The Editor’s Introduction to the Winter 2004/5 edition of Drug Discovery World ended on a ‘hopeful and constructive note’. Regrettably this has not proved to be particularly prophetic. Not long into the New Year came the news that the MS drug being developed by Biogen and Elan had run into problems thus adding to the list of product failures which dented confidence in the pharmaceutical and medical biotechnology industries in 2004. Anecdotal evidence suggests that potential investors in early and even later stage biotech companies, after a brief period of increased confidence, have once more retreated into their shells and have become extremely wary about funding ventures in these fields. There is an increasing tendency for investors in healthcare companies on both sides of the Atlantic to prefer fewer, larger investments in companies with products or, at least, near market opportunities. The demand for early stage funding far outweighs the supply of available funds making it very difficult for potential start up companies to get off the ground. In the long run this must, it has to be assumed, reduce the number of truly innovative new products entering the pipelines of pharmaceutical and biotech companies – a point to be borne in mind when considering some of the comments made below relating to productivity.

We try in these introductory comments to reflect the mood of the R&D community in the industry and to highlight issues which are at the top of their contemporary agendas. Over the years we have learned that these burning issues are likely to be reflected in the topics covered in the articles submitted for publication in our journal. Of late the themes have changed very little, being focused around what one of the authors in this edition describes as ‘pointed questions about productivity and efficiency’. The same author quotes figures issued by The Pharmaceutical Research and Manufacturers of America indicating that in 2004 their members spent $38.8 billion on R&D compared with $34.5 billion the previous year – an increase of 12%. Almost inevitably the point is made that this has not been accompanied by an increase in numbers of applications for licensing new products. The other point made regularly is that the costs of bringing a new drug to market are rising inexorably – current estimates vary between about $0.8 to 1.15 billion.

Everybody in the industry is, of course, well aware of these facts – there is certainly no complacency. Drawing on the evidence provided by the topics covered by our authors we can see that there is no shortage of suggestions as to how the situation may be improved. All eight articles in this edition of DDW are focused in one way or another on improving productivity and efficiency in the R&D process either by the use of new technologies, by improvements in existing technologies or by learning from past experience.

It is a truism to state that a thorough understanding of a disease process is a prerequisite to developing a new and effective treatment and, to that end, biomarkers have gained increasing prominence over the last few years. Two of our authors discuss the pros and cons and complexities of the use of biomarkers. It is agreed that, in principle, this approach is sensible and likely to be productive but there are still questions regarding the definition and classification of biomarkers and more work needs to be done on their validation.

Three relatively new techniques are reviewed. The first, Cryo Electron Tomography (ET), addresses the problem of determining the structure of the very large number of proteins that the genome encodes. In comparison with other methods it is said to be relatively fast and straightforward and can provide additional information relating, for example, to interactions between proteins. Such information is likely to be critical to drug development.

The second technique is physiologically-based pharmacokinetic modelling (PBPK) which, although requiring more effort than conventional pharmacokinetic studies, has the potential to yield more relevant information. It is well known that large numbers of drugs fail early in the development process because of deficiencies in their ADME profiles. Anything which can be done to weed out such drugs before they enter the development stage would be of great benefit in improving productivity and efficiency.

RNA interference is the third technology reviewed. This has the potential to determine gene function both in vitro and in vivo and is now widely used in drug discovery. Our author considers its strengths and weaknesses and attempts to put it into context in the decision making process in drug discovery. This represents one example of looking back to identify areas where even small improvements would result in big positive effects.

Another approach to learning from the past is exemplified by our article on Cox-2 inhibitor toxicity – described by the authors as a ‘warning shot over pharma’s bow’. The point is made that with available microarray assays there are prospects for providing diagnostic information to identify patients likely to benefit from new drugs but also to identify any sub-group in which use of the drug may be contraindicated.

As just indicated diagnostic genetics are likely to become more widely used and this has led to questions regarding the treatment of the intellectual property involved. Our authors conclude that ‘going it alone will become the less favoured mode of doing business’ and suggest that the use of ‘patent pools’ will become more common. In such arrangements multiple patent owners will agree to license patents to one another or to third parties.

Lastly, modern drug discovery results in the generation of extremely large compound libraries – more than a million compounds can be held by big pharmaceutical companies. Maintaining the integrity of these compounds represents a major challenge. We include an article which reviews some of the latest technologies being applied to compound management.

Finally, I’d like to take this opportunity of warmly welcoming both Dr Amber Salzman and Professor Stephen Naylor to DDW’s Editorial Advisory Board. Amber is currently Senior Vice-President of R&D Information Technology at GSK while Stephen is Adjunct Professor of Genetics and Genomics at Boston University of Medicine as well as a Visiting Faculty Member in the Division of Biological Engineering at MIT. Between them they bring a wealth of knowledge and experience to the team and we look forward to working with them in the future.

Dr Roger Bramblecombe PhD, DSc, FRCPath, FIBio