# The industrialization of drug discovery

'The ethical pharmaceutical industry is facing unheralded challenges unlike any it has seen before.'

**Jeffrey S. Handen**, Principal Consultant, PricewaterhouseCoopers

Recent technological advances in combinatorial chemistry and HTS, along with the explosion of genomic data and the increasing empowerment of the patient (or consumer), have all converged to exert significant pressure on the traditional drug development paradigm of 'one size fits all'. With the recent completion of the first draft of the Human Genome Project, these forces now pose both an unparalleled challenge and opportunity to the pharmaceutical industry.

The opportunity to both industry and society is to translate these new technologies into tangible rewards for mass customization in drug development; in short, personalized medicine. The challenge will be how to dramatically increase the speed, volume, and quality of R&D both to exploit the new technological opportunities afforded by advances in automation, computing and genomics, and serve the growing market expectations for personalized medicine.

## Rising costs

The ethical pharmaceutical industry is facing unheralded challenges unlike any it has seen before. Discovery and development costs are spiralling upwards at an annual rate of ~11% [1]. This is partly because of increased regulatory burdens, skills shortages and intensive investments in new techniques and technologies, such as genomics, combinatorial chemistry and ultra-HTS. Meanwhile, pricing pressures continue and increasing competition has led to drastically shortened periods of market exclusivity for new chemical entities (NCEs) [1]. Indeed, the number of NCEs developed by the top 20 ethical pharmaceutical companies has continued a 15-year downward trend, and there is no evidence of greater numbers of compounds entering clinical development to fill the widening productivity gap [1]. This absence of gains in productivity could reflect the fact that investments in genomics and HTS have, as yet, not had sufficient time to yield the expected returns in the market. However, there is no evidence of increases in productivity in either preclinical or Phase I development [2].

In addition, the ethical pharmaceutical industry is facing high expectations from both the financial markets and the 'new' consumer. Analysts and shareholders continue to demand rates of 20–30% in revenue growth to maintain total shareholder value. This becomes more difficult in the face of diminishing portfolios from patent expiry and a continued reliance on the 'blockbuster' model of drug development, in which <10% of products recoup their initial investment costs.

## The empowered consumer

Added to these factors are the growing market demands and expectations of the empowered consumer in the major markets. The patient of the 21st century is a highly knowledgeable and proactive drug consumer. This is a result of both the coming of age of the Internet, where medical and prescribing information is available at the touch of a button, and the industry's own efforts in direct-to-consumer advertising. In recent years the pharmaceutical industry has extended significant resources and efforts in educating and empowering the lay public. This empowered consumer, who the pharmaceutical industry helped to create, is now demanding the fruits of investments such as the Human Genome Project and the promise of personalized medicine. With rising healthcare costs, significant subpopulations of non-responders failing to benefit from a particular drug, and a growing realization of the morbidity and mortality associated with pharmacotherapy (pharmaceutical drugs remain the sixth largest cause of death in the USA [3]), consumer demands for more and better, or personalized, medicine cannot be ignored. Consumers will continue to exert pressure on elected officials and regulators already struggling with risk versus benefit equations in deciding issues such as pricing controls, return on investment (from public taxes allocated to research), and limiting corporate liabilities.

## Confronting the challenge: industrialization

The challenge facing the pharmaceutical industry is how to bring more products to market faster and at reduced

1359-6446/02/$ – see front matter  PII: S1359-6446(01)02099-2 

cost. Spending US$700 million to bring a drug to market that shows efficacy in only 50% of patients, and which has a 10% chance of recouping its development cost, will no longer be a tenable option to either the consumer, the regulator, or the industry itself [4]. All marketed pharmaceuticals work on ~400 targets. The explosion in genomics, proteomics and all the other 'omics' will result in excess of tens of thousands of potential targets. As a result, there is an increased need to discern high-quality leads and to leverage information effectively. The mega-mergers have created scale but not economies of scale in drug discovery efforts, and the new technologies are succeeding in creating fresh bottlenecks.

## Lessons learned

There is a growing realization that the available technology, in isolation, is failing to deliver the goods. Initial efforts to manage the vastly increased throughput of targets and discern the 'hits' have been less than fruitful. They have been marked by difficulties in evaluating and implementing complex capital equipment and software within research-based user communities, problems integrating new equipment piecemeal into existing facilities and departments, difficulties in working across functional, departmental, national and parochial boundaries, and ineffective attempts at using equipment as catalysts for cultural and organizational change. The cost of discovery continues to rise and target time-reductions are not being achieved.

The pharmaceutical industry's initial efforts at automation have strong parallels with the automation of the automobile industry in the late-1970s, when the Japanese completely reconfigured the competitive landscape of the global automotive market. Initial investments in robotics and computer-controlled machine tools failed to yield expected returns. As a result, a whole new school of management thinking evolved – Total Quality Management (TQM), which is characterized by new techniques in integration based on scheduling, bottleneck management, process simulation, statistical process control and production control. This new school of thought helped realize the promised savings of automation. Simply automating silos resulted in the transfer of bottlenecks, realizations by users post-installation that the perceived endpoint was, in fact, just the start, and discernment that theoretical throughputs did not take into account how parameters, such as set-up time, would integrate into the overall process.

However, industrialization, resulting from effective automation coupled with integrated process planning and management, as well as change management, led to a shift in emphasis from saving direct labor to reducing indirect costs and an ability to handle frequent product or process change, but at the same time this did not take the science and engineering out of the process. It allowed the science and engineers more time to concentrate on high-value, low-process work. The success of this new school of thought can be gauged by the observation that in the 1950s the big three car manufacturers (Ford, Chrysler and General Motors) controlled 95% of the US market. The first Japanese import did not reach America until Toyota entered the US market in 1957, and in less than 30 years the imports accounted for almost 50% of the American market. The dominance of the former fortress markets of the big three American manufacturers had not only been breached, but demolished.

The experience of the automotive industry showed that industrialization is more than mere implementation of automation; it is more than the newest hardware. It is a continual process of reconfiguration, addressing change management, enabling technologies, interchangeability and supporting infrastructure to compress cycle-times, reduce defects and expand margins.

The techniques and lessons learned in the automotive industry all have equal applicability in drug discovery. Considered in the light of the erosion of the fortress markets of the American automotive industry in the later part of the 20th century, market dominance, no matter how extreme, is transient to those companies, which remain stagnant.

## The way forward

The future of drug discovery can be based on these lessons. Using the knowledge gained from other industries, the ethical pharmaceutical industry now has the potential to make industrialization a reality. Industrialization can provide an effective catalyst to meet the growing market and financial demands, but the industry must realize that industrialization requires profound organizational change and not just stand-alone investments in robotics and technology. It requires:

- A new culture – a shift to a factory-based culture in those parts of the process adaptable to industrialization;
- A focus on throughput and quality and the realization that this does not take the science out of the process, but allows the scientists more freedom to concentrate on high-value activities;
- New skills in discovery – engineering, automation, logistics and production management;
- New disciplines in discovery – Hi-tech facility design, capital projects management and integrated supply chain management;

- A refocusing of high-value staff on high-value skills – allowing scientists to focus on target validation, assay development and lead optimization;
- A focus on scarce skills – chemo/bioinformatics and data management.

It also requires a clear vision to align the R&D strategy with an IT and technology strategy. It requires definition and measurement of benefits, communication of the need and urgency to implement change, establishment of a full-time team to deliver all aspects of that change, and recognition of the size and complexity of the task with the commitment to budget accordingly.

In conclusion, the ethical pharmaceutical industry will fail to meet the demands imposed by the changing socio-economic landscape of the 21st century if it remains bound to a 20th century business model. Industrialization provides part of the solution by focusing on throughput, quality and resource efficiency in key process parts, while also leveraging experience from other industries.

## Acknowledgements

Richard Archer, CEO of The Automation Partnership, was one of the earliest proponents of the concept of bringing integrated industrialization to drug discovery. The Automation Partnership coined the term 'Drug Discovery Factory' in the mid-1990s to, in part, convey the application of these principles to pharmaceutical research and drug discovery.

## References

1 PricewaterhouseCoopers LLP (1998) *Pharma 2005: An Industrial Revolution* (http://www.pwc.consulting.com)
2 Ashton, G. (2000) Vital data for effective strategic planning highlighted in latest pharmaceutical investment and output survey. *CMR Intl News* 18, 14–15
3 CDC, National Center for Health Statistics (1999) Death and death rates for the 10 leading causes of death in specified age groups by race and sex: United States, 1997. *Nat. Vital Stat. Rep.* 47, 27–38
4 The Boston Consulting Group (2001) A revolution in R&D – the impact of genomics. *BCG Focus* June issue, 1–15

***Jeffrey S. Handen***
*PriceWaterhouseCoopers, LLP*
*Two Commerce Square*
*Suite 1700*
*2001 Market Street*
*Philadelphia*
*PA 19103-7042, USA*
*tel: +1 267 330 6725*
*e-mail: jeffrey.s.handen@us.pwcglobal.com*