# Developing the Broad Process Excellence Program

By

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Submitted to the MIT Sloan School of Management and the Department of Engineering Systems Division in Partial Fulfillment of the Requirements for the Degrees of

Master of Business Administration
and
Master of Science in Engineering Systems

In Conjunction with the Leaders for Manufacturing Program at the
Massachusetts Institute of Technology
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**Abstract**

This thesis is based on the author's experience as an intern at the Broad Institute of MIT and Harvard. The Broad Institute has been working on applying and implementing traditional manufacturing process improvement tools to customize and select tools that can be adapted to its needs. Its unique production environment necessitates the requirement to customize and select tools that can be adapted to its needs. The objective of the thesis is to identify such tools and recommend methods to sustain them. The scope includes the following:

- Conduct a benchmarking survey to understand what other organizations are doing in the area.
- Conduct a stakeholder analysis involving relevant team members in Sequencing Operations.
- Design a system that brings together the lessons learnt from the benchmarking and stakeholder analysis exercises.
- Conduct a project to showcase some of the tools. The objective of the project is to identify key process levers and improve the performance of the Duncan Cycler, a key DNA processing step. This problem solving exercise acts as a proxy for situations where tools recommended by the program can be used.

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|---|---|
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# Chapter 1

# Introduction

In 2003, researchers at Whitehead Institute/MIT Center for Genome Research, Institute of Cell Biology at Harvard University and its associated hospitals decided to join hands to form a new collaborative initiative that would bring together some of the best minds in the country. Helped by a founding gift of $100M from Eli and Edythe Broad, the vision was to combine complementary resources and talents to create a world class institute to tackle some of the major challenges of genomic medicine. The result of this effort was the Broad Institute of MIT and Harvard, which has today become one of the foremost organizations in the area of finding new ways not only to cure but also hopefully prevent diseases. The secret to this effort is its ability to successfully and efficiently map and interpret genes, the basic building blocks of living organisms.

This endeavor started with the successful mapping of the Human Genome, wherein the Broad Institute researchers played a pivotal role, with more than 60% of the mapping conducted within the premises of this institution. The Institute has since increased its scope by sequencing the DNA for a wide variety of organisms, including:

- Other mammals such as elephant, armadillo, hedgehog, shrew, dog, cat, guinea pig, mouse, squirrel, rabbit and chimpanzee.
- Other Vertebrates and invertebrates including different types of fishes and fruit fly
- Microbial organisms such as fungi, bacteria, viruses, parasites and insect vectors.

The internship was based at the Sequencing Operations Platform at the Broad Institute. The majority of the content of the thesis will thus be based on this platform.

A part of a non-profit organization, the Sequencing Operations Platform is dependent on grants from national and international sources. In order to continue to be the top choice for funding agencies, it needs to keep a close tab on the following success factors:

- Quality of DNA sequence or read

- Operational clockspeed in development of new technologies
- Total cost of operations measured on the basis of cost per read

Achieving these success factors have become even more critical as more and more organizations try to develop disruptive technologies to go after the same goals more efficiently. These efforts have been further encouraged by organizations that are trying to push the boundaries of innovation in genomic research. Examples include the X-Prize Foundation who recently announced the launch of the Archon X-Prize for Genomics with the largest medical prize in history for any organization that comes up with a process to map 100 human genomes in 10 days instead of the several months that it takes today.

Efforts led by previous LFM interns have shown that traditional operational improvement tools, such as Lean Manufacturing and Six Sigma among others, can be used to achieve these factors more efficiently. Previous internships have thus focused on implementing these tools in different areas of the organization. It was, however, found that a majority of the initiatives have had sustainability challenges over time. It was additionally observed that there were several islands of success within the organization. These were typically areas where previous LFM interns had interned. The thesis aims at uncovering reasons for poor sustainability. It finds that piecemeal approach to process improvement can result in achieving sub-optimal solutions. For the Broad Institute to firmly establish and maintain its position of pre-eminence in genomics, it is thus critical that it address the issues identified in this thesis and work on putting into practice a common process engineering language. The Broad Process Excellence Handbook, additionally developed by this author has been implemented by the Genome Sequencing Operations Platform as a first step towards realizing this common language.

By following an approach shown in Figure 1, the thesis takes a strategic view of process excellence at the Broad Institute by taking a system level approach to analyzing the needs of processes followed at different steps of the Broad value chain in Genome Sequencing Platform. It brings together the knowledge gained through previous LFM internships, literature study and benchmarking of best practices at leading organizations across industries. Some of the issues identified by the thesis include:

- Communication issues such as knowledge of organizational goals and overall big picture
- Challenges in prioritization of activities
- Absence of common language
- Resistance to change due to top-down pressure for implementing tools not necessarily seen as fully applicable

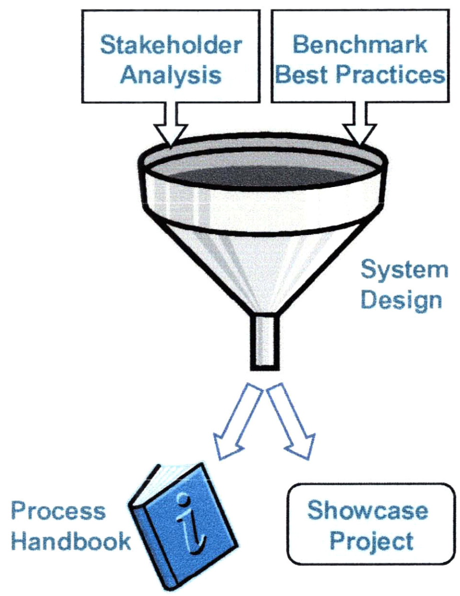



**Figure 1. Approach used to develop the Broad Process Excellence Program**

The culmination of the thesis is in the form of an operational excellence handbook that provides a system map of the organization with details of applicable tools. In addition to being a custom tool kit, this handbook presents a good overview of the complete value chain and is aimed at helping communication by making available a common process excellence language. Also included as a part of this thesis is a project on improving the performance of the Duncan Cycler (a key DNA processing step) to showcase some of the tools presented in the system design. This project serves as a data point for highlighting the impact of implementing Broad Process Excellence on day-to-day problem solving at Broad.

The thesis has been structured as follows:

**Chapter 2** uses the MIT Three Lens Analysis framework to establish the background for analyzing the structure, culture and politics in the Sequencing Operations Platform.
**Chapter 3** digs a little bit deeper by analyzing the stakeholders and understanding their needs, dependencies and challenges.
**Chapter 4** takes an external view into process excellence and attempts to understand best practices at 14 leading organizations across industries.
**Chapter 5** brings together the knowledge gained in all the previous chapters and presents a system design for the Sequencing Operations Platform.
**Chapter 6** shows the implementation of some of the tools recommended in Chapter 5 to solve a complex previously unsolved problem with the Duncan Cycler as a proxy for its application to problem solving at the Broad.
**Chapter 7** concludes with some recommendations for the future.

# Chapter 2

# Three Lens Analysis

This chapter uses the Three Lens approach to analyze the different aspects of the Operations Sequencing Platform at the Broad Institute. This sets the stage for analyzing the organization, which is the first step towards developing the Broad Process Excellence Program.

## *2.1 Strategic Lens*

The purpose of the strategic lens analysis is to analyze the strategic design of the organization including, but not limited to the following:

- Strategic grouping by activity and output
- Strategic linkage – formal reporting structure

As an organization, The Broad Institute is composed of 6 platforms and 10 scientific programs. Although the platforms and programs are organized in a matrix fashion as shown in Figure 2, they act almost like customers to each other. It is interesting to note that the linkage between the platforms and programs is fairly unstructured and from the platforms' perspective is mostly limited to management.

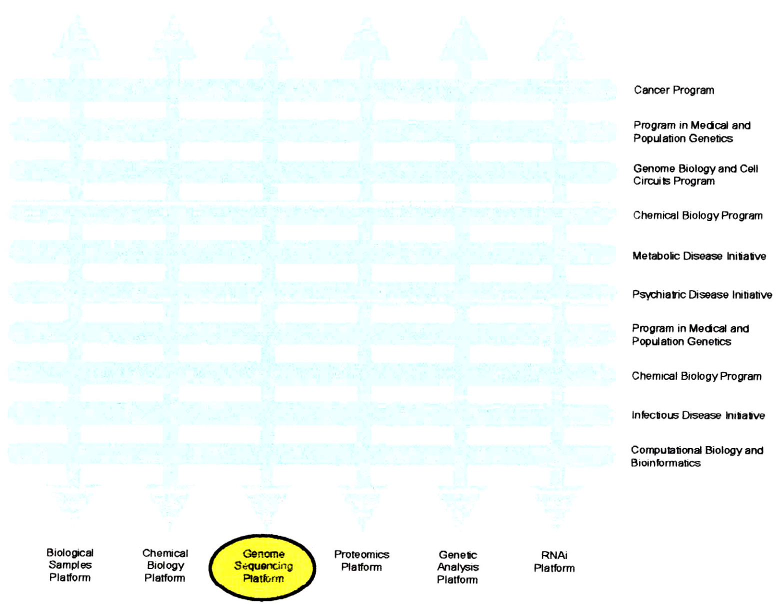



**Figure 2. Broad Organization**

The internship was conducted with the Genome Sequencing Platform (GSP), the largest of all platforms.

GSP is one of the foremost organizations in the world in the area of quickly introducing and scaling genome sequencing technologies. In order to achieve this effectively, the platform relies on extensive automation and a process focused structure to get things done. From an organizational perspective, GPS is divided into eight groups – Scientific Affairs, Technical Development (comprised of four sub-groups – Next Generation Sequencing, Process Development, Quality Assurance/Quality Control and Automation), Core Sequencing, Bio-informatics, Special Projects Group, Molecular Biology Production Group, Supply and Quality Management, and Finishing. Each of the groups with the exception of Technical Development (headed by an Asst. Director) is headed by a Manager, each of whom manages a group of several operators (number varies by group and function). The schematic in Figure 3 shows the strategic groups within GSP. The work streams (shown in Figure 4) however are not perfectly aligned with potential opportunities to reduce overlapping work functions created due to some recently created groups.

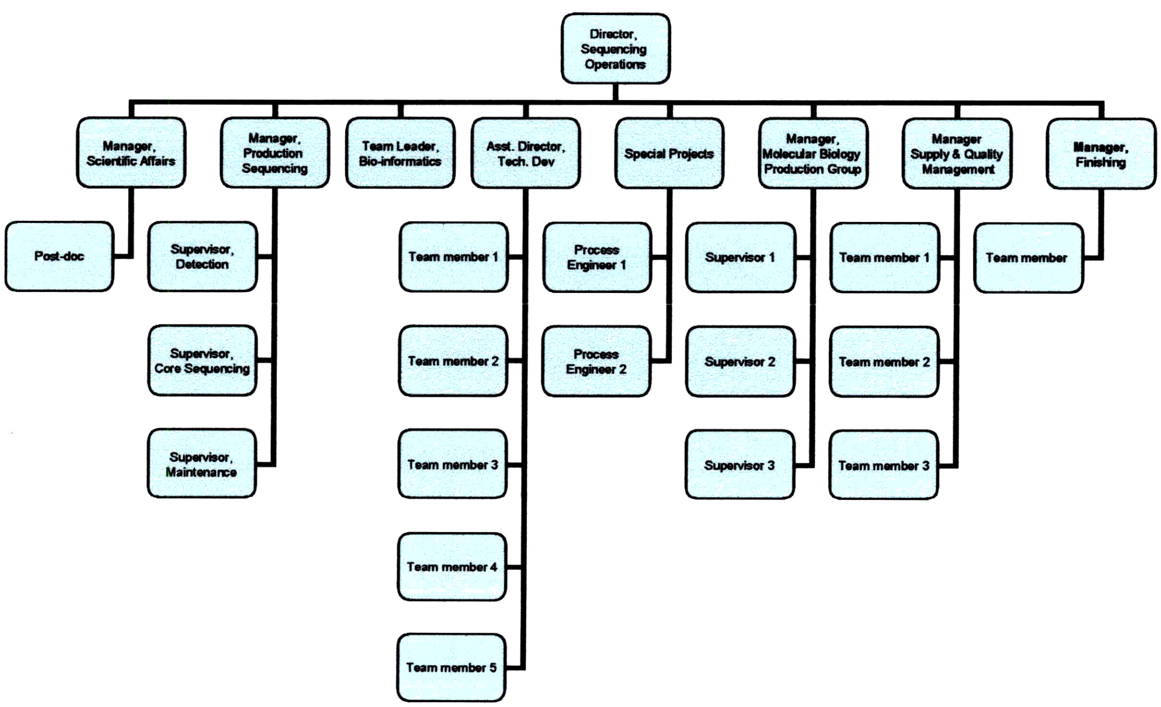



**Figure 3. Organizational structure within GSP**

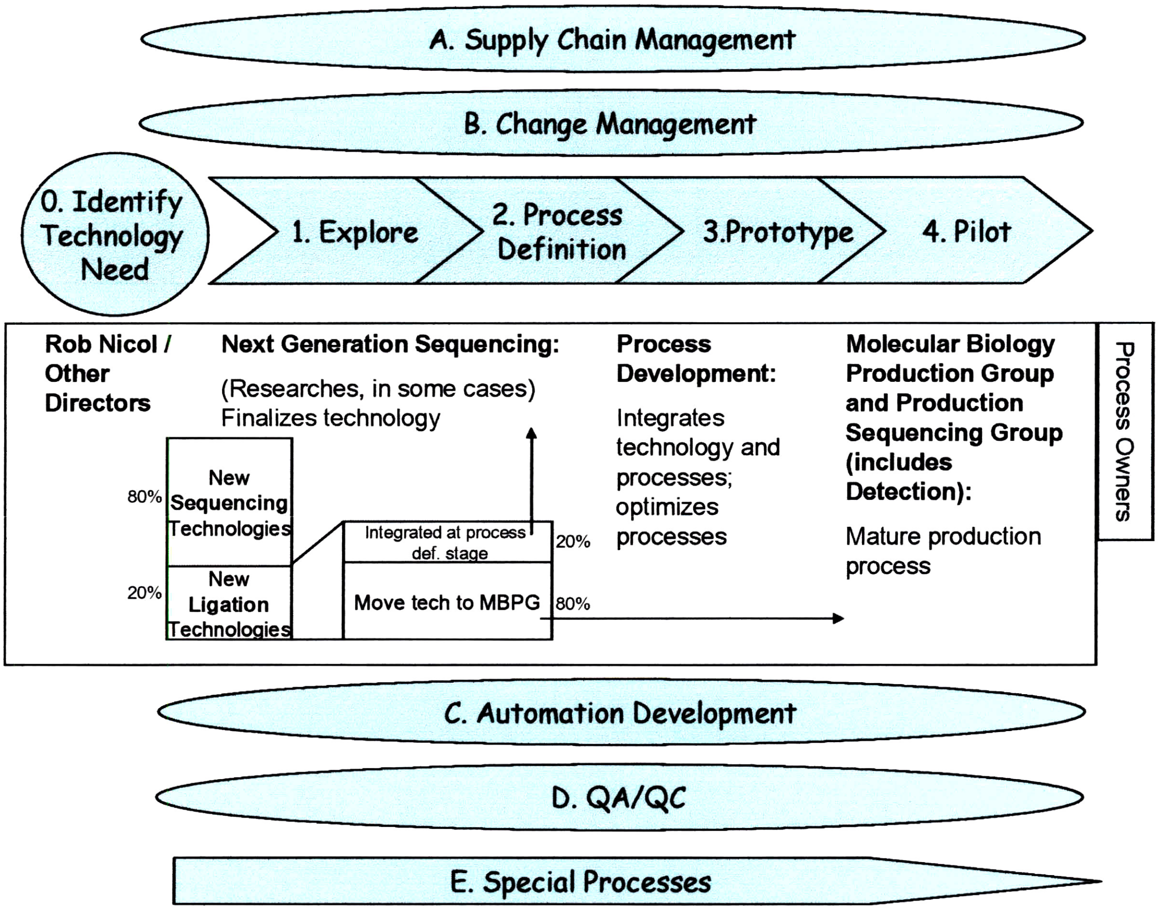



**Figure 4. Work-streams within GSP**

## *2.2 Cultural Lens*

The Broad Institute was originally set up as an academic research center with a strong emphasis on the academic part. There is a feeling of working in a research lab much like in a school with every group pretty much doing its own thing. Stakeholder analysis revealed the following interesting facts about the culture at Broad:

- Average work force is very motivated and enjoys their work.
- Informal (reflected in dress code and attitude to work)
- Very collaborative and friendly workforce
- Everyone wants to be involved in “cool” new technologies
- Clash between scientific approach and business sense
- Existence of departmental barriers

- Sometimes, a short term focus comes in the way of achieving the organization's longer term objectives. Consequently, several groups complained about challenges in prioritizing work and experimental design with greater emphasis on small quick changes as opposed to more detailed systematic experiment design. The result has been a distinct bias for experimental work, which is not always optimal.
- Communication of ideas across groups/departments is a challenge.

One of the global metrics for success at Broad is flexibility to quickly develop and ramp new technologies. Management has decided to achieve this by maintaining flexibility in staffing through cross training.

## *2.3 Political Lens*

Broad has different work structures for different process stages. As an example, while the production areas follow strict protocols, technical development areas do not. The organization has made significant efforts to increase communication through the use of all-hands meetings. There are, however, some challenges in having free flowing communication of ideas up and down the organization.

## *2.4 Final Observations*

Upon analyzing the three lenses for the Broad Institute, the following details emerge:

- The Institute follows a strong hierarchical structure and with an appropriate chain of command on decisions
- There is a strong culture that sometime bring with it elements of resistance to change.
- There is a lot of importance given to theoretical solutions to problems.

# Chapter 3
# Stakeholder Analysis

Previous internships by Leaders for Manufacturing students have introduced different aspects of process excellence to various areas of the Broad Institute of MIT and Harvard. As mentioned earlier in the thesis, sustainability of such efforts has been a challenge. This chapter presents application of the stakeholder analysis theory to better understand the needs and challenges of different stakeholders who constitute the Sequencing Operations Platform. We look at existing literature on stakeholder analysis theory and discuss the results of a stakeholder survey conducted based on the presented theory. The chapter concludes with a list of recommendations on how some of the existing challenges can be alleviated.

## *3.1 Background*

The Broad Institute over the past several years has made significant progress transforming several areas of its organization by introducing lean practices and six sigma principles for variability reduction. As a consequence, the organization has seen a big improvement in cycle time reduction, improved quality and overall reduced costs. These improvements have made the Broad Institute one of the top genomic sequencing centers of the world.

These efforts have been primarily targeted within Core Operations - also called Production Operations (Molecular Biology Production Group and Production Sequencing Group) and Process Development. One of the principal elements of these initiatives has been to focus on value maximization for the sequencing operations value stream by looking at these parts of the value chain. Several tools such as Value Stream Mapping, Kanban and Spaghetti Diagrams have been implemented in the pilot operations area to conduct this activity. Audit mechanisms such as 5S have also been implemented to help sustain some of the activities[1].

[1] LFM Thesis – previous LFM interns

So far, little attention has been paid to areas outside Production Operations and Process Development. Research, as indicated in Figure 5, has shown that a major portion of the total cost of most product/service is disposed over at the initial stages of the design and production process. Stated in another way, what this indicates is that although the costs incurred at the design stage of a process are a small percentage of the total cost, their impact on the total cost is much higher. It is thus essential to understand how the value stream extends to and impacts all parts of the organization. It is important to map the end-to-end value chain in its entirety and conduct a detailed stakeholder analysis to understand their relevance, structure and contribution. Womack and Jones define a product or service value stream as a "set of end-to-end and linked actions, processes and functions necessary to transform raw materials and other resources into finished products or services delivered to the customer." Without taking the time to identify all the different components of the sequencing value stream, it is difficult to analyze for any activities that do not contribute directly or indirectly to an activity that the end customer i.e. Projects Group or the funding agency (organizations such as the National Human Genome Research Institute) is ready to pay for.

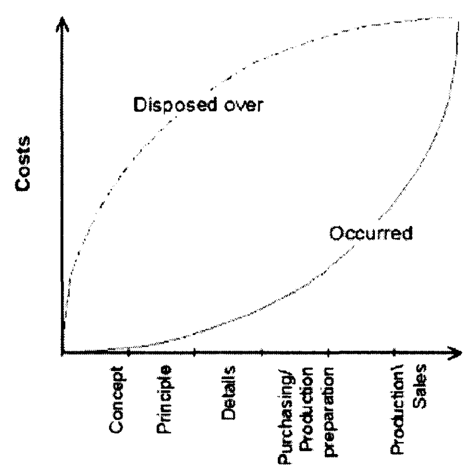



**Figure 5. Disposed and occurred costs through the product design process**[2]

The term "*stakeholder*" refers to any person or entity that has a stake or legitimate interest in the results of the strategic, operations and business actions of the enterprise.

[2] ANDREASEN, M.M. and OLESEN, J., 1990, The concept of dispositions. Journal of Engineering Design, 1, 17–36.

Stakeholder theory is not new to organizational theory and several researchers have done in-depth analysis of this concept in order to incorporate the interests of all interested parties in the workings of an enterprise. Grossi presented several definitions of the term "*stakeholder*". They are shown in Table 1. It is interesting to note that different researchers have provided a different definition, usually tailored to their area of study[3].

**Table 1 Different definitions of the stakeholder term**

| Date | Author(s) | Definition |
|---|---|---|
| 1963 | Stanford memo | "those groups without whose support the organization would cease to exist" |
| 1964 | Rhenman | "are depending on the firm in order to achieve their personal goals and on whom the firm is depending for its existence" |
| 1971 | Ahlstedt & Jahnukainen | "driven by their own interests and goals are participants in a firm, and thus depending on it and whom for its sake the firm is depending |
| 1983 | Freeman & Reed | Wide: "can affect the achievement of an organization's objectives or who is affected by the achievement of an organization's objectives"<br>Narrow: "on which the organization is dependent for its continued survival" |
| 1984 | Freeman | "can affect or is affected by the achievement of the organization's objectives" |
| 1987 | Freeman & Gilbert | "can affect or is affected by a business" |
| 1987 | Cornell & Shapiro | "claimants" who have "contracts" |
| 1988 | Evan & Freeman | "have a stake in or claim on the firm" |
| 1988 | Evan & Freeman | "benefit from or are harmed by, and whose rights are violated or respected by, corporate actions" |
| 1988 | Bowie | "without whose support the organization would cease to exist" |
| 1989 | Alkhafaji | "groups to whom the corporation is responsible" |
| 1989 | Carroll | "asserts to have one or more of these kinds of stakes" – "ranging from an interest to a right (legal or moral) to ownership or legal title to the company's assets or property" |
| 1990 | Freeman & Evan | Contract holders |
| 1991 | Thompson et al. | In "relationship with an organization" |
| 1991 | Savage et al. | "have an interest in the actions of an organization and... the ability to influence it" |
| 1992 | Hill & Jones | "constituents who have a legitimate claim on the firm... established through the existence of an exchange relationship" who supply "the firm with critical resources (contributions) and in exchange each expects its interests to be satisfied (by inducements)" |
| 1993 | Brenner | "having some legitimate, non-trivial relationship with an organization [such as] exchange transactions, action impacts, and moral responsibilities" |
| 1993 | Carroll | "asserts to have one or more of the kinds of stakes in business" – may be affected or affect... |

[3] GROSSI, I., 2003, Stakeholder Analysis in the context of the Lean Enterprise, MS in Engineering and Management Thesis, MIT.

| | | |
|---|---|---|
| 1994 | Freeman | Participants in "the human process of joint value creation" |
| 1994 | Wicks et al. | "interact with and give meaning and definition to the corporation" |
| 1994 | Langtry | The firm is significantly responsible for their well-being, or they hold a moral or legal claim on the firm |
| 1994 | Starik | "can and are making their actual stakes known" – "are or might be influenced by , or are or potentially are influencers of, some organization" |
| 1994 | Clarkson | "bear some form of risk as a result of having invested some form of capital, human or financial, something of value, in a firm" or "are placed at risk as a result of a firm's activities" |
| 1995 | Clarkson | "have, or claim, ownership, rights, or interests in a corporation and its activities" |
| 1995 | Näsi | "interact with the firm and thus make its operation possible" |
| 1995 | Brenner | "are or which could impact or be impacted by the firm/organization" |
| 1995 | Donaldson & Preston | "persons or groups with legitimate interests in procedural and/or substantive aspects of corporate activity" |
| *Source: Mitchell, Agle, and Wood, 1997* [4] | | |
| 2003 | Grossi | " any group or individual who directly or indirectly affects or is affected by the level of achievement of an enterprise's value creation process" |

As can be noted from Table 1, stakeholder definition has over the years become broader to cover different aspects of the value creation process. One thing that is not very clear though is the definition of the individual/entity for which value is being created. This question becomes particularly important for research based organizations such as the Broad Institute where the secret to competitiveness is the ability to build technological capabilities within the enterprise itself. We would thus like to add that the enterprise value creation process should include value creation not only for the external customer but also for the enterprise itself. The attributes of the stakeholder and the interdependencies between the stakeholders themselves and the enterprise can thus be defined as shown in Figure 6. It is critical for every stakeholder to have a clear understanding of where they fit in the overall structure and how their activities impact / get impacted by the global metrics of the enterprise.

[4] MITCHELL R.K., AGLE B. R., AND WOOD D.J., Toward a Theory of Stakeholder Identification and Salience: Defining the Principle of Who and What Really Counts, Academy of Management Review, Vol. 22, No. 4, pp. 853-886, 1997

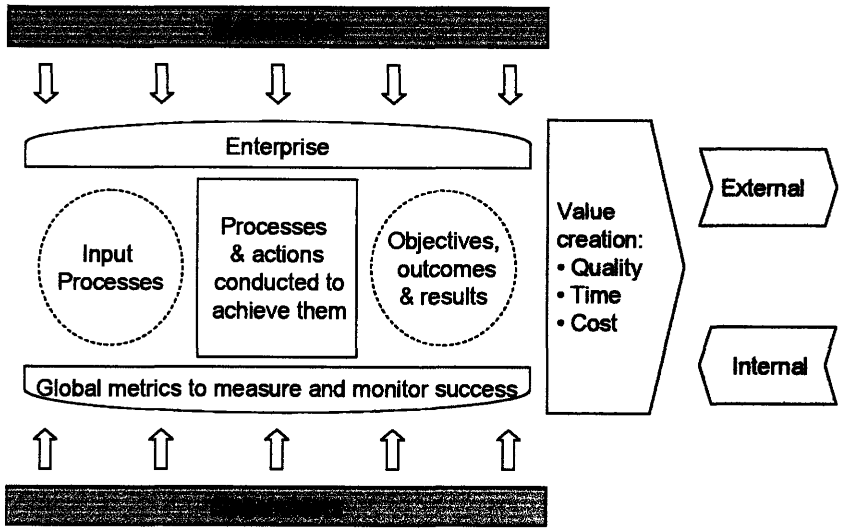



**Figure 6. Stakeholder definition**

## *3.2 Stakeholder Identification*

With so many different approaches to definition of the word "stakeholder", it is no surprise that there is no consensus in describing methods to identifying stakeholders. Mitchell, Agle and Wood in their monumental paper on the theory of stakeholder identification have analyzed different rationales for stakeholder identification. Shown in Table 2, this shows that the different rationales can be sorted on the following basis:

- Relationship
- Power dependence where the stakeholder is dominant
- Power dependence where the form is dominant
- Mutual stakeholder and firm power dominance
- Legitimacy of relationship
- Stakeholder interests with legitimacy not necessarily implied

Table 2. Different rationales for identifying stakeholders

**A Relationship Exists**

**The firm and stakeholder are in relationship:**

Thompson et al., 1991: 209—in "relationship with an organization"

Brenner, 1993: 205—"having some legitimate, non-trivial relationship with an organization [such as] exchange transactions, action impacts, and moral responsibilities"

Freeman, 1994: 415—participants in "the human process of joint value creation"

Wicks et al., 1994: 483—"interact with and give meaning and definition to the corporation"

**The stakeholder exercises voice with respect to the firm:**

Starik, 1994: 90—"can and are making their actual stakes known"—"are or might be influenced by, or are or potentially are influencers of, some organization"

**Power Dependence: Stakeholder Dominant**

**The firm is dependent on the stakeholder:**

Stanford memo, 1963—"those groups without whose support the organization would cease to exist" (cited in Freeman & Reed, 1983, and Freeman, 1984)

Freeman & Reed, 1983: 91—Narrow: "on which the organization is dependent for its continued survival"

Bowie, 1988: 112, n. 2—"without whose support the organization would cease to exist"

Näsi, 1995: 19—"interact with the firm and thus make its operation possible"

**The stakeholder has power over the firm:**

Freeman, 1984: 46—"can affect or is affected by the achievement of the organization's objectives"

Freeman & Gilbert, 1987: 397—"can affect or is affected by a business"

Savage et al., 1991: 61—"have an interest in the actions of an organization and . . . the ability to influence it"

Carroll, 1993: 60—"asserts to have one or more of the kinds of stakes in business"—may be affected or affect . . .

Starik, 1994: 90—"can and are making their actual stakes known"—"are or might be influenced by, or are or potentially are influencers of, some organization"

Brenner, 1995: 76, n. 1—"are or which could impact or be impacted by the firm/organization"

**Power Dependence: Firm Dominant**

**The stakeholder is dependent on the firm:**

Langtry, 1994: 433—the firm is significantly responsible for their well-being, or they hold a moral or legal claim on the firm

**The firm has power over the stakeholder:**

Freeman & Reed, 1983: 91—Wide: "can affect the achievement of an organization's objectives or who is affected by the achievement of an organization's objectives"

Freeman, 1984: 46—"can affect or is affected by the achievement of the organization's objectives"

Freeman & Gilbert, 1987: 397—"can affect or is affected by a business"

Carroll, 1993: 60—"asserts to have one or more of the kinds of stakes in business"—may be affected or affect . . .

Starik, 1994: 90—"can and are making their actual stakes known"—"are or might be influenced by, or are or potentially are influencers of, some organization"
Brenner, 1995: 76, n. 1.—"are or which could impact or be impacted by the firm/organization"

**Mutual Power-Dependence Relationship**

**The firm and stakeholder are mutually dependent:**

Rhenman, 1964—"are depending on the firm in order to achieve their personal goals and on whom the firm is depending for its existence" (cited in Näsi, 1995)
Ahlstedt & Jahnukainen, 1971—"driven by their own interests and goals are participants in a firm, and thus depending on it and whom for its sake the firm is depending" (cited in Näsi, 1995)

**Basis for Legitimacy of Relationship**

**The firm and stakeholder are in contractual relationship:**

Cornell & Shapiro, 1987: 5—"claimants" who have "contracts"
Carroll, 1989: 57—"asserts to have one or more of these kinds of stakes"—"ranging from an interest to a right (legal or moral) to ownership or legal title to the company's assets or property"
Freeman & Evan, 1990—contract holders
Hill & Jones, 1992: 133—"constituents who have a legitimate claim on the firm ... established through the existence of an exchange relationship" who supply "the firm with critical resources (contributions) and in exchange each expects its interests to be satisfied (by inducements)"

**The stakeholder has a claim on the firm:**

Evan & Freeman, 1988: 75–76—"have a stake in or claim on the firm"
Alkhafaji, 1989: 36—"groups to whom the corporation is responsible"
Carroll, 1989: 57—"asserts to have one or more of these kinds of stakes"—"ranging from an interest to a right (legal or moral) to ownership or legal title to the company's assets or property"
Hill & Jones, 1992: 133—"constituents who have a legitimate claim on the firm ... established through the existence of an exchange relationship" who supply "the firm with critical resources (contributions) and in exchange each expects its interests to be satisfied (by inducements)"
Langtry, 1994: 433—the firm is significantly responsible for their well-being, or they hold a moral or legal claim on the firm
Clarkson, 1995: 106—"have, or claim, ownership, rights, or interests in a corporation and its activities"

**The stakeholder has something at risk:**

Clarkson, 1994: 5—"bear some form of risk as a result of having invested some form of capital, human or financial, something of value, in a firm" or "are placed at risk as a result of a firm's activities"

**The stakeholder has a moral claim on the firm:**

Evan & Freeman, 1988: 79—"benefit from or are harmed by, and whose rights are violated or respected by, corporate actions"
Carroll, 1989: 57—"asserts to have one or more of these kinds of stakes"—"ranging from an interest to a right (legal or moral) to ownership or legal title to the company's assets or property"

Langtry, 1994: 433—the firm is significantly responsible for their well-being, or they hold a moral or legal claim on the firm
Clarkson, 1995: 106—"have, or claim, ownership, rights, or interests in a corporation and its activities"
Donaldson & Preston, 1995: 85—"identified through the actual or potential harms and benefits that they experience or anticipate experiencing as a result of the firm's actions or inactions"

**Stakeholder Interests—Legitimacy Not Implied**

**The stakeholder has an interest in the firm:**

Carroll, 1989: 57—"asserts to have one or more of these kinds of stakes"—"ranging from an interest to a right (legal or moral) to ownership or legal title to the company's assets or property"
Savage et al., 1991: 61—"have an interest in the actions of an organization and ... have the ability to influence it"
Carroll, 1993: 60—"asserts to have one or more of the kinds of stakes in business"—may be affected or affect ...
Clarkson, 1995: 106—"have, or claim, ownership, rights, or interests in a corporation and its activities"

Based on their research, Mitchell, Agle and Wood propose an attribute based method to sort stakeholders that considers the following attributes:

- The stakeholder's *power* to influence the firm:
  Defined by Pfeffer[5] as "relationship among social actors in which one social actor, A, can get another social actor, B, to do something that B would not have otherwise done", power can be of three types:
    - Coercive Power – "based on physical resources of force, violence or restraint";
    - Utilitarian Power – "based on material or financial resources"; and
    - Normative Power – " based on symbolic resources" [6]
- The *legitimacy* of stakeholder's relationship with the firm:
  The Merriam-Webster Dictionary defines "legitimacy" as conforming to recognized principles or accepted rules and standards.
- The *urgency* of the the stakeholder's claim on the firm:
  According to Mitchell, Agle and Wood, "urgency" exits when the following two conditions are met:

[5] PFEFFER, J. 1981 Power in organizations. Marshfield, MA: Pitman
[6] ETZIONI, A. 1964 Modern organizations. Englewood Cliff, NJ: Prentice Hall

- Time sensitivity – degree to which managerial delay in attending to the claim or relationship is unacceptable to the stakeholder
- Criticality – the importance of the claim or relationship to the stakeholder

To add to this theory, we further assert that none of these attributes should be considered in isolation. Considering any one in isolation will give an incomplete picture of the stakeholder and his/her salience.

## *3.3 Stakeholder structure*

As identified in previous sections, relationships are an important aspect of stakeholder theory. Social network analysis offers very interesting tools to explore the nature of stakeholder structures and their impact on the enterprise as an entity rather than individual stakeholders[7]. One way to represent relationships is through the use of network diagrams. One of the earliest and most popular approaches is shown in Figure 7.

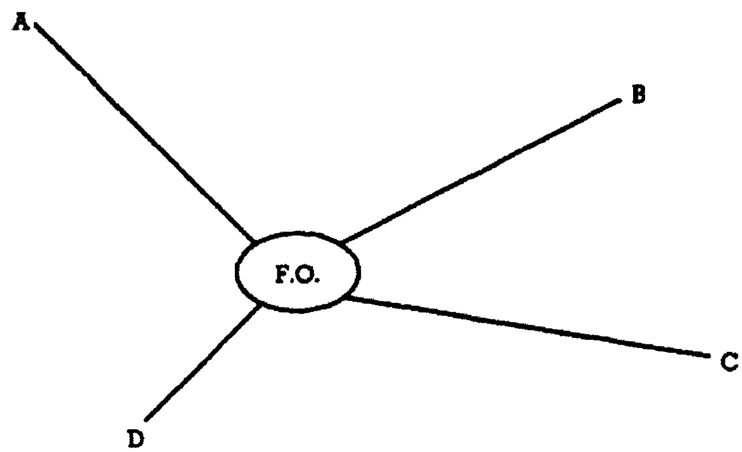



**Figure 7. Stakeholder structure 1[6]**

Since relationships rarely occur as dyadic as shown in Figure 7, but instead in a network of relationships spread across the enterprise, Freeman and Evan[8] suggested that the stakeholder environment comprises of several "multilateral contracts among stakeholders". This is illustrated in Figure 8.

[7] ROWLEY, T.J. Moving beyond Dyadic Ties: A Network Theory of Stakeholder Influences, Academy of Management Review 1997, Volume 22, No. 4, 887-910
[8] FREEMAN, R.E., EVAN, W.M. Corporate governance: A stakeholder interpretation. The Journal of Behavioral Economics, 19: 337-359.

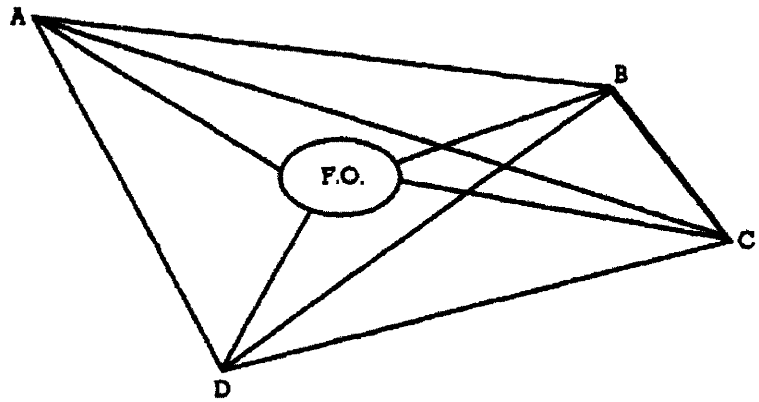



**Figure 8. Stakeholder structure 2** [6]

However, Rowley suggests that "in reality it is unlikely that all stakeholders will be linked directly" as shown in Figure 8. Rowley additionally found that in many cases, the focal organization is more than simply the central point of its own stakeholders; it is also the stakeholder of many other focal points in its relevant social system. Thus, treating the enterprise as a variable in its complex system with an opportunity to understand fully how patterns of a stakeholder interactions impact the enterprise. This is represented in Figure 9.

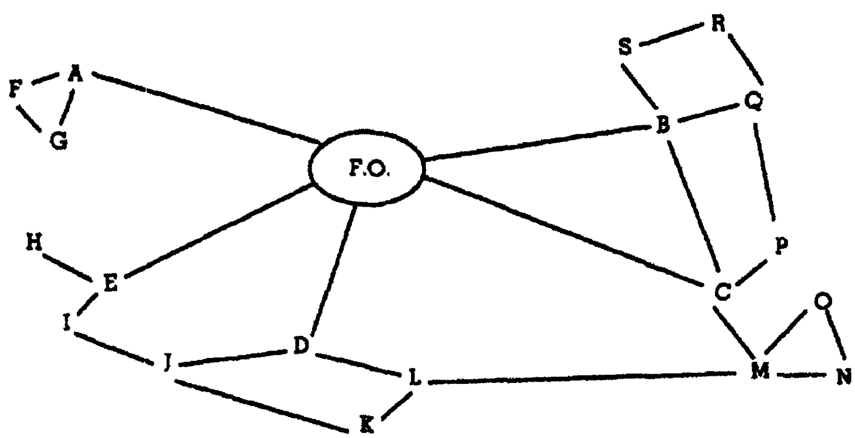



**Figure 9. Stakeholder structure 3** [6]

We would like to take this a step further by suggesting that the enterprise by itself has no existence. It is nothing but a collection of all the stakeholders involved. We can thus redraw Rowley's representation of the stakeholder structure by the one shown in Figure 9. As we continue our analysis of the Broad Sequencing Operations Platform enterprise, we will use the stakeholder structure defined in Figure 10.

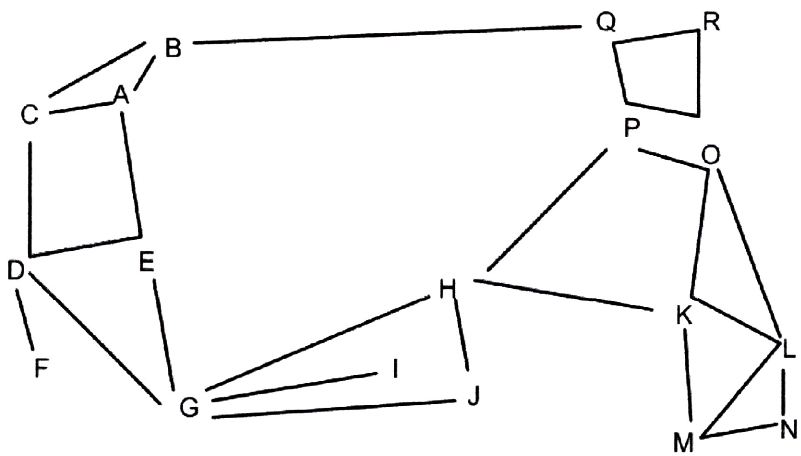



**Figure 10. Stakeholder structure 4**

## 3.4 Analyzing the Stakeholders in the Broad Sequencing Operations Platform Enterprise

We used the hierarchical organization structure, shown in Figure 11, as a starting point to understand the stakeholders and their structure. It is interesting to contrast this organization chart with the stakeholder structure that emerged based on stakeholder surveys.

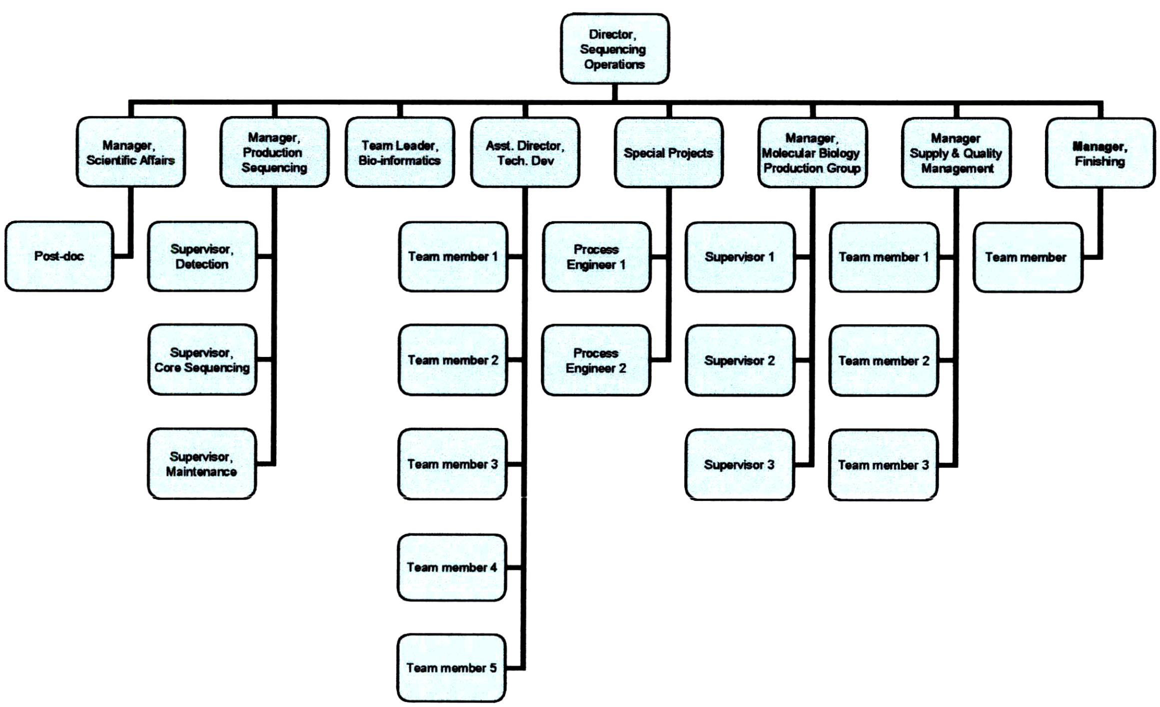



**Figure 11. Organization chart for the Broad Sequencing Operations Platform**

A detailed survey was conducted to understand and analyze the stakeholder structure and relationships. The survey questionnaire, shown in Table 3, covered the following areas:

- Knowledge of value engineering concepts
- Stakeholder structure
- Process excellence
    - Burning platform for change
    - Needs and expectations for new integrated process excellence system
    - Program development and sustainability
- Metrics – local, global and their interdependency

**Table 3. Stakeholder Questionnaire**

| |
|---|
| Background and knowledge level |
| • What is value chain and how do you perceive it?<br>• Where in the overall value chain do you as a stakeholder fit? |
| Stakeholder structure |
| • Who are your stakeholders?<br>• What products/services do you share with other stakeholders?<br>• What does each of your stakeholders care most about? Please rate them on a scale of 1-7.<br>• How do you interact with your stakeholders? At what level?<br>• Please rate the support you are getting in process improvement from your stakeholders on a scale of 1-7<br>• What types of feedback mechanisms do you have in place with your stakeholders?<br>• How often do you seek feedback? How do you incorporate the feedback?<br>• How do you track feedback? |
| Process excellence – Burning platform for change |
| • What are your biggest pain points i.e. issues/weaknesses that hinder your work?<br>• What is their impact on your success factors? Please report these in as quantitative terms as possible.<br>• What solutions have you tried to solve these pain points? Why? What was the impact? Please be specific or please rate on a scale of 1-7.<br>• Please rate your success on a scale of 1-7? Why? |
| Process excellence - Needs and expectations for new integrated process excellence system |
| • What would you like the process excellence program to do for you?<br>• What are the areas that will be impacted due to this effort?<br>• How will this impact your stakeholders?<br>• Present the matrix of areas impacted by process excellence in terms of Customer, Internal Processes, Learning and Growth, Financials and other factors of importance to Broad with quantified impact. Please rate this on a scale of 1-7. |

| Process excellence - Program development and sustainability |
|---|
| • What are your biggest fears for an integrated process excellence system? What would you want it NOT to be? Please rate them on a scale of 1-5.<br>• Have you had any previous experience with lean/six sigma/process design?<br>  - How many years of experience do you have in this area?<br>  - What did you do? Please be specific: Lean/DFSS/DMAIC<br>  - Why did you do it?<br>  - What was the outcome? Please rate on a scale of 1-7.<br>  - What did you do to sustain them? Rating and results. Please quantify.<br>• How would you like to be involved and contribute to the program development and sustenance? |
| Metrics |
| • What are the key success factors of your group?<br>• How do you measure them?<br>• What is the relative importance of these metrics (scale of 1-7)?<br>• Please rate the how proactive these metrics are on a scale of 1-7 (1 being 100% reactive and 7 being 100% proactive)<br>• How do these metrics relate to your global metrics?<br>• Do you tie the initiatives with HR metrics? If not, why not? If yes, which metrics? Why? |

## *3.5 Stakeholder Survey Results*

### 3.5.1 Background and knowledge level

The results, shown in Figure 12, showed a wide variation in the level of understanding of value maximization amongst stakeholders. Since the survey was conducted in an interactive format, the knowledge gap was filled through discussions over the period of the survey.

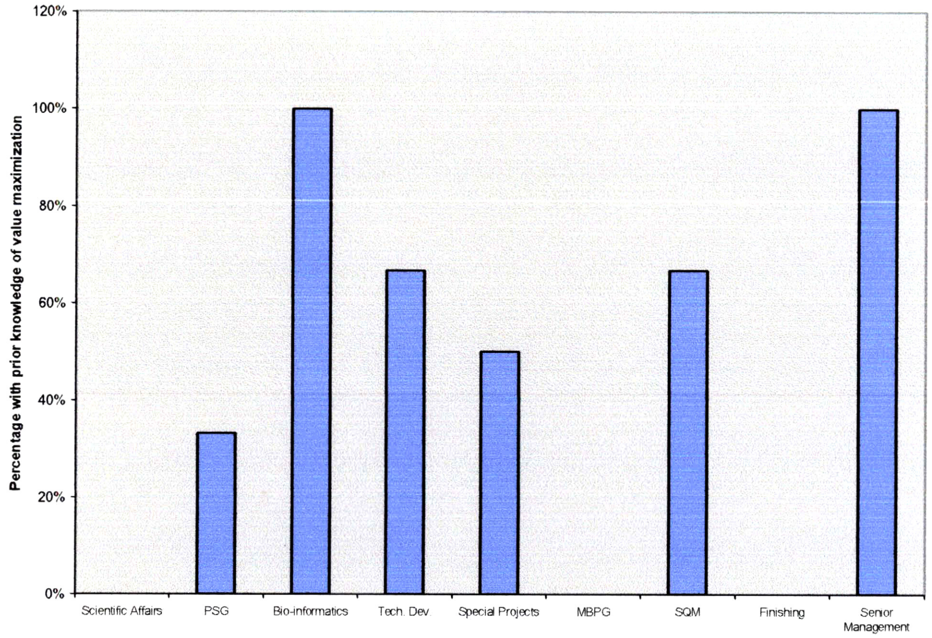



**Figure 12. Survey results on level of fundamental understanding of concepts of value maximization across different groups**

## 3.5.2 Stakeholder structure, expectations and needs

Much as suggested in the literature, the survey results suggested a much more cross linked organization that the organization chart presented in Figure 11. In order to analyze the stakeholder structure, we will start at a broader level by first understanding the enterprise structure – high level and granular; and then will move on to look at the stakeholder structure at a detailed individual level.

The Operations Sequencing Platform at the Broad Institute is a grant driven organization that is charged with the responsibility of sequencing DNA of new organisms, each of which is unique. The sequencing process thus needs some adjustment every time Broad gets a new project. Additionally, new technology platforms are constantly emerging and need to be optimized as they are implemented. With maturity of the project, the fuzziness in its definition reduces. This can be qualitatively plotted as shown in Figure 13. This description is critical as we go forward to understand the enterprise structure of the organization.

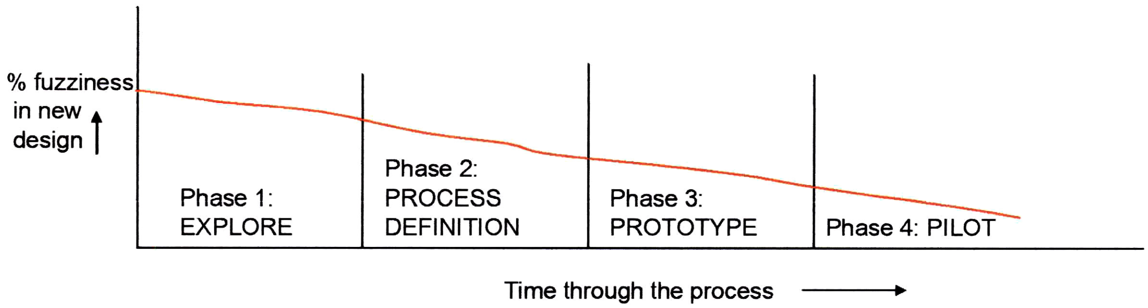



**Figure 13 Reduction in fuzziness as project matures**

As shown in Figure14 (a) and (b), the Broad Sequencing Operations Platform can be divided into two broad work streams:

- Core processes
- Supporting processes

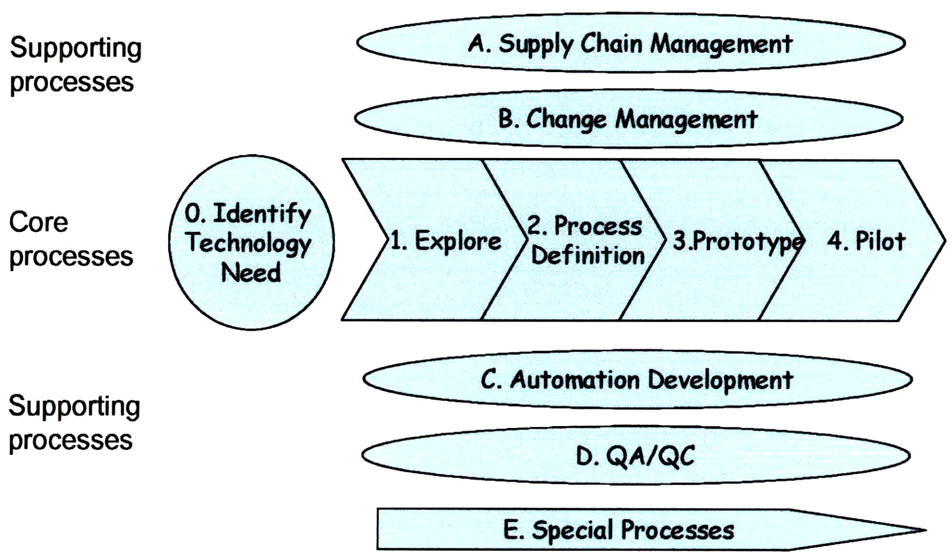



**Figure 14 (a) Overall enterprise structure**

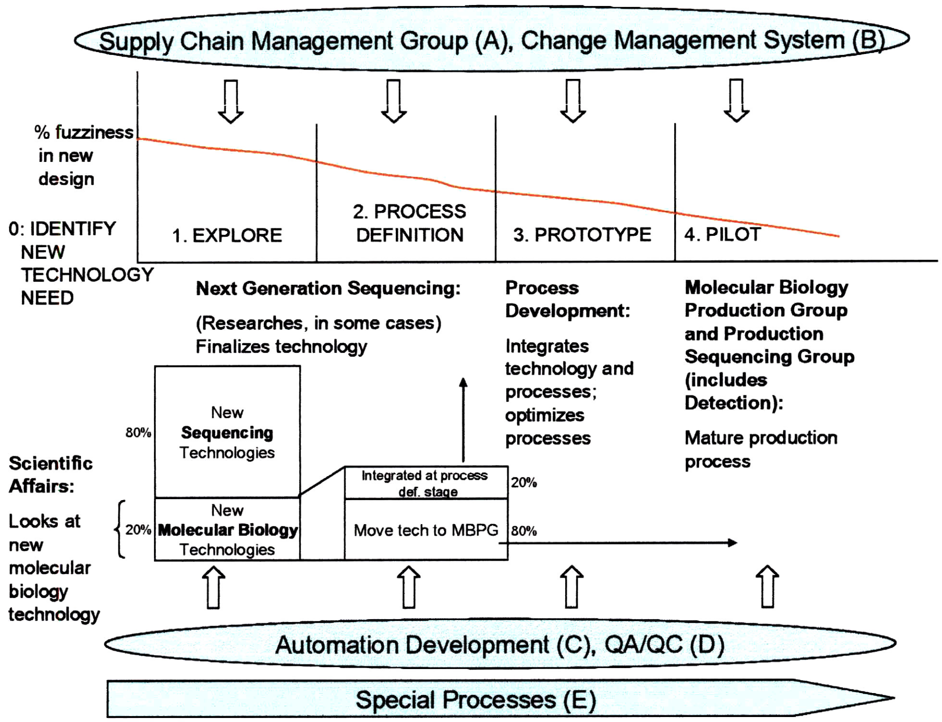



**Figure 14 (b) Enterprise structure with details on core processes**

Detailed questioning suggested that a lot of work has gone into trying to define the specific roles and interactions across different groups. Figure 15 shows the inter-dependencies between them. This means that that the enterprise as a whole will remain at a sub-optimum level if the following are not taken care of:

- Effective channels of communication that are simple and easy to follow
- Existence of common language – both technical and process
- Clear mechanism for prioritization of projects/work

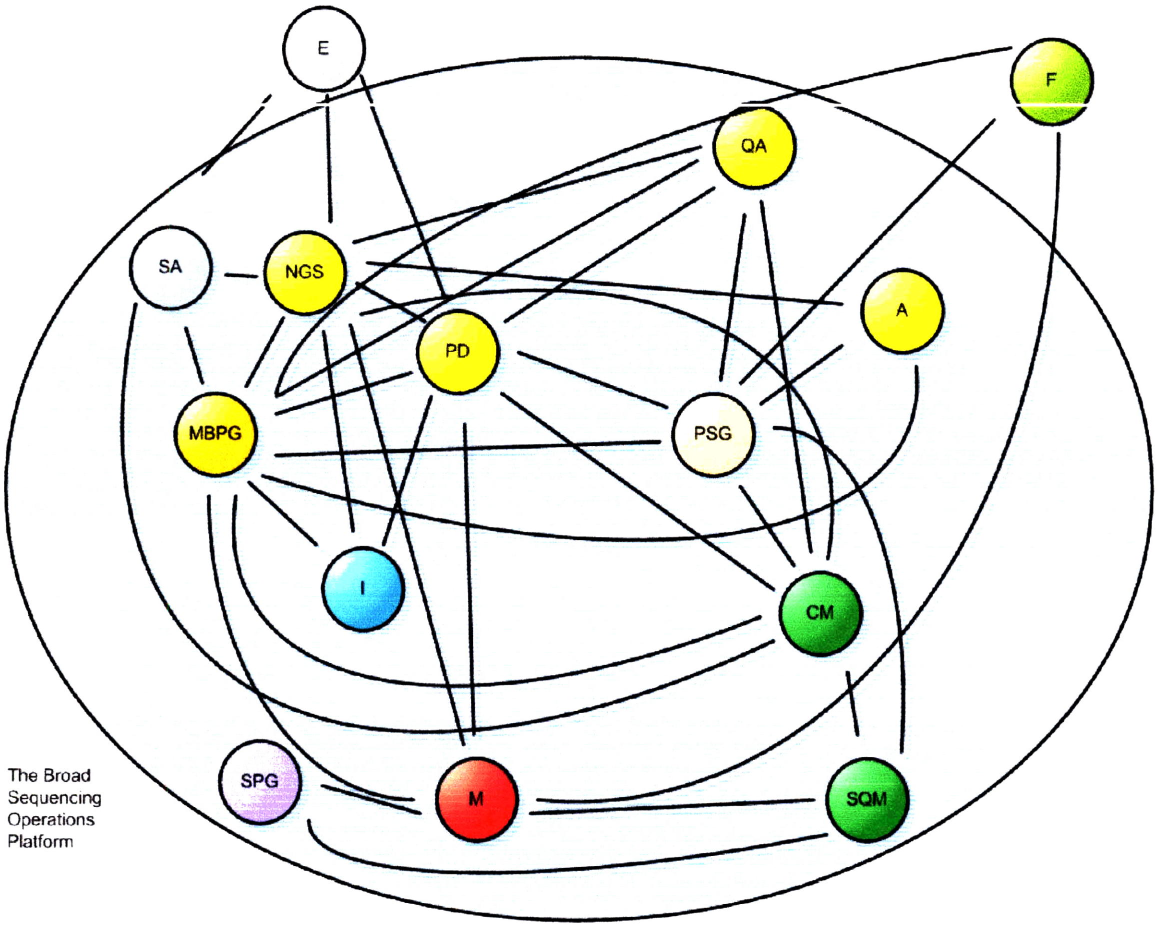



**Figure 15. Stakeholder structure where SA: Scientific Affairs; NGS: Next Generation Sequencing; PD: Process Development; MBPG: Molecular Biology Production Group; PSG: Production Sequencing Group; SQM: Supply and Quality Group; CM: Change Management; A: Automation; QA: Quality Assurance and Quality Control; SPG: Special Processes Group; E: External Collaborators; I: Informatics; M: Senior Management; F: Finishing Group**

Analyzing the stakeholder structure in Figure 15, it becomes clear that the institute has systems in place to facilitate corporate communication through a "Change Management Team" that is responsible for ensuring appropriate communication of processes and relevant changes. However, the data analyzing the pain points and needs of stakeholders, shown in Figure 16, showed that more than 70% of pain points related to communication and culture.

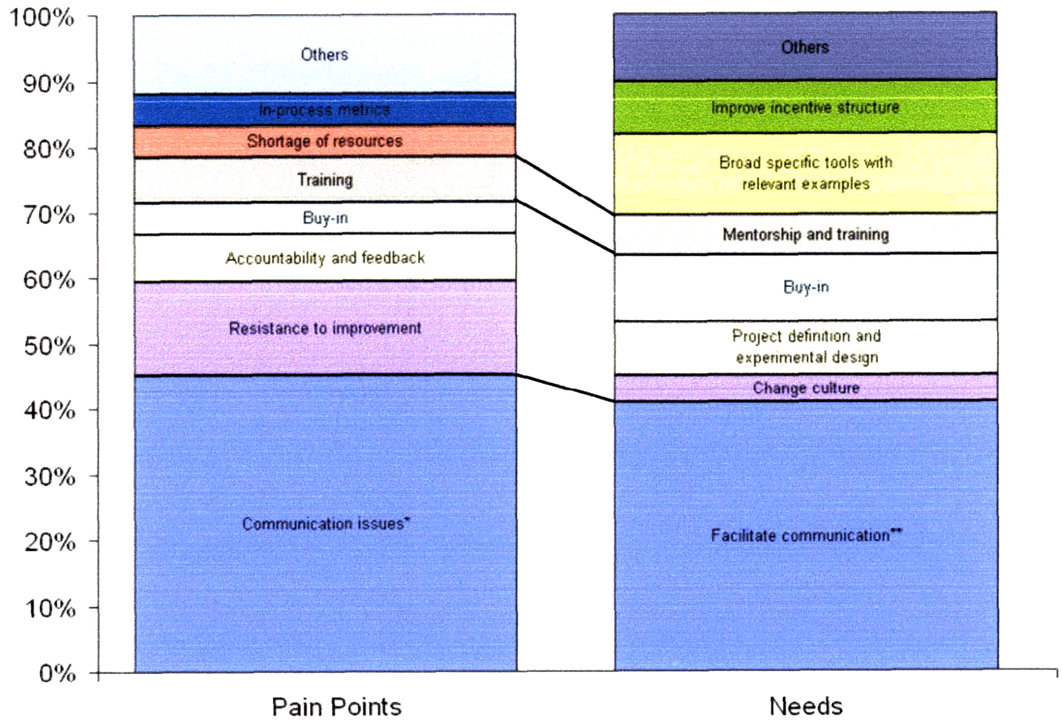



**Figure 16. Comparing stakeholder pain points and needs. * Includes direct communication of organizational goals, people not being on the same page, choosing right priorities ** Includes communication channels, need for same language, awareness of big picture and organizational goals. The category "Others" for pain points includes: motivation of staff, compensation, management of small projects, sample quality, variability in machine performance. The category "Others" for Needs includes: participation of all team members, update of protocols, metrics, career development and flexibility**

Analyzing the stakeholder expectations from process excellence, shown in Figure 17, we find that the top two expectations are more of implementation related concerns. This could be due to either or both of the following reasons:

- Insufficient communication of process goals and expectations in previous implementation exercises
- Inability to relate process excellence to current work

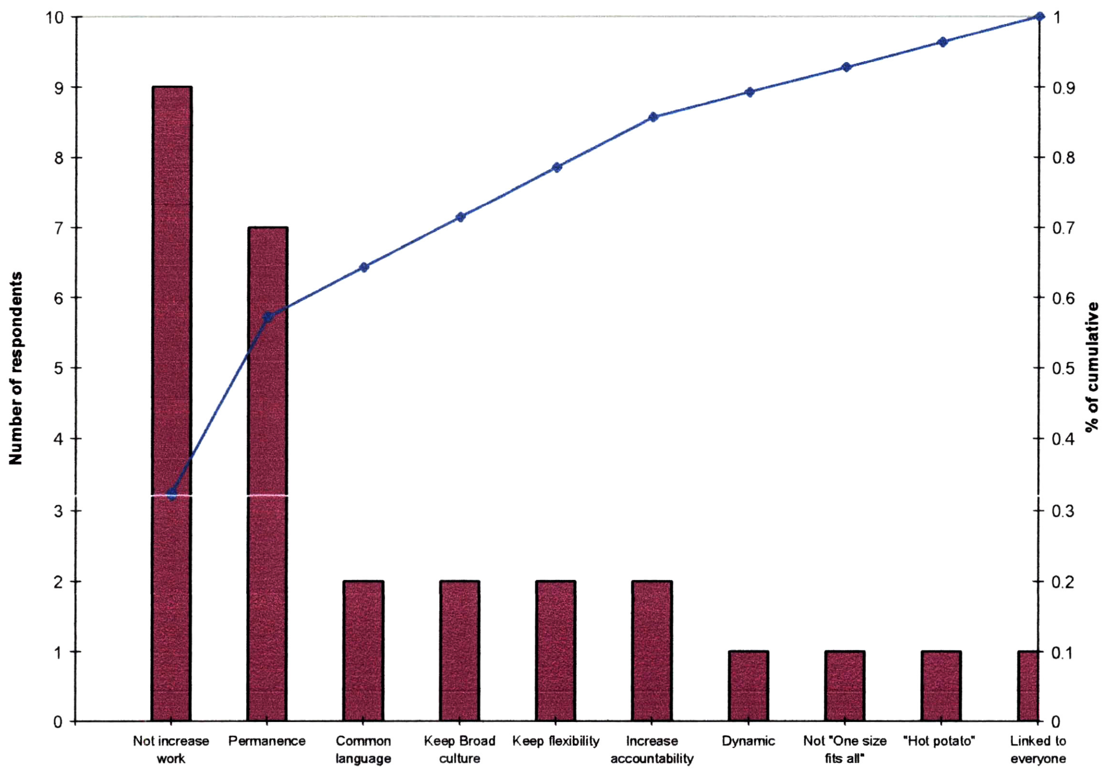



**Figure 17. Stakeholder expectations from process excellence**

### 3.5.3 Metrics

The goal of the metrics section of the survey was to answer the following questions about the Broad Sequencing Operations Platform:

- Are the current metrics effectively measuring the key success factors for the stakeholders?
- How do the stakeholder's metrics at a group level relate upwards (to global metrics of the enterprise) and downwards (to metrics at the individual stakeholder level)?

*Stakeholder metrics and Success Factors:*

The survey results indicated that, as of the time of the survey in late summer 2006, 60% of respondents effectively measured more than 50% of their individual success factors. We assert that the answer to this gap lies in Figure 18, which shows the list of stakeholder success factors that are not being measured. In particular it is interesting to contrast Figure 16 and 18, which shows a strong correlation between stakeholder pain points and the success factors that are not being measured.

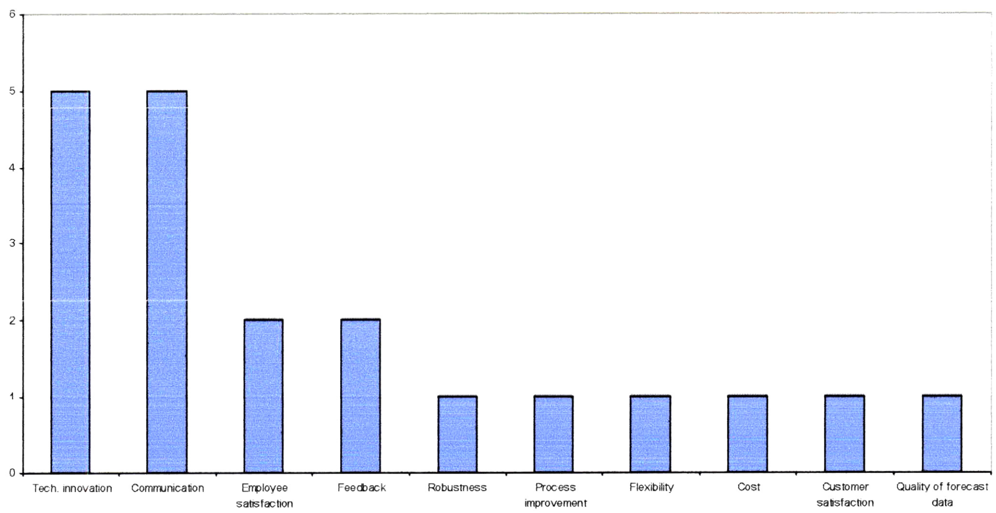



**Figure 18. Success factors that are not being measured today**

*Relationship between stakeholder metrics and those up and down the organization:*
As shown in Figure 19, almost 50% of the stakeholders mentioned that there is no tie between their metrics and those of the enterprise. We assert that this is due to communication issues that the majority of the stakeholders reported. Thus, instituting communication systems that are easy to follow and not seen as additional work should help alleviate this problem.

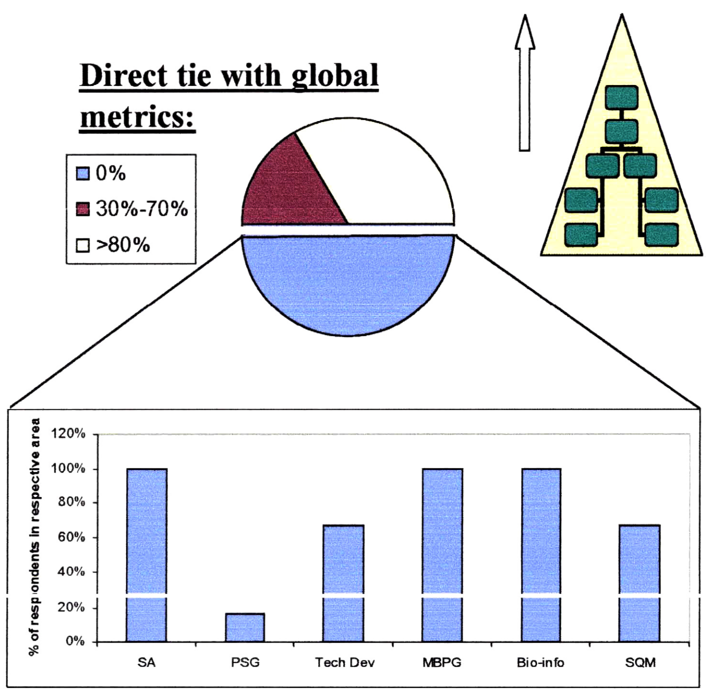



**Figure 19. Tie between stakeholder's individual metrics and the global metrics for the enterprise**

Survey results and follow-up discussions on the issue of metrics further revealed that the global metrics and group metrics for different stakeholders is measured on the basis of process results that are not measured till the very end of the production step i.e. detection. Under the current system, it is thus very difficult to separate contributions by the different stakeholders towards the global metrics. Individual stakeholder metrics are thus on the lines of resource utilization and qualitative description of work. It is thus not a surprise that no stakeholder reported any tie between process metrics or stakeholder success metrics and their individual metrics.

### 3.6 Conclusions

The challenges that form the root causes for poor sustainability of previous process improvement programs can thus be summarized as follows:

- Communication issues such as knowledge of organizational goals and overall big picture
- Challenges in prioritization of activities
- Absence of common language
- Resistance to change due to top-down pressure for implementing tools not necessarily seen as fully applicable
- Absence of in-process metrics that can be identified at the stakeholder level

We assert that such issues can be alleviated by ensuring the following as a part of the Broad Process Excellence Program:

- Include improvement tools such that they are integrated into the current workload
- Develop simplistic communication mechanisms that include knowledge sharing and increased touch points between management and stakeholders
- Implement process tools that can help develop in-process metrics that can be tied to global and individual metrics

These solutions being longer term than the duration of the internship permits, it was decided that we would start by developing a Process Excellence Handbook that would be distributed and implemented in all parts of the organization. Using this handbook as a guide, each of the groups will be able to address concerns and expectations of the stakeholders as they carry on their daily activities. This will help implement the new process in a manner that makes process excellence a part of their daily work.

# Chapter 4

# Benchmarking Best Practices in Process Excellence

A survey was conducted to capture lessons learnt while implementing best practices in operations excellence practiced at different organizations. This chapter presents information on background and results of the survey. The chapter concludes with key takeaways from the survey and in addition to the previous chapter on "Stakeholder Analysis" provides the foundation for Broad Process Improvement Framework presented in the next chapter.

## *4.1 Background and motivation*

Over the past several decades, corporate America has seen repeated waves of foreign competition first in the form of foreign companies and then in the form of low cost labor pools. These factors have required companies to continuously reinvent themselves and come up with innovative ways to improve their productivity. Such actions have given birth to several initiatives that have taken explicit forms and have additionally changed names several times.

Traditionally process improvement and quality improvement has gone hand in hand. The origin of this approach lies in corporate America's direct response to the growing demand for higher quality electronics and automotive products coming in from Japan. The response started with application of statistical tools to problem solving. However, it was quickly realized that such approaches were based on lagging indicators. Consequently, the solutions proved to be prescriptive as opposed to predictive. It was additionally realized that such initiatives would not succeed without the active involvement of team members beyond the quality organization. Such realization gave place to "Quality Circles", in which small teams of workers were formed to tackle manufacturing problems. Empowered by authority to make necessary changes and statistical monitoring tools such as Statistical Process Control developed by Walter Shewhart, the teams set about solving problems faced on the shop floor. Over time, these initiatives transformed into a broader toolbox called, "Total Quality Management (TQM)" that embraced the entire organization. By the end of the 1990s, TQM started being considered a fad by many business leaders. It is interesting to note that although, TQM by itself started becoming obsolete, its practices still continue. Next came the "Malcolm Baldridge National Quality Award" program that included business results criterion to its measures of applicant success. This was followed by the "Six Sigma" program pioneered by Motorola who shared this program as the secret to their winning the Baldridge award in 1998. Along the way also came ISO 9000 that added the aspect of customer satisfaction. But with its features being so closely tied to TQM, its existence as an independent process improvement tool diminished. Other programs being practiced in the industry include those brought forward by the International Motor Vehicle Program and the Lean Aerospace Institute at MIT such as "Lean Manufacturing", "Toyota Production System", and "Lean Enterprises". Other leading programs that developed along the way include CMMI and Reengineering. Figure 20 shows a timeline of different process improvement methods that were developed, introduced and implemented in corporate America over the past 100 years.

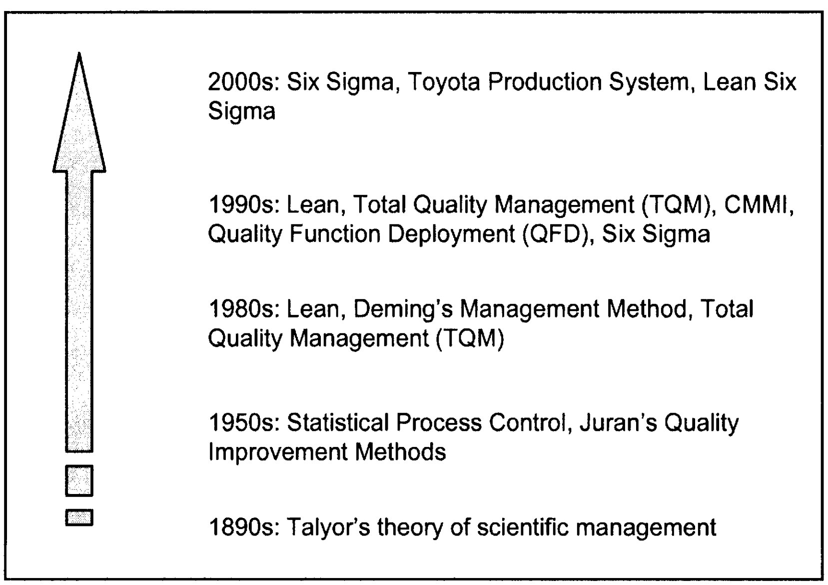



**Figure 20. Timeline of development of various process improvement methods**

Table 4 shows the comparison as presented by Uzair in SM Thesis.

**Table 4. Detailed comparison of some popular process improvement programs (Source: Uzair[9])**

| Change Program | Brief History | Basic Objectives | Fundamental Concepts / Principles | Performance Metrics Supported | Degree of change brought about | Tools / Methodologies | Scope of Application in an enterprise |
|---|---|---|---|---|---|---|---|
| Total Quality Management | Dates back to Edward Deming and his quality philosophy. | Bring about and sustain a company's winning position by continuously improving customer satisfaction. | Data-driven, employee-based, continuous incremental improvement in all enterprise operations with a focus on customer satisfaction. | Customer satisfaction is the primary performance metric. | Slow, incremental. | The seven famous TQM tools are: histograms, flow charts, scatter diagrams, cause and effect diagrams, Pareto charts, control charts, and check sheets. Basic methodology is plan, do, check and act. | The whole enterprise including all core, support, and strategic planning process. |
| Six Sigma | Theorized by Mike Harry and Rich Shroeder, Six Sigma concepts were | To improve market share and profitability of an enterprise by | A defect is anything going against customer satisfaction. The basic concept of | Number of "defects" is the primary metric for Six Sigma. | Could be dramatic as well as incremental, depending | Statistical analysis is the primary tool. All seven TQM tools | The whole enterprise including all core, support, |

[9] UZAIR, K.M., Development of a Framework for Comparing Performance Improvement Programs, M.S. Thesis, MIT September 2001.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | first implemented and perfected by Motorola, and later on by GE and Allied Signal (Honeywell) | continuously reducing the number of defects in its products and processes. | Six Sigma is that number of these defects should keep on decreasing in all products and processes going on in the enterprise. The ultimate target for such reductions should be in the six sigma level of a normal distribution, which is 3.4 defects per million. | The term "defect", in turn could be defined differently in different contexts. $C_{pk}$ is an important gauge for tracking the primary metric. | upon the tools and methodologies adopted for reducing the number of defects. | mentioned above are however considered basic in all data analysis. The general methodology for bringing about improvements is Define, Measure, Analyze, Improve and Control. | and strategic planning processes. |
| Reengineering | Pioneered by Michael Hammer in the early '90s; he built upon his ideas based on Peter Drucker's work and on the general need of corporate America to reinvent itself in | To achieve dramatic leaps in performance by redesigning an enterprise process. | Quantum leaps in performance and dramatic improvements in competitive position can never be achieved by fixing problems in a system; it can only be achieved by | Varies from case to case, and cannot be generalized. Most commonly, cost of production, lead time to deliver, and quick | Very fast and radical. | No fixed tool or methodology applies. It's all about designing something afresh. Information technology is, however, a useful enabler | The whole enterprise including all core, support, and strategic planning processes. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | the face of Japanese competition. | | starting over, by rethinking the fundamental design of processes, by reinventing the way things are done. The most notable of the changes required are from Adam Smith's theory of specialization of labor to generalization & empowerment. | changeover are the performance metrics required to be improved. | | in most of the cases. | |
| Quick Response Manufacturing | Built upon the Toyota Production System by giving the same philosophy a new dimension. Initiated by the Boston Consulting Group in the late '80s and later on further developed by Rajan Suri, | To capture market share and improve profitability by taking lead time as the primary performance metric for improving all enterprise operations. | Lead time is the primary waste in all industrial operations. Reducing lead time for manufacture & product development results in bringing products to the market faster than the competitors and | Lead time is the primary performance metric in this philosophy. | Could be dramatic as well as incremental, depending upon the tools and methodologies adopted. | PDCA (Plan, Do, Check, Act) is the primary tool. However, any possible tool helpful in achieving the objective is recommended. Examples are Kanban, JIT, SMED, SPC, etc. | The whole enterprise including all core support and strategic planning processes. |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Suzanne de Trivelle, and other academicians. | | in improving customer satisfaction. Also, reducing changeover/setup times reduce inventories thus reducing costs. | | | | |
| Agility | Started in the '90s by DoD and NSF. An Agility Forum was established by them in response to a conference's recommendation. Lehigh University has been at the forefront of this movement. | Objective here is to improve and sustain an enterprise's competitive position by making it flexible enough to meet any and all the changing customer demands and to cope with any sudden changes in external or internal environment. | The basic concept of the agile movement is that instead of having any fixed objectives and a set methodology for continuously improving one's competitiveness, the best strategy is to develop an ability to cope with changing customer expectations and other externalities. | Flexibility of systems and processes as well as the enterprise policies is the primary metric here. | Could be fast or slow depending upon the situation. It is actually not a change process, but the ability to cope with change. | Any possible tool helping to achieve the objectives is applicable. The best tool, however, is the right strategy at the planning level at a micro manufacturing level. At a micro-manufacturing level, SMED, empowerment, etc, are useful. | The whole enterprise including all core, support, and strategic planning processes. |
| Variance Reduction | This new approach was discovered and advocated by Stephen Ruffa | To reduce cost of production, so as to improve the overall | The basic concept is that it is hard to reduce inventory or to slash lead time | Variance reduction is the primary metric for performance | Could be drastic as well as incremental, depending | A whole set of techniques or initiatives like concurrent engineering, | The whole enterprise including all core, support, |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | and Michael Perozzielo of the aerospace industry in the late '90s. It was discovered by them while researching on reducing cost of production in the aero industry. | competitiveness of the organization. | unless variability is reduced from the processes. Once variance is reduced from the processes, it becomes a lot easier to device ways to improve lead time or inventory. Cost of production goes down as soon as variance, lead/cycle times, and inventories are reduced. | here. The two secondary metrics are cycle time reduction and inventory reduction. | upon the need and the method used. | SPC, MRP II, Cellular Manufacturing, etc. leads to six different process enablers. The enablers help in improving the three metrics. The six enablers are: Design for Manufacturing; Quality Improvement, Control of Manufacturing Operations, Cont. of inventory, Supplier Improvements, & Improvement in Production Flows. | and strategic planning processes. |
| Lean | The philosophy of Lean has its roots in the International | The objective is to increase the overall competitiveness | The five basic principles of lean thinking: specify value for the | Value created for a customer is the primary | Could drastic as well as incremental, depending | Value Stream Mapping and all popular tools. | The whole enterprise, including all core, |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Motor Vehicle Program researchers at MIT on Japanese auto manufacturing. The concepts were first presented in the IMVP book, "The machine that changed the world" | of an enterprise by reducing waste and increasing the overall value created for the customer. | customer by specific product, make value flow without interruptions and let the customer pull value through the stream. | metric | upon the tools and methodologies adopted. | Technologies, especially from Toyota Production System, as and when applicable. | support, and strategic planning processes. |

A squeeze in revenues during the 2000s due to an economic slowdown and an increase in pressure from shareholders to generate returns have challenged corporate America to generate higher productivity at a faster pace. With so much variety out there, organizations have tended to constantly jump between these different initiatives. An inclination towards trying to employ these ideas as off the shelf "silver bullet" solutions has resulted in poor success rate and a large majority of employees getting disoriented and cynical about process improvement.

In order to not fall into the trap of finding a quick fix off the shelf solution, a benchmarking survey was conducted to learn from the experiences of some of the leading organizations across multiple industries. The results showed that industries have come a full circle in process improvement – starting with individual process improvement initiatives (not necessarily efficient); moving to standard off the shelf programs such as Lean or Six Sigma and now back to custom programs (a hybrid version of different programs). The next sections cover the survey in detail.

## *4.2 Industrial Survey*

A survey was undertaken to benchmark best practices in process improvement at some of the leading organizations across industries. Table 5 represents the categories of organizations interviewed. The names of organization have been hidden for confidentiality reasons.

**Table 5. Organizations interviewed to benchmark best practices**

| Type | Number of companies |
|---|---|
| Pharmaceutical companies | 3 |
| Hi-technology companies | 3 |
| Automotive | 2 |
| Aerospace | 3 |
| Healthcare provider | 1 |
| Retailer | 1 |

The survey content was designed to gain an understanding of the following:

- Change initiatives being followed

  The goal of this section was to get a perspective on the types of change initiatives followed, key tools from an implementation standpoint, targeted impact and key challenges experienced during its implementation. Table 6 provides the list of questions asked:

**Table 6. Questions on change initiatives and implementation**

| Objective | Question |
|---|---|
| Initiative | • What are the different process excellence initiatives your organization is involved with? (Lean/DMAIC/DFSS/TQM/hybrid etc.) |
| Targeted impact | • What problems were you targeting to solve through these initiatives? |
| History | • How long have these programs been in existence?<br>• Did you have any specific process excellence program before this? If yes, what happened to it? Why?<br>• Did you try integrating your previous improvement initiatives to your new program? Please rate the success of integration on a scale of 1-7. Please provide reasons. |
| Implementation | • What are the key areas within the organization where process excellence is being implemented?<br>• Do you have a blanket program or does each area have their own? Why?<br>• Please list specific tools or techniques being used for implementation and rate each on a scale of 1-7 for effectiveness. |

- Stakeholders and people involved

  The goal of this section was to understand categories of stakeholders, leadership and accountability and customer response. Table 7 shows the list of questions asked in this category.

**Table 7. Questions on stakeholders and people involved**

| Objective | Question |
|---|---|
| Stakeholder | • What categories of personnel are involved in this process, and what types of skills are needed? Please also rate the support you are getting for each category.<br>• Please rate the support and involvement for each of the following hierarchical levels:<br>o Leadership - specific<br>o Middle Management<br>o Shop floor/lab tech |
| Leadership & Accountability | • Who typically leads these efforts? Which group?<br>• How do you ensure accountability if the person in charge belongs to a different department? |

- Metrics

The objective of this section was to learn how leading organizations measure their key success factors and how such metrics relate to individual and global metrics. Table 8 shows the list of questions asked in this category.

**Table 8. Questions on metrics**

| Objective | Question |
|---|---|
| Metrics & success factors | • What are the key success factors?<br>• How do you measure the performance of each of these initiatives? Please rate your performance on a scale of 1-7<br>• Please rate the how proactive these metrics are on a scale of 1-7 (1 being 100% reactive and 7 being 100% proactive) |
| Vertical and horizontal alignment of metrics | • Please rate uniformity of metrics across the organization on a scale of 1-7<br>• How do these metrics relate to the global metrics of your organization?<br>• Do you tie the initiatives with HR metrics? If not, why not? If yes, which metrics? Why? |

- Sustainability of initiatives

  The primary goal of this section was to understand the challenging issue of ensuring initiatives can be sustained over time. Table 9 shows a list of questions asked in this category.

**Table 9. Questions on sustainability**

| Objective | Question |
|---|---|
| Processes & feedback | • What processes do you have in place to help sustain these initiatives?<br>• Do you have any processes to take feedback from your employees on these initiatives?<br>• How often do you seek feedback? How do you incorporate the feedback?<br>• How do you track feedback? |
| Training | • What types of training do you have in place?<br>• How do people access the training? How do you measure success? |

## *4.3 Industrial Survey Results and Key Insights*

### 4.3.1 Change initiatives and implementation

Successful process improvement is achieved by focusing resources on the day-to-day activities that have a clear link to delivering/improving value to the customer end-user. All processes/activities in an organization should be adding value to customer product/services or supporting those processes that add value. This objective however is fairly broad and needs to be focused to specific objectives. Figure 21 shows some of the targeted objectives identified by the benchmarked organizations.

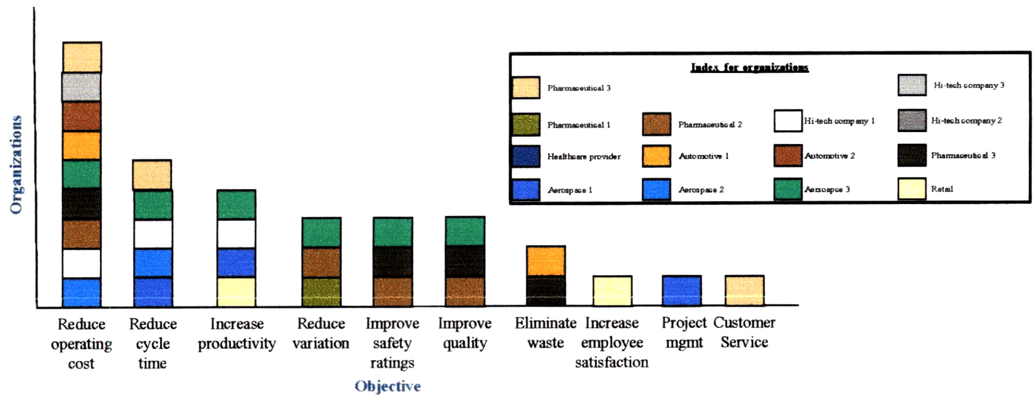



**Figure 21. Key target objectives for implementing process excellence**

Figure 21 further shows that the top 3 objectives for implementing process excellence are reducing operating cost, reducing cycle time and increase productivity. Such operations-centric objectives are in-line with the fact that 100% of the organizations reported that process excellence is primarily being implemented and led by the operations area. It will be interesting to observe change in objectives as process excellence moves to other areas of the organizations. As shown in Figure 22, the organizations interviewed follow a wide variety of initiatives to reach these objectives. It is however important that organizations additionally spend a considerable amount of time to get a clear understanding of customer requirements and expectations, and create a channel to effectively communicate it across the enterprise. The existence of this activity is validated by the high degree of popularity of programs such as Lean, Six Sigma and Toyota Production System.

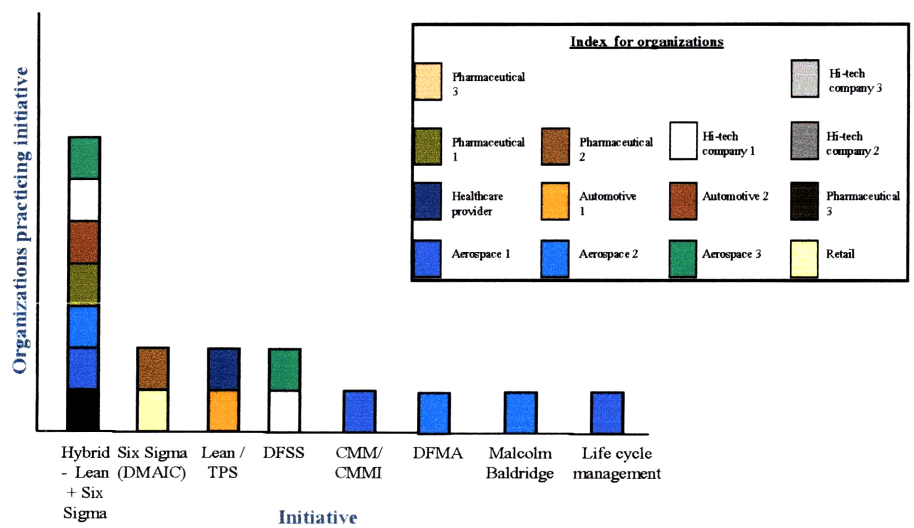



**Figure 22. Initiatives followed at the benchmarked organizations; DMAIC – Define, Measure, Analyze, Improve and Control; DFSS: Design for Six Sigma, CMM: Capability Maturity Model; DFMA: Design for Manufacturing & Assembly**

The interviews and surveys further revealed that leading organizations tended to follow different initiatives at different parts of the organization. This group of organizations was divided into two sub-groups – one that called the different initiatives by their original names (Malcolm Baldridge, Lean etc.) and the second, the larger of the two, which followed a more custom hybrid approach. Such cherry-picking of tools can be tricky since it can result in building isolated islands of improvement instead of improving the whole production flow to reap the biggest benefits. It was thus interesting to note that industry leaders while cherry-picking tools to develop custom programs, additionally employ systemic big-picture tools such as value stream mapping – a mapping tool that helps the user visualize day-to-day activities and their linkage as they add value to the end customer. This inclination is shown in Figure 23, which illustrates the industry's preference for simple to use visual system level tools. These were rated as effective because these tools explicitly map between existing processes and eliminating activities that do not deliver/improve customer end-user value. Companies that do not rate these tools as effective should look at whether they are deploying these tools in a way that accomplishes the key objective of increasing value for the end-customer. Discussions with respondents further suggested that other analytical tools (whether Lean Six Sigma or not) should be experimented with and added as they prove helpful in making this link between day-to-day actions and customer end-user value more obvious to everyone involved.

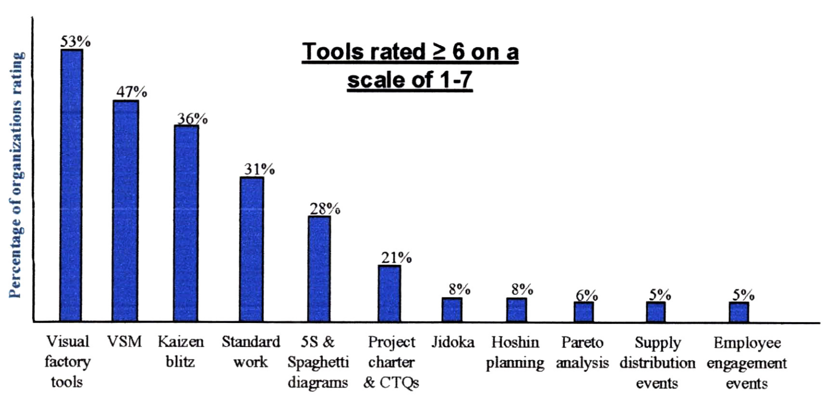



**Figure 23. Respondent rating of tools on a scale of 1-7**

*History & transition from previous process improvement processes*

Several literature sources[10] have talked about how organizations fueled by the need to provide higher quality at lower cost and higher efficiency have gone after the latest off-shelf management solution such as TQM, Lean, Six Sigma etc. However, additional study [11] showed that things were not going as well as previously thought. The problem was that such initiatives were being looked at as the universal truth and the solution to all problems. Managers were in the process of stretching the techniques, by applying them too broadly to more creative areas such as research and new-product development. As an example, one of the senior executives at Agilent Technologies suggested that managers should not rely too much on Six Sigma for tasks that are difficult to measure[12]. The industrial survey, as illustrated in Figure 24, suggested a similar trend with leading organizations moving away from the previously popular off-the-shelf initiatives such as Lean and Six Sigma to more hybrid approaches that included custom elements of several initiatives.

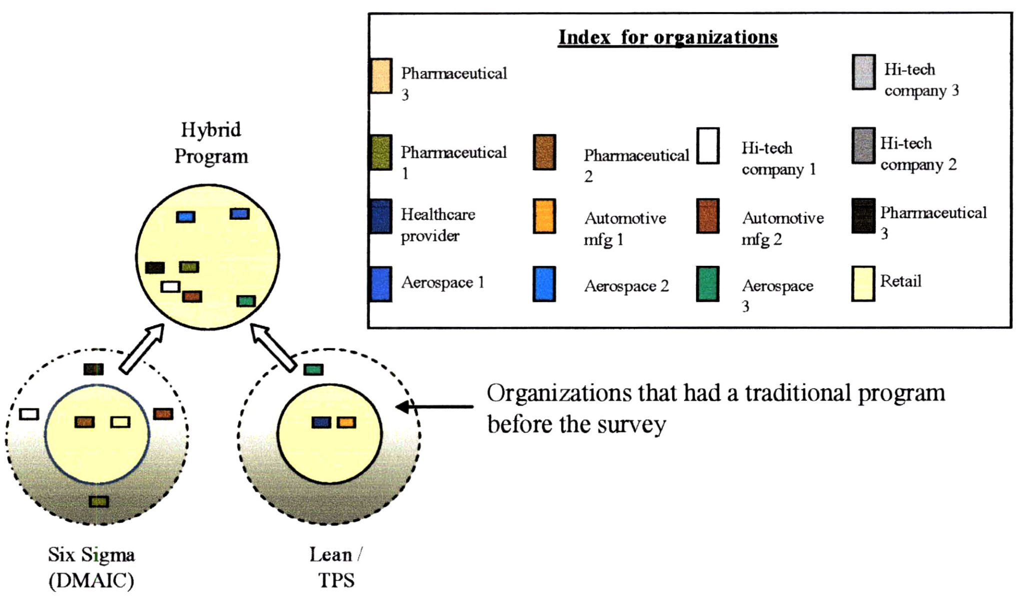



**Figure 24. Organizations that have moved away from traditional off-the-shelf initiatives**

[10] "Machine that changed the world" (Womack et al), "Pursuing the competitive edge" (Hayes et al)
[11] "Don't Get Hammered by Management Fads", The Wall Street Journal, May 21, 2001; "Many Companies Try Management Fads, Only to See them Flop", The Wall Street Journal, July 6, 1993.
[12] "Rethinking Quality Improvement", The Wall Street Journal, September 19, 2005

Such evidence in both literature and benchmarked companies suggests that one good approach to maximizing value for the final consumer would be to have a three dimensional approach with the following key elements –

- A holistic tool such as lean or TPS to provide the breadth
- A problem solving tool such as in Six Sigma to provide the depth in selected problems
- Aligned metrics to help monitor improvement and growth in the right direction.

It must however be noted that this approach can be a challenge in situations where there are no metrics available. Absence of metrics can mean either of the following two situations:

- the activities are very subjective- here it is possible that it does not make economic sense to work towards developing quantitative metrics. It is recommended to do a detailed cost-benefit analysis before embarking on a metrics finding session.
- the activities are objective – respondents suggested the use of voice of customer analysis to understand the key levers to measure.

### 4.3.2 Stakeholders and people involved

<u>Stakeholders</u>

Process Excellence is a cross-functional activity that is wholly dependent on active participation of team members from all relevant areas of organizations. This was overwhelmingly supported by the survey data that showed that 100% of benchmarked organizations implement process excellence as an inclusive activity involving key members from several departments. 100% of respondents also mentioned that for widespread success it is very important to effectively involve stakeholders from all vertical levels – shop floor, middle management and senior leadership. Some correlation was found between the level of support of personnel from the different levels and the maturity of the process excellence initiative. Maturity was measured by the number of years since the initiative was implemented. The behavior and the extent of correlation was however different for the different vertical levels. As indicated in Figure 25, the amount of correlation for the senior leadership data not only was insignificant, but overall senior leadership support was rated in the 6-7 for majority of the organizations interviewed. This supports the need for leadership to invest resources in linking day-to-day processes more explicitly to customer end-user, and to play a leading role in adjusting policies as needed to eliminate current tasks that do not add value. Such top-down support and involvement is critical to success of process excellence.

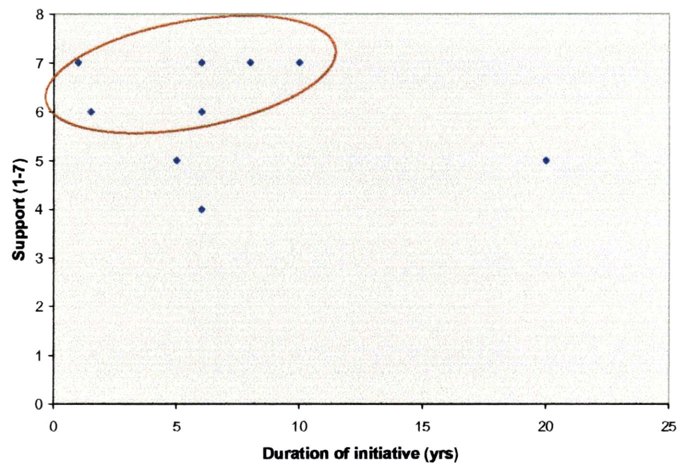



**Figure 25. Relationship between senior leadership support and duration of initiative**

The relationship between the middle management support and the duration of the initiative on the other hand was, as shown in Figure 26, much more correlated. A similar result was observed for that of shop floor support as well. This is illustrated in Figure 27.

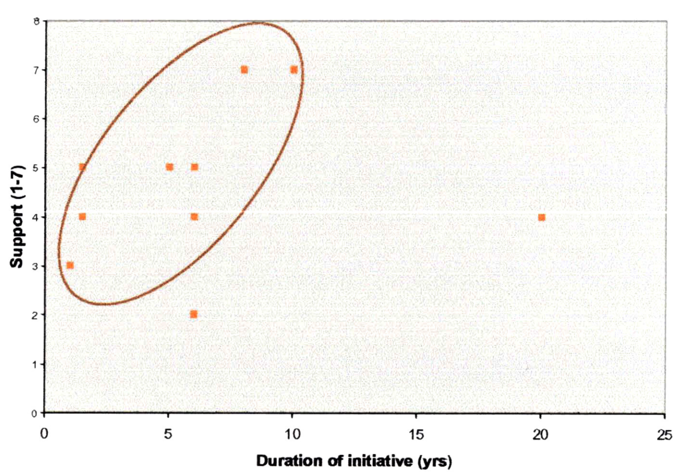



**Figure 26. Relationship between middle management support and duration of initiative**

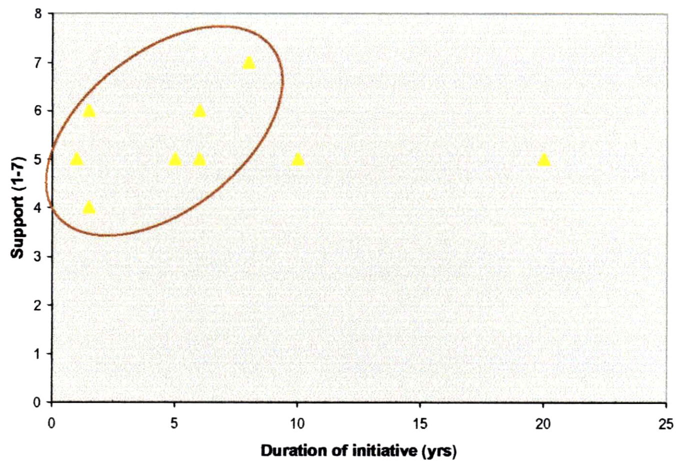



**Figure 27. Relationship between shop floor support and duration of initiative**

Figure 28 shows the relationship for middle management support and the shop floor. This highlights a very important observation that the average middle management support is less than that for the shop floor for the same duration of initiative. Such observation highlights the importance of paying importance to political issues when implementing process excellence.

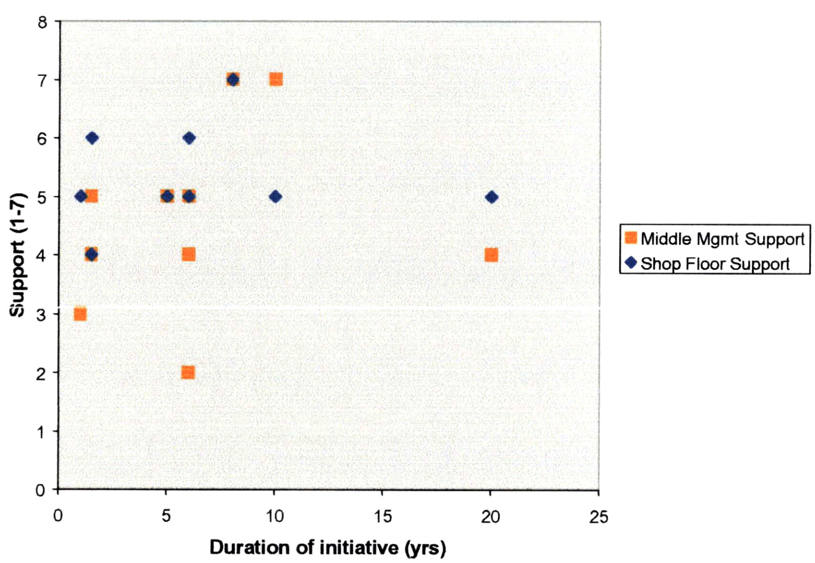



**Figure 28. Contrasting middle management support with shop floor support at different durations of process excellence initiatives**

<u>Leadership & Accountability</u>

The data presented so far has shown that process excellence is a team activity that involves all relevant stakeholders – both across functions and hierarchical levels of the organization. This high degree of wide-spread involvement brings up the very important topic of accountability which has a big role to play in ensuring both short term and long term success of process excellence. The first step to ensuring accountability is to have the right person leading such an effort. Unfortunately, there is no right answer to who the right person is. It could be a third party such as an external or internal consultant such as a Black Belt, the General Manager of the facility, functional leads etc. Our proposal based on several interviews with benchmarked organizations, other process improvement practitioners and academicians, is that such activities should be led by people who are closest to the process and have a vested interest in its success. This is because such leaders - 1) have the highest level of knowledge (both formal and informal) about the process; 2) have established credibility with the front line; 3) are measured by the success of the process they manage. Since the goal of process excellence is to maximize value for the end-customer, such factors prove to be immensely useful. This proposal was supported by the benchmark data, which, as illustrated in Figure 29, showed that the top three groups that take leadership are Internal Process Owners, Senior Divisional Managers and Black Belt/Change Agents. Several benchmarked organizations additionally mentioned that they are in the process of developing functional Black Belts with the plan to eventually transfer them to functional lead roles. The stint as a Black Belt or official change agents helps provide training and added incentives for future growth when they transition to functional positions.

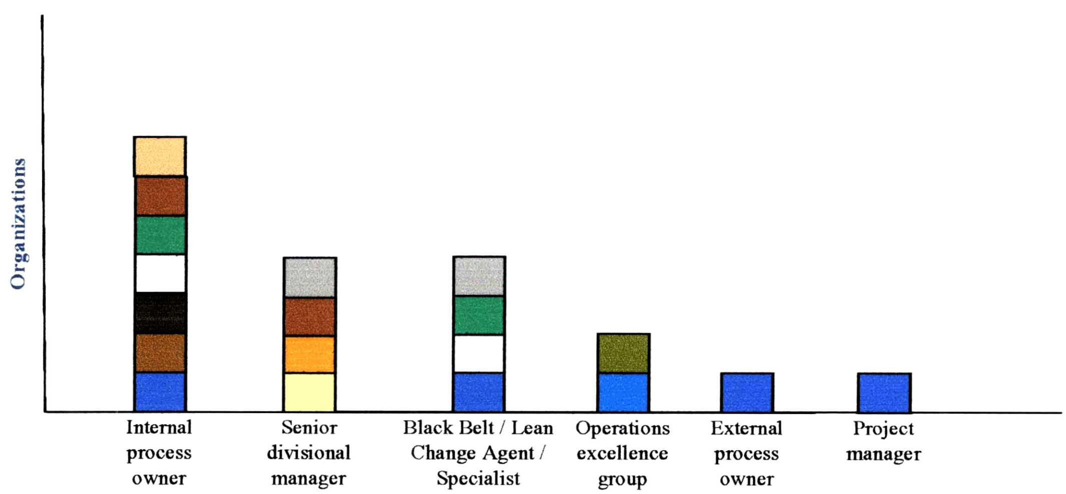



**Figure 29. Leadership of process excellence initiatives**

### 4.3.3 Metrics

Success Factors & Metrics

Metrics are key part of measuring the pace of improvement and ensuring accountability. Interviews suggested that this area of process excellence to be fairly grey with organizations reporting multiple levels of metrics. Some organizations reported as many as 54 metrics that they track to ensure success. Although 99% of organizations reported that there is a direct tie between their organization's success factors and their metrics, our proposal is that maintaining such a large number of metrics can be both confusing and expensive. We propose that organizations follow a multi-tiered metrics that can be cascaded down the organization. The merits of this proposal were validated by 40% of the organizations that reported a move in this direction.

The survey additionally showed that more than 80% of the metrics followed by the leading organizations are reactive as opposed to being proactive. It is thus not surprising that several organizations reported always being in a reactionary mode of operation.

We propose that in order to effectively identify problems, metrics at each level should have the following attributes:

- Should not be more than 3 to 4 at each level
- Should be simple to understand
- Should have well defined upper and lower control limits
- Should be as independent of each other as possible
- Should be proactive

Horizontal and vertical alignment of metrics

Maximization of value for the end customer requires that the entire organization across different departments and hierarchical levels speak the same process language and are directly impacted by the process results. A way to ensure that is to have a good alignment of metrics across the organization. Survey results, as illustrated in Figure 30, validated a high degree of alignment at different levels for the different benchmarked organizations.

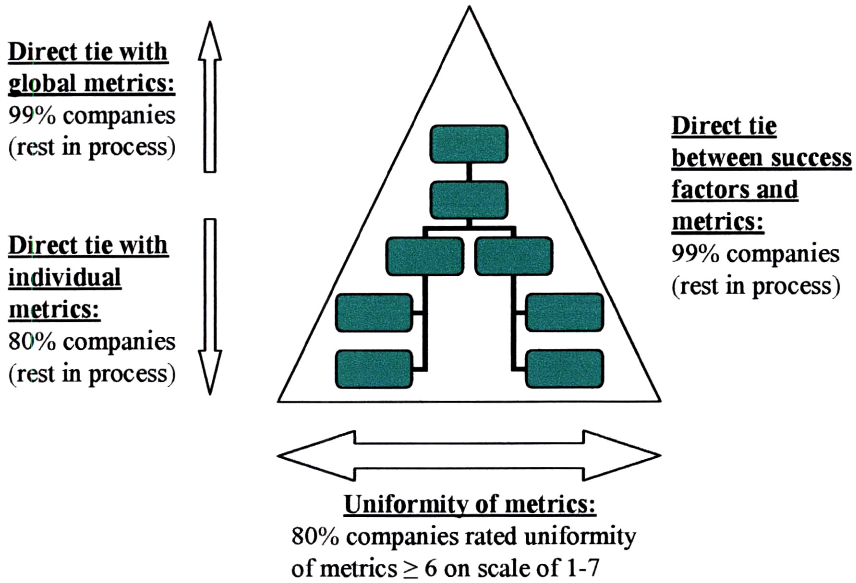



**Figure 30 Alignment of metrics across organization**

### 4.3.4 Sustainability of initiatives

Sustainability is the most challenging part of process excellence. As illustrated in Figure 31, the top 3 challenges reported by the benchmarked organizations were balancing priorities, goal alignment and communication. It was interesting to note that some of these issues were also mentioned by the different stakeholders at the Sequencing Platform during the stakeholder analysis described in Chapter 3.

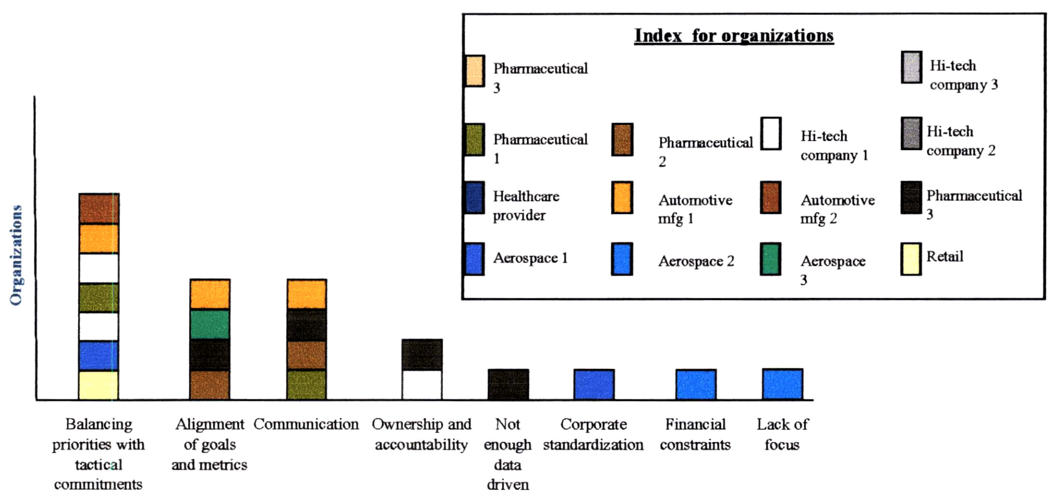



**Figure 31. Key challenges to sustaining process excellence**

The solution to such issues is to work with stakeholders to develop clear control structures through active stakeholder involvement, alignment of incentives, and project overview. It is additionally important to keep cultural, strategic and political issues in mind. Such solutions were validated by survey results, which, as illustrated in Figure 32, identified the top 3 sustainability initiatives to be:

- Cross functional steering committee to improve involvement and control
- Tie to performance metrics to better align incentives
- Audit of completed projects for better feedback and oversight

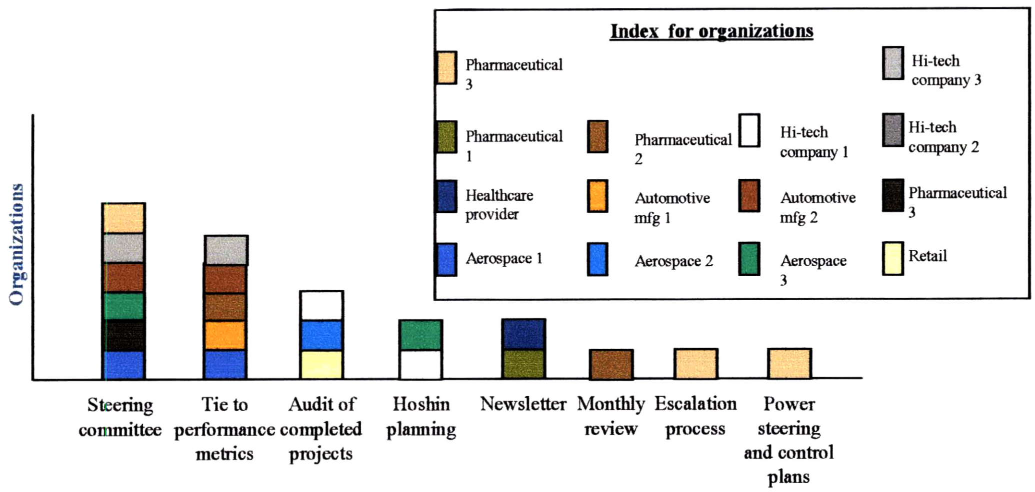



**Figure 32. Key sustainability measures followed by benchmarked organizations**

<u>Training</u>

Training is a key part of sustaining process excellence. The survey showed that 100% of benchmarked organizations have some form of training for the key stakeholders. The training methods however varied across organizations. 38.5% of respondents reported providing online training and the remaining 61.5% emphasized classroom training. Both methods have their pluses and minuses. Online training is cost effective and can be a good medium for individual learning; it is not very good for understanding complex team concepts where students can learn a lot from other's experiences. A combined online-classroom training medium thus can provide the best of both worlds.

## *4.4 Conclusions*

Benchmarking best practices using the industrial survey provided the following learnings that could potentially be implemented in the Broad Process Excellence Program:

- Develop a custom hybrid program that takes the best parts of several process improvement methodologies. It is important for this program to be cognizant of the following two important conclusions:
    - No tools can be universally applicable. Hence, the program should include multiple tools that apply to the diverse set of activities at the Broad Institute.
    - The program should include holistic and visual tools.
- There should be a strong buy-in from senior management.
- The initiatives should be led by functional process experts. An approach could be to have senior process owners to have a rotating sabbatical position within the group to identify process challenges and work on them.
- There should be high degree of alignment between success factors, process and individual metrics.
- Stakeholder teams should be formed to ensure stakeholder involvement and project oversight.

# Chapter 5

# System Design

In this chapter, knowledge gained from stakeholder analysis and benchmarking of industry best practices have been combined to come up with a system design for the Operations Sequencing Platform. The result is a detailed framework that starts with the enterprise design described in Chapter 3, identifies the key stakeholders and work-streams for each process step and based on benchmarking interviews and results recommends appropriate tools. Most of the information presented in this chapter has been taken from the Broad Process Excellence Handbook developed by the author for use by the Operations Sequencing Platform team members. Since the information is based on analysis already described in Chapters 3 and 4, the majority of the information in this chapter being will be in the form of tables.

## *5.1 The Operations Sequencing Platform Enterprise*

The largest of all platforms, Broad's Genome Sequencing Operations platform is a world leader in large-scale genome sequencing and analysis. It collaborates on a wide range of projects, including understanding the human genome by evolutionary comparison, decoding the genomes of pathogens, and discovering mutations in cancers. In order to continue to be the top choice for funding agencies, it needs to keep a close tab on the following success factors:

- Quality of read
- Operational clockspeed in development of new technologies
- Total cost of operations measured on the basis of cost per read

The enterprise structure of the Sequencing Operations Platform can be depicted as shown in Figure 33(a) and (b). This was originally introduced in Chapter 3 and will serve as the framework for our proposal.

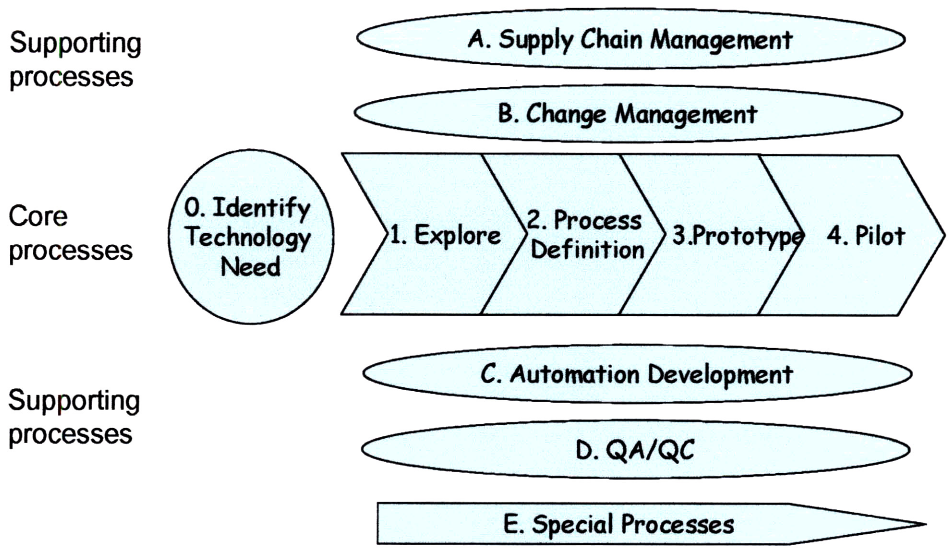



**Figure 33 (a) Overall enterprise structure**

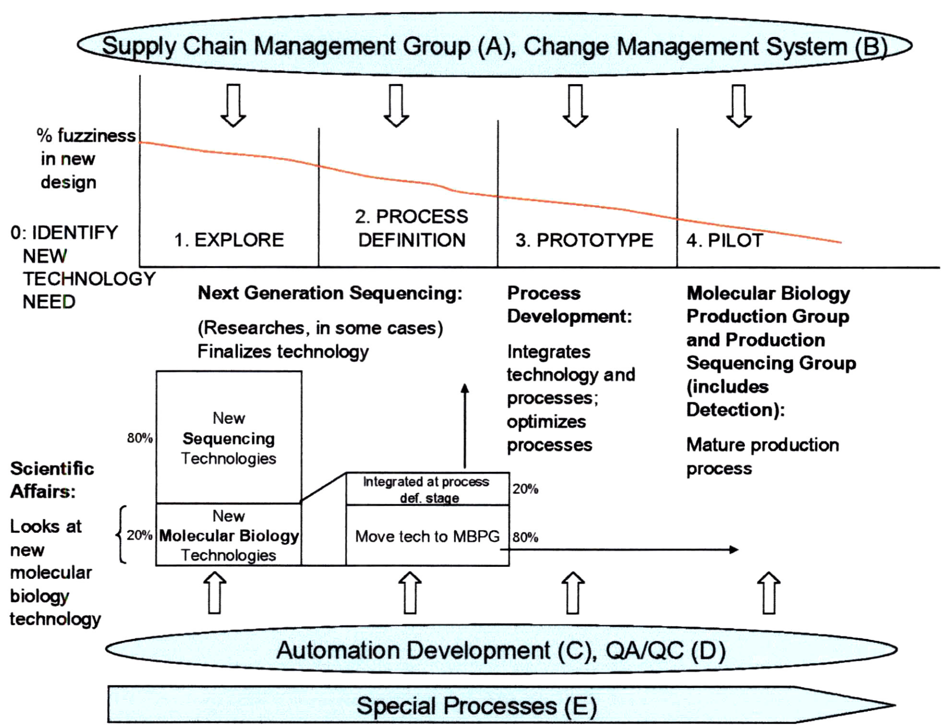



**Figure 33 (b) Enterprise structure with details on core processes**

The next sections will provide a list of recommended tools for the different process divisions of the enterprise.

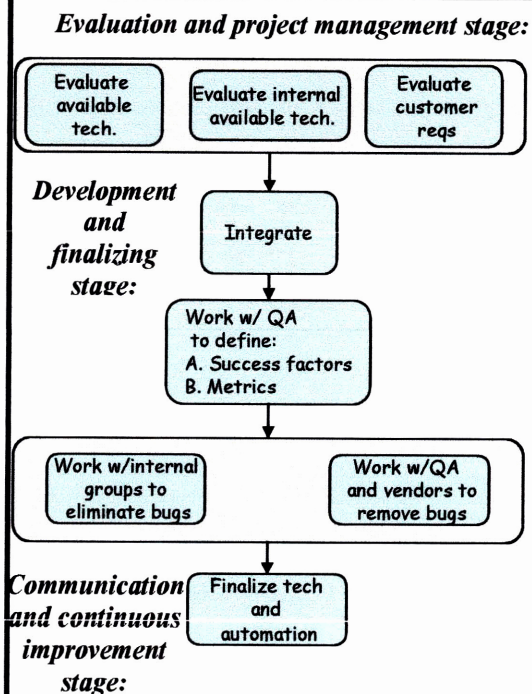
## 5.2 Recommended tools

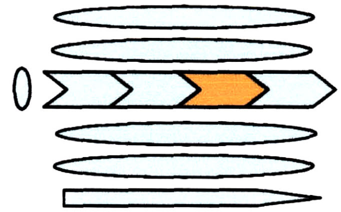
### 5.2.1 Explore New Technologies and Process Definition

5.2.1.1 New ligation techniques

| Stakeholders | Project Scale: Large / Incremental | Project Scale: Incremental: Medium | Project Scale: New: Medium | Project Scale: Prototype | Key Activities (work streams) | Tools recommended: |
|---|---|---|---|---|---|---|
| 1. External collaborators<br>2. R&D group of MBPG<br>3. Next Generation Sequencing | ☑ | | ☑ | ☑ | *Evaluation and project management stage:*<br>Literature review; Evaluate potential process improvements; Evaluate customer reqs | **1. Evaluation and project management stage:**<br>Project Management tools such as WBS, PERT and other resource utilization tools – can be used as built-in test) |
| | ☑ | ☑ | ☑ | ☑ | *Development and finalizing stage:*<br>Integrate and select top 2-3 options | **2. Development and finalizing stage**<br>a) DFSS tools<br>b) Visual workplace tools (Standard work, 5S and spaghetti diagram) to eliminate non-value added actions. This needs to be fairly flexible. |
| | ☑ | | ☑ | ☑ | Conduct feasibility tests | |
| | ☑ | | | ☑ | Finalize Design | |
| | ☑ | | | | Optimize for production | |
| | ☑ | | | | Pre-production test | |
| | ☑ | | | | Re-optimize process | |
| | ☑ | | | | Training, implement troubleshoot<br>*Communication and continuous improvement stage:* | **3. Communication and continuous improvement stage**<br>a) Communication of learning<br>b) Kaizen events |

5.2.2.2. Explore and finalize new sequencing technologies

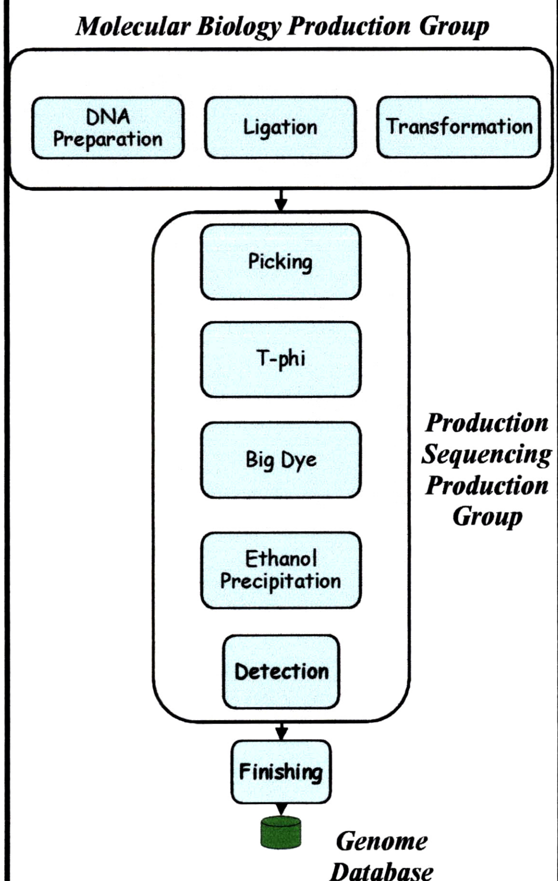
| Stakeholders | Key Activities (work streams) | Tools recommended: |
|---|---|---|
| 1. External collaborators<br>2. R&D group of MBPG<br>3. Scientific Affairs<br>4. Bio-informatics<br>5. Process Development<br>6. QA/QC<br>7. Senior management<br>8. Automation |  | ***1. Evaluation and project management stage:***<br><br>Project Management tools such as WBS, PERT and other resource utilization tools<br><br>**2. Development and finalizing stage**<br><br>a) DFSS tools<br>b) Visual workplace tools (Standard work, 5S and spaghetti diagram) to eliminate non-value added actions. This needs to be fairly flexible.<br><br>**3. Communication and continuous improvement stage**<br><br>a) Communication of learning<br>b) Kaizen events |



## 5.2.2 Process Development

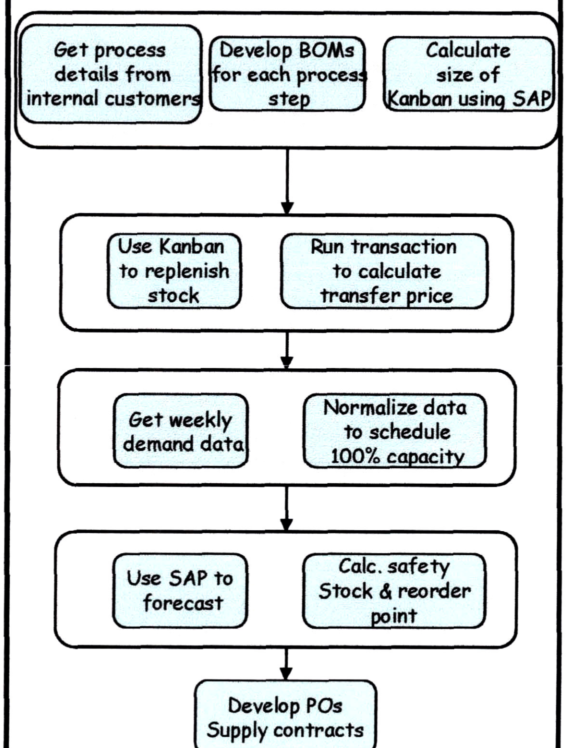
| Stakeholders | Key Activities (work streams) | Tools recommended: |
|---|---|---|
| 1. External collaborators<br>2. Senior management / Projects group<br>3. Next Generation Sequencing (NGS)<br>4. Bio-informatics<br>5. Automation<br>6. QA/QC<br>7. Production Sequencing Group | ***Evaluation and project management stage:***<br>Analyze tech Finalized by NGS<br>Define customer required success factor & metrics<br>↓<br>***Development and finalizing stage:***<br>Analyze resource availability<br>↓<br>Conduct feasibility studies<br>↓<br>Design & develop processes<br>↓<br>Optimize, Develop Metrics & acceptable data ranges<br>↓<br>***Communication and continuous improvement stage:***<br>Validate & implement<br>↓<br>Monitor & troubleshoot | ***1. Evaluation and project management stage:***<br><br>Project Management tools such as WBS, PERT and other resource utilization tools<br><br>***2. Development and finalizing stage:***<br><br>a) DFSS tools for process development<br>b) DMAIC tools for root cause analysis of problems coming in from pilot operations<br>c) Visual workplace tools (Standard work, 5S and spaghetti diagram) to eliminate non-value added actions. This needs to be fairly flexible.<br><br>***3. Communication and continuous improvement stage:***<br><br>a) Communication of learning<br>b) Kaizen events |

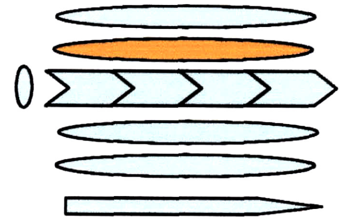
## 5.2.3 Pilot Operations – Molecular Biology Production Group and Production Sequencing Group

<table>
<tr><th>Stakeholders</th><th>Key Activities (work streams)</th><th>Tools recommended:</th></tr>
<tr>
<td>1. External collaborators<br>2. Senior management / Projects group<br>3. Bio-informatics<br>4. Automation<br>5. QA/QC<br>6. Process Development</td>
<td>
</td>
<td>1. Beginning new projects:<br>Project Management tools such as WBS, PERT and other resource utilization tools<br><br>2. Controlling processes:<br>Built-in tests such as in-process metrics for methods, end process metrics for output and resource utilization for pathways. Use Axiomatic Analysis to develop in-process metrics.<br><br>3. Eliminate non-value added actions:<br>Visual Workplace tools (Value stream map, Standard work, 5S and Spaghetti diagram[13])<br><br>4. Flag changes in protocol:<br>Mistake proofing to force stakeholders to flag system every time there is a change in protocol<br><br>5. Flag problems<br>Resource utilization and quality documents<br><br>6. Root cause analysis for problems:<br>DMAIC tools<br><br>7. Communication and continuous improvement<br><br>a) Communication of learning<br>b) Kaizen events</td>
</tr>
</table>

[13] A spaghetti diagram is graphical tool used to indicate movement of material or personnel as a product moves through its various production steps.

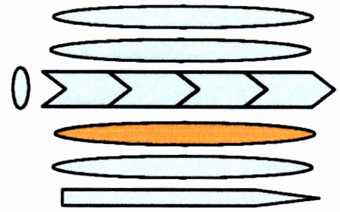
## 5.2.4 Supply & Quality Management

| Stakeholders | Key Activities (work streams) | Tools recommended: |
|---|---|---|
| 1. External collaborators<br>2. Senior management / Projects group<br>3. Next generation sequencing<br>4. PSG<br>5. MBPG<br>6. QA/QC<br>7. Process Development |  | ***1. Supplier selection and order placing pre-RFQ***<br><br>a) Spend and usage analysis to segment procured items<br>b) Optimize product packages for standard items<br>c) e-auction for standard parts<br>d) Kitting and bundling of low value items with high value items as a step towards long term contracts for high value items. Different types of contracts can be looked at protect against fluctuation in price and supply of high value items.<br><br>***2. Continuous improvement and sustaining improvement***<br><br>a) Visual Workplace tools (Standard work, 5S and spaghetti diagram) to eliminate non-value added actions<br>b) In-process metrics to flag problems<br>c) Communication of learning<br>d) Kaizen events |



## 5.2.5 Change Management and Communication

| Stakeholders | Key Activities (work streams) | Tools recommended: |
|---|---|---|
| 1. External collaborators<br>2. Senior management / Projects group<br>3. Next generation sequencing<br>4. PSG<br>5. MBPG<br>6. QA/QC<br>7. Process Development | Develop mailing list to collect changes from Process Owners<br>↓<br>Collect protocol change information using std template<br>↓<br>Enter information in eNovator and assign tasks | 1. Metrics and ownership alignment to take care of agency problem.<br>2. One solution is to use a combination of bar codes and access database to monitor changes and flag changes. The logistics will be as follows:<br>a. User scans bar code of material when he/she takes it from the mini-mart. This can have dual purposes:<br>i. Allow system to monitor demand<br>ii. Give a signal to the Kanban system that mini-mart needs to be replenished<br>b. Since the Kanban system was originally based on usage range for every material, it should be fairly easy for the system to flag whenever usage is outside the pre-defined range. This flag can mean either of two things:<br>i. The originally defined range was not appropriate<br>ii. There has been a change in the protocol. |



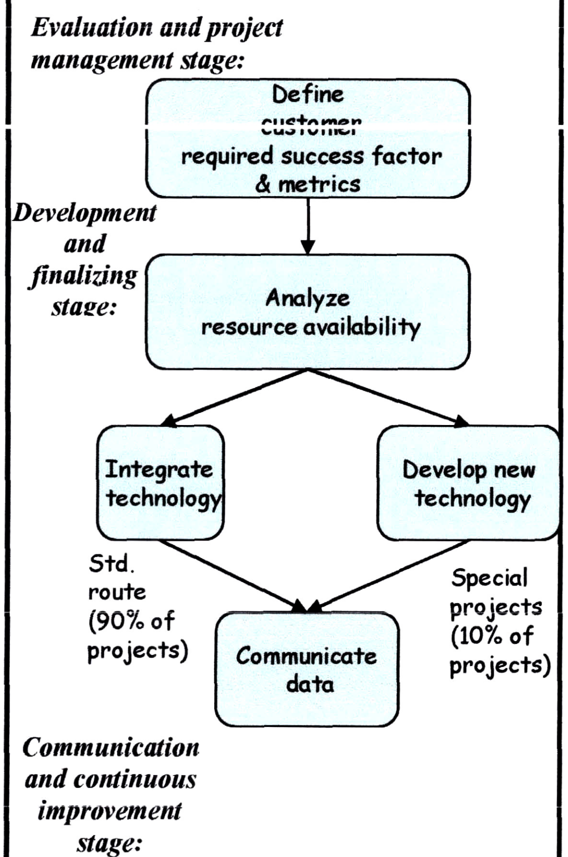
### 5.2.6 Automation

| Stakeholders | Key Activities (work streams) | Tools recommended: |
|---|---|---|
| 1. External collaborators<br>2. Senior management / Projects group<br>3. Next generation sequencing<br>4. PSG<br>5. MBPG<br>6. QA/QC<br>7. Process Development | ***Evaluation and project management stage:***<br>Define customer requirements<br>↓<br>***Development and finalizing stage:***<br>Research and provide options<br>↓<br>Evaluate and implement<br>↓<br>***Communication and continuous improvement stage:***<br>Troubleshoot and support | ***1. Evaluation and project management stage***<br><br>Project Management tools such as WBS, PERT and other resource utilization tools (can be used as built-in test)<br><br>***2. Development and finalizing stage***<br><br>a) DFSS tools for process development<br>b) DMAIC tools for root cause analysis of problems coming in from pilot operations<br>c) Visual workplace tools (Standard work, 5S and spaghetti diagram) to eliminate non-value added actions. This needs to be fairly flexible.<br><br>***3. Communication and continuous improvement stage***<br>a) Communication of learning<br>b) Kaizen events |

## 5.2.7 Quality Assurance and Quality Control

| Stakeholders | Key Activities (work streams) | Tools recommended: |
|---|---|---|
| 1. External collaborators<br>2. Senior management / Projects group<br>3. Next generation sequencing<br>4. PSG<br>5. MBPG<br>6. Process development | Develop metrics with customer (tech and process dev) for new technologies and processes<br>↓<br>Measure and track data for both new technologies and current processes<br>↓<br>Troubleshoot and support | 1. DMAIC tools for root cause analysis<br>2. Visual Workplace tools (Standard work, 5S and spaghetti diagram) to eliminate non-value added actions. This needs to be fairly flexible.<br>3. Communication of learning |

## 5.2.8 Special Processes

<table>
<tr><th>Stakeholders</th><th>Key Activities (work streams)</th><th>Tools recommended:</th></tr>
<tr>
<td>1. External collaborators<br>2. Senior Management / Projects group<br>3. Production sequencing group</td>
<td>
</td>
<td>1. Evaluation and project management stage:<br><br>a) Project Management tools such as WBS, PERT and other resource utilization tools<br>b) In-coming inspection and std feedback that includes these results<br>c) Top-down analysis to prioritize projects based on breakdown of projects based on success factors<br><br>2. Development and finalizing stage:<br><br>a) DFSS tools<br>b) Visual Workplace tools (Standard work, 5S and spaghetti diagram) to eliminate non-value added actions. This needs to be fairly flexible.<br><br>3. Communication and continuous improvement stage:<br><br>a) DMAIC tools for root cause analysis<br>b) Communication of learning</td>
</tr>
</table>

## *5.3 Conclusions*

The information presented in this chapter forms the foundation to implement the Broad Process Excellence Program and shows that the processes in Operations Sequencing Platform are fairly different from each other. This warrants the need for custom hybrid tools based on the marriage of stakeholder analysis and benchmarking of best practices described in Chapters 3 and 4. The next chapter showcases the usage of some of the tools mentioned in this chapter to solve a typical problem experienced by the organization.

# Chapter 6

# Improving the performance of the Duncan

This chapter showcases some of the tools recommended in Chapter 5 to solve the problem of variability and poor performance of the Duncan, a key DNA processing step. The problem had remained unsolved after 3 months of extensive research before our team started working on it. The chapter covers the background and motivation for the project, desired outcomes and usage of tools such as Work Breakdown Structure, Process Flow, Axiomatic Analysis, Cause & Effect Analysis, Failure Mode and Effect Analysis, Measurement System Analysis and additional targeted experiments to solve the problem. The chapter assumes the reader has a fundamental understanding of the concept of DNA and its processing.

## *6.1 Background and motivation for the project*

The Duncan, shown in Figure 34, is a thermal cycler that performs a modified polymerase chain reaction[14] (PCR) to conduct one of the most important steps of Sanger Sequencing – amplification of DNA and adding chain termination dyes for the detector to determine the nucleotide order of a given DNA sequence. The steps are described in the next sections.

**Figure 34. The Duncan Thermal Cycler**

[14] Sumanas, Inc., NHGRI, Broad Internal Documentation

### 6.1.1 Duncan cycling

The Duncan Cycler is a thermal cycler which can be used to amplify a single copy of the target genomic DNA into billions of identical copies of different lengths with fluorescent dDDTP attached to the end for ease of detection during sequencing. Figure 35 and 36 illustrates a sample DNA segment with the target DNA zoomed in.

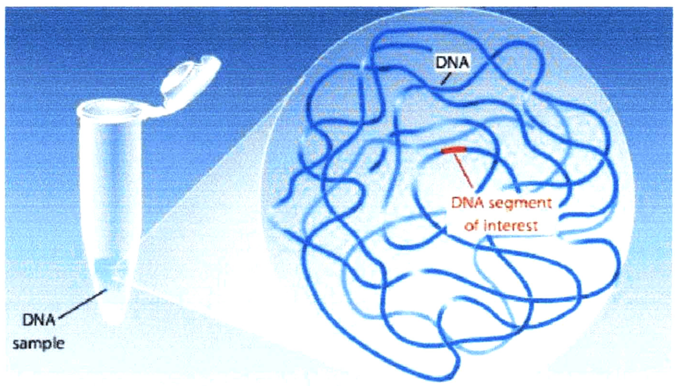



**Figure 35. Genomic DNA**

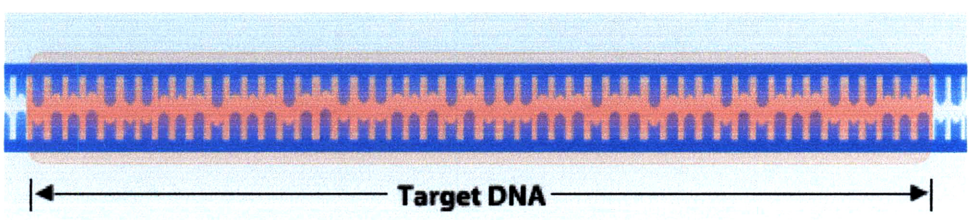



**Figure 36. Target DNA**

The following nucleosides and enzymes are added to the sample DNA as an input to the Duncan process:

- DNA Polymerase I
- dATP
- dGTP
- dCTP
- dTTP
- Limiting amounts of fluorescently labeled ddATP, ddGTP, ddCTP, ddTTP (these dideoxynucleosides act as terminating nucleosides and attach to the respective base-

pairs i.e. ddATP to Thymine (T), ddGTP to Cytosine (C), ddCTP to Guanine (G), and ddTTP to Adenine (A)

- DNA primer – usually 20 nucleosides long (comprising of A, T, C, G) and are complimentary in sequence to the ends of the target DNA

The mixture comprising of the DNA sample and reagents mentioned above will be referred to as PCR mix for the rest of this chapter.

The Duncan process consists of three temperature dependent cycles repeated 25 times in the order mentioned below:

- Cycle 1: Denature

Denature refers to breaking the hydrogen bonds that hold the DNA strands together. For this to happen successfully, the PCR mix is heated at around 96° C and held at this temperature for ~20 seconds. The step is illustrated in Figure 37.

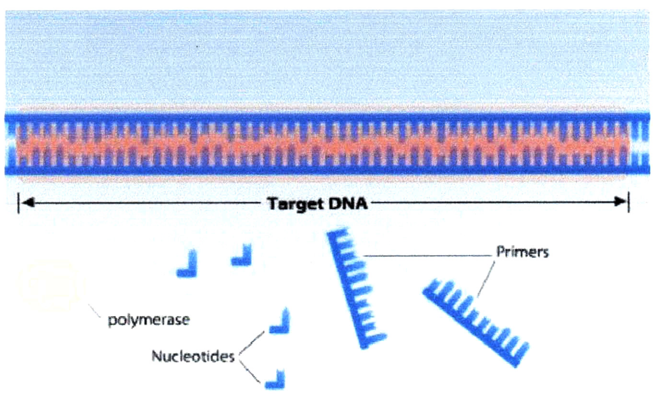



**Figure 37. Denature**

- Cycle 2: Primer Anneal

As illustrated in Figure 38, this step results in DNA primers forming hydrogen bonds with their complementary sequences in the denatured target DNA. The hydrogen bond formation follows the base-pairing rule i.e. base A pairs with base T while base C pairs with base G. Primer anneal is temperature sensitive and occurs at a PCR mix temperature of 50° C with a holding time of ~15 seconds.

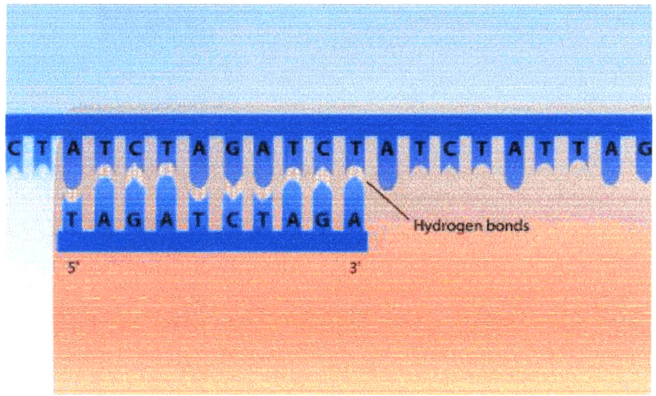



**Figure 38. Primer Anneal**

- Cycle 3: Polymerase Chain Reaction

In this step, the dATP, dGTP, dCTP and dTTP along with the fluorescently labeled ddATP, ddGTP, ddCTP, ddTTP present in the PCR mix form hydrogen bonds with the target DNA with the primer sites acting as the starting positions. This results in formation of double stranded DNA as illustrated in Figure 39. This occurs by holding the PCR mix at 60° C for 4 minutes.

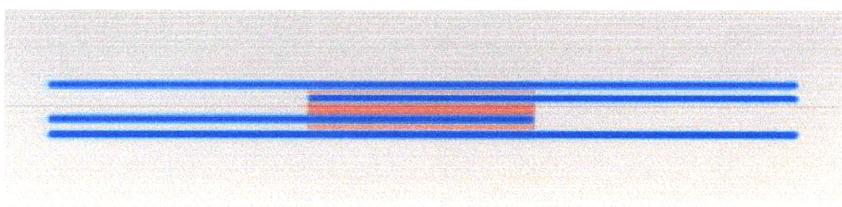


**Figure 39. Hydrogen bonds development to result in multiple copies of double stranded target DNA**

However, one important point to note in this step is that the florescent labeled ddNTPs act as terminating nucleosides, as shown in Figure 40.

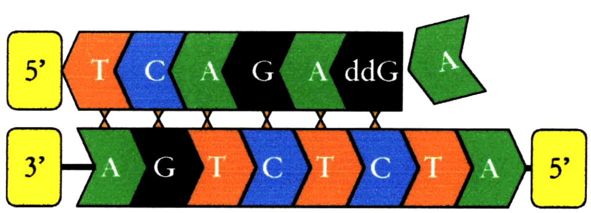



**Figure 40. Dideoxynucleosides prevent further chain extension**

This results in the formation of billions of copies of the target DNA fragments with varying lengths as illustrated in Figure 41.

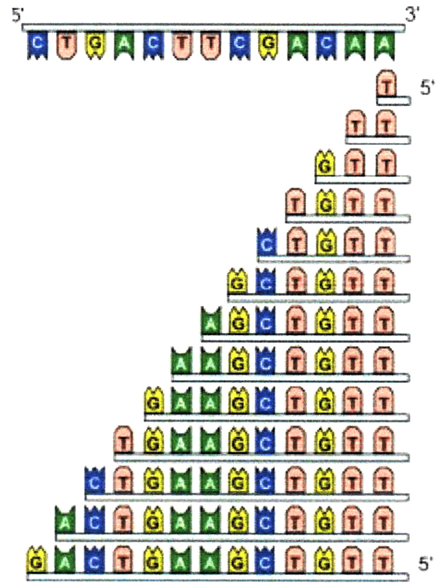


**Figure 41. Multiple copies of DNA having varying lengths**

As mentioned earlier, cycles 1 through 3 are repeated 25 times before the processed DNA is moved to the next step – detection of sequence.

### 6.1.3 Processing Metrics

Due to absence of in-process metrics, the performance of the Duncan is measured using sequence quality at the end of the detection step. In order to better understand these metrics, it is important to understand the detection process. Detection comprises of the following three key steps:

- Separation of the DNA fragments according to lengths by a process called gel electrophoresis.
- Exposure of the DNA fragments to a laser that excites the fluorescent dyes in the fragments as they pass.
- Collection of the emission intensities at four different wavelengths by the detector.

The final output are usually processed traces displayed in the form of chromatograms consisting of four curves of different colors, each curve representing the signal for one of the four bases and drawn left to right in the direction of increasing time to detection. This is illustrated in Figure 42. A special software program called "base-caller algorithm" looks for peaks in the output trace as indication of the base type.

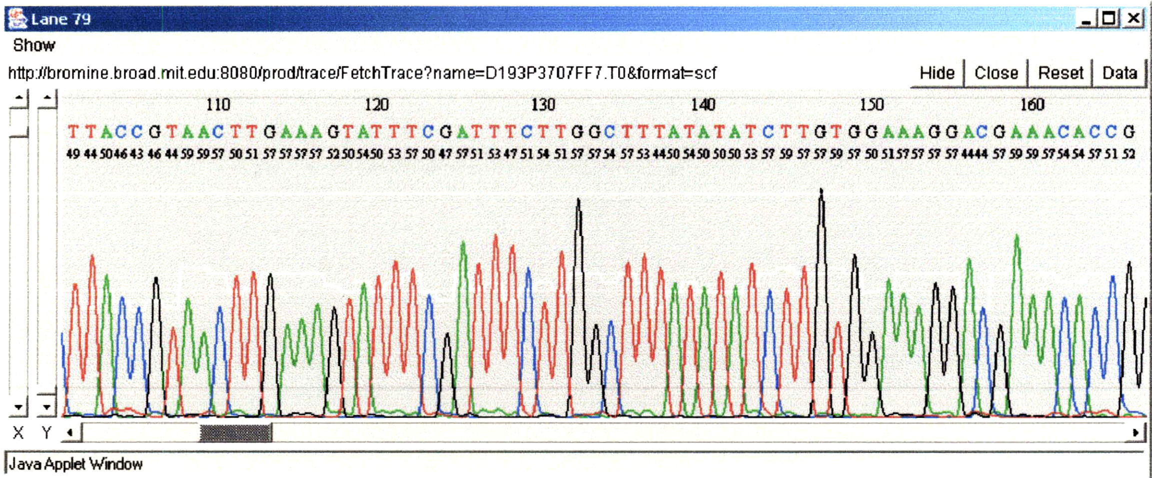



**Figure 42. A typical detection output**

An idealized output trace consists of evenly spaced, non-overlapping peaks. However, reality is rarely so. This departure from reality can be due to several reasons, the primary being imperfections in previous sequencing reaction steps such as in the Duncan. The detection metrics are thus indirectly representative of the Duncan cycling quality. The principal sequencing quality metrics are phred score[15], read length and sequence pass. The metrics are described below:

- Phred score:

Phred is a base-calling program for DNA sequence traces. It uses a four-phase procedure to determine a sequence of base-calls from the processed output trace. These 4 phases happen very quickly taking less than half a second to complete. The 4 phases are:

1. Phase 1 – determine idealized peak locations (predicted peaks). The idea is to use the fact that fragments are locally relatively evenly spaced, on average, in most regions of the gel, to determine the correct number of bases and their idealized evenly spaced locations in regions where the peaks are not well resolved, noisy, or displaced (as in compressions).
2. Phase 2 – observe peaks identified in the trace.

[15] Brent Ewing, LaDeana Hillier, Michael C. Wendl and Phil Green, Base-Calling of Automated Sequencer Traces, Using Phred. I. Accuracy Assessment, GENOMIC RESEARCH 8:175–185. Brent Ewing and Phil Green, Base-Calling of Automated Sequencer Traces, Using Phred. II. Error Probabilities, GENOME RESEARCH 8:186–194

3. Phase 3 - observe peaks matched to the predicted peak locations, omitting some peaks and splitting others. Associate peaks with 1 of the 4 bases and thus use the ordered list of matched observed peaks to determine a base sequence for the trace.
4. Phase 4 – observe the uncalled (i.e., unmatched) peaks and check for any peak that appears to represent a base but could not be assigned to a predicted peak in the third phase, and, if found, insert the corresponding base into the read sequence.

Simply stated, phred considers peak-to-peak spacing (bases) versus uncalled bases, and the resolution of the bases. The program uses these parameters to score and estimate the accuracy of the called base. The accuracy or simply probability of calling a wrong base is measured by a quality score, also known as Q score, which is measured as follows:

$Q = -10 \times \log_{10}(p)$ ..............................................................(1)

where p = Probability of error i.e. calling a wrong base; Q = Quality (phred) score

This being a logarithm scale follows the score set shown in Table 10.

**Table 10. Q scores**

| Quality Score | % Accuracy | Error Rate | Comments |
|---|---|---|---|
| Q10 | 90% | 1 in 10 | |
| Q20 | 99% | 1 in 100 | Minimum Quality Standard |
| Q30 | 99.9% | 1 in 1000 | |
| Q40 | 99.99% | 1 in 10,000 | |

The quality metric thus used is the number of bases with a Q score of 20 or simply Q20. The Broad Institute uses a 384 well plate shown in Figure 43 to analyze DNA. Each well has an individual Q20 score. In order to get an overall quality snapshot, the Institute uses a metric called Q20 All, which is the average number of bases with a Q20 score across all 384 wells in a plate. 126 such plates are loaded in a cage during DNA processing. Figure 44 and 45 shows illustrates loading of plates in a cage and then in the Duncan. This large scale processing helps significantly increase the DNA processing efficiency.

**Figure 43. A 384 well plate used at the Broad Institute**

**Figure 44. Step 1 of loading DNA processing plates – 42 plates loaded and locked in mini-cage**

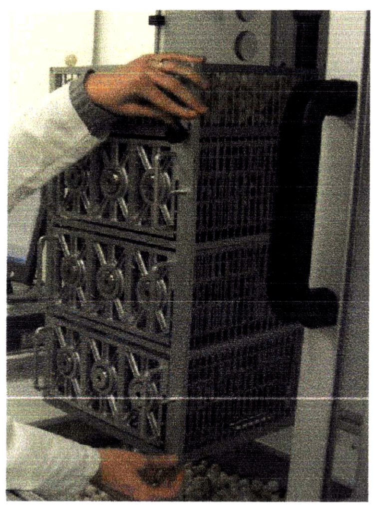


**Figure 45. Step 2 of loading DNA processing plates – 3 mini-cages loaded and locked in a larger cage in the Duncan**

- Read Length

The Read Length is determined by analyzing the Q score of a sliding window of 20 bases across a DNA fragment and iteratively measuring the length of read bases till the average Q score of the 20 base-window is less than Q15. This is illustrated in Figure 46.

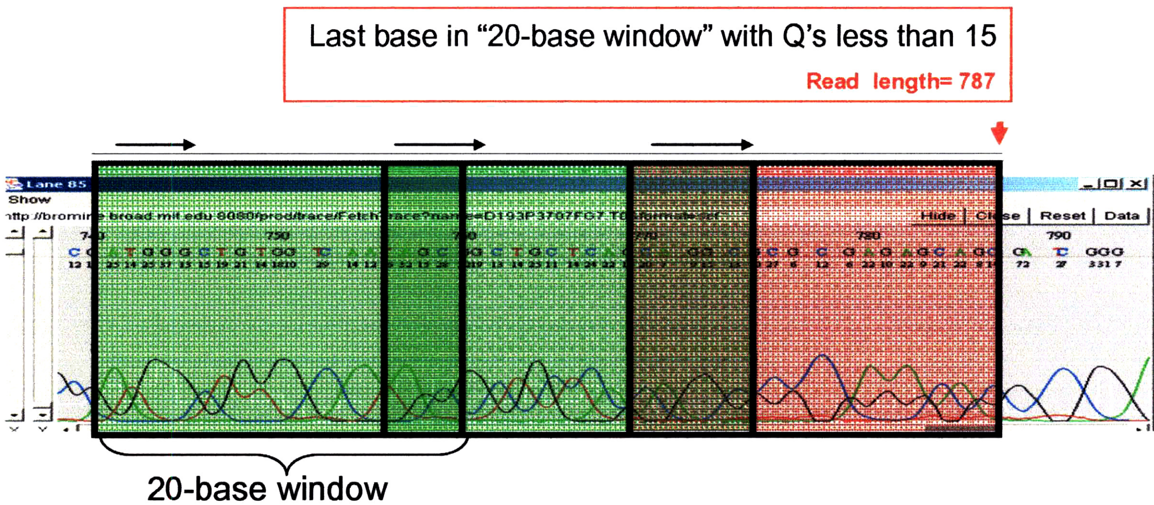



**Figure 46. Read length**

- Sequence Pass

If the average Q score for the bases # 100-300 of the DNA fragments in a well is greater than or equal to Q20, the well is rated as passed. Sequence Pass is rated as a pass percent given by the following equation:

$$\text{Pass rate \%} = \frac{\text{\# of passing wells}}{96} \quad \text{(2)}$$

### 6.1.4 The problem and initial efforts

The quality metrics of the Duncan had always been a challenge. Table 11 shows the average quality measurements for July and August, 2006.

**Table 11. Average quality performance for the Duncan in July and August 2006**

| Metric | Mean Score | Preferred Score |
|---|---|---|
| Q20 All | **599** | As close to 700 as possible |
| Read Length | 853 | Greater than 700 |
| Sequence Pass | **88.9%** | Greater than or equal to 94% |

As can be seen from Table 11, the Q20 All and Sequence Pass were not meeting the specifications. An internal Broad team comprising of team members from the Sequencing Operations Platform was formed to solve the problem. The team brainstormed and identified the following possible reasons for such performance:

- Time delay between Duncan cycling and reaction cleanup
- Position of plates before loading and after unloading
- Position of the DNA plate inside the Duncan during processing
- Seal
- Centrifuging DNA plates post-Duncan cycling

Section 6.2 describes the results for experiments conducted to solve these potential causes.

## *6.2 Background experiments*

Between August and December 2006, a series of experiments were conducted to solve potential causes for poor Duncan performance. In a majority of the cases, the Duncan results were compared to the Hybaid, a thermal cycler also used for conducting PCR processing of DNA. The Hybaid has had a relatively consistent quality performance and thus served as a capable benchmark. The experiments serve as a background to the project conducted as a part of the thesis and also represents a typical problem solving exercise at the Broad. This section describes the results for the experiments.

### 6.2.1 Time delay between Duncan cycling and reaction cleanup

Reaction cleanup is an intermediary step between Duncan cycling and Detection. Herein the plates subjected to a centrifuging process to remove any excess water or liquid on top of the processed DNA. Figure 47 shows a picture of the centrifuging machine with plates.

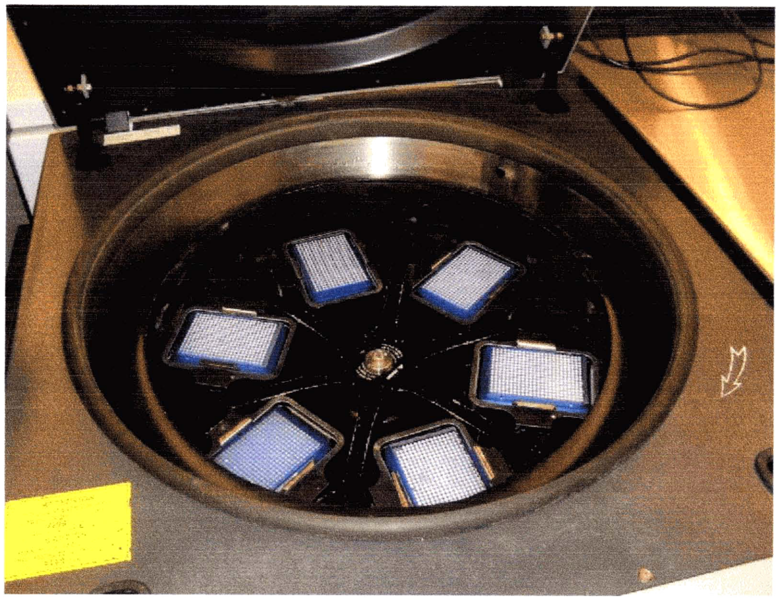


**Figure 47. Centrifuging machine with plates**

Although the reaction cleanup step occurs at 4° C, the plates typically sit in room temperature between Duncan cycling and reaction cleanup. The hypothesis was that DNA would get degraded during this time delay and thus give less than acceptable results. A series of tests with different time delays was conducted to test this hypothesis. Figure 48 and 49 shows the effect of time delay on Sequence Pass and Q20 All. The data shown is for days with maximum variability. As can be observed the effect on mean performance was not very significant.

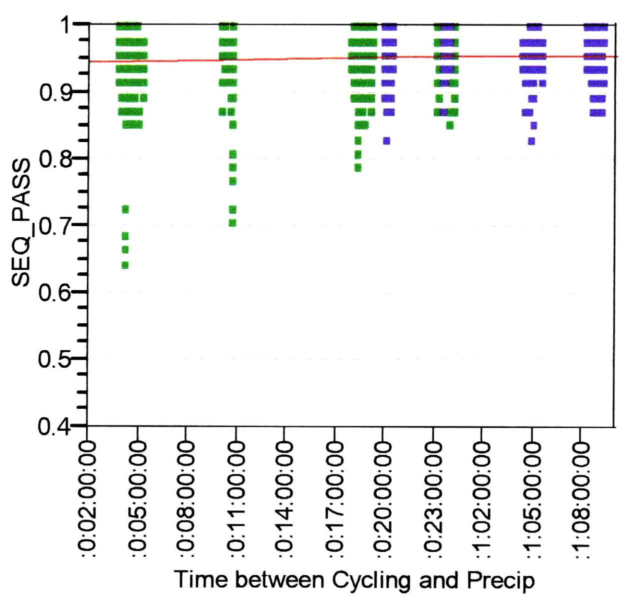



**Figure 48. Effect of time delay on Sequence Pass**

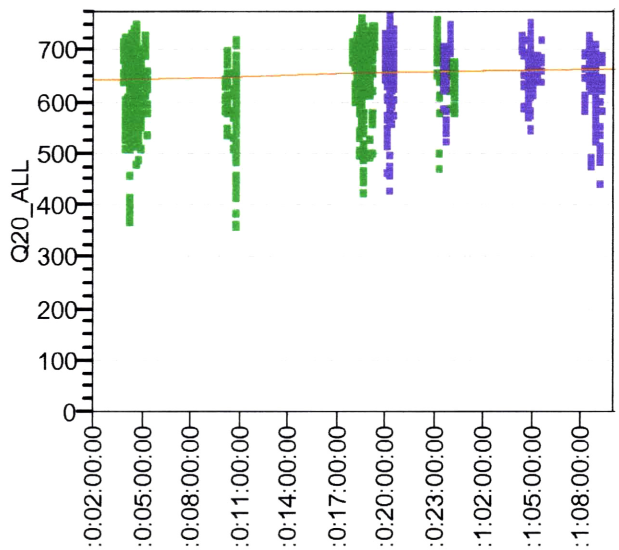



**Figure 49. Effect of time delay on Q20 All**

### 6.2.2 Position of plates before loading and after unloading

2 plates are placed on top of each other during loading in the Duncan cages. There are two ways in which they can be oriented during the loading process – horizontal with one of the plates placed upside-down or sideways. This is illustrated in Figure 50.

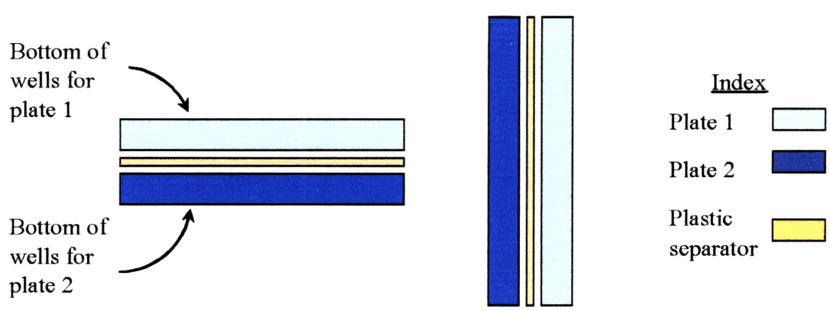



**Figure 50. Orientation options while loading DNA plates in cage**

The hypothesis was that it was possible for the PCR mix in plate 1 (refer Figure 50) to fall out of the wells while waiting to be loaded in the Duncan. As shown in Figure 51 and 52, results showed that changing the plate orientation during loading and unloading of Duncan cages from horizontal to sideways improved the mean Q20 All score by 25% and mean Sequence Pass by 14.3%.

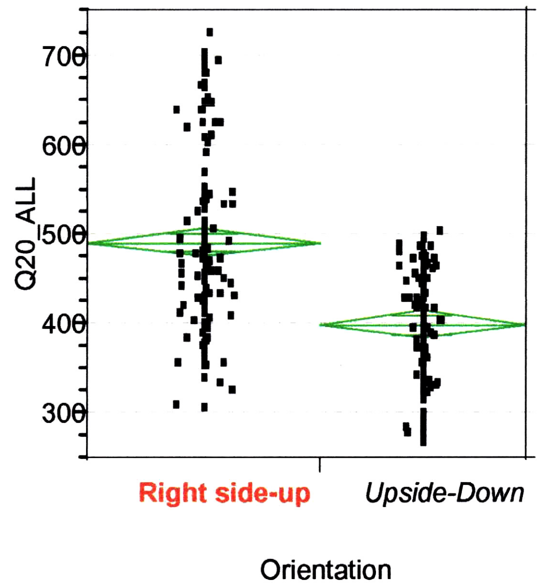



**Figure 51. Impact of plate orientation during loading on Q20 All**

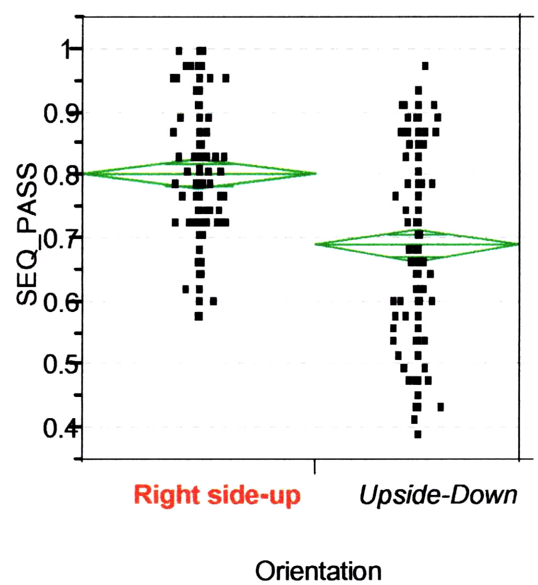



**Figure 52. Impact of plate orientation during loading on Q20 All**

## 6.2.3 Position of the DNA plate inside the Duncan during processing

Based on the hypothesis that the temperature in different parts of the well could be different, a series of experiments was to conducted to understand the impact of position of the DNA plate in the Duncan cage. As shown in Figures 53 and 54, the position of the DNA plate had marginal impact on both Q20 All and Sequence Pass. It is however interesting to note that there were several outlier points in the data for both Q20 All and

Sequence Pass. Since the data used for determining quality of data is based on box plot analysis, these outliers were not considered. This is a fairly standard practice at the Broad Institute.

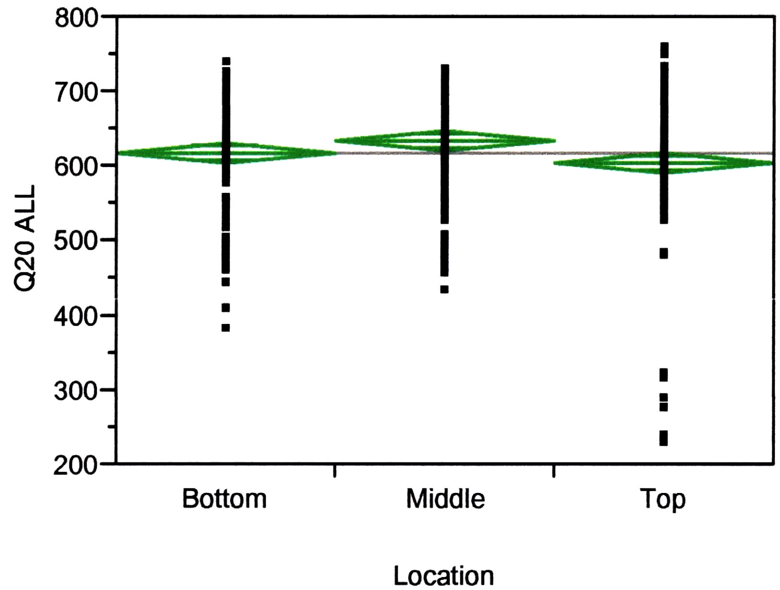



**Figure 53. Impact of position of DNA plate on Q20 All**

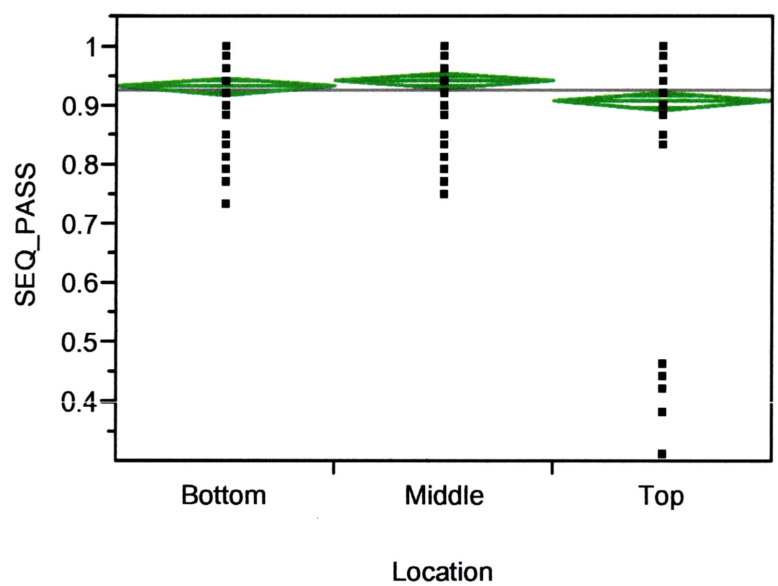



**Figure 54. Impact of position of DNA plate on Sequence Pass**

### 6.2.4 Seal

Preliminary test results showed that the seal type had a significant on the consistency of the quality results. The Core/Pilot Sequencing Group is as a consequence analyzing different seal options, which shall remain outside the scope of the Duncan project.

### 6.2.5 Centrifuging DNA plates post-Duncan cycling

Test DNA plates were centrifuged to test the hypothesis that such action would help better separate the heavier DNA fragments. As illustrated in Figure 55, this action proved to further worsen Q20 All measurements.

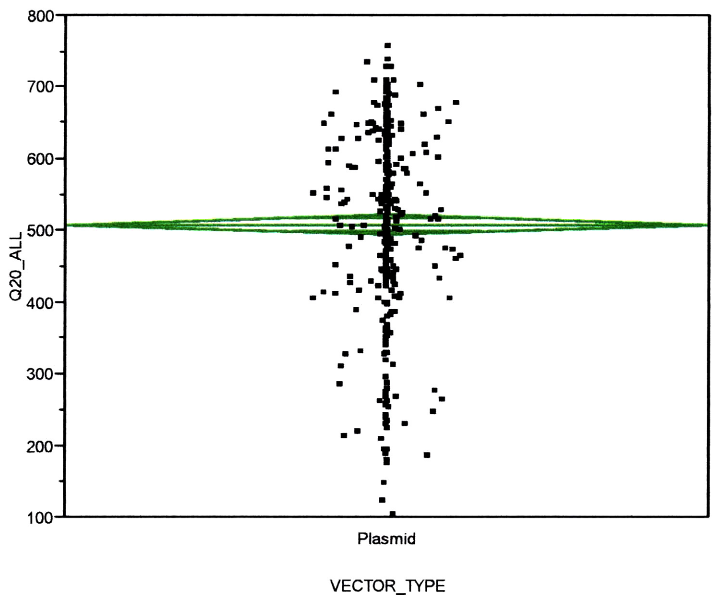



**Figure 55. Impact of post-Duncan centrifuging on Q20 All**

## 6.3 Improving the performance of the Duncan Cycler

The rest of this chapter describes the efforts to improve the performance of the Duncan Cycler using tools recommended in Chapter 5. As a first step, the Work Breakdown Structure (WBS) shown in Figure 56 was created to develop a structure for conducting the project. The next sections provide more details for each step of the WBS as the key variables are identified and a solution is found.

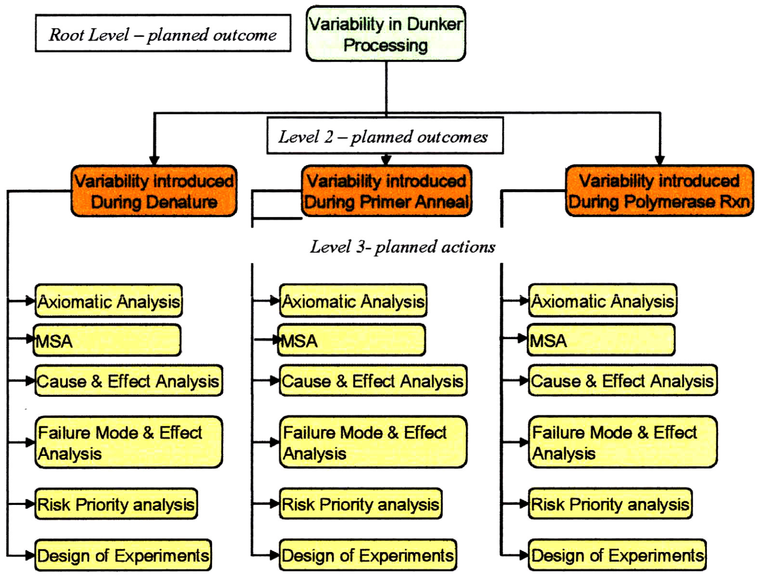



**Figure 56. Work Breakdown Structure for improving the performance of the Duncan Cycler**

It is important to note that while the WBS states Design of Experiments (DOE), it was later found out that the cost of conducting a DOE would be much greater than the expected cost savings. It was decided not to conduct a DOE. Instead a series of experiments were conducted to develop necessary data and manipulate the key levers identified.

### 6.3.1 Axiomatic Analysis

A useful Design for Six Sigma tool, Axiomatic Analysis was used to map the functional requirements for Denature, Primer Anneal and Polymerase Reaction with design parameters. The goal was to set the stage for identifying key parameters for conducting the Cause & Effect Analysis described in the next section.

Figure 57, 58 and 59 show the Axiomatic Analysis results for Denature, Primer Anneal and Polymerase Reaction.

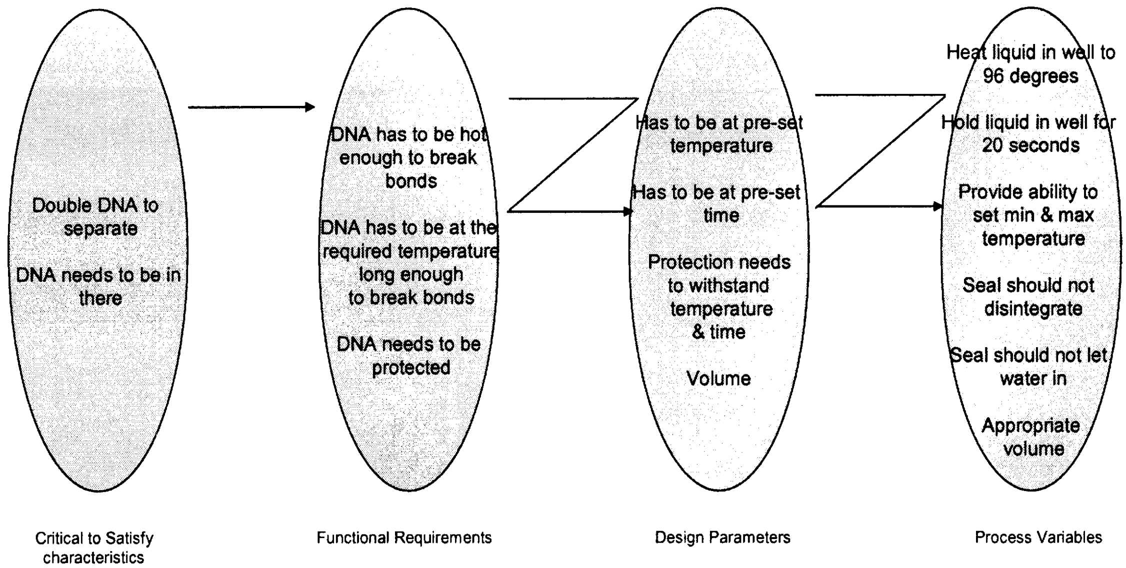



**Figure 57. Axiomatic Analysis for the Denature process**

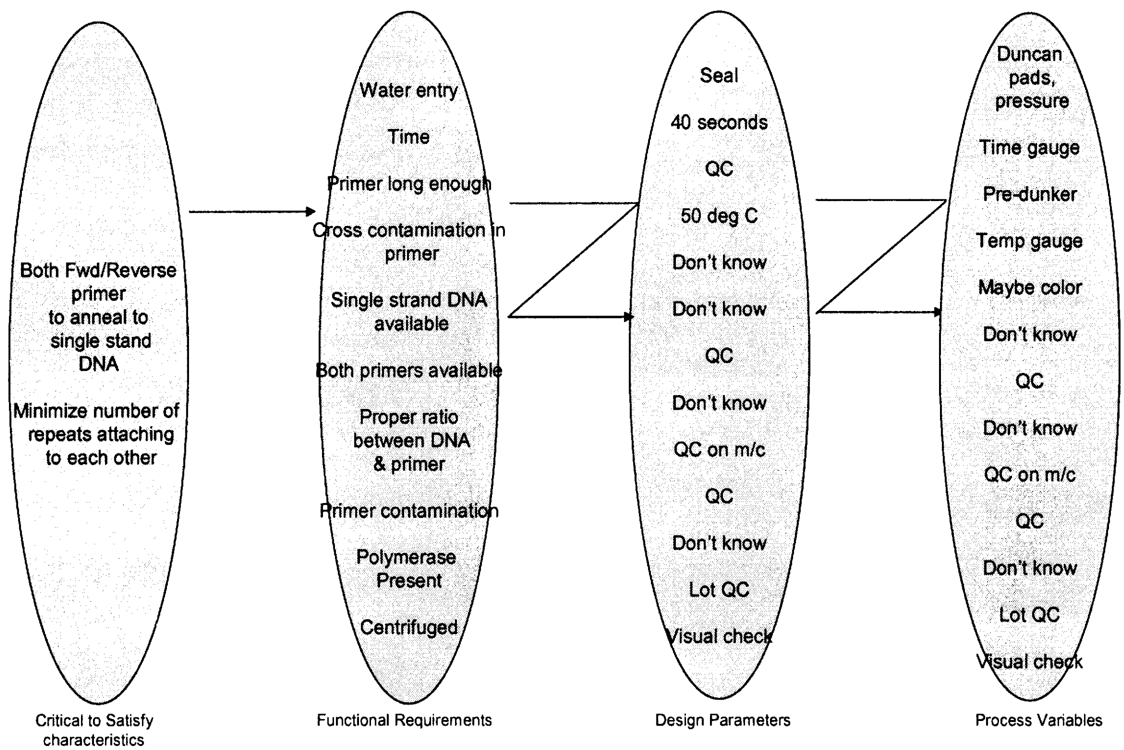



**Figure 58. Axiomatic Analysis for the Primer Anneal process**

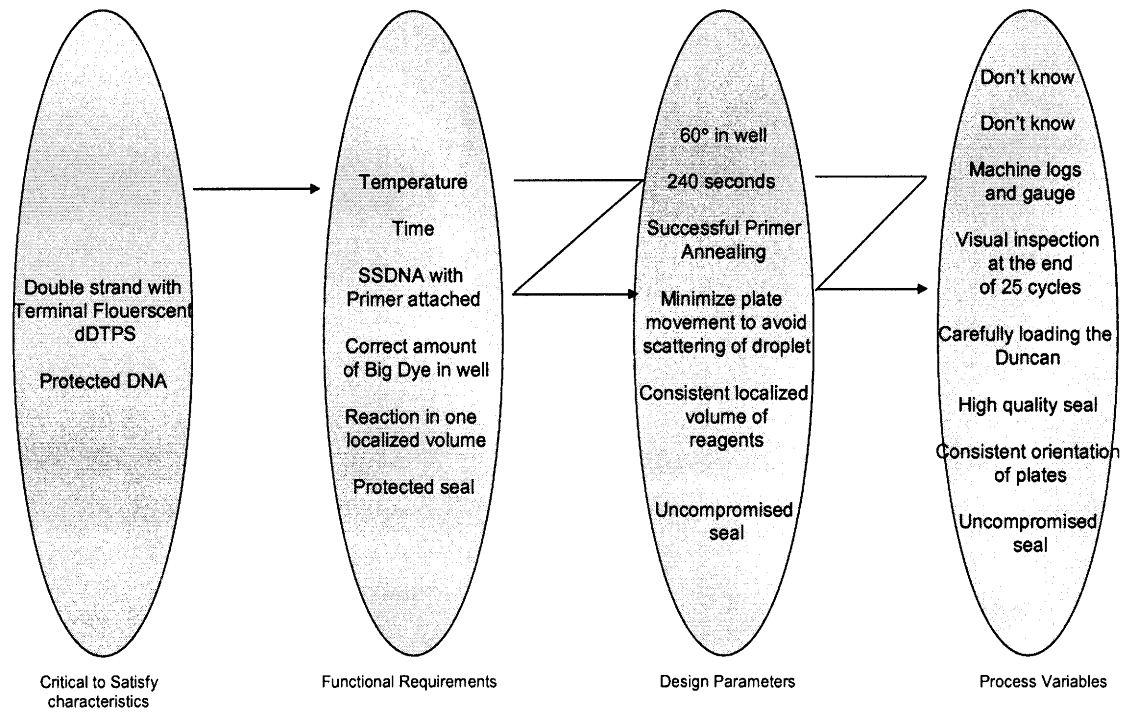



**Figure 59. Axiomatic Analysis for the Polymerase Reaction process**

The results showed that the key factors in these processes were:

- Reaction time
- Reaction temperature in the well
- Seal quality
- Volume of PCR mix

It was additionally observed that there were no processes in place to measure several key design parameters.

### 6.3.2 Cause & Effect Analysis

Cause & Effect Analysis was the next root-cause analysis tool used to understand the reasons that could potentially cause poor performance in different steps of the Duncan cycling process. Figure 60, 61 and 62 show the Cause & Effect Analysis charts for the different cycles of the Duncan.

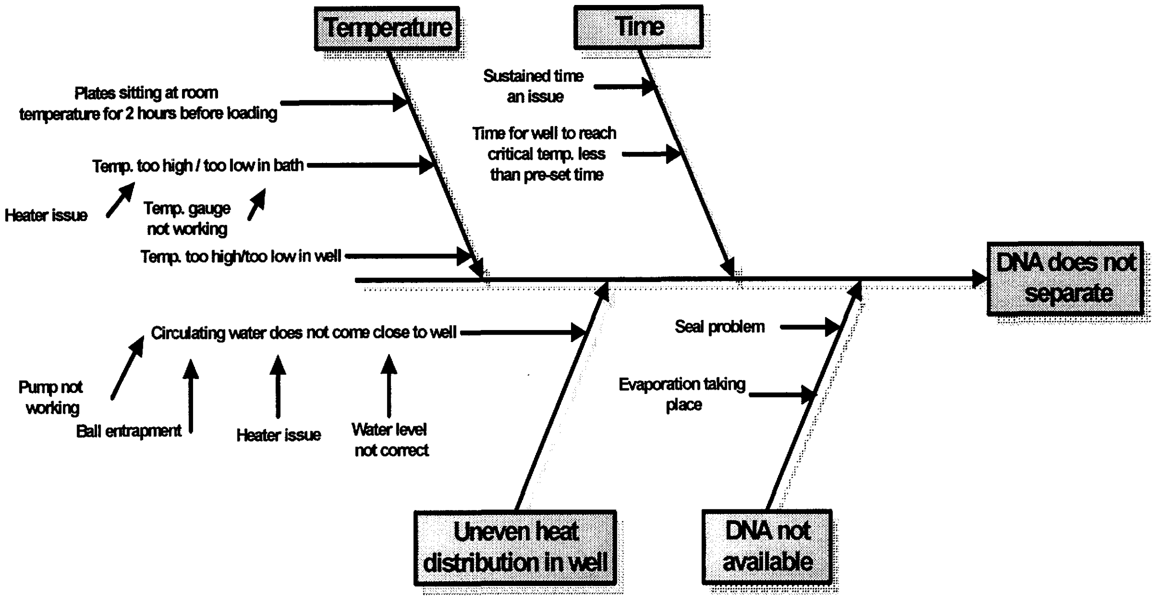



**Figure 60. Cause & Effect Analysis for Denature step**

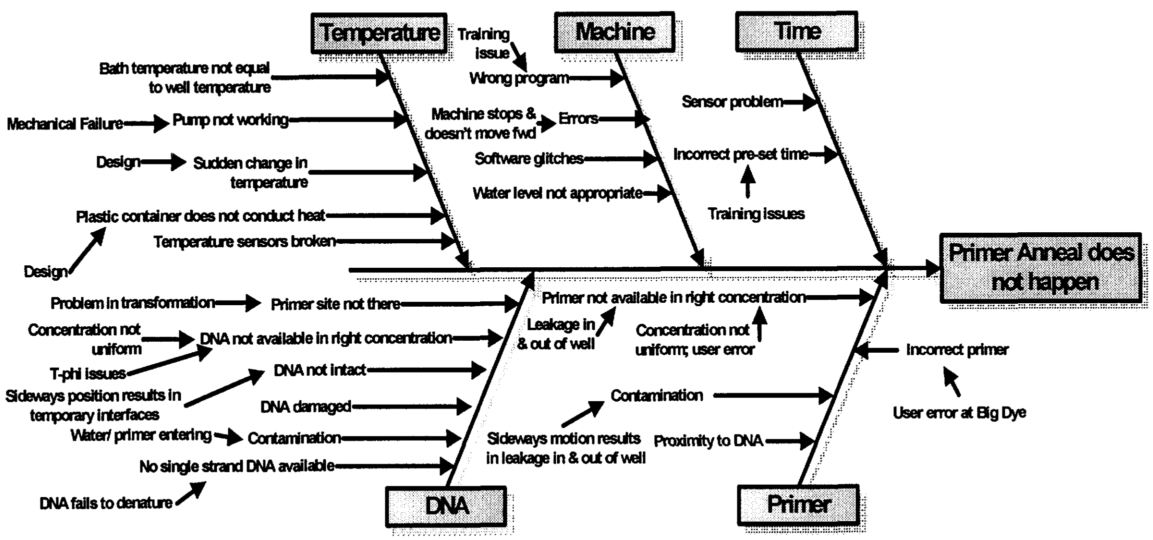



**Figure 61. Cause & Effect Analysis for Primer Anneal step**

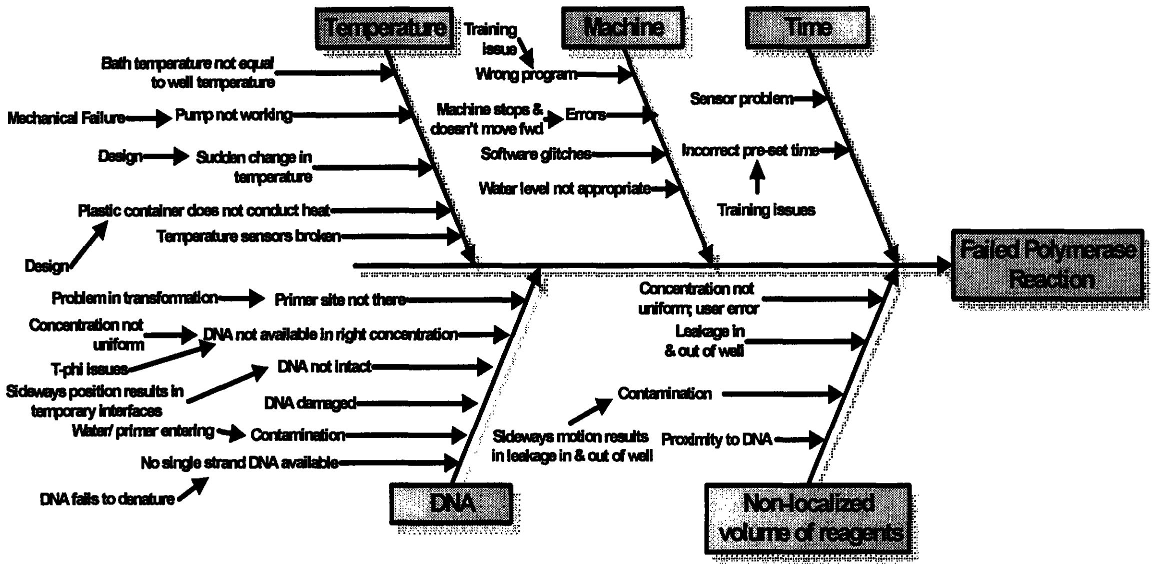
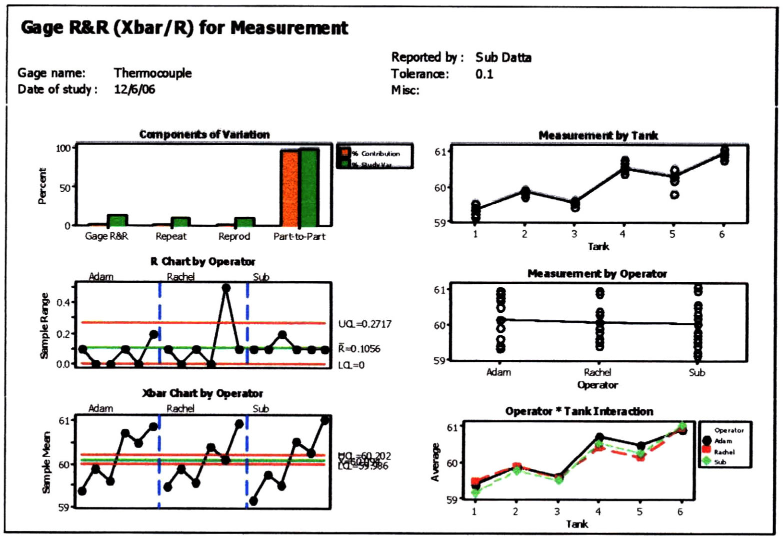



**Figure 62. Cause & Effect Analysis for Polymerase Reaction step**

## 6.3.3 Measurement Systems Analysis

Since the holding time and well temperature were not only proving to be two of the most important parameters, but also something for which not much data was available. A J-type thermocouple was decided to be the measurement system of choice. Introducing a new measuring device always brings in a new variable in the situation that could potentially add to the variability in the process. Measurement Systems Analysis (MSA) is a good tool to ensure that the variability introduced by the measuring device is negligible as compared to the target sample variation. A Xbar/R analysis was conducted to analyze the MSA. Figure 63 shows the MSA results for the Thermocouple used. 3 operators were used for the tests.




**Results**

| Source | StdDev (SD) | (6 * SD) | (%SV) |
|---|---|---|---|
| Total Gage R&R | 0.088126 | 0.52875 | 14.26 |
| Repeatability | 0.062348 | 0.37409 | 10.09 |
| Reproducibility | 0.062280 | 0.37368 | 10.08 |
| Part-To-Part | 0.611735 | 3.67041 | 98.98 |
| Total Variation | 0.618050 | 3.70830 | 100.00 |

Number of Distinct Categories = 9

**Figure 63. MSA results**

The results showed that the thermocouple not only introduced negligible variation but also had an acceptable level of resolution to track small changes in temperature. It could thus be used as a capable temperature measuring instrument.

## 6.3.4 Failure Mode & Effect Analysis

In order to quantify the results obtained through the Cause & Effect Analysis process, a Failure Mode & Effect Analysis was conducted for each of the Duncan process steps. Table 12, 13 and 14 show the rating scale used for the severity, frequency of occurrence and detect ability of the different failure modes.

**Table 12. Rating scale for measuring severity of failure modes**

| Rating | Severity |
|---|---|
| 1 | No impact |
| 3 | 30% fail - beginnning or end of the cycle (say machine failure) |
| 5 | 50% fail |
| 7 | Within cycle (say water leaking) |
| 9 | Every plate will fail |

**Table 13. Rating scale for measuring severity of failure modes**

| Rating | Frequency of Occurrence |
|---|---|
| 1 | Never |
| 3 | <25% |
| 5 | 25-50% |
| 7 | 51-75% |
| 9 | 75-100% |

**Table 14. Rating scale for measuring severity of failure modes**

| Rating | Detectability |
|---|---|
| 9 | Very Low |
| 7 | Low |
| 5 | Medium |
| 3 | High |
| 1 | Very High |

Figure 64, 65 and 66 show the Pareto charts for the Risk Priority Numbers (product of the severity, frequency of occurrence and detect ability of the different failure modes).

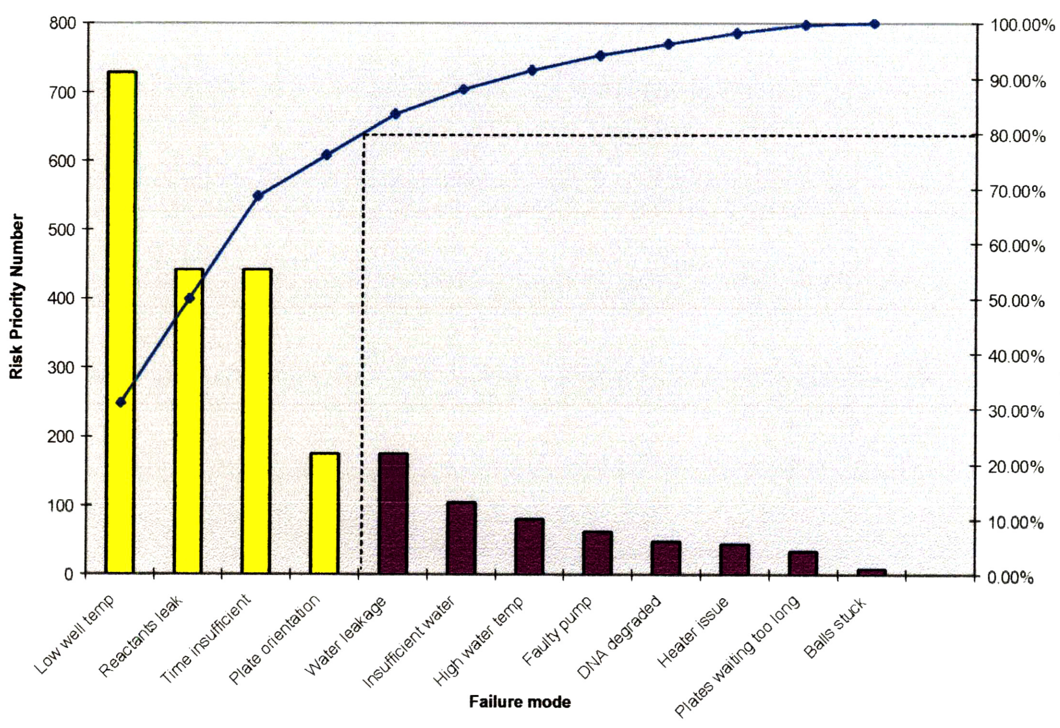



**Figure 64. Pareto of Risk Priority Numbers for failure modes during Denature Process**

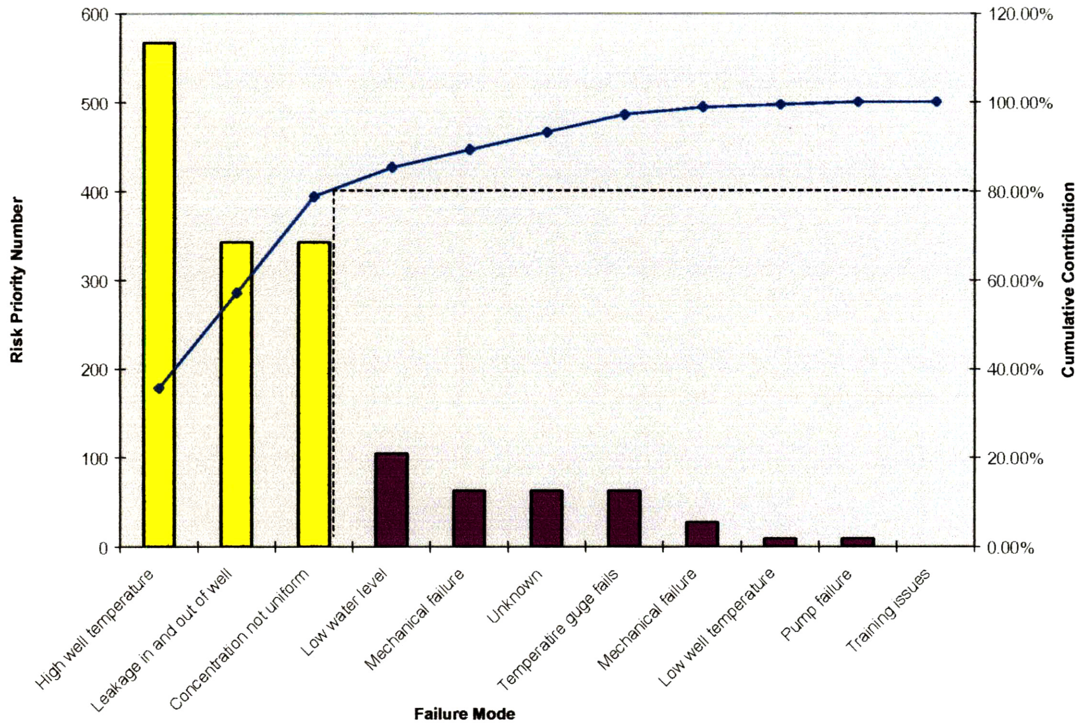



**Figure 65. Pareto of Risk Priority Numbers for failure modes during Primer Anneal Process**

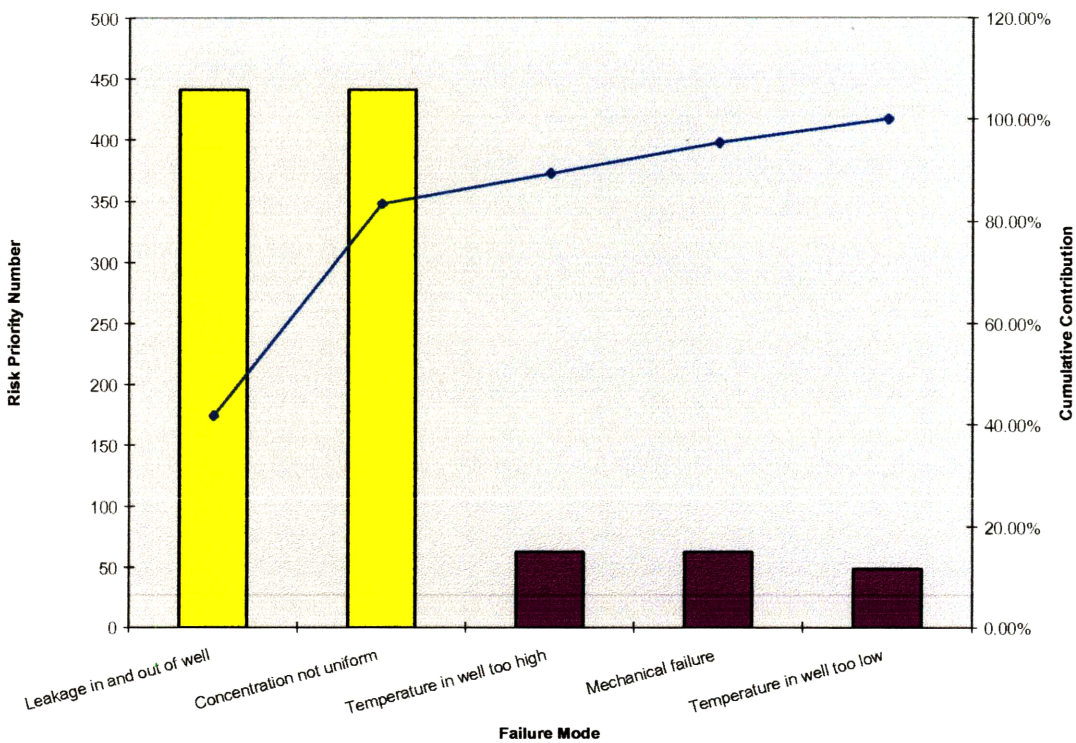



**Figure 66. Pareto of Risk Priority Numbers for failure modes during Polymerase Reaction Process**

Based on these test results, the following two areas were identified for further investigation:

- Effect of sideways racking of plates during Duncan cycling

- Time – temperature relationship in well

However, in light of the fact that there was no data available to understand these areas, two sets of experiments were conducted. These have been described in detail in the section 6.3.5.

### 6.3.5 Exploring the effect of sideways racking of plates during Duncan cycling

It was decided to understand this effect by filling 10 plates with a fluorescent dye and processing them using the Duncan and the Hybaid. The dyes would proxy for the PCR mix. If the amount of dye splashing was high in either of the processes, it would indicate that the following 2 phenomena were happening:

- The PCR mix was not localized for effective reactions to take place
- There was loss of PCR mix on the seal

Figure 67 compares the Duncan plate results with the Hybaid.

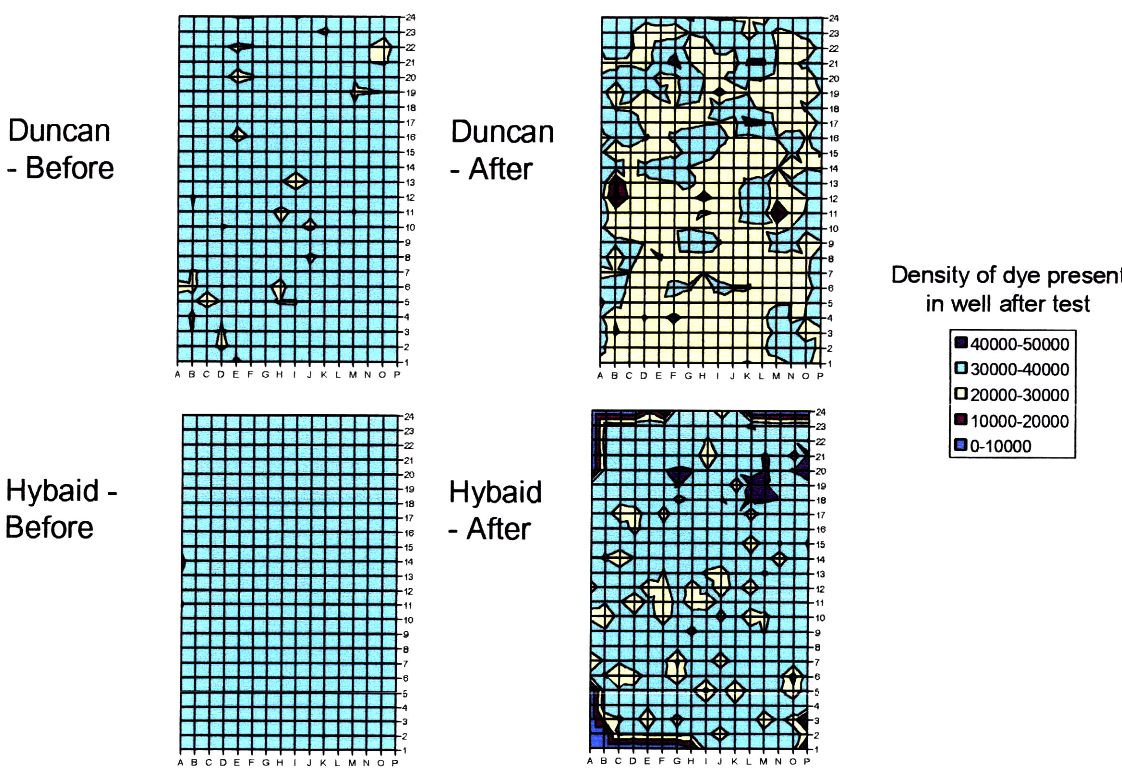



**Figure 67. Effect of sideways racking of plates during processing – Duncan vs. Hybaid**

The following conclusions were reached on the basis of this data:

- There was significantly higher loss of PCR mix in the Duncan
- It suggested the possibility that it is possible that the concentration of reactants across the cross section of the well may actually be significantly different in the Dunker as opposed to in the Hybaid

### 6.3.6 Time-temperature relationship in well

Analysis of the various root-cause analysis tools suggested that the two most important levers for the Duncan cycling process were temperature in the well and the holding time at the stated temperature. However, at the point of this study, there was no set procedure to measure the temperature in the DNA well. There were two basic assumptions in place when the team started working on the project:

1. The temperature in the DNA well was equal to the external heat source for the Duncan i.e. the water bath in which it was dunked.
2. The holding time was equal to the time the well plates stayed in the water bath. As a consequence, the cycle times were as follows:
    a. Denature bath – 20 seconds
    b. Primer Anneal bath – 15 seconds
    c. Polymerase reaction bath – 4 minutes

    These times incidentally were equal to the literature recommended holding times for the DNA wells and were in line with the first assumption that the temperature of the DNA well was equal to the temperature of the water bath.

A set of tests with the following temperature recording set-ups were conducted to test the validity of these assumptions on the two most important levers of Duncan cycling:

- 4 thermocouples in 4 well locations in test plate to record change in well temperature during thermal cycling
- 2 thermocouples on cage to record change in temperature of bath /heat source during thermal cycling

Similar tests were run on the Hybaid as a point of comparison. Figures 68, 69, 70 show the time-temperature curves for the three Duncan water baths in comparison with the Hybaid.

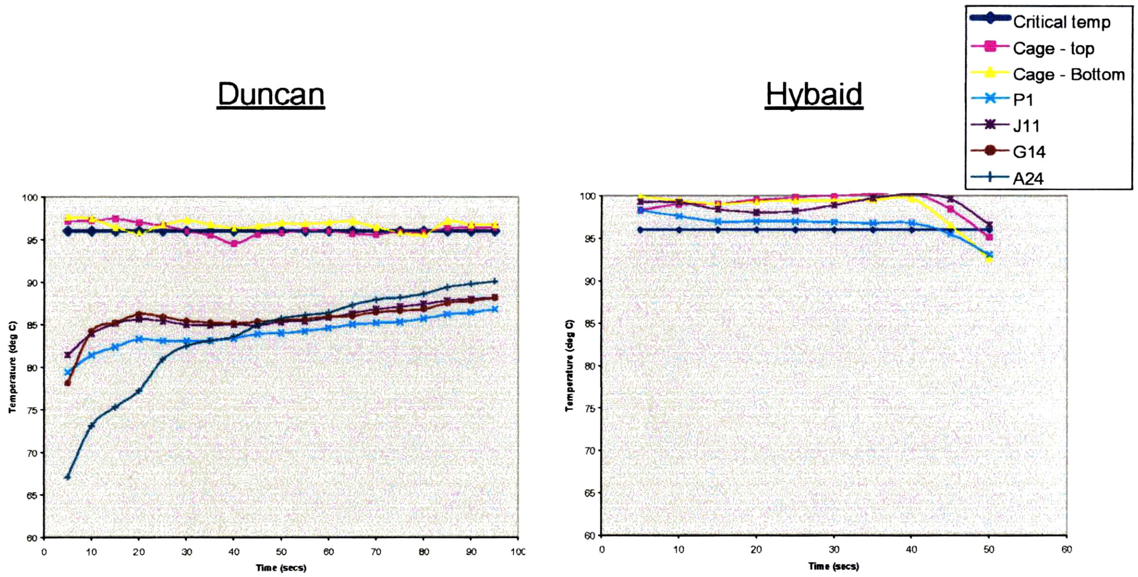



**Figure 68. Cycle 1: Denature - Comparison of change in well temperature with change in temperature of heat source for the Duncan and the Hybaid**

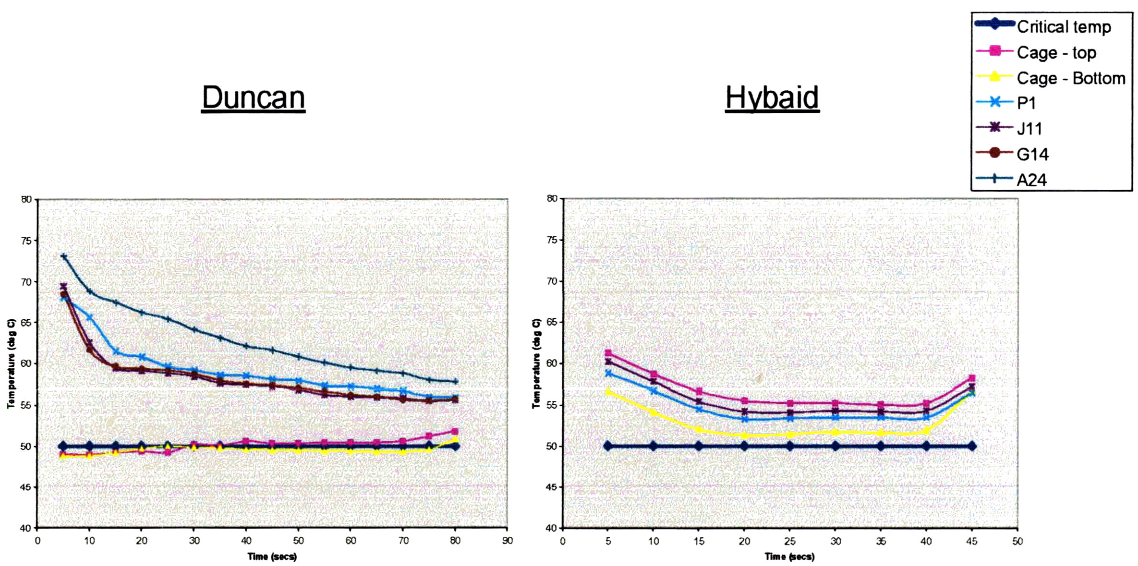



**Figure 69. Cycle 2: Primer Anneal - Comparison of change in well temperature with change in temperature of heat source for the Duncan and the Hybaid**

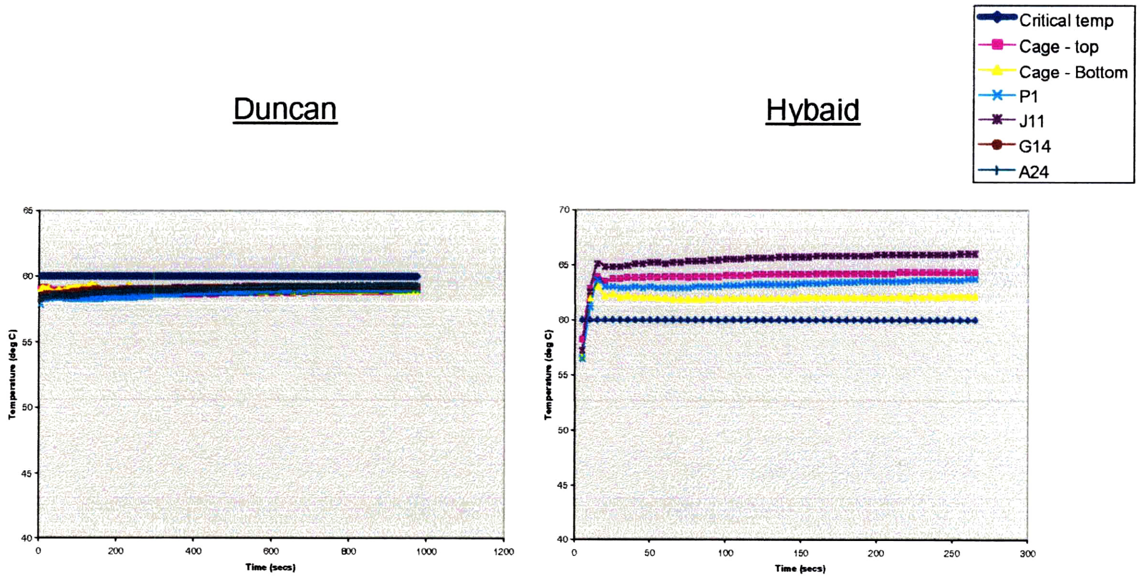



**Figure 70. Cycle 3: Polymerase Reaction - Comparison of change in well temperature with change in temperature of heat source for the Duncan and the Hybaid**

The following observations were made for the Duncan cycles based on the above shown data:

- Cycle 1 – Denature: Well temperature reaches an average temperature of 90 deg (6 deg < Critical temperature)
- Cycle 2: Primer Anneal: Well temperature reaches an average temperature of 55 deg (5 deg > Critical temperature)
- Cycle 3: Polymerase Reaction: Well temperature very close to critical temperature

The data thus conclusively proved that the assumption that the well temperature was equal to the Duncan bath temperature was not true for 2 out of the 3 cycles. This makes sense since the well is made using polypropylene, which is actually a fairly good insulator[16]. It additionally suggested that controlling the time-temperature curve could be the answer to improving the performance of the Duncan. In order to prove this new hypothesis, the following tests were planned:

- Experiment 1: Conduct one cycle with a holding time of 10 minutes in the Denature bath and 3 minutes in the Primer Anneal bath. This would help get an idea of the time temperature curve for the two stages in the Duncan.

[16] Material properties per Materials Handbook.

- Experiment 2: Change water bath temperature in the Denature and Primer Anneal baths to offset the increase in the processing time resulting from increased holding times.

Figure 71 and 72 show the DNA well time-temperature curves for the Denature and the Primer Anneal water baths. As a point of comparison, the figures additionally compare the current holding times with the suggested holding time per the graphs.

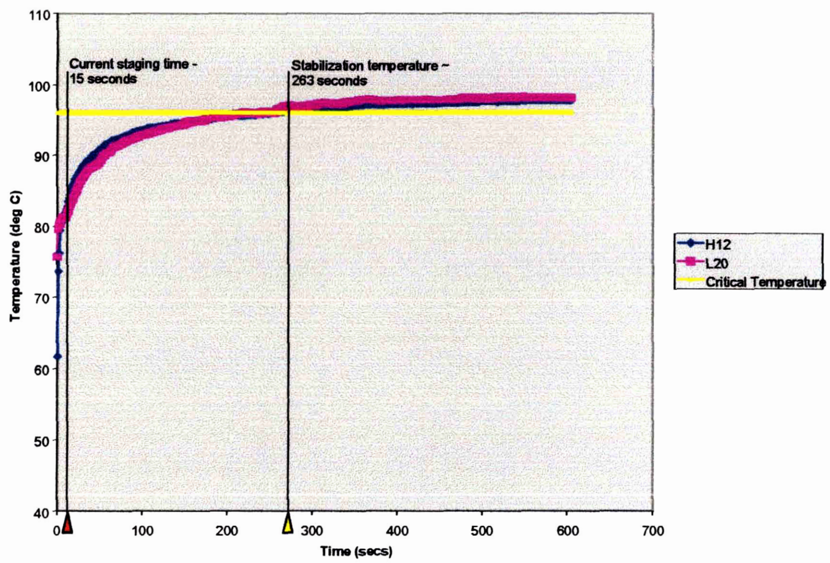



**Figure 71. Time-temperature curve for DNA well during processing in the Denature step suggesting the holding time in the tank be increased to 263 seconds instead of the current holding time of 15 seconds.**

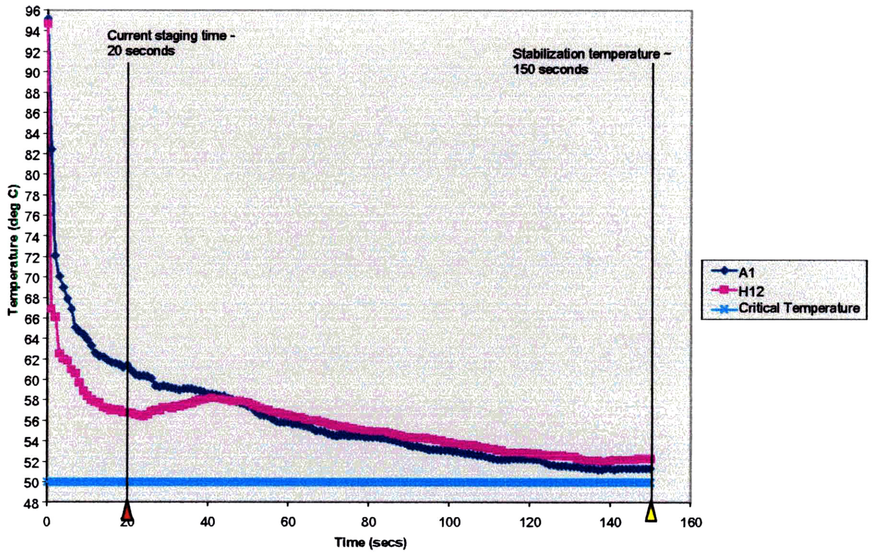



**Figure 72. Time-temperature curve for DNA well during processing in the Primer Anneal step suggesting the holding time in the tank be increased to 150 seconds instead of the current holding time of 20 seconds.**

DNA samples were processed using holding times suggested by the DNA well time-temperature curve to understand the impact on Duncan performance. Table 15 shows the results for the test.

**Table 15. Quality metrics for DNA sample plates processed with holding times of 263 seconds in the Denature bath and 150 seconds in the Primer Anneal bath**

| Metric | Mean Performance | Impact |
|---|---|---|
| Q20 All | 595.7 | Reduced by 1% |
| Read Length | 804.6 | Acceptable |
| Sequence Pass | 94.8% | Acceptable with an improvement of 7% |

Table X showed an improvement in one of the two metrics being targeted by the tests, which suggested that the tests were on the right track.

To continue with the investigation, the temperature of the Denature bath was increased to 98°C and that of the Primer Anneal bath was reduced to 45°C. The DNA well time-temperature curves at these settings suggested that the holding times for the Denature and Primer Anneal baths could be reduced to 155 seconds and 60 seconds respectively. In addition to reducing the processing time, this would have the additional benefit of reducing the chance of the DNA getting degraded exposure to high temperatures for a long time. Table 16 shows the impact of these holding time-temperature settings on quality metrics. As indicated, the outcome of the experiments was very positive with all metrics achieving the desired performance levels.

**Table 16. Quality metrics for DNA sample plates processed with holding times of 155 seconds in the Denature bath at 98°C and 60 seconds in the Primer Anneal bath at 45°C**

| Metric | Mean Performance | Impact |
|---|---|---|
| Q20 All | 674.8 | Acceptable with an improvement of 12.7% |
| Read Length | 831.4 | Acceptable |
| Sequence Pass | 94% | Acceptable with an improvement of 6% |

## 6.4 Summary of results and benefits showcased

The impact of the project on improvement of the Duncan Cycler can be summarized as follows:

- The project helped identify the 2 main levers that impact the performance of the Duncan for ongoing improvement.
- It showcased the usage of 8 key process improvement tools. These examples have been incorporated in the Process Handbook as illustrative examples and will help users at the Broad Institute better relate to them.
- It improved quality performance of the Duncan:
    - Improved Q20 All score by 12.7%
    - Improved Sequence Pass performance by 6%
- As indicated in Figure 73 that contrasts the amount and type of effort involved in using an approach suggested by the Broad Process Excellence Program with similar information for a typical problem solving effort at the Broad, following the tools suggested by the Program can:
    - Reduce problem solving time by 52%; and
    - Reduce experimental activity by 67%.

Thus, effective use of the tools implemented through the Broad Process Excellence Program can help solve complex problems while using significantly less labor, material and time resources. The implications of such activities on a non-profit organization like the Broad can be immense.

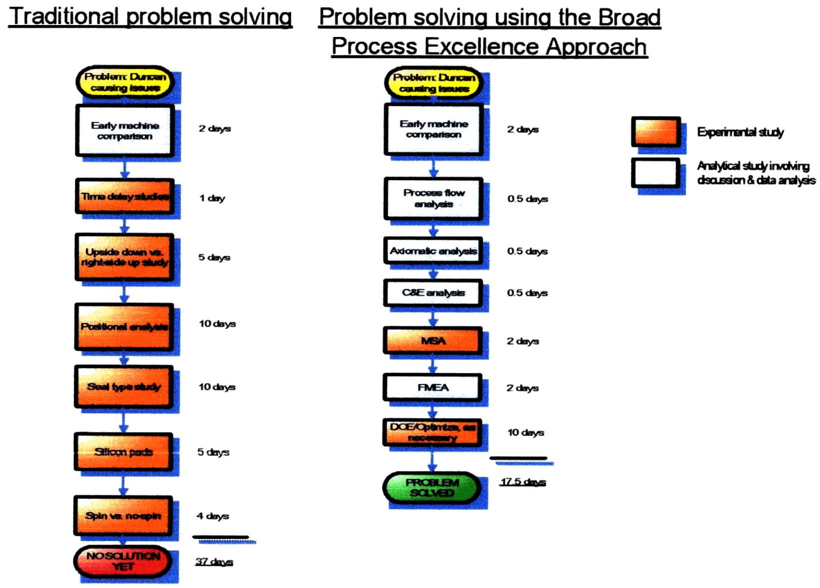



**Figure 73. Comparison resources used by traditional problem solving methods to solve complex problems such as the improvement of Duncan performance with problem solving using the Broad Process Excellence Program**

# Chapter 7

# Recommendations for the future

The previous chapters have introduced the background and stages through the development of the Broad Process Excellence Program. This chapter talks about some of the recommendations on what Broad can do as it implements the Program, areas it should be careful about and can consider analyzing as it improves its competitiveness by adapting operational innovations to improve its performance.

## *7.1 Learnings and recommendations*

The internship project effectively proved that despite some skepticism observed at the beginning of the project, manufacturing operations tools have a lot of promise in having a significant positive impact on the success factors of bio-technology organizations. Developing and implementing a process handbook that provides a foundation for the program is the first step in this direction. In order for the program to be successful, the Broad Institute is recommended to additionally do the following a part of the implementation process. These recommendations can also act as areas for future research:

- Training program:
  - The Broad Institute already has a Six Sigma training program in place. Although this training curriculum is fairly generic, it gives the trainees a good background into some of the available tools that can be useful. It is recommended that the institute additionally invest in basic operations training into some of the other tools referred to in the Process Excellence Handbook. MIT is an excellent resource that could be utilized in this respect.
- Improve communication across different areas of the Operations Sequencing Platform:
  - Develop a platform that requires members of different parts of the Operations Sequencing Platform to interact more with each other. This could be through

different projects and also by starting a sabbatical program where team members spend some time in a different group.

  - Develop a shared learning resource center. For this to be something that everyone participates in without the need for active push from management, the elements should be simple and easy without the stakeholders considering it to be additional work.

- Metrics and alignment:
  - Once a common language has been implemented in the organization, the next step for the organization is to work on aligning group metrics with global and individual metrics. Several benchmarked organizations suggested Hoshin Planning as a way to get there.

All of these areas require careful planning and have their own implementation challenges. It is thus recommended that the Operations Sequencing Platform involve trained personnel such as LFM and other MIT interns in implementation of some of these areas. The Broad Institute is one of the foremost areas for genomic research in the world. Such continuous improvement steps can help cement the institute at the top in this area and further increase its competitive advantage.

# Chapter 8

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# Chapter 9

# Author's Biography

The author is a native of Kolkata, India and graduated from the Indian Institute of Technology (IIT-R), Roorkee in 1998 with a Bachelor of Engineering degree in Metallurgical Engineering. While a IIT-R Merit Scholar at IIT, Roorkee, he was a student research assistant in multiple research programs and between 1995 and 1997, worked as an intern with the Bhabha Atomic Research Center in Mumbai, India and then with the Vizag Steel Plant in Visakhapatnam, India in various process engineering and materials research roles.

He moved to the US in 1998 and graduated from The Ohio State University in Columbus, Ohio with a MS degree in Materials Science and Engineering. While at The Ohio State University, he worked with Prof. Glenn Daehn's Hyperplasticity Research Group (www.osu.edu/hyperplasticity) in the area of Impulse-Based Metal Forming.

From 2000 to 2005, he worked with Cessna Aircraft Company as a Senior Materials and Process Engineer in various strategic sourcing, and advance manufacturing design roles. Finally, he joined the Leaders for Manufacturing Program at MIT for his MBA and MS in Engineering Systems degrees, where this thesis was completed in May, 2007. Upon graduation from MIT, the author will be joining A.T. Kearney as a management consultant in the firm's Boston office. The author can be reached at sdatta@sloan.mit.edu.

Publications co-authored by the author:

1. "The Effect of Forming Pressure on Springback in 2xxx Aluminum Alloys", SAE World Aviation Congress and Exposition, November 2004, Reno, NV.
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1. "Method of Predicting Springback in Hydroforming", US Patent 7,130,714 B1.
2. "Wrinkling-Predicting Process for Hydroforming", US Patent approval in process.