introduction

This edition of ***Drug Discovery World*** marks our second anniversary. During these two years we have published around 65 articles, which we hope, and believe, have been of value and interest to all who are concerned with the discovery and development of new therapeutic agents but also to those who market, sell, regulate and prescribe them. (If this is the first time you have seen ***DDW*** or do not receive regular copies then please make sure you complete the FREE subscription form within.)

Inevitably a large number of our articles have been concerned with genomics and proteomics and with associated technologies which, hopefully, will facilitate the process of producing useful new medicines from these apparently fruitful sources.

Many new technologies, however, can be misused or abused and in this edition the article by George Poste serves as a timely reminder that technological advances in the general field of biotechnology can increase the threat from bioterrorism. By the same token, advances in the development of vaccines and anti-infectives, for example, can afford better protection from infectious disease agents used as weapons of war or bioterrorism.

High throughput screening (HTS) has played a major role in modern drug discovery but its scale has also produced a new set of problems. Many companies are now in the hitherto unheard of situation of having more apparently promising leads than they can cope with. This has lead to the development of secondary screens which are intended to optimise leads and to reduce their number to a manageable level. Such secondary screens might include ones which can give early indications of toxicity or of the ADME profile.

In these pages Sandra Fox and her colleagues report the results of an HTS study in which 51 HTS directors were interviewed. An astonishing statistic from the study indicates that large laboratories expect to be screening one million compounds per target by 2003. This will be achieved by implementing miniaturisation strategies using 1536-well plates containing very small volumes. The latter has lead to the development of a new technology – nanolitre dispensing. The various developments in this field are reviewed by John Comley.

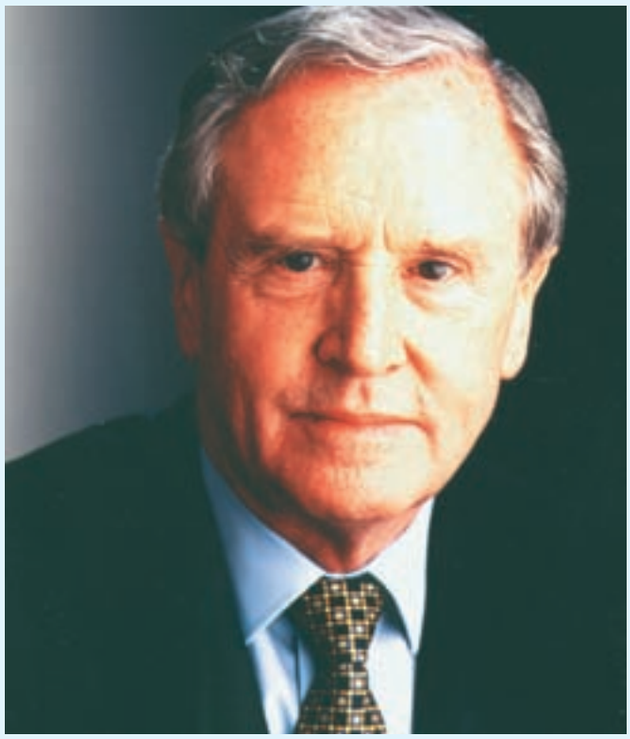
Jeffrey Handen also discusses the challenges for the future which face HTS. He points out that simply screening more compounds will only increase costs and result in more non-viable 'leads'. The thrust must be to develop new screens which filter out all but 'drug-like' compounds.

Mark Beggs and Audrey Long compare the relatively long established HTS with the newer discipline of high throughput genomics. There are differences but also similarities.

The most important similarity is that to be of any value both technologies must produce quality data. This has lead to the recognition of bioinformatics, a subject which has been discussed from various points of view in earlier issues of ***DDW***.

The third generation of human genome maps is represented by single nucleotide polymorphism (SNP) maps. Public databases now contain information on more than two million SNPs on specific locations in the human DNA sequence. In their article Nicholas Dracopoli and Kim Zerba suggest that SNP genotyping will lead to a better understanding of, and potentially development of useful therapies for, complex (ie non-monogenic) diseases.

Monoclonal antibodies seem to have been just below, or just appearing over, the therapeutic horizon for a long time now. Ten are now approved and almost 20 are in Phase III clinical studies. Here Fiona Adair addresses the question as to whether these 'magic bullets are finally hitting the mark'. Not surprisingly they concentrate on the immunogenicity issue which was a major reason for early clinical failures. A variety of strategies to reduce or eliminate immunogenicity have been, and continue to be,



adopted but the conclusion of the author is there are still issues to be addressed before these drugs achieve their full potential.

In recent issues of ***DDW*** we have included a series of articles which discuss advances in areas of unmet medical need. Here Jorn-Peter Halle discusses skin diseases, many of which are poorly treated and where such treatments are available often only relieve symptoms. It is hoped that functional genomics will lead to the development of drugs which will actively modify the course of such common dermatological conditions as psoriasis, atopic dermatitis, etc.

Pharmaceutical and biotechnology companies and various observers of these industries constantly attempt to analyse the productivity of their R&D. The stark fact is that during the last decade R&D spending worldwide increased two-and-a-half-fold but productivity, as measured by the number of products approved, nowhere near kept pace with this increase. Roger Edwards reports the results of a studying which chemistry functions in nine large pharmaceutical companies were benchmarked and conclusions drawn regarding strategy and tactics, processes and resources. It would be of great interest if the author and his colleagues, or others could carry out a similar study on the other disciplines involved in drug discovery.

Finally, I have to report some changes in our Editorial Advisory Board. Dr Simon Campbell who has been with us from the start has felt obliged to resign due to pressure of other commitments. We thank him for his contributions. We are very pleased to welcome to our Board Dr George Poste (see above) and look forward to working with him. Dr Poste is, I am sure, well-known to many of you, not least of all as having been President, R&D and Chief Science and Technology Officer at SmithKline Beecham.

Dr Roger Brimblecombe PhD, DSc, FRCPath, FIBio