Implementing Lean Sigma in pharmaceutical research and development: a review by practitioners

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The authors recount their experience of the implementation of lean thinking and Six Sigma in pharmaceutical development research and development (R&D). Use of Lean Sigma in pharmaceutical manufacturing is widespread and generally noncontentious. Lean Sigma is used successfully to improve the development of new pharmaceutical manufacturing processes. However, the value of the application of lean and Six Sigma ideas to research & development is controversial. Published material is reviewed, and then the methods, tools, barriers and benefits are discussed, with recommendations for implementation of Lean Sigma into an R&D organisation.

1. Introduction

This paper introduces the concepts of lean thinking and Six Sigma, and briefly reviews their value for business process improvement. On the application of business process improvement methods to research and development (R&D), there appears to be no consensus in the literature on whether or not these methods support or stifle innovation and creativity. We review the literature, and in that context we reflect on our experience of the application of lean and Six Sigma in a pharmaceutical development department, with a discussion of the methods, drivers and barriers, and including recommendations for success.

2. Lean and Six Sigma – some background

As is well known, Six Sigma originated in Motorola in 1986 (Motorola Inc., 2008). 'Six Sigma' as a business activity encompasses an intent to move an organisation to very high levels of process quality (Pyzdek, 1999). Brady and Allen (2006) survey the literature, and report that 'Six Sigma is an organized and systematic method for strategic process improvement and new product and service development that relies on statistical methods and the scientific method to make dramatic reductions in customer defined defect rates'. Six Sigma, a Motorola trademark, was further developed in General Electric from 1995

(Hahn, 2005), initially applied to manufacturing and then widely across the organisation. Hayes (2002) recounts: 'Motorola reported, through their Six Sigma briefings, that savings for a 10-year period from 1985 to 1995 were $11 billion. GE in 1999 reported $2 billion in savings attributable to Six Sigma, and in their 2001 annual report discussed the completion of over 6,000 Six Sigma projects probably yielding over $3 billion in savings by conservative estimates'.

Six Sigma is now also widely applied to transactional processes such as office operations, insurance, banking and services (e.g. Tennant, 2001) with substantial cost benefits. The application of Six Sigma to the development of new products has been reported to be highly beneficial. For example: 'Design For Six Sigma (DFSS) helped GE deliver record financial results in 1999 . . . products are different – they capture customer needs better and can be brought to market faster than ever before' (Smith, 2004). Hahn (2005) mentions 22 new medical products introduced by GE in 2000 using DFSS.

A core method of Six Sigma is the DMAIC process: Define, Measure, Analyze, Improve and Control. Six Sigma training allows process improvement practitioners to use statistical methods in the workplace without being expert statisticians. Six Sigma practitioners are qualified in GlaxoSmithKline (GSK) as: Green Belt (typically 2 weeks' training and successful project experience and delivery of benefits); Black Belt (typically 4–6 weeks of intensive training; multiple improvement project experience; generated savings of $million upwards); and Master Black Belt (full-time role; has generated major benefits from multiple projects; experienced in training, mentoring senior staff and project selection). The authors know of no international standard for qualification of Belts. Of course, the training of Belts is not an end in itself but merely a means to enhance delivery of substantial benefits to the company.

The term 'lean' was applied by Womack and Jones in 1990 and further developed in their highly regarded book 'lean thinking' (Womack and Jones, 1996). Lean thinking is defining value for the customer, focusing on adding value, driving out wastes, reducing cycle times and ensuring smooth flow of work at the pull of the customer (Bicheno, 2000). The ideas of lean originate in the Toyota Production System (TPS) (Monden, 1998), often associated with the 'just in time' concept, but actually much more than this (Liker, 2004).

Lean thinking is now widely applied in manufacturing, transactional processes (banking, insurance, finance, sales, marketing and customer service), product development (Liker and Morgan, 2006), healthcare (e.g. The Lean Enterprise Academy, 2006) and laboratories (e.g. Gras and Philippe, 2007).

3. Lean Sigma and its application

Lean thinking and Six Sigma are now frequently used in combination, as 'Lean Six Sigma' (LSS) or 'Lean Sigma'. The lean approach seeks to convert inputs to outputs for the customer with minimum waste (reduced 'DOTWIMP'). Six Sigma seeks to understand how the process outputs Y relate to inputs X.

Figure 1 shows Lean Sigma as a mechanistic application, but, importantly, Lean and Six Sigma are far more than a set of process improvement methods to be applied to existing processes and procedures. Successful applications show that the beneficial implementation of lean thinking and Six Sigma requires a high degree of personal commitment, training and changed behaviour at all levels of management (Pyzdek, 1999; Pande et al., 2002; Bendell, 2005). Six Sigma requires Champions who vigorously promote the methods, top-level sponsorship, Black Belt practitioners and widespread training. Lean requires involvement of all staff in improvement activities

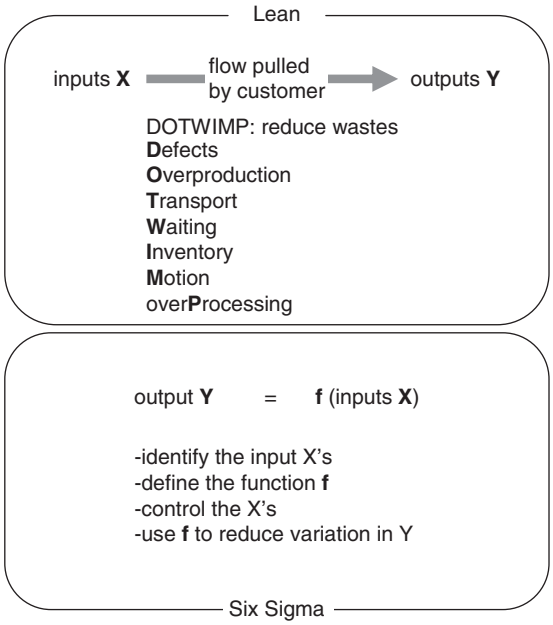


Figure 1. Lean thinking and Six Sigma.

with a management commitment to the principles of the TPS (Liker, 2004).

There is a large literature on lean thinking and Six Sigma. Google shows more than six million links for Six Sigma. In January 2008, Amazon.com listed 374 books relating to Six Sigma, and a large number on lean. The references cited in this article are therefore a very small part of the available literature, and are the books and articles that the authors have found interesting and useful.

Lean and Six Sigma methods and tools have been further augmented by the theory of constraints (ToC) (Goldratt and Cox, 2004). ToC addresses the importance of identifying and understanding the constraint to the flow of product. There is a philosophical structure and set of thinking processes associated with ToC as developed by Goldratt (e.g. Scheinkopf, 1999). ToC is an important partner tool for Lean Sigma. The current authors have applied ToC thinking to the flow of the drug knowledge development process, with the aim of finding and relieving the bottlenecks to progress.

Thus, the application of lean thinking and Six Sigma to manufacturing operations (e.g. Drakulich, 2007), transactional processes and services is well established (e.g. Hahn, 2005, for GE). A quick search on the web will illustrate that nearly all major corporations appear to be using lean and Six Sigma methods. Indeed, the literature shows little controversy on the benefits of Lean Sigma ideas in manufacturing, transactional processes and service industries. Lean and Six Sigma are being applied widely in the healthcare industry (de Koning et al., 2006; Jacobson and Johnson, 2006; The Lean Enterprise Academy, 2006; Gras and Philippe, 2007). Lean and Six Sigma certainly benefit the development of new manufacturing processes, for example by DFSS, by 'Quality by Design' with its Six Sigma concepts for pharmaceuticals (Hussein, 2005) and improved process understanding, for example by Britest (Thomas, 2005).

4. Lean Sigma, innovation and R&D

Some reports describe the benefits of Lean Sigma methods for R&D, while others strongly advise against applying process improvement to R&D, as we show below. Lean Sigma methods *do* improve product development, but do they improve 'idea development'?

Part of the debate around lean and Six Sigma in R&D centres on innovation, and whether ideas are encouraged or suppressed by business process improvement. Pyzdek (1999) stated that he would never apply Six Sigma to research because it would kill creativity (Johnson and Swisher, 2003). Benner and Tushman (2003) argue that process management (such as Six Sigma) is 'fundamentally inconsistent with all but incremental innovation and change ... process management activities must be buffered from exploratory activities ...'. They recommend partitioning innovative activities 'without Six Sigma constraints' (see also Anon, 2005). A pharmaceutical R&D Executive wrote recently 'An even more stifling trend [than mismanagement] has been the recent importation of the 'six sigma' business improvement methodology into aspects of pharma R&D ... six sigma has been well documented to quench innovation' (Bernal, 2007). At 3M, Six Sigma is being 'loosened', reports Hindo (2007), to improve innovation by research scientists.

In contrast, Calabrese et al. (2007) state 'Six Sigma is designed to aid drug development in getting back on track ... Six Sigma is one quality tool that can have a positive impact on the drug development process'. DePalma (2006) reports on use of LSS in Dowpharma GE Healthcare, and West Pharmaceutical Services, including the quotation 'Six Sigma doesn't inhibit creativity, it frees creativity for more productive work'. Johnson (2006) reviews the benefits of Six Sigma to R&D across a wide range of industries, concluding 'R&D activities naturally defy systematic improvement efforts, and Six Sigma is not the only ingredient in an effective recipe for competitive advantage ... Six Sigma and Design for Six Sigma, linked with corporate strategy in an R&D context, have helped companies generate superior products ...'. Is this true for pharmaceutical R&D, we ask?

Lander and Liker (2007) discuss the application of Lean to high-variability and low-volume environments. They propose going beyond what is now seen as 'conventional' lean [define customer value, identify the value stream, flow, pull, strive for perfection (Womack and Jones, 1996) to use the principles that led to the establishment of the TPS (Liker, 2004)]. To quote: 'Create flow and move materials and information fast ... so that problems surface right away'; '... understanding and adapting to dynamic external environments is a prerequisite for success'; '... change in work routines (and the corresponding improvement in performance) is the true hallmark of organisational learning'; '... evolution through

improvement and learning ... is at the core of Toyota's system'. Lander and Liker (2007) show that '... it is possible to adapt the tools of TPS and use them in novel environments'. Their example of the application of Lean/TPS to a custom tile manufacturer indicates that the Lean/TPS principles should indeed be applicable to R&D, a low-volume high-variability process.

Liker and Morgan (2006) present the Toyota Product Development System and show how Toyota has the capability to develop innovative and superior products faster than competitors. 'The challenge in product development is to reduce variation while preserving the creativity that is necessary to the creative process ... Toyota creates high-level system flexibility by standardizing lower-level tasks'. We can interpret this to mean that application of lean thinking releases time for innovation.

Reinertsen and Schaeffer (2005), in a thought-provoking paper, present 10 principles of lean, adapted for R&D, which we can briefly reprise:

1. Reduce batch size: process pharmaceutical leads frequently in small batches; take smaller steps with faster feedback of information.
2. Reduce the wastes of unwanted variability to increase capacity for desired variability producing valuable information.
3. Focus on flow. Monitor flow of work and buildup of queues and respond adaptively rather than preplanning everything far in advance. This tends to average out the arrival of technical problems and use of resources.
4. Pull, do not push. Rather than strategy driving roadmaps driving plans driving monthly resourcing, use project pull to allocate resources frequently, giving shorter cycle times.
5. Ensure fast feedback of new information so that scientists can control rapid development.
6. 'User requirements' are not stable as in manufacturing: goals must adapt rapidly to all new information.
7. Invest in sufficient flexibility of people in R&D so that bottlenecks can be relieved.
8. Achieve adequate failure rates. An experiment generates knowledge most efficient when its probability of success is 50%. Efficient failure rates create less waste than trying to 'do it right first time'.
9. Understand the economics of waste. In R&D, expenses are low compared with the cost of cycle times of months or years where people are the dominant cost. Focus on reducing cycle time even if this entails additional expense.
10. Control the right parameter – understand the critical path. For example, avoid local maximisation of the efficiency of support groups that can reduce responsiveness and increase the overall cycle time.

5. Lean Sigma in pharmaceutical R&D

Does the 'industrialisation' of pharmaceutical R&D quench innovation? All major pharmaceutical companies are probably applying lean thinking and Six Sigma to *manufacturing*, in order to remain competitive. However, the application of process improvement methodologies to pharmaceutical *R&D* is unproven.

Representatives from AstraZeneca, Johnson and Johnson and Pfizer R&D have presented on lean and Six Sigma at conferences. The meeting 'Lean Six Sigma in Pharmaceutical R&D' (2008) included speakers from Amgen, AstraZeneca, Bristol-Myers Squibb, Cardinal Health, Centocor and Pfizer, with delegates from Aspreva, Genentech, Merck & Co., Novo Nordisk, Takeda and Vertex. This indicates a high level of interest in Lean Sigma for pharmaceutical R&D, and application at least by the corporations with speakers on the topic.

Of lean thinking in R&D (McGee, 2005), a Bristol-Myers Squibb spokesman is quoted as 'It's quite amazing when you start to apply this criteria [lean] to how we do drug discovery. You essentially see how inefficiently we do it'. McGee adds 'Those inefficiencies became clear when BMS performed a ''rigorous'' analysis of its drug discovery process'.... 'By retooling its R&D process, BMS increased development candidates entering the clinic from 50% to 80%'. Further benefits of the application of lean manufacturing concepts to pharmaceutical R&D are described in Weller et al. (2006). Petrillo (2007) (formerly of Bristol-Myers Squibb) states: 'The application of lean thinking ... will enhance the value of the knowledge product of drug discovery, and lead to better success rates for clinical candidates'. Petrillo shows a value stream map for drug discovery lead optimisation, with the sub-processes giving the greatest benefit from lean transformation, and states 'The application of lean thinking to drug discovery will be a powerful complement to other approaches to improving industry productivity .... Drug discovery is indeed ready for lean thinking'.

TAP Pharmaceutical Products Inc. (Lake Forest, IL, USA; jointly owned by Abbott and Takeda) applied lean to improve their R&D.

Shankar et al. (2006) review the benefits. 'The lean drug development tools are not only easy to understand and use but have proven to be very beneficial to TAP'.

Hence, there is controversy about the value of lean and Six Sigma in R&D generally, but within pharmaceuticals R&D there appears to be a high level of interest. However, there is only a small number of reports on applications, possibly because of the confidentiality of R&D.

6. Lean Sigma in GSK R&D

6.1. GSK

GSK was formed by the merger of GlaxoWellcome and SmithKlineBeecham in 2001, and is the second largest research-based pharmaceutical company in the world (GlaxoSmithKline, 2008). The GSK R&D corporate vision includes entrepreneurialism, urgency and innovation. Here we are discussing here the relationship between innovation, which is at the core of research-driven pharmaceutical development, and business process improvement methods such as Lean Sigma.

Pharmaceutical Development is one department within R&D. Figure 2 shows the flow of product discovery and development (GlaxoSmithKline, 2006).

It can take 12–15 years to bring a new medicine to market and costs as much as £500 million. (GlaxoSmithKline, 2008). Most new developments are never commercialised, mostly because of lack of clinical efficacy or adverse side-effects, and so 'fast-to-fail' is an internal management driver to minimise wastage of scarce resources of time, money and people. GSK R&D employs hybrid product and functional structures to improve productivity. The rationale is to allow specialisation of the Centres of Excellence for Drug Discovery (CEDDs) to drive innovation, but functional structures (e.g. in PharmDev) to drive speed and efficiency. Because of the interactions required between the numerous knowledge-based specialisms required to discover and develop new products, they are integrated within various product matrix teams. As discussed later, this matrix structure complicates the implementation of Lean Sigma.

The pharmaceuticals industry is characterised as being an innovative but highly regulated sector. The current evolution of pharma business model away from blockbuster products to 'personalised medicine' will require radically new innovations

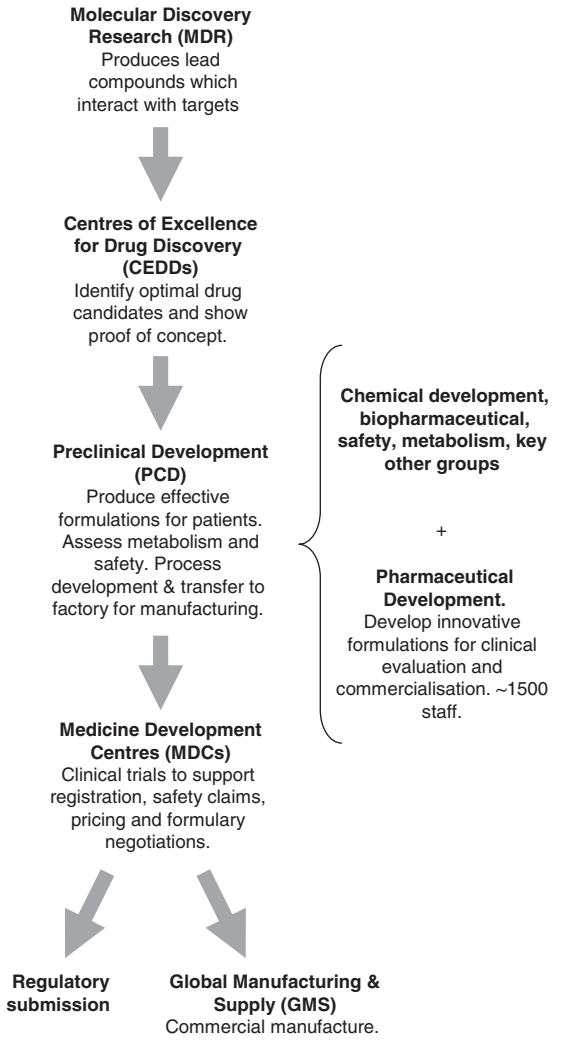


Figure 2. Pharmaceutical Development and research and development in GlaxoSmithKline (drawn from GlaxoSmithKline, 2006).

such as genomics and niche-therapies (Economist, 2007). This trend, together with the urgent need to reduce operating costs, highlights the need for GSK R&D, as with other pharma companies, to adopt broad strategies to improve innovation and balance investment in innovation with control of expense by operational excellence (OE).

The US Food and Drug Administration (FDA) are leading the way in the introduction of new regulatory expectations that have Quality by Design (QbD) at their heart (Hussein, 2005). Enshrined within this, and emerging from ICH (International Conference on Harmonization), are expectations for achieving greater understanding of pharmaceutical process capability and control, and for embedding continuous improvement. The Six Sigma toolkit contains valuable methods and tools for QbD, as DFSS.

6.2. Lean Sigma in GSK

Here the authors lay out the experience of applying Lean Sigma within Pharmaceutical Development, part of the drug development R&D organisation in GSK, including some historical background.

Lean Sigma is well established within the GSK factory organisation [Global Manufacturing and Supply (GMS)]. In some factories, Lean and Six Sigma tools were used from 1991. Immediately following the merger forming GSK, the OE group was established to oversee the implementation of Lean Sigma across the entire factory network. The harmonisation, competency development, accreditation and knowledge management support for this programme have been coordinated via OE with highly organised training and deployment leading to large benefits in manufacturing. For example, annualised cost savings of £300 million by 2004 through operational efficiencies with its network of manufacturing sites were reported (GlaxoSmithKline, 2004). 'OE' is the current major improvement strategy across the Company (GlaxoSmithKline, 2007).

In the early 1990s, process improvement methodology met little enthusiasm in R&D, and uptake was minimal. In 2001, the GSK factory Lean Sigma programme was assessed for application in R&D, and in 2003 the programme was formally adapted and customised for use, being launched in R&D under the brand name 'Enhance'. Within Pharmaceutical Development, six members of staff (including the authors) were recruited from the business lines, trained in Lean and Six Sigma tools including change management and deployed full-time as dedicated practitioners. Similar groups were established in the other pre-clinical functions and in central R&D.

In 2003 (2 years after the merger of GlaxoWellcome with SmithKline Beecham), the anticipated benefits in R&D Pharmaceutical Development were characterised as being:

- Process harmonisation: reduce waste and inefficiency (therefore reduce operating costs).
- Increased productivity by greater focus on value-adding activities (therefore reduced cycle times).
- Accelerating the cultural shift toward becoming a learning organisation (see also Argyris and Schön, 1978; Senge, 1990).

Business process improvement via Lean Sigma methods and tools supported all these aims.

The Enhance customisation provided greater focus on lean thinking and change management (e.g. IMA, 2008), while somewhat reducing focus on the Six Sigma statistical tools. Statistics were already being taught and used via a separate programme, and the valuable statistical aspects of Six Sigma were later incorporated into a 'quality by design' programme for product process development and technology transfer to the factory.

6.3. Lean Sigma in GSK R&D pharmaceutical development

6.3.1. Methods and tools used

Some of the Lean Sigma methods and tools used in the DMAIC process are shown in Figure 3. It is evident that much of the Lean Sigma toolkit is useful in pharmaceutical development R&D. Particular attention was paid to the people aspects of change management ('soft skills'). Figure 4 summarises the support of Lean Sigma for R&D innovation.

6.3.2. Drivers and barriers

A forcefield analysis (Lewin, 1943) can be used at the start of a project to identify drivers for, and barriers against, the project succeeding. We have used the forcefield analysis framework to describe how the Lean Sigma implementation programme maximised drivers and overcame barriers (Tables 1 and 2).

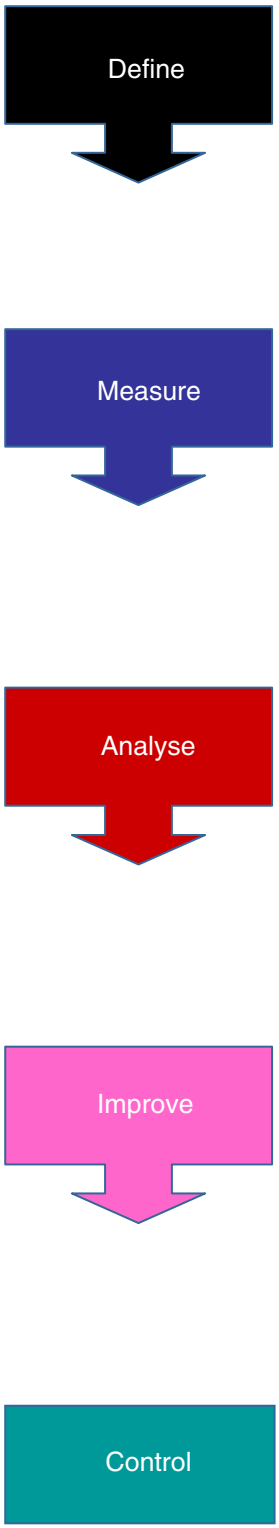
6.3.3. After action review and recommendations

The 'After Action Review' (AAR) was developed by the US Army, and is now used in Shell Oil and many other organisations. The authors in his paper have essentially made an AAR of Lean Sigma in pharmaceutical development.

Practical aspects of the implementation of Lean Sigma in GSK Pharmaceutical Development are given elsewhere (Altria et al., 2008) with projects and benefits. A key benefit was the increased capacity for project work from time saved on repetitive tasks, and reduction of cycle times. Lean Sigma facilitated the better use of laboratory space. Less tangible benefits were easier working following simplification and harmonisation of routine tasks for scientists, better sharing of knowledge and best practice and improved teamworking and individual involvement. Staffs were familiar with the common language of Lean Sigma.

Our recommendations from practical experience with the implementation of Lean Sigma are the folowing:

1. Collect baseline facts and data to show the compelling need to change.



Methods and tools found useful in R&D:

Project Initiation Form, Project Charter, sponsorship
Supplier-Input-Process-Output-Customer map
Situation-Target-Proposal
Stakeholder mapping
RACI (Responsible, Accountable, Consulted, Informed) diagram.
Cost-benefits estimates.
Milestone planning.
Risks analysis (e.g. Failure Mode Effect Analysis FMEA).
Voice of the Customer (VoC), surveys, web-based questionnaires.
Structured interviewing, 5 whys.
Database for knowledge sharing.
Value stream mapping.
Observations in the workplace, gemba.
Identify wastes (DOTWIMP)
Process flow maps (logical, spaghetti, time value).
Theory of Constraints (ToC).
Check sheets, diarying
Pareto diagram, histograms, run charts
Scatter diagram, run chart
Regression modelling, design of experiments (DoE), measurement systems analysis (MSA)
Quality function deployment (QFD)
Problem statement & root cause analysis
Kepner-Tregoe problem analysis
5 whys, reality tree, logic fault tree
Brainstorming, fishbone (Ishikawa) diagram.
Undesirable Effects (UDEs) and affinity diagram
Change management tools e.g. Accelerated Implementation Methodology (IMA, 2008), Eight Steps of Change (Kotter, 1996)
5S (sort, store, shine, standardize, sustain)
Kaizen Blitz type workshops
Kanban, mistake-proofing (poka yoke)
Standard work as first intent
Solution finding and weighted selection matrix.
de Bono Six Thinking Hats
Visual workplace. SOPs. Auditing. Metrics.
Forcefield analysis.
After Action Review

Figure 3. Lean Sigma tools found useful in research and development (R&D).

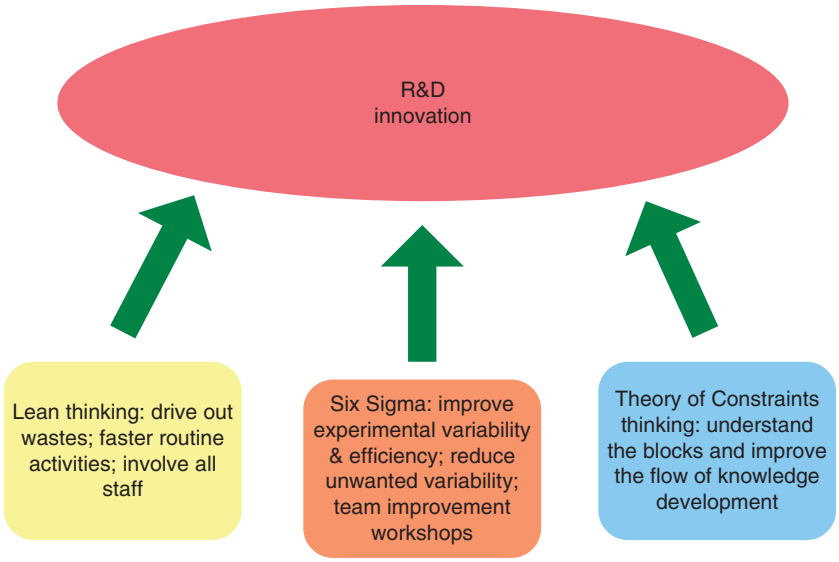


Figure 4. Lean Sigma supports research and development (R&D).

Table 1. Drivers for success

Driver	Tactic adopted to maximise driver
Senior management sponsorship	Senior management communications to staff endorsing and encouraging the Lean Sigma approach. Senior staff communicating praise for Lean Sigma projects when completed
High level of experience and knowledge of Lean Sigma within the GSK factory network (GMS)	Secondment of Lean Sigma black belts from GMS into R&D. Adaptation of GMS training materials to R&D. Implementation of GMS Lean Sigma accreditation scheme (Green and Black Belts) in R&D
Full-time appointment of staff to Lean Sigma-based role within R&D	'Internal consultant' role with senior management to identify projects. Motivation of Lean Sigma staff through accreditation scheme
Establishment of knowledge sharing	Establishment of network of champions, and community of practice. Sharing of best practices and learning through seminars, workshops and intranet databases

GMS = global manufacturing and supply; GSK = Glaxo SmithKline; R&D = research and development.

2. Ensure excellent sponsorship and communicate well with all staff involved.
3. Allocate full-time staff to support implementation.
4. Coordinate the implementation with consistent training, documentation and internal 'branding'.
5. Inform, involve or train all staff about the overall improvement programme, and embed Lean Sigma methods and tools.
6. Focus first on reducing bureaucracy and routine repetitive tasks, and phase the implementation building on successes.
7. Support experimentation by reducing *unwanted* variation of inputs and processes.
8. Ensure that 'sustain' mechanisms are built in to maintain benefits.
9. Change the culture by multiple communications, staff involvement, rewards and recognition.
10. Use, and hence show the value of, the Lean Sigma tools wherever possible to support product development, even if not part of a formal 'DMAIC' improvement project.

7. Conclusions

It is now widely accepted that Lean Sigma is of considerable benefit in pharmaceutical manufacturing and in the optimisation of generic processes for drug development, as shown by the above review. In this paper, we have looked at the implementation of Lean Sigma in R&D Pharmaceutical Development. Scientists with an in-depth technical knowledge of their specialisms must be creative and innovative in meeting the

Table 2. Barriers to success of Lean Sigma, and their mitigation

Barrier	Tactic adopted to mitigate barrier
Scientific culture does not welcome 'continuous improvement'	Encourage a cultural shift. Consistent training and branding of materials. Use of change management principles and multiple channels of communication. Phased implementation building on successes.
Lack of knowledge or understanding of business process improvement concepts in senior managers. Managers typically ex-scientists with limited business training	Education on continuous improvement. Build awareness of the methods & tools. Training was carefully customised for the R&D audience—supported by visible sponsorship and vivid examples.
Individual scientists were sceptical. Often believe that knowing the scientific method is sufficient to do the job well	Concentrate on facts and data to show benefits of early lean sigma projects. Education and awareness by many communication routes. Training was customised for the audience—focused on pertinent examples of project activity and benefits in their area of R&D. Use team activities and human aspects of Lean Sigma to get involvement.
Difficulty demonstrating benefits in a culture unfamiliar with metrics and governance. Fewer 'hard' efficiency measures in R&D than in the factories	Developed standard calculating and reporting procedures to communicate benefits. Time saved was converted into—FTEs (one person full time) to show increased capacity for development.
Difficult to find quantifiable financial benefits in a non-commercial operation	FTE capacity gains were converted to cost benefit for senior management. Where cost and capacity measures were difficult to obtain, demonstrated intangible benefits (improved teamwork, better knowledge sharing, increased motivation and easier experimentation).
Some middle management perceived as a 'black hole' (not persuaded of the benefits) while senior management are sponsoring and scientists are carrying out improvement projects	Attendance of middle management at advocate training (three days). Sponsorship of projects to encourage ownership and involvement. Mentoring by full-time lean sigma staff.
Perceived lack of routine processes in R&D with high throughput and low variability suitable for Lean Sigma projects	Implementation of 'systems thinking' e.g. SIPOC, to highlight underlying routine aspects of operations as target for improvement. Practical application to the many routine activities.

R&D = research and development; FTE = full-time equivalents.

challenges of new drug development and yet sensitive to the need for operational efficiency.

The formal tools of Lean Sigma have been found to be of great benefit where there are routine operations within R&D. Lean tools were used to reduce waste associated with routine tasks in the laboratories and so allow more time for creative product development work. Lean thinking improved support activities including transactional processes such as experimental documentation, office bureaucracy and GMP procedures. The statistical tools of Six Sigma are of course essential in 'Quality by Design' development of more robust manufacturing processes.

The implementation of Lean Sigma in a scientific research environment has been found to be more challenging than in the factory for the following reasons:

- In R&D, the management structure is less hierarchical than the factory.
- There is a strong matrix process and culture across lines and product teams that dilutes sponsorship.
- Cycle times for product development are protracted, so feedback is necessarily slow.
- Scientists who are excellent in their technical field may resist the perceived imposition of improvement methods that they believe force-

fits a routine system approach to a creative, innovative activity.

These barriers were mitigated by strong sponsorship and stakeholder management, attention to business change management principles, focusing on creating time and space for thinking and a phased implementation using surrogate metrics to publicise success.

The 'product' of R&D is knowledge, and addressing the flow and constraints on the development of knowledge has been useful. For example, Lean Sigma principles have been applied to the 'soft' people aspects of processes, to improve teamworking, to share information better, and to improve individuals' engagement in the overall development process. These attributes are enablers in the development of the Learning Laboratory. Customer-focused process thinking is now the norm in GSK PharmDev.

Therefore, does Lean Sigma support or stifle innovation? There are firm published views one way or the other. We have shown that Lean Sigma can be beneficial in the R&D environment. While not catalysing creativity directly, Lean Sigma methods and tools can be used to improve knowledge management and teamwork, and to improve all routine aspects of the overall operation. The result is more time for scientists to innovate, and reduction of cycle times, which increases the speed of development.

Thus, with the background controversy around the value of process improvement in R&D, the authors have shown that the implementation of Lean Sigma in pharmaceutical R&D can be beneficial if done with the right focus and sensitivity to the needs of scientists. Perhaps Lean Sigma does not promote creativity per se, but it certainly supports efficient problem definition, problem solving and the dissemination of ideas. More research is needed in this area, and more public discussion by those in industry, in order to reach a consensus of the role of business process improvement methods in R&D.

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