'Is it really possible to reverse the downward trend in productivity…?'

editorial

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How can we avoid the productivity gap?

Over the past few years, the term 'productivity gap' has entered the vocabulary of virtually everyone involved in the pharmaceutical or biotechnology industries. As I am sure you are aware, the term refers to a reduction in the number of medicines entering the market on a year-by-year basis. In itself this would be a significant problem, but ever-increasing R&D expenditure compounds the issue. As a result, the cost of developing new medicines is spiralling, with current estimates of US$800 million per drug [1]. In view of the increasing proportion of biological therapies entering the market, the situation is even more acute for companies producing small organic molecules for treating disease. Taking into account that many 'big pharma' companies are facing major product patent expiries imminently, the future would not appear to be rosy.

Post-genomic expectations

In the past ten years or so, expectations have been raised, in that most companies have invested significantly in high-throughput technologies that it was hoped would harvest the benefits of the information derived from the completion of the sequencing of the human genome. It would be unfair to claim that such initiatives have been failures; however, it is probably true that the results of such high-throughput technologies have, up to now, been disappointing. A recent article by Gribbon and Sewing [2] in *Drug Discovery Today* outlined the quality and druggability of leads from Pfizer's significant experience in this area. As with any fledgling technology, it takes some time to assess the issues and values of such approaches. I think that now, the power of these technologies is better understood and they are being placed more appropriately and efficiently in the drug discovery process.

So it would appear that companies are now well placed to take advantage of the plethora of new targets that have appeared in the post-genomic era. However, recent research from Accenture and CMR International (www.eyeforpharma.com/search.asp?/news=44801) has suggested that only 3% of projects aimed at new targets will enter preclinical development compared with 17% for projects on established targets. Obviously, bald statistics such as these do not give the complete picture, in that established targets frequently have set medicinal chemistry approaches that are generally not available for new targets. However, what is more perturbing in the current environment is that new targets, on average, take 16 months longer than established targets to deliver a preclinical drug development

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candidate. Given this, and the reduced likelihood of delivering a preclinical drug development candidate, the result could be some degree of temptation to concentrate on more established targets to reduce risk in the development portfolio.

The question of innovation

In this themed issue of *Drug Discovery Today*, we will be examining some of these concerns. Included in this issue are two excellent papers, the first, a keynote from Esther Schmid and Dennis Smith [3] of Pfizer, which questions whether there has been a decline in innovation. Second, Frank Sams-Dodd [4], from Boehringer Ingelheim, examines whether companies are positioned optimally to benefit from innovation.

So, why is there a productivity gap in the pharmaceutical industry? Well, to be blindingly obvious, there are not enough new medicines coming to market. However, what are the underlying factors resulting in this shortfall? It has been proposed that there might be a reduction in productivity of the individual scientists. This is not a view that I would endorse, nor would Peter Corr of Pfizer, who, when interviewed in this issue of *Drug Discovery Today* [5], commented: '…because I know how hard people in the industry work, day and night…'. Although I quite understand that working hard is definitely not the same as being productive, it would be my view that scientists working in the industry in the past ten years have been more focused, monitored and measured than ever before. The ratio of blue sky:skunkworks is, in my opinion, continually, and unfortunately, shrinking. This would, therefore, broach the question of innovation. Innovation is the life blood of the industry and, as commented by Francis Bacon (1561–1626): 'He that will not apply new remedies must expect new evils; for time is the great innovator'. Clearly, the issue is not a new one. However, the human race shows a clear history of ever-increasing innovation. Does it seem reasonable that scientists in the pharmaceutical industry are any less innovative? Of course it does not, I would contend that pharmaceutical industry scientists are among the most motivated and innovative individuals in the world. Again, the keynote article by Schmid and Smith [3] in this issue addresses the issues surrounding innovation in the pharmaceutical industry. Innovation *per se* and application are, in themselves, probably not the issue, it is more likely that the problems stem from the systems set up to harness the fruits of such innovation and commitment. Frank Sams-Dodd [4] outlines a model by which pharmaceutical companies can exploit more effectively the innovation of their employees. I would suggest that such a model has many attractive features and represents a useful framework for pharmaceutical R&D.

The path for development of a new drug molecule is a well-trodden one. The stages have been outlined for all to see and the general model is used by most, if not all, companies involved in development of small organic molecules as drugs. Is it really possible to reverse the downward trend in productivity by modifying the process that is superimposed across discovery and development? On the face of it, such an approach sounds simple – so why has it not been done before? I would suggest that it has been done before, but often this approach is like turning a supertanker, in that it takes a long time to turn around performance and achieve results. However, for a concrete example of how improved process can have results and can achieve them rapidly we need to look at the example of Wyeth.

The value of process

At the recent *PharmaDiscovery* meeting organized by Elsevier and *Drug Discovery Today*, held on 10–12 May 2005 in Washington DC, USA (www.pharmadiscovery2005.com), Bob Ruffolo (Wyeth) gave a passionate keynote presentation entitled: '*Maximizing the Tools of Drug Discovery to Improve Productivity*'. Ruffolo questioned whether the industry should re-engineer the discovery and development process to address productivity issues. The task of convincing discovery scientists that they should conform to a well-defined, highly managed process is potentially challenging, yet essential. Claims that such processes stifle the creativity or the ability to innovate in a discovery setting is one I am sure most people will have heard (or even said). However, the challenge for senior management is to demonstrate that a suitable framework can allow for personal expression of innovation while achieving the results that are essential to fulfilling the objectives of the company and providing value to its shareholders. Ruffolo showed some spectacular results of how Wyeth R&D had been turned around from, by his own admission, something of a comparative underperformer in the business to one of the leaders in terms of research productivity measures, such as success rates, Phase I candidates per year, and so on. Such improvements are not only important for the R&D divisions but for the company as a whole, because confidence in the pipeline is enhanced by a history of success and delivery. One must always bear in mind that bottom-line costs for development are positively influenced by success rate. As Peter Corr of Pfizer mentioned [5]: 'So, essentially, we're paying a lot for failures'. There is no reason to assume that other companies will be unable to follow Wyeth's lead, although their particular solutions might deviate from the Wyeth model.

The broad issue of the productivity gap and the aspects that are contributing to it was the overall theme of the *PharmaDiscovery* conference, and the issues and some possible routes of solution were hotly debated by leading scientists in the field. A new model was adopted in this conference whereby the content was tightly linked to issues surrounding the development of new molecules. It was intended that specific debate would be encouraged within the sessions, which would be reported by the

respective chairpeople to all the delegates at the end of the daily sessions. Active voting systems enabled us to collect, anonymously, the opinions of the delegates that were present. A summary of the sum-up sessions and results of the voting are presented elsewhere in this issue [6]. We believe that this approach will help to identify issues facing the pharmaceutical industry, identify solutions and make delegates more aware of problems facing their colleagues in different disciplines. Thus, we hope that we will in some way be helping to break down the silos that can so often develop between such specialized disciplines.

References

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