WHAT IS MEDICAL INNOVATION?

Allison Jeynes-Ellis
Medical & Innovation Director, ABPI

The story of the discovery in 1928 of penicillin – the original 'wonder-drug' if ever there was one – is today part of the lore of medicine. Most people know how Sir Alexander Fleming discovered the killing powers of the penicillium mould in an accidentally-contaminated bacterial culture. Fleming received the Nobel prize for medicine for his work in 1945. Yet it is a very long way from a mouldy petri dish to today's modern armoury of antibiotics. Fleming's part in the story, though seminal, is but a fraction of it. Moreover, the urgent quest for new antibiotics to combat resistant strains, highlighted by Professor Laura Piddock and Tracey Guise in the Autumn 2011 edition of *Science in Parliament*, shows us that continuous innovation in drug development is both vital and inevitable.

The profound impact antibiotics have had on our lives is no longer the product of chance discovery but has come about thanks to mankind's ceaselessly probing nature. Every one of today's medicines is the result of countless small steps forward: an incessant process of learning and improving so that each new agent takes us further than we have gone before. Innovation is not about eureka moments. There is no switch that puts the bulb on or off. It is more like turning up the dimmer control: gradually intensifying our capacity to understand, overcome and treat.

The Office of Health Economics will shortly publish the second edition of its report *The Many Faces of Innovation*. It will describe how it is this process of incremental innovation that has given us the vast array of medical treatments at our disposal today. Drawing on examples from several therapeutic areas, the report will show how in every case step-by-step improvements have brought important benefits over and above the original concept. These benefits have several dimensions to them. Incremental innovation can lead to a medicine that is more effective than the one before, or which has fewer side-effects. A newer product might be easier to take, making it more convenient for the patient and aiding adherence. It may be more cost-effective. It may have particular value treating specific groups of people with the underlying disease.

These added advantages are seen both in new classes of medicine and within class. Later types of agent for hypertension, for example, have led to improved health outcomes, with a significantly reduced risk of death from events associated with raised blood pressure. The new generation of anti-epileptic drugs were better tolerated than their predecessors, with less risk of harmful interactions with other medicines. This was particularly important for elderly patients, for example, who are more likely to be taking a variety of medication.

The cholesterol-lowering statins meanwhile provide an excellent example of how innovation expands our options within one class of medicine. Later statins were more potent than the earlier versions, with a corresponding impact on outcomes. If there had only ever been one statin, that would have been good in itself; but nowhere near as good as the spectrum of products available today, allowing doctors to tailor treatment to their patients' needs.

Incremental innovation is not only the essence of medicine development. It is also important in public policy, and about to become more so as the Government embarks upon reform of how prescription medicines in the UK are paid for. This will be a challenge not just for the pharmaceutical industry, which is under increasing pressure in a finance-dominated environment to justify itself as innovative, but for policy-makers too. They must find ways of providing incentives for the progress and innovation that will help improve NHS productivity in the medium term, while bearing down on costs in the shorter term.

The Government wants a new system of 'value-based pricing' to be in place two years from now. The shape of things to come is starting to emerge. The Government's consultation paper issued in December 2010, for example, states that the new system would '[aim] to recognise and reward innovation, in particular by encouraging a focus towards genuine breakthrough drugs, which address areas of significant unmet need'. Later the same document talks about focusing on 'achieving genuine step changes in clinical performance, rather than seeking just to make incremental changes'. This is in the context of growing reluctance on the part of payers across Europe to recognise and reward innovation beyond a very limited definition of the term.

It is welcome that a paper on pricing recognises innovation as something that matters; however, the nature of some of these comments suggests that a restrictive definition of innovation may be used. How the government defines innovation in the new scheme will be critical to whether it achieves its stated objectives. It is therefore important that the government has a thorough understanding of the nature of pharmaceutical innovation, to inform its policy approach.

Pharmaceutical R&D has four key characteristics: it is highly complex and uncertain due to a significant scientific challenge at early stage and recurrent risk of failure at clinical phases; timelines to develop new products are long (over 12 years

on average); it costs much more than in other sectors to bring a new product to market (£1.15bn per new medicine, including the costs of failure and capital); and there are very close links between the private and academic sectors.

The uncertainty and length of time involved means the outcome of a research project will not be known until many years after the decision to invest has been made, and significant sums have been spent. Companies aim to have a portfolio of high-risk and low-risk projects and the extent of innovation is unpredictable at the point when the investment in R&D is made. Understanding this is important in order to provide the right economic incentives to generate socially valuable R&D.

Pricing systems provide signals to the pharmaceutical industry about whether and where to invest in R&D, depending on what is rewarded and how. The relationship between pricing mechanisms and rewards for innovation was discussed in the WHO Priority Medicines Report of 2004. This report argues, among other things, that prices in Europe are set at levels that do not fully reward innovation. This, along with delays to reimbursement decisions, leads to uncertainty among stakeholders and encourages companies to launch their products first in non-European markets.

Given the importance of pharmaceutical R&D investment to the UK economy, these considerations should command the attention of policymakers. To encourage continued pharmaceutical investment in innovation, the steady process of incremental advance and the different dimensions of innovation will need to be recognised and rewarded. Looking at the history of medicine development shows that it is just such incremental advances that have led to the considerable improvements in, for example, antibiotics, anti-epileptics and statins, that have had such major patient benefits.

Therefore, a value-based pricing system will need to allow for a broad definition of innovation. Any policy that does not recognise all aspects of value in a new medicine, including value that accrues outside the health system, and that might increase the uncertainty of reward that companies face, might end up discouraging potential worthwhile R&D investment.

It is still early days for value-based pricing and the new system can – and must – be designed to recognise the reality of incremental innovation. Innovation is a complex, multi-faceted and uncertain matter and valuing it will undoubtedly be a daunting challenge. It is vital we succeed. Whether it is antibiotics or cancer, HIV or heart disease, our success in pushing medicine to its limits is inextricably tied to how well we recognise and incentivise innovation. Only rewarding eureka moments would choke off that potential.

The stakes are high, not just for our health, but for our pharmaceutical and biopharmaceutical industries as well. Late last year, the Prime Minister launched the Government's life sciences strategy, acknowledging the importance of these industries to growth and jobs. Finding the way through to incentivise incremental innovation in pricing will be an important test of that strategy's durability and strength.

IMPLICATIONS OF THE NEW EU DIRECTIVE REGULATING ANIMAL EXPERIMENTS FOR THE UK

Dr Maggy Jennings OBE
Head of Research Animals Department, RSPCA

On 9 November 2010 a new European Directive on the Protection of Animals used for Scientific Purposes (2010/63/EU)[1] came into force. If this is implemented in line with the intentions encompassed in its recitals, there will be a significant improvement in the regulation of animal experiments in many Member States. However, in the UK, which already has a well-developed law regulating animal use, there could be serious negative consequences.

The Directive is largely based on the UK Animals (Scientific Procedures) Act 1986 (ASPA), but as Home Office Minister Lynne Featherstone MP has acknowledged, a number of its provisions are 'potentially less stringent'.[2] For example, a higher level of suffering could be caused than is currently permitted – an exemption clause allows researchers to make a case for using procedures involving long-lasting severe pain, suffering or distress that cannot be ameliorated –