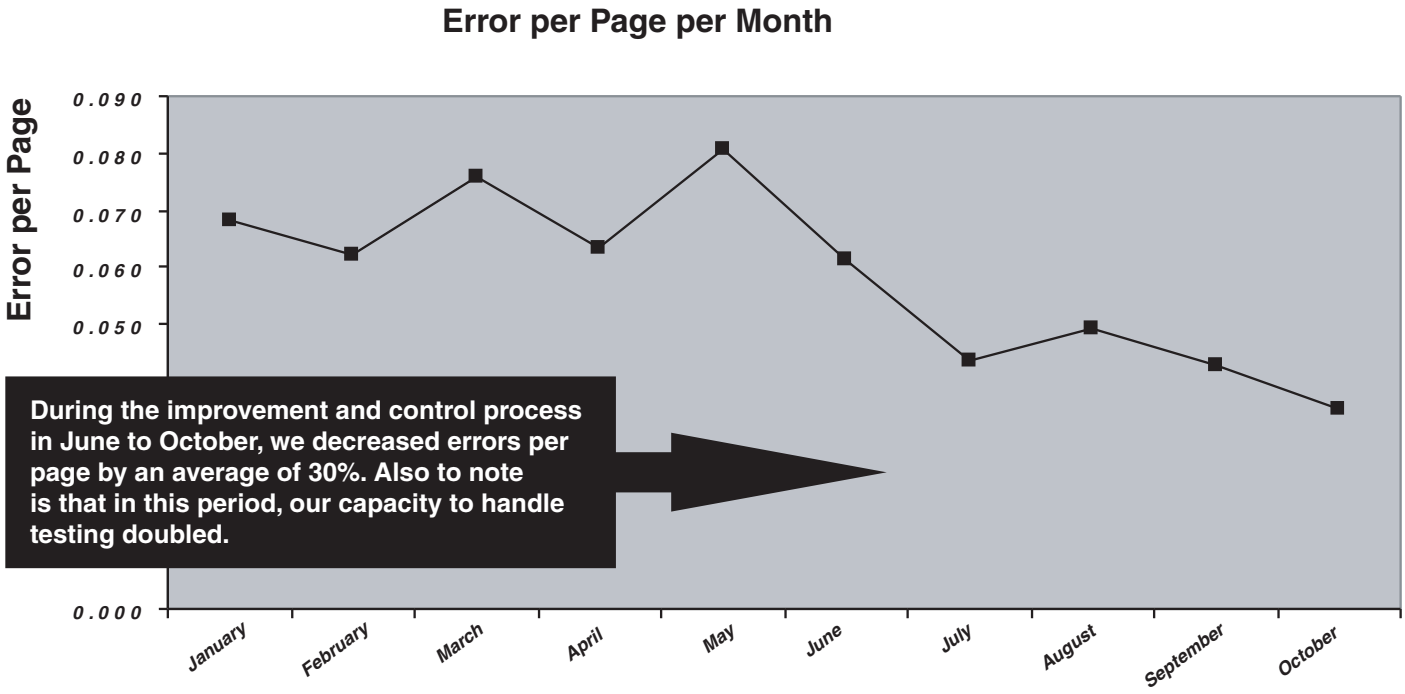
Figure 7

Improvement and Control Results



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Suggested Reading

1. *GAMP 4 Guide for Validation of Automated Systems*, ISPE, December 2001.
2. Craig R.D., Jaskiel S.P., *Systematic Software Testing*, Artech House Publishers, 2002.
3. Grady R.B., Caswell D.L., *Software Metrics: Establishing a Company Wide Program*, Prentice-Hall Inc., 1987.
4. Dustin E., *Effective Software Testing: 50 Specific Ways to Improve Your Testing*, Pearson Education, Inc., 2003.
5. Highsmith J., Schwaber K., *Lean Software Development: An Agile Toolkit*, Addison-Wesley, May 2003.
6. George M.L., *Lean Six Sigma*, McGraw-Hill, 2002.
7. George M.L., *Lean Six Sigma for Service*, McGraw-Hill, 2003.
8. Pande S.P., Neuman R.P., Cavanagh R.R., *The Six Sigma Way: Team Fieldbook*, McGraw-Hill, 2002.
9. Six Sigma Academy, *The Black Belt Memory Jogger: A Pocket Guide for Six Sigma Success*, Goal/QPC, 2002.

Article Acronym Listing

CIO:	Chief Information Officer
DMAIC:	Define, Measure, Analyze, Improve, Control
DPMO:	Defects per Million Opportunities
DPU:	Defects per Unit
FMEA:	Failure Mode and Effects Analysis
GR&R:	Gage Reproducibility and Repeatability (study)
KPIV:	Key Process Input Variable
KPOV:	Key Process Output Variable
RTY:	Rolled Throughout Yield
SDLC:	System Development Life Cycle

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