



Creativity, innovation and lean sigma: a controversial combination?

Craig Johnstone¹, Garry Pairaudeau¹ and Jonas A. Pettersson²

¹ CVGI Research Area, Mereside, AstraZeneca R&D Alderley Park, Alderley Edge, SK10 4TG, UK

² Continuous Improvement, DECS, AstraZeneca R&D Mölndal, SE-431 83 Mölndal, Sweden

The application of lean sigma is gaining momentum in drug discovery and development but it remains controversial because of perceptions that process improvement will suppress much-needed creativity and innovation. We review the conditions required to support creativity and innovation and the principles and benefits of lean sigma in a drug discovery environment. We conclude that it is desirable to create a unified climate that encourages and enables both innovation and continuous improvement and that this is possible if three key tensions are handled carefully and with due respect to the needs of research. These three potential traps occur in the interpretation of standardization, the role of variation and the choice of how to use liberated capacity.

Introduction

The pharmaceutical industry faces enormous challenges, and some observers have gone as far as to state that the common operating model of drug discovery and development is broken. Certainly, there seems to be agreement that the escalating costs of bringing new products to late-stage development, recently estimated to be typically more than \$1 billion USD per product [1], are reaching unsustainable levels for profitable business and adequate return to investors [1,2]. In addition, through their actions and guidance, payer organizations and government agencies (e.g., see <http://www.nice.org.uk>) are exerting increasing control over prescribing activity and demanding greater value and benefits in return for the money spent on pharmaceuticals. Patients' expectations of therapeutic advances are also on the rise, as is their influence through patient interest groups. When taken together, the industry is being challenged with two simultaneous demands from multiple customer groups: more innovative products, which need to be delivered at a lower cost than today.

Several strategies for improving the efficiency and effectiveness of drug discovery and development are being explored across the industry. We [3–5] and others [6–12] have attempted to adopt the principles of continuous process improvement, such as lean and

six sigma, which have successfully revolutionized the cost and quality of manufacturing and service provision in recent decades.

This trend for increasing process improvement is not without controversy, however, particularly when one considers the demand for increased innovation as well as cost effectiveness of delivery. There is a genuine and understandable concern that methodologies such as lean (six) sigma, which include standardization and the reduction of variation in their guiding principles, will restrict the freedoms required for innovative ideas to survive and flourish. In the editorial pages of this journal in 2005 [13], the commonly expressed view of tension between process and creativity was acknowledged. In an article about their own experiences of deploying lean sigma in pharmaceutical development at GSK, Carleysmith *et al.* [14] cite several typical examples of some of the concerns expressed about deploying lean in innovative environments. Early in our own lean sigma deployment, *Business Week* [15] carried an article claiming that the recent adoption of six sigma had suppressed innovation at 3M, a company often regarded as being one of the most successful innovators over many decades. More recently, further commentary has contributed to the view that improved process performance and innovation are inherently contradictory ambitions. Hoffman and Bishop [16] state that 'The greatest tension in discovery research in Big Pharma companies...seems to result from...the competing goals of efficiency and innovation'. Ullman and Boutellier [11] refer to the

Corresponding author: Johnstone, C. (craig.johnstone@astrazeneca.com)

'trade-off' between the required levels of coordination in large companies and the negative impact that that coordination has on freedom, personal initiative and creativity. They refer to the retention of operational independence of acquired biotechs from the larger parent company as one way to protect the smaller innovative companies from the politics and bureaucracy of the parent company. Although beyond the scope of this article, much has been written about organizational structure and its role in facilitating innovation in large organizations (<http://www.the-innovation-machine.com/?p=86>; <http://www.innovation.cc/discussion-papers/organizational-design.htm>).

In this article, we consider the conditions required for improved organizational creativity and innovation and explore whether lean sigma deployment has characteristics that make it inherently anti-innovative or a supportive pro-innovative force.

Innovation in the pharmaceutical industry

Within the context of drug discovery in the pharmaceutical industry, we have defined innovation as 'the introduction of novel therapies, targets, insights or processes that make a meaningful difference to patient lives and bring value to the business'. Much has been written about the steps required to bring an innovation to fruition, and there is broad agreement that ideas traverse several distinct phases (<http://www.communities.gov.uk/publications/localgovernment/innovationits>; http://www.innovationexchange.net/the_innovation_process) [17]. In Fig. 1, we have amalgamated numerous models into a 'consensus' representation.

Within any organization wishing to support innovation, it can be useful to consider how the organization as a whole supports these stages in terms of its systems, processes and culture and the behaviours of its members. In addition, we should recognize that an individual's propensity and desire to think and act innovatively is largely driven by the environmental conditions they experience and their motivation, particularly intrinsic motivation [18]. When viewed in this context, there are particular contextual challenges that face large organizations as distinct from smaller biotechs, which have been perceived as more innovative.

The stages of innovation

Often when one thinks about innovation, it is tempting to skip directly to the creative ideation stage – 'How can we have more ideas?' – but this misses a crucial step in the process. Within an industry as complex as drug discovery, containing multiple parameters and variables coupled with protracted timelines, vast

investment and fierce competition, separating the important problems from the trivial ones is a challenging but crucial task. This challenge can be amplified in a big organization: there are multiple stakeholders, complex governance processes, isolated departments owning segments of the value chain and so on. Without clarity of vision about what is important, several things tend to happen in complex environments: creative individuals might pursue their personal interests, and well-meaning intentions without business-aligned purpose can lead to senior management frustration at what it perceives as a 'university environment' full of unfocused or uncoordinated activity; alternatively, staff might feel unable to make their own mind up about what is important and resort to asking for ever-increasing degrees of clarity from management who (with good intention) will try to clarify the situation with increasing levels of detail, resulting in an explosion of bureaucracy, policies, protocols, role descriptions and so on. The role of leaders in resolving this dilemma by creating a meaningful purpose and vision is clear [19,20]. There is also a behavioural component to the identification of important problems. Individuals need to feel able to highlight that there is an issue and feel supported in doing so. Often, an organization focused on delivery does not want to hear about a problem that needs solving [21] and misses a valuable opportunity to innovate or continues with the problem-laden product, which fails later at higher cost and consequence.

There is little doubt that people need time and space and some autonomy over how to spend that time to have creative ideas, and there are different ways that this can be achieved. It can be formalized, as in the much-publicized 15–20% free time at Google and 3M, or can be less formally delivered through permissiveness. The common desired outcome is the individuals belief and experience that 'it is OK to spend time being creative here'. In considering how to improve this aspect, one needs to consider the current prevailing context: if the company culture already embodies a high level of permissiveness, then perhaps all that is needed is appropriate time management to ensure that employees are not overloaded. If the culture is highly delivery and efficiency focused, however, then more explicit interventions might be required to install a change in climate and behaviour.

Even within an environment that cultivates idea creation, there always comes a time when the person with the idea must break his or her silence and share the idea with someone else. This creates the need for self-confidence and constructive behaviour on the part of the proposer and the receiver. The proposers need to be

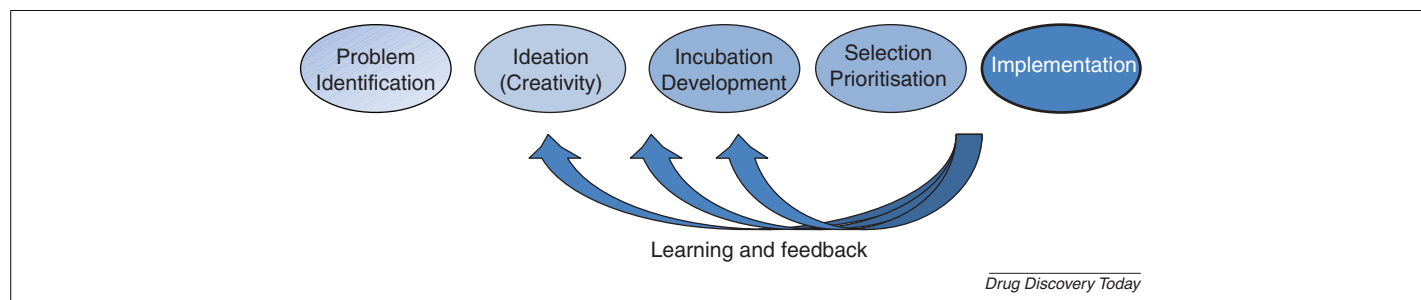


FIG. 1

Innovation, the conversion of new ideas into useful outcomes, occurs through a series of distinct phases as the idea matures, but is rarely a "once-through" linear process. Incorporating feedback and learning into earlier phases enhances the quality, and thus increases the probability of success, of the eventual solution.

confident enough to expose their private thoughts to critique, recognizing their idea will be imperfect, so as to avoid over-defensiveness at the first criticism, and the receivers need to constructively listen to the idea, and if they consider it worthy of further debate, display sufficient self-confidence to support it emotionally and verbally and, potentially, with resources.

All new ideas need some development or prototyping before it is possible to assess whether they have any merit. This is an area in which a large organization should excel because it is blessed with plentiful resources and an array of diverse skills. Why, then, can launching a new idea feel so difficult? The answer is multidimensional, of course, but is at least in part a function of the complexity of the organization and the ability of the individual to navigate it. Organizations that delegate budgetary control and decision-making downwards will be more likely to succeed, and if this is coupled with coaching of individuals in business entrepreneurship and a focus on building personal networks across functions, ideas are more likely to be developed to a stage where prioritization is feasible. Strong cultural drivers also exist in organizations, and the behaviours exhibited by peers and particularly leaders [20] play a big part in encouraging a climate in which expression is risk free and open.

Assuming it can create a fertile breeding ground of new ideas, an organization needs to decide where to spend its finite resources. Sufficient resources to progress every idea are not available, and indeed, not all new ideas will fulfil their early promise. Therefore, it is important to select and further resource the good ideas, but it will also be necessary to stop the progression of many others. In areas of high novelty, a 'stop' decision might indeed be the most frequent outcome; therefore, the stop decision needs to be handled skillfully and constructively to prevent demotivation of the ideas' proponents. Furthermore, there needs to be a mechanism in place to acknowledge and reward the effort invested and achievements made, regardless of the final outcome, to encourage and incentivize future ideation and progression.

Learning underpins any truly innovative organization. The desire at the individual and organizational level to try an experiment secure in the knowledge that, whatever the outcome, something of value will have been learnt is what generates the necessary confidence to step into the unknown. Systems for capturing outcomes and sharing knowledge support this principle, and the combined knowledge of a community helps inform and define the next phase of challenges and opportunities. This combined knowledge, if capitalized upon, should confer big pharmaceutical companies with an advantage over more nimble and agile biotechs, and is one of their key assets. The recognition of its importance is also a primary driver behind recent increases in cross-company information sharing and the emergence of pre-competitive consortia.

Organizations can strive to create a conducive atmosphere, but it is evident that individual motivation is an extremely important factor in creativity and innovation. The factors that are proposed to govern personal motivation [18,22] – namely, autonomy (a level of freedom to make choices), purpose (a clear context in which one can make a contribution), progress (a sense of achievement) and mastery (becoming good at something) – are strikingly similar to those conditions that support innovation. It is likely that there is a synergy between innovation and motivation, a kind of cyclical

drive: staff that are engaged, involved and empowered are much more likely to be innovative, and the satisfaction derived from seeing new ideas comes to fruition that is, in turn, deeply motivating.

We have considered the factors that are conducive to organizational creativity and innovation, but it is important to comment briefly on the fragility of ideas. Unfortunately, it is much easier to suppress and crush ideas, often unintentionally, than to cultivate them [23]. A low frequency of negative behaviours or anti-innovative comments might be enough to undo extensive efforts to create a supportive environment, and co-operative and supportive efforts need to prevail throughout the organizational hierarchy. Most readers of this article will recognize to what we refer: 'we've tried that before' and 'that's a rubbish idea' are innovation killers, and the more influential the person who says them, the greater and longer lasting the negative impact.

Lean sigma in R&D

Lean sigma is a well-established methodology for improving the speed, quality and cost of manufacturing and service industries. In these environments, the underlying work processes are often characterized by high-frequency or repetitive events, so the use of process improvement methods is non-controversial. Nevertheless, such approaches are not magic bullets in any environment. Implementation failures are not often described, but can occur for several reasons (http://www.applied-lean.com/concept/when_lean_fails.html). Recently, an increasing body of evidence has emerged that suggests that continuous improvement, lean, six sigma and process excellence are making a positive impact on drug discovery and development [3–12]. Most of the reported benefits in the public domain are in cycle time improvement. The relative magnitude of these reported improvements is considerable: reports of doubling speed (50% reduction in time) are commonplace (Table 1). This makes sense in our industry for several reasons: true benefit as expressed by increased profitable product launches to customers is rare and takes a long time to realize, so leading indicators such as cycle time are required; and our industry is highly competitive and confers considerable advantages in being first to market, so reduction of cycle time is in itself value-adding to the product. Paul *et al.* [1] have attempted to relate pharma productivity to various key parameters, of which one is cycle time, and increasing speed to enable faster feedback loops has also been suggested as a strategy to reduce uncertainty earlier in drug discovery and development [24]. Going faster can also reduce waste because it can provide information that keeps the direction of research on a more fruitful track, thus reducing wasteful side-avenues of unnecessary exploration [25].

Examples of reduced costs or improved overall efficiency are rarer, but some claims are beginning to emerge. Lilly claim to have gained more than \$1 billion in cumulative benefits from five years of six sigma work (<http://www.investor.lilly.com/annuals.cfm>, 2009 Annual Report), and Covance estimate \$30 million in savings as a result of an 'intensified focus on process excellence' (http://www.covance.com/docs/investors/CVD_Annual_Report_2009.pdf). In our own experience in the cardiovascular and gastrointestinal research department in AstraZeneca, we have seen our operating unit cost (the total budget for the research area divided by the number of preclinical development candidates that com-

TABLE 1

Cycle time improvements from lean sigma process improvements

Process	Cycle time reduction	Refs.
Bioanalytical turnaround time for routine PK studies	Reduced from 3.5 days (mean) to 1.4 days (mean)	[34]
Chemical library provision	18 days to 7 days	[6]
Synthesis of novel molecules	17 days to 9 days median	[4]
Compound receipt to data publication	40% reduction	[7]
Rodent pharmacokinetic study turnaround times	>50% reduction in mean cycle time	[3]
Design-make-test-analyse cycle	25–40% reduction in time taken to test hypothesis from idea to data in database	[35]
Decision-making assay cycle time	61 days to 24 days (median)	[36]
Hit assessment phase	Eight months to four months	[37]
Optimization to proof of concept	Prospective 34 month workplan reduced and achieved in 24 months	[38]
Lead optimization residence time	50% reduction from 2004 baseline	[39]
Reduced early development timelines	More than 12 month reduction	[9]

mence good laboratory practice (GLP) safety studies, expressed as a three-year rolling average) drop by 30% from 2007 baseline to 2009 (at constant rate of exchange), primarily owing to an increase in output. The lack of reported cost reduction is, at least in part, caused by the re-investment of the benefits that have been released from improvement or because the improvement delivered cost avoidance: for example, an improvement project that delivered increased capacity would enable more work to be done by the existing workforce, thus avoiding the need to expand the workforce further to accommodate the increased volume.

Above all, our industry craves improved survival of drug candidates throughout the value chain to launch, but evidence that process improvement has positively impacted on this ultimate test – or, indeed, has the potential to do so – is lacking at this point. Insufficient time and volume of examples have passed to credibly claim that lean thinking has the potential to transform the performance of drug discovery and development. There are some reasons for optimism, however: lean sigma principles encourage us to drill down to the root causes of our recent failures as an industry and provide a framework and tools to enable us to better understand which of our well-intended interventions and investments actually make a tangible difference to outcomes, specifically in the eyes of our customers; the lean principle of making problems visible will make us more self-critical of unproductive compounds, targets and studies and all their associated waste and, as a result, should drive more robust selection and improve decision-making at key investment points, which would in turn reduce attrition; and the proven ability of lean sigma to reduce cycle times will extend to the end-to-end process, reducing time to launch and thereby improving return on investment. For any company to realize these kinds of benefits, lean philosophy and tools will need to be understood and employed throughout the value chain and at all levels in the organizational hierarchy. A new culture will need to emerge and prevail.

Lean sigma, people-centricity and culture change in the context of R&D

Most, if not all, of the texts that have been written about lean thinking and prominent lean companies refer to an evolution from process improvement tools to a culture of continuous

improvement or a ‘lean philosophy’ over time, but it is also commonly recognized that not all companies that embark on process improvement strategies make this transition successfully. Tangible benefits can be realized even from a single cycle of improving operational effectiveness, and for some, it is sufficient return. Alternatively, managers might move on to promoting the next ‘initiative’, thus inadvertently taking the attention and momentum away from sustained improvement. Some lean principles, such as reducing batch size, feel countercultural to long-established ways of working such as batch-and-queue and, as a result, they meet considerable cultural resistance. A lean sigma deployment should be considered to be a cultural transformation [21], therefore, and because most transformation efforts fail [26], the decision to embark on a lean journey should not be taken lightly. Success will depend on capable and experienced change management and leadership and insight into effecting culture change. The importance of the cultural context into which the change is being introduced can be illustrated with the truism often attributed to Peter Drucker: ‘culture eats strategy for breakfast’.

Culture has been said to be the hardest attribute of any organization to change because at its deepest level, there are unspoken rules and tacit assumptions about what is the ‘correct’ way for employees to act and feel in a variety of situations. It might be necessary, therefore, to change how work is done, as well as how people feel about it, to make any impact on culture [21]. Seminal work by Schein [27] highlights the failure to acknowledge the importance of tacit assumptions and norms as one of the primary reasons for failed culture change efforts.

Despite the real and tangible benefits that have been reported, we have also observed noteworthy intangible benefits during our lean journey. In our view, in an innovation-seeking industry that is heavily reliant on problem solving, scientific insight, knowledge and experience, it is possible that some of these intangible benefits are crucial for long-term innovation, productivity and business success. It is somewhat surprising to us, therefore, that these intangible benefits often go unreported or command few column inches in articles. Scientific training probably makes us shy away from making claims that are inherently difficult to justify, but it is those ‘soft’ aspects that have often, in our experience, been tipping points in securing the support and engagement of senior leaders.

In his article, 'Lean in R&D: the surprising fit' [9], Barnhart describes that during three-day value stream workshops with drug discovery teams, 'a unified team forms'. He reports that social bonds appear and cross-functional frictions are reduced as people better understand that it is not the individual who is the enemy or the source of the problem, but the process, and – importantly – that the process is under their control. This is in stark contrast to the interpersonal frictions that were reported when a team in GSK attempted to deliver a lead optimization project in 12 months without first improving the processes and infrastructure [28]. In that case, it is likely that the processes were not fully capable of supporting the team's ambitions and that the interpersonal friction was the result.

On reflecting on the impact of lean sigma improvements in a pharmacokinetics team, our colleagues reported a better, less stressful working environment, which created the time for them to develop new assays and investigate new technologies [3]. In our annual, anonymous survey of employee opinions three years after we began our lean journey, there were notable, strongly favourable responses to key questions, which, if lean sigma were genuinely anti-innovative or anti-creative, would have been a means through which we would have detected a negative impact. Instead, we were pleased to find remarkably positive responses to key statements (Table 2).

These examples of positive impact on the human aspects of work – when combined with our own positive (but hard-to-measure) experiences of improved engagement, teamwork, motivation and confidence as a result of lean sigma improvement work – have reinforced our faith in a people-centric lean philosophy, which was so important to the early proponents such as Deming and Ohno and is still at the heart of current 'true lean' thinking [29]. We believe it is this people-centric foundation on which a unified improvement and innovation culture can be built.

Lean sigma and innovation

The conditions that encourage, support and enable creativity and innovation in large organizations are subtle and complex, but we believe there are some features that offer clear overlap with lean sigma and continuous improvement (Box 1), and others have reported similar findings. Byrne *et al.* [30] analyzed the innovation performance of several companies that had embraced lean six sigma and found that the most successful companies were those that had deliberately extended lean sigma principles into their innovation agenda and had used it to enable breakthrough inno-

ventions and, importantly, change the culture towards one that supported continual innovation. Similarly, Reinertsen and Shaefter [25] highlight how low-cost, rapid cycles of learning achieved through lean improvements and philosophy can directly reduce risk aversion and enhance innovation because the cost and consequences of a negative outcome are reduced. The synergistic potential of lean (six) sigma and innovation is also receiving some attention in the blogosphere, presumably because of the high profile innovation has in most industries at present (<http://www.sixsigmaiq.com/article.cfm?externalID=493>; http://www.sixsigmaiq.com/sponsor_article.cfm?externalID=1720). In his people-centred book, Kofman [31] highlights the potential benefits to an organization that recognizes and captures the importance of learning in its culture. In his words, such an environment 'is every leaders dream: effectiveness, flexibility, innovation, high quality and profitability, low costs and employee rotation, competitiveness, continuous improvement and personal and organizational growth'. It seems we are not alone in believing improvement and innovation can be made to co-exist and even positively cooperate, if handled well.

Concluding remarks

As acknowledged earlier in this article, there is a body of opinion that process improvement methodologies such as lean sigma are inherently anti-innovative, but there are also reports to the contrary. We think these differences are understandable because deploying lean thinking does not, as a direct consequence, enhance or drive innovation, nor is it contraindicated. Instead, we believe that the fate of innovation under a continuous improvement drive (or vice versa) depends on the choices that are made and the climate that is created during the deployment journey. We firmly believe there is much in the continuous improvement philosophy that can be interpreted and implemented to support and even enable more innovation (Fig. 2; Box 1), but we also recognize that there are some traps that could inadvertently divert a well-intentioned continuous improvement deployment in an anti-innovative direction. If the lean deployment has an ambition to help people to contribute at their best, several basic principles of lean thinking can support innovation: it encourages deep, root-cause exploration of problems, which creates a rich and constructive stimulus for new ideas; it puts powerful tools in the hands of the staff who are closest to the problems and can create the autonomy and flexibility for them to tackle them; it values and encourages relentless reflection for learning and sees risk taking as

TABLE 2

Results from employee opinion survey, 2006–2009.

Statement	Proportion of positive responses		
	2006	2008	2009
People continually strive to ensure our processes are as efficient as possible	51%	92%	94%
People are recognised for innovation, finding new and better ways of doing things	66%	76%	88%
I feel my ideas are actively considered	*	84%	88%

Employees were asked to respond anonymously to an electronic survey in September 2006, 2008 and 2009 (no surveys were conducted in 2007). They were asked for their level of agreement with statements on a scale of 1–5, from strongly disagree to strongly agree. Results are reported as a proportion of positive responses received. These data were taken from the surveys of the CV&GI Medicinal Chemistry Group at Alderley Park, UK, which has been engaged in lean sigma improvements since August 2007. Lean sigma improvements formed the most substantial change intervention during this period. Response rate in 2009 was 88%.

* Question not posed in 2006 survey.

BOX 1

The keys to an innovative organization, and how lean can help**Selecting the most important problems to address**

In complex environments, there are many problems, and the selection of the most important ones to tackle is important and non-trivial. Getting to the root cause of problems using lean sigma tools such as the fishbone diagram or '5 Whys' provides deep insight into problems to avoid jumping to superficial solutions or 'patching'.

The organization's attitude to problems

Innovative organizations regard problems as sources of learning and inspiration, rather than inconveniences to be avoided or hidden from view. Furthermore, the organization needs to transmit that it values that learning and ideas highly. Lean organizations consider problems as gifts, sources of further improvement.

Opportunities for cross-boundary interactions

Few innovations are achieved by single individuals working alone, and many innovative solutions are inspired by seeing the potential modification of a pre-existing solution to an analogous problem; therefore, novel perspectives, interactions, networks and teamwork should be encouraged to foster innovation. Many lean solutions involve improved teamwork, cross-training and 'horizontal', anti-silo thinking.

Some available capacity or resources to try new things

Many ideas require incubation and development before their value can be assessed. There are many ways this can be achieved, such as tolerating 'underground' activity, allowing a percentage of exploratory time or a more structured 'dragons den'-like competitive pitching for funds. Whatever the method, ideas need some resources to germinate. The capacity for this kind of work needs to be created, ideally without incurring extra costs. Improvement work typically removes waste, thus liberating vital resources, and lean organizations aspire to operate at 70–80% capacity, thus creating the space for innovation, as well as dealing with surges in demand.

Confidence

People with unconventional, innovative ideas need to be sufficiently self-confident to share their thoughts with others

for those ideas to begin the long journey towards implementation or failure. At the same time, the resource holders (who are often accountable for the quality and volume of the output of the workgroup) need to be sufficiently confident to allow such activities to take place despite the risk of failure. The structured, team-based approach common in lean sigma improvement projects provides an unbiased framework in which ideas are assessed, evaluated and selected for progression. Furthermore, participants who see their contributions make a measurable impact in improvement activities then feel more confident in making bigger, more risky contributions in the future.

Motivation and engagement

Engaged, passionate people are more likely to be innovative and, in turn, an innovative environment stimulates engagement and passion. In general, lean organizations report high levels of employee engagement.

Reduction of frustration

Good underlying processes can enable people's contributions and reduce frustration, just as poor processes can inhibit and dishearten. Frustration exerts a negative drive on creativity and innovation, so process improvement can be considered as a means to reduce an anti-innovative force.

Infrastructure

There is an apparent contradiction between freedom for ideation and structure, but some supporting structure is required to support innovation. Ideas that lack supporting structure such as peer review and input and available resources required for further development will ultimately wither and die. Similarly, ideas that have progressed but are found to be unfruitful need to be stopped in a constructive and timely manner to avoid demotivating those involved and wasting resources. Openly accessible visual planning media and structured lean tools can be used to manage the progression of ideas through the stages of the innovation process laid out in Fig. 1.

a learning opportunity; and it creates a more involved, engaged and committed workforce who take pride in their achievements, thus driving self-confidence and further cycles of ideation and innovation.

The potential traps reside in how three elements of process thinking are interpreted, what choices are made and with what spirit they are deployed. The three elements of process thinking are the meaning of standardization, the role of variation and the choice of how to use liberated capacity. The principle of standardization is often interpreted as being directly anti-innovative because of the implication that the standard way is the 'right way' and, therefore, suggestions for new ways are not welcome. In the context of continuous improvement, however, the standardized state is not a desired final destination but is a meta-stable situation intended to provide a platform for further improvement [32] because it makes it easier to propagate any improvements when they are discovered. To circumvent this potential trap, 'gold-plated' standard procedures should be avoided. Instead, standardized ways of working should be positioned as a way to ensure that everyone conducts their work in line with today's best practice, but everyone should also strive to improve upon it every day and communicate their improvements, when proven. In this way, standardization supports continuous improvement and innovation.

The core aim of six sigma quality (3.4 defects in a million opportunities) is to drive down variation, and it seems to have little relevance to research, especially when one considers the high attrition, or defect rate, at every step in the R&D process. Some research activities involve inherently high variation because they are new and uncertain in outcome. There are some aspects of research work in which low variation is desirable, however, such as in the execution of regular, routine tests or in the turnaround time of results from key experiments. Once the distinction between desirable and undesirable variation is recognized, the benefit of process improvements to provide fast, reproducible, stable and comparable results in a predictable and dependable manner is self-evident, as is the overlap with faster learning cycles and more effective innovation [24,25]. We find that this distinction is so easy for research scientists to understand that it passes unnoticed, but it might pose a trap for the six sigma purist trying to deploy their skills in an R&D environment.

Increases in capacity often arise when unnecessary and wasteful work is taken out of a process. There is a choice to be made about what to use that extra capacity for. If that capacity is entirely taken up by doing more of the same work, productivity will increase but the opportunity for enhanced innovation will be missed because there will still be a lack of resources to conduct exploratory work

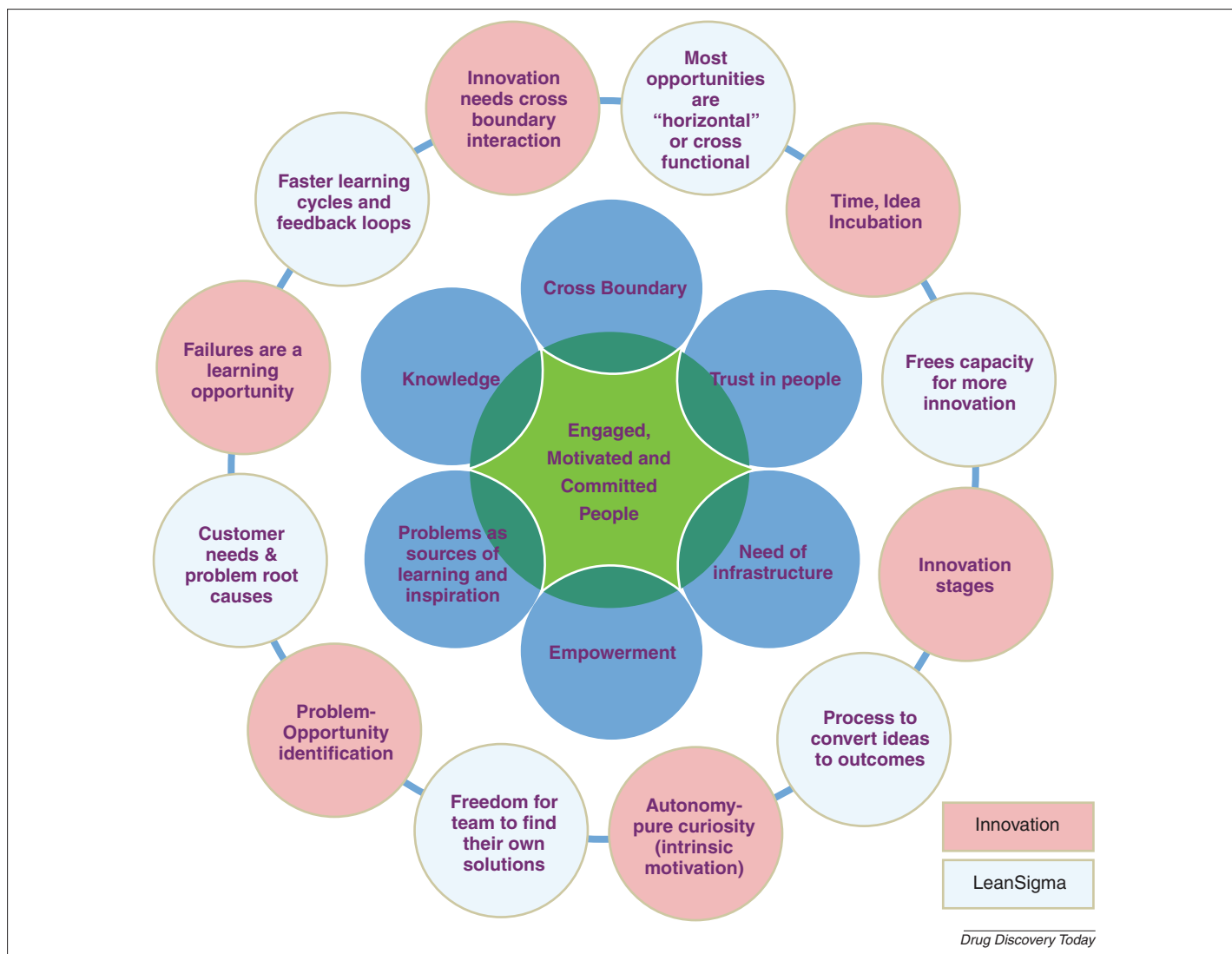


FIG. 2

Relationships between requirements for innovation and lean sigma.

and develop new ideas. The disadvantages of operating at maximal capacity are not only limited to restricted freedom for exploration, however, but also include the inevitable creation of queues and waiting when problems arise [33]; in research, because of the nature of the work, unpredicted events and problems arise frequently. Therefore, a golden opportunity is presented to the R&D manager when capacity is increased because it provides the chance to create more time and space for innovation and reduce the time delays caused by problem-solving work. Successfully exercising this choice and using this extra capacity to explore new, innovative ideas is still a cultural challenge, however, especially in a result-orientated environment. Success is dependent on creating a climate that encourages the use of some or all of the liberated time in this less constrained way and requires strong signals from leaders at all levels that core delivery and innovation are both valued. These signals need to come consistently from what is said, done, recognized, rewarded and resourced.

At the outset of this article, we highlighted that our industry faces two simultaneous demands: to be more innovative and to be more cost effective. We believe it is possible to create a coherent

organizational climate that is capable of rising to and meeting these two challenges by actively pursuing a unified 'innovation and improvement' agenda in the way we have described. Despite the differences in opinion in the literature, the theory seems straightforward, but we fully recognize that the major challenge is in implementation – in 'walking the talk'. Success will depend on skillful and clear communication, gaining widespread commitment to the vision, consistently acting in line with the vision and embarking on the journey for the long term. We also see that the rewards for such an effort are tremendous, however: in addition to the clear business benefits, we think this vision of a creative, innovative, continuously improving place to work sounds like a good, fun, energizing, rewarding and productive place to go and do research each day.

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References

- 1 Paul, S.M. *et al.* (2010) How to improve R&D productivity: the pharmaceutical industry's grand challenge. *Nat. Rev. Drug Discov.* 9, 203–214
- 2 Cavalla, D. and Minhas, R. (2010) Does R&D pay? *Drug Discov. Today* 15, 230–234
- 3 Hammond, C. and O'Donnell, C.J. (2008) Lean six sigma – its application to drug discovery. *Drug Disc. World Spring* 11–18
- 4 Andersson, S. *et al.* (2009) Making medicinal chemistry more effective – application of lean sigma to improve processes speed and quality. *Drug Discov. Today* 14, 598–604
- 5 Russell, K. (2008) Improving pharmaceutical R&D using lean sigma. *PharmaFocus Asia* 7, 48–51
- 6 Weller, H.N. *et al.* (2006) Application of Lean manufacturing concepts to drug discovery: rapid analogue library synthesis. *J. Comb. Chem.* 8, 664–669
- 7 Sewing, A. *et al.* (2008) Helping science to succeed: improving processes in R&D. *Drug Discov. Today* 13, 227–233
- 8 Sewing, A. (2008) Evolution in thinking and processes? *Drug Discov. Today. Technol.* 5, e9–e14
- 9 Barnhart, T. (2008) Lean in R&D: the surprising fit. *Future State Spring* 1–3
- 10 Allen, M. and Wigglesworth, M.J. (2009) Innovation leading the way: application of lean manufacturing to sample management. *J. Biomol. Screen.* 14, 515–522
- 11 Ullman, F. and Boutellier, R. (2008) A case study of lean drug discovery: from project driven research to innovation studios and process factories. *Drug Discov. Today* 13, 543–550
- 12 Petrillo, E.W. (2007) Lean thinking for drug discovery – better productivity for pharma. *Drug Disc. World Spring* 9–14
- 13 Carney, S. (2005) How can we avoid the productivity gap? *Drug Discov. Today* 10, 1011–1013
- 14 Carleysmith, S.W. *et al.* (2009) Implementing lean sigma in pharmaceutical research and development: a review by practitioners. *R&D Manag.* 39, 95–105
- 15 Hinds, B. (2007) 3M: struggle between efficiency and creativity. *Business Week* September
- 16 Hoffmann, T. and Bishop, C. (2010) The future of discovery chemistry: quo vadis? Academic to industrial – the maturation of medicinal chemistry to chemical biology. *Drug Discov. Today* 15, 260–264
- 17 Silverstein, D. *et al.* (2009) *The Innovator's Toolkit*. John Wiley and Sons
- 18 Hennessey, B.A. and Amabile, T.M. (1998) Reward, intrinsic motivation, and creativity. *Am. Psychol.* 53, 674–675
- 19 Sundgren, M. and Styhre, A. (2006) Leadership as de-paradoxification, leading new drug development work at three pharmaceutical companies. *Leadership* 2, 31–52
- 20 Amabile, T.M. and Khaire, M. (2008) Creativity and the role of the leader. *HBR* 101–109
- 21 Shook, J. (2010) How to change a culture: lessons from NUMMI. *MIT Sloan Manag. Rev.* 51, 63–68
- 22 Pink, D. (2009) *Drive: The Surprising Truth About What Motivates Us*. Riverhead Books
- 23 Amabile, T.M. (1998) How to kill creativity. *HBR* 76, 76–87
- 24 Schmid, E.F. and Smith, D.A. (2004) Is pharmaceutical R&D just a game of chance or can strategy make a difference? *Drug Discov. Today* 9, 18–26
- 25 Reinertsen, D. and Shaeffer, L. (2005) Making R&D lean. *Res.-Technol. Manage.* 48, 51–57
- 26 Kotter, J.P. (1996) *Leading Change*. Harvard Business Press
- 27 Schein, E.H. (2004) *Organizational Culture and Leadership*. Jossey Bass
- 28 Macdonald, S.J.F. and Smith, P.W. (2001) Lead optimization in 12 months? True confessions of a chemistry team. *Drug Discov. Today* 6, 947–953
- 29 Hines, P. *et al.* (2009) *Staying Lean: Thriving Not Just Surviving*. Pitman Publishing
- 30 Byrne, G. *et al.* (2007) Using a lean six sigma approach to drive innovation. *Strategy Leadersh.* 35, 5–10
- 31 Kofman, F. (2006) *Conscious Business: How to Build Value Through Values*. Sounds True
- 32 Liker, J.K. (2004) *The Toyota Way*. McGraw-Hill 140–148
- 33 Mudie, P. and Pirrie, A. (2006) *Services Marketing Management*. Butterworth-Heinemann pp. 157–159
- 34 Yergey, J. (2010) Merck experience of application of lean-sigma principles to DMPK workflows in support of drug discovery. *239th American Chemical Society National Meeting, San Francisco, CA*, Paper 304.
- 35 McKerrcher, D. *et al.* (2009) Improving design and enhancing analysis: IDEAs on hypothesis-based multidisciplinary design and analysis. *15th RSC-SCI Medicinal Chemistry Symposium, Cambridge, UK*, Poster 19.
- 36 Sloan, L.S. (2010) Accelerating research through continuous improvement. *239th American Chemical Society National Meeting, San Francisco, CA*, Paper 303.
- 37 Savin, K.A. (2010) Lean-6-sigma and the improvement of processes in early lead generation drug discovery efforts. *239th American Chemical Society National Meeting, San Francisco, CA*, Paper 301.
- 38 Street, S. (2010) Keeping with the times – integrated strategies to improve speed and survival in drug discovery. *Global Drug Discovery and Development Innovation Forum, Edinburgh, UK*. Oral presentation.
- 39 Johnstone, C. (2009) Lean thinking in drug discovery. *10th Drug Discovery Leaders Summit, Montreux, Switzerland*. Oral presentation.