

Healthcare Innovation in the UK - A Royal Society of Chemistry Position Paper

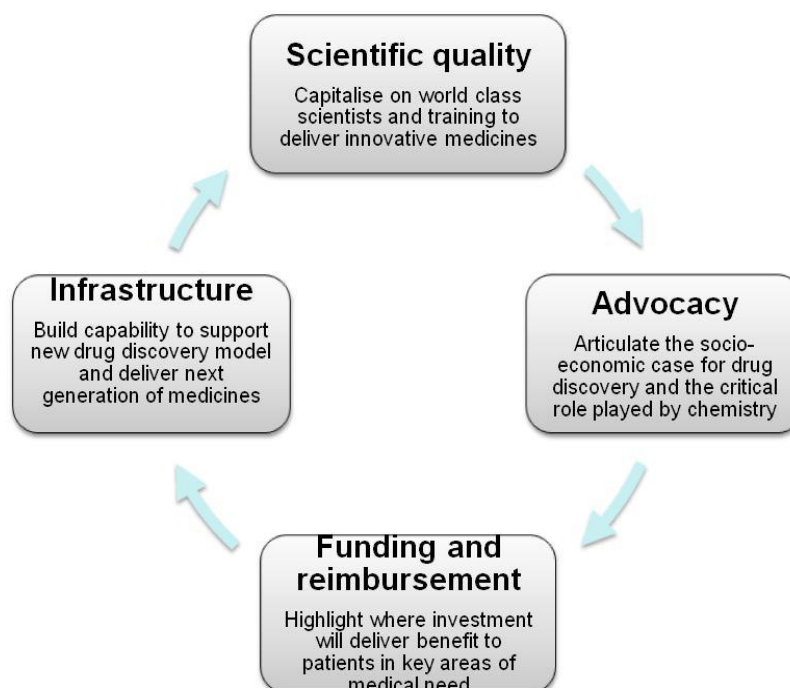
Introduction

The pharmaceutical industry (Pharma) has made important contributions to quality of life, longevity, economic growth and education at all levels, and is a key component of the government's growth strategy. However, the industry is now under considerable pressure as the number of novel drug molecules or 'New Chemical Entities (NCEs)' has not increased over the past decade and there have been significant revenue losses as important drugs lose patent protection. Consequently, the sector has experienced significant reductions in R&D budgets, closure of research sites and the loss of thousands of skilled jobs. While these phenomena are not restricted to the UK, the UK does have a compelling need to evolve to safeguard its leadership position. A new and sustainable funding model with public sector participation is urgently required for the UK's world class scientists to invent and develop innovative medicines that meet the medical needs of the 21st Century, and contribute to economic growth

The positive benefits of such an exciting initiative would include: UK discoveries would help meet the healthcare challenges of the 21st Century; quality of life would be improved even within constrained healthcare budgets; important diseases areas abandoned by Pharma would receive proper attention with consequent patient benefits; assets not being pursued by Pharma would be revived and developed; economic benefits would flow as UK innovations enter world markets; the UK science base would be strengthened with exciting career opportunities for world class scientists to reap the benefits of our internationally competitive science education; new biology emerging from UK laboratories would be expertly exploited by world class medicinal chemists; the biotech sector would be revitalised as an additional source of innovation/discovery with a sustainable return on investment.

Background

The position paper centres around four inter-related themes as summarised below:



Scientific quality

For decades, the UK had been a world leader in medicines discovery and research with at least 10 of the top-selling drugs worldwide (>\$1bn annual sales at peak) having UK-trained

PhD organic chemists as named inventors. The basis of this success has been the ability of the UK-based pharmaceutical industry to retain a rich pool of highly talented and well-trained scientists, ensuring that healthcare challenges have been addressed through the application of world-class science. As the complexity of medicines research grows and as other nations play an increasingly active role, the UK approach to healthcare innovation needs to evolve in order to safeguard its global leadership position.

Advocacy

It is critically important for the medicines research community to articulate clearly and consistently how the invention and development of new drug treatments has served to benefit patients and that continued investment in key areas of medical need will be required to address the existing and future needs of patients. It is also important to emphasise that investment in drugs and therapies has paid dividends for the UK economy and will continue to do so as long as the UK's leadership is maintained. The indispensable role chemistry plays in the process is often overlooked but without chemical enablement, medicines research in the UK would flounder. In particular, new disease targets would lack tools for validation and would be devoid of chemical lead matter - the bedrock of drug discovery programmes.

Funding and reimbursement

At a time of rising R&D costs and diminishing research budgets, there is a clear need for the UK to develop a national strategy for investment and reimbursement that will serve to incentivise medicines research in defined areas of high medical need. A coherent approach would help funding bodies to align their investment priorities and so ensure benefit to patients is realised and return on investment is maximised.

Infrastructure

In order to safeguard the UK's scientific leadership in medicines research and underwrite the next wave of innovative medicines, a step-change in research infrastructure will be required to ensure the UK remains at the forefront of the latest scientific advances. This will require funding bodies and policy-makers to work in concert, across traditional discipline boundaries, to establish a capability across the UK that can sustain a new model of drug discovery and help to attract and retain world-class scientists.

Status

The global pharmaceutical industry has come under considerable regulatory and economic pressures over the past years, and continued contraction is now threatening healthcare innovation. Additionally there are increasing government drivers to contain healthcare budgets particularly in light of an ageing population, and drug prices are continually being forced down. Increasing emphasis is now placed on cost/benefit analyses to justify reimbursement, but negative regulatory decisions after multi-year drug development programmes are wasteful of R&D investment. Safety demands have also escalated such that a single clinical trial for a new cardiovascular agent can involve up to 20,000 patients, while new drugs for diabetes now have to undergo an additional 2-year safety study before approval. Consequently, the costs of discovering and developing a new medicine have escalated to well over \$1bn, but return on investment has deteriorated sharply in the face of fierce economic and regulatory pressures. Indeed, the EU Commission for Industry and Entrepreneurship recently recognised tensions between making affordable medicines widely available while providing Pharma with incentives to innovate, but gave no direction for future action.

In addition to external pressures, Pharma is losing billions of dollars in revenues as major drugs come off patent, but which are not being replaced at an equivalent rate despite escalating R&D budgets over the past two decades. Biotech was once regarded as an endless source of potential products for Pharma to acquire, but both sectors have weakened in parallel as venture capitalists are unwilling to wait between 5-10 years for an

adequate return on high risk investments. It is essential that UK Biotech is revived through innovative funding mechanisms that balance risk and a sustainable return on investment so that the sector can continue to make major contributions to future healthcare needs.

A common reaction to internal and external pressures was through mergers and acquisitions to create monolithic organisations driven largely by commercial considerations rather than R&D productivity. For example, a recent mega-acquisition created a world-wide research group of over 12,000 scientists with a combined pre-merger R&D budget of \$11bn. However, drug discovery cannot be industrialised in the same way as cars or steel and productivity has not increased in Pharma over the past decade, although R&D expenditure has ballooned to unsustainable levels. In future, drug discovery will be carried out by smaller and more nimble organisations with clear objectives, reporting lines and accountability.

In response to these economic, regulatory and organisational threats, Pharma is going through an extensive round of downsizing with site closures, redundancies and significant budget reductions. The UK has been particularly hard hit with closures by AstraZeneca, GlaxoSmithKline, Pfizer, Merck and Roche in recent years, with thousands of skilled scientists losing their jobs and livelihoods. Whilst these events present significant challenges, there is also a unique opportunity now to redeploy world class medicinal chemists released by Pharma as part of a re-shaping of the UK's medicines research landscape. One attractive option is build this medicinal chemistry expertise into a series of dedicated drug discovery hubs co-localised with therapeutic area clusters as this fundamental skills base barely exists in UK academia. Of course, individual hardship is also reflected by reduced tax inflow at national and local levels, erosion of a positive balance of payments, reduced industry support for science education at all levels, and for community activities. Contraction of Pharma is also a major concern for the next generation of UK-trained research scientists as employment prospects have been seriously threatened, and the nation's science base will be weakened.

The economic consequences of Pharma downsizing are obviously serious, but such dramatic reductions in research capacity also threaten future healthcare innovation in the UK, particularly in light of an ageing population. Not only has the Pharma research base contracted but therapeutic areas such as neuroscience and obesity are being downsized, despite high medical need, limited effectiveness of current therapies, and significant healthcare costs. Meagre returns on investment have largely forced Pharma to exit antibiotic R&D, even though the World Health Organisation has forecast a disaster due to rapid and unchecked increases in microbial resistance. Indeed, the devastating effects of HIV and MRSA, for example, underline the need for a strong pharmaceutical R&D sector to invent new drugs to control known and unexpectedly medical challenges in the 21st Century. Given the scale of Pharma contraction in the UK, the shortfall in healthcare innovation cannot be made up by academia and charities in their current format as there is neither the scale nor experience. In addition, these bodies largely focus on and diseases of the developing world and cancer, and there are little or no drug discovery initiatives in the public sector addressing serious conditions such as obesity and schizophrenia, for example.

The developing gap in healthcare innovation is particularly concerning as the UK has an outstanding record with novel inventions ranging from cardiovascular drugs to anti-infective agents addressing relevant medical needs and generating billions of dollars in revenue. There are strong academia/industry/clinical research partnerships in drug discovery and development that have taken years to build, but which simply do not exist in developing countries such as China and India. The UK Pharma work force is skilled and innovative, but if these world class drug discovery teams are allowed to fragment it will be extremely difficult to re-build such quality from scratch all over again. It is essential that the UK's unique medicinal chemistry talent pool is nurtured, supported, and integrated into multidisciplinary translational initiatives as a fundamental core skill to facilitate and exploit

innovative biology emerging from UK laboratories. UK medicinal chemists are particularly successful in inventing the synthetic molecules that provide cost effective oral therapies that are the mainstay of any healthcare system. While biological based drugs are making a significant impact, this therapeutic class will not remove the need for affordable small molecule “drug pills” taken by mouth for chronic diseases.

Pharma’s response to stagnant productivity was to create monolithic organisations, but the number of NCEs approved by the Food and Drug Administration has barely changed over the past decade, and attrition during discovery and development has remained above 90%. Greater consideration needs to be given to the reasons for compound failure which include poor target validation, suboptimal animal and human safety, heterogeneous clinical trials rather than targeted patient sub-groups, and insensitive methodologies where placebo response can confound a positive signal to a novel mechanism of action. . In addition, “chemistry space” needs to be expanded significantly to access hundreds of novel biological targets that are involved in important diseases, but are beyond the reach of current drug templates. International pre-competitive collaborations such as the European InnoMedPredTox, the Innovative Medicines Initiative and the Structural Genomics Consortium are addressing some of these issues, as are as a series of precompetitive workshops being coordinated by the RSC across the UK but investment needs to be increased. All of these initiatives would reduce R&D risk and the cost of drug discovery and development, so as to generate an acceptable return on investment to fund future innovation. Pharma exactly matches the government’s demand for research with economic and social benefits, and therefore drug discovery should be an obvious area for growth.

Summary

The government considers that investment in Pharma R&D should be a key component of its growth strategy as new medicines bring significant health, social and economic benefits as well as providing rewarding employment for world class scientists trained in our schools and universities. Officials from the Department of Business, Innovation and Skills and the Department of Health are considering how the UK can take advantage of the changing Pharma R&D sector, and the RSC is committed to work with all parties to develop a national strategy for drug discovery that capitalises on world class talent with pump priming investment from government, funding councils, charities and the private sector. The fundamental challenges are to balance drug prices, R&D expenditure and risk, with a fair return on investment to fund continued innovation. Therefore, key stakeholders should work together to develop a sustainable funding model with enhanced public sector participation that will support world class UK scientists in the discovery and development of innovative new medicines to meet the medical needs of the 21st Century and to contribute to economic growth.

The Strategic Themes below summarise options for prioritisation, and development into an integrated plan to revitalise Pharma R&D in the UK.

Strategic Themes for Healthcare Innovation in the UK (RSC-led, Partner participation)

Advocacy

- **Build consensus of expert stakeholders** with the common objective of supporting world class healthcare innovation in the UK
- **Stress importance of innovative biopharmaceutical R&D** as a key component of the government's growth strategy and for competitive exploitation of the UK science base
- **Highlight for government, funding bodies and charities that innovative chemists** are the fundamental enabling scientists that invent the range of novel structures required to modulate biological processes at every level

Scientific Quality

- **Continue to build industry/academic pre-competitive collaborations**, focusing on target selection/validation, and predictive toxicology to reduce attrition
- **Embed experienced industrial scientists in biomedical centres of excellence** by creating new chairs in medicinal chemistry, enabling them to engage in translational initiatives and transform innovative biology into new medicines
- **Invest in fundamental new chemistry** to address novel biological targets currently beyond traditional drug templates

Infrastructure

- **Stimulate a new model of medicines research** through a network of Academies of Drug Discovery where expert medicinal chemists can facilitate and exploit innovative biology emerging from UK laboratories and where the education and training of next generations of research scientists can be delivered.
- **Invest in a nationwide compound bank and screening capability** that enables a systematic approach to tool/lead identification to validate and advance new biological targets

Funding and Reimbursement

- **Work with government, European Investment Fund, Technology Strategy Board, Wellcome Trust, Research Councils, private sector etc** to establish a sustainable funding model to world class drug discovery capabilities at the public/private interface and also to revitalise biotech

Partner-led (RSC participation)

Funding and Reimbursement

- **Prioritise therapeutic areas of significant medical need** where innovative new medicines will improve quality of life and economic benefits
- **Define efficacy/safety/health economic criteria** for new agents that would command fair reimbursement and an sustainable return on investment

Scientific Quality

- **Build industry/academic/clinical pre-competitive collaborations** to identify patient sub-groups that respond to agents with novel mechanisms

Infrastructure

- **Evaluate opportunities to reposition experienced pharmaceutical scientists** and state of the art facilities into a combination of Innovative Drug Discovery Centres, Spin Outs and CROs