

Consultation Meeting for the Cooksey Review:

“Lost In Translation”

The Royal Society, London. 31st July 2006.

As part of the consultation exercise for the Cooksey Review, a one day stakeholder meeting, entitled “Lost in Translation,” was jointly hosted by the Academy of Medical Sciences and the Royal Society. It was held at the Royal Society, London on Monday, 31st July, 2006.

A. Meeting Format

More than seventy leading representatives from science, medicine, medical research charities, the NHS, universities, policy-makers and the commercial life sciences sector attended the meeting. Each invitee was asked to consider four questions prior to, and during, the event. These were:

- 1. The UK has demonstrated its ability to fund and carry out excellent basic research. There have been successful examples of this basic research being translated for patient and economic benefit. The paramount requirement of this Review is to improve our success in translation and application of research discoveries. How do we achieve this?*
- 2. What career, cultural and financial incentives do we need to have in place to ensure that the basic and applied research communities work together as a continuum?*
- 3. What incentives do we need for the institutions concerned, universities, hospitals and industry to work seamlessly together to realise the broadest possible benefit to society?*
- 4. This is a fast moving field where other national governments are competing for the success of their own systems, e.g. NIH, CIHR, etc. Yet all the investment is long term. Metrics must be developed to measure past success, position our current activity and demonstrate what needs to be done to succeed in the future.*

Four eminent figures in the world of health research were invited to give presentations on their thoughts and ideas for health research, particularly in relation to translational research. These were: Professor John Bell FMedSci, Regius Professor of Clinical Medicine, University of Oxford; Dr Alan Bernstein, President of the Canadian Institutes of Health Research; Sir William Castell, Chairman, Wellcome Trust & former President and CEO, GE Healthcare; and Professor John Savill FMedSci, Vice Principal, University of Edinburgh & Head of the College of Medicine & Veterinary Medicine. After these presentations, attendees were asked to discuss each of the above four questions in small “breakout groups”. Each breakout group then fed back a summary of their discussions to the entire assembly.

General points captured during both the four presentations and the ensuing discussions are presented below. These points are not intended to represent a consensus view of the meeting attendees. Neither do they necessarily represent an expression of the views of the Cooksey Review Team, the Royal Society, or the Academy of Medical Sciences.

B. Points of Discussion

1. Basic science

- The UK is the second most important country to the USA in basic science. It has several international lead positions, such as in embryonic stem cell research.
- There is an increasing need to maintain that strong foundation in basic research, not just in biomedicine, but also in the physical and social sciences.
- The increasing speed and power of biomedical research is both a promise and a challenge for healthcare delivery. There is a gulf between the pace of change in basic research and its application to both healthcare policy and healthcare practice.
- Rather than separate basic science from clinical research, excellence should be supported wherever it may be on the research continuum.

2. Healthcare Trends

- Healthcare expenditure is expanding faster than GDP in many countries, leading to international concerns that healthcare costs will soon be unaffordable. This growth is coupled with an increased expectation for accountability of public funding.
- In the near future, there will be a movement away from the focus of developing treatments for terminal diseases, like cancer, to management of chronic conditions, like diabetes or infection.
- The UK is in a strong position to take advantage of health research, because its government is a provider, insurer and legislator for healthcare. This universal healthcare system provided by the NHS is the unique selling point for undertaking biomedical research in the UK. Information Technology will be a key component in industrialised countries for the effective operation of healthcare systems in the future. Data from the NHS could be used to answer important research questions, such as those relating to combination drug therapy.
- International health is an increasingly important issue for the benefit of both the developing world and the UK. China and India will join the USA as the dominant major economies in the world within twenty years, yet most medical research still targets the 5% of the world's population living in the USA. The UK is an even smaller market than the USA and is a more expensive location for research than China or India. Therefore, research into international health requires substantial additional investment.

3. Research strategy

- The UK needs a clear national strategy for health research so that resources can best be allocated. Industry would be more interested in pre-competitive collaboration if there were a defined national strategy as areas of mutual interest would be clearer.
- Blue skies research can often be better undertaken in the public sector.
- Publicly-funded health research also has a significant role to play in research underpinning healthy ageing, mental health and cognitive

decline, developing stem cell therapies, improving capacity in predictive toxicology, exploring public health and prevention strategies through studies of disease-related behaviours, and in developing personalised medicines.

- A culture of R&D must be seen as an asset in the NHS. More of basic research should be needs-led. Unfortunately, at present, basic researchers do not know what the clinicians want. The UK needs a demand-side 'pull', not just science-side 'push' in a publicly funded health system. It would be important to consider how best to stimulate this demand. Future research directions should not be all be 'top-down'. 'Bottom-up' approaches seem better for basic research while 'top-down' approaches are more appropriate for applied research.
- Translation of research is a bi-directional process. There is need for a 'bedside to bench' approach, and not just *vice versa*.
- Prevention, such as changing health behaviours, is an important aspect of translational research. Yet a recent report by UKCRC indicated only around 2.5% of UK health research was in prevention.
- Government procurement could be greatly strengthened as the UK is traditionally a late and slow adopter of new health technology. Here, there is a role for NICE, or another organisation, to enable the NHS to act as an 'intelligent customer'.
- Change champions, including young faculty, are vital to achieving cultural change.

4. Career paths

- There has been a dramatic decrease in the numbers of clinical academics, who are a key cadre for the translational research mandate. More properly trained clinician scientists are needed. The number of research Fellowships needs to be expanded. Future clinician scientists need to be identified early. The career path for budding clinician scientists is not always clear and the current clinical research training environment remains somewhat patchy. The Walport awards are an encouraging development that needs to become widely embedded quickly. The

distribution of role models, many of whom were educated and trained under a different system, is also irregular. MD PhD awards take too long to complete. The fast pace of research will often make much of the experience gained in the PhD component redundant before the whole programme is completed.

- There is a trend towards increasing the multidisciplinary and size of research teams, independent of the translational issue.
- Tenure and promotion currently tend to be based on what individual researchers have done, rather than what their contribution has been as part of a team. This will need to change to reflect the increasing importance and changing profile of research teams.
- UK health researchers should be given the opportunity to train and work overseas with colleagues in the developing world.

5. Incentives

- Incentives must be provided at every level of the research enterprise, from individuals, to teams, to departments and hospitals. All must be rewarded appropriately. Incentives should include rewards for collaborations between hospitals and universities.
- A culture must be established that encourages NHS Trust Managers to support research. Research activity and quality should be included in NHS Trust ratings. More support is needed from the Healthcare Commission in terms of valuing R&D activity.
- Research can bring Trusts increased 'kudos', which encourages patients to choose Trusts with high research activity. Trusts must be educated in the positive impact of research activity on recruitment and retention of high-quality staff. Evidence from the new medical schools suggests that research has a significant impact in this respect.
- General practitioners also need incentives to become involved in research. The General Practice Research Database became so successful in part because GPs were given free computers if they participated, but the computers had to be returned if practices withdrew from the scheme.

- The decline in number of research training (merit) awards has opened a gap between the rewards received by academic and non-academic consultants, thereby reducing the incentive to follow a clinical academic career.
- Grants are difficult to obtain, so young basic scientists find it hard to establish themselves, which reduces the incentive to follow a research career. Basic scientists also need better individual rewards. Scientists and their laboratories need clear rewards for translating their research, something that MRC Technology often does well. A mechanism is needed that both allows scientists to continue to be involved in translating their own ideas or, where appropriate, takes them forward on their behalf.

6. Infrastructure

- The higher education system is currently formulated around disciplines, but questions in health research are increasingly 'horizontal', that is, based on specific unmet needs which are to be answered. This calls for people of different disciplines working together. There need to be structures at higher education institutions that promote horizontal integration.
- There are benefits in establishing five to six 'centres of excellence' in research located around the country. The co-location of basic and applied research will break down interfaces between the basic and applied communities, promote interactions between groups, and increase multidisciplinary working. The effect of putting people together overcomes the problem most researchers identify which is the physical distance between research groups. Creation of such facilities would create an environment for innovative treatments. It is important that the system does not stagnate, so there must be continued opportunity for other locations to become centres of excellence.
- However, in parallel to the development of these centres of excellence, research networks must be widely supported. The advantage of the geographical breadth of the NHS must be exploited. Lessons from the Canadian Institutes of Health Research show that virtual networks can be as effective as physical ones.

- Translation research structures should be owned and managed jointly by universities and the NHS. Increased levels of multi-institutional collaborations are taking place because it is difficult for one campus to have all the necessary infrastructure. One idea would be for university and health boards to have cross membership, with a single R&D office. R&D strategy should be owned at the top level within the health board, with locally organised research funding that is transparent, activity-driven and flexible. Partnerships with the Regional Development Agencies are also vital. The Scottish Executive's activity is a good example.

7. Funding

- Funding awards need to cover the full economic costs of research. Assuming limited resources, it would be better to fund less research but at full cost.
- The health research community needs to be realistic about the substantial resources required to support research properly. Oxford University, as an example, demonstrates it is possible to obtain resources from a number of sources by systematically targeting support from charities, research councils and industry.
- Although the BBSRC and MRC offer some opportunities in translational research, current funding to help move ideas on from the laboratory is limited. Research Councils are still perceived as being weak at supporting interdisciplinary research.
- Cultural change is easier in an expanding financial environment as the Canadian Institutes of Health Research has recently found.
- However, relatively modest pre-seed funds from government could help establish proof-of-concept experimentation and encourage innovation.

8. Knowledge transfer

- Knowledge transfer is a vital process in improving the translation of basic research into healthcare benefit. It is a 'sticky' operation, often being driven by the personal interaction and trust between colleagues. Simple

accumulation of facts can be generated from standard sources, such as the internet.

- Knowledge transfer tends not to be as highly valued in academia as knowledge production. However, it is essential for the research community to be engaged in Knowledge Transfer.
- There are numerous possibilities for enhancing the profile of knowledge transfer, such as via prizes for best examples of knowledge transfer, separate bodies or sources of funding for knowledge transfer, or 'champions' or vice-presidents of knowledge transfer, to act as 'lightning rods' within institutions.

9. The Commercial Sector

- The contributions of the different sub-disciplines within basic science to drug development have changed over the years. In the 1960s and 70s, drug development took place principally using chemistry to identify lead compounds, followed by animal screening. Between the 1970s and 80s, clinical pharmacology was the key discipline underpinning drug development. Over the 1980s and 90s, biotechnology grew in importance and between the 1990s and now, systems biology has grown in prominence.
- The big pharmaceutical companies are no longer in a rapid expansion phase as has been seen over the previous decades. Although traffic is not one-way, much of the pharmaceutical industry is moving from Europe to the US. Drivers are complex, but include cost, animal activism, size and location of markets, availability of skilled staff and regulation.
- The UK remains attractive to the pharmaceutical industry as a place to carry out Phase I and II Clinical Trial Research. It is much less expensive and often quicker to carry out Phase III research abroad, but Phase III research might follow in the UK if it was not so expensive and if conditions were improved.
- However, the biotechnology, medical diagnostics and devices industries are of increasing economic importance in the life sciences sector.

- The venture capital community has also shifted its investment strategy away from basic science and more towards applied research.
- The movement of people between industry and academia is to be encouraged, as more clinician scientists are needed in industry and there should be increased mobility between the two sectors at all levels.
- Industry needs to engage with NICE earlier to get better healthcare to the consumer.

10. Collaboration

- Academic-industry collaboration is about collaboration to solve a common problem rather than a one-way movement of funds from industry to academia. Translational research problems such as biomarker validation or the development of enabling technologies offer opportunities for pre-competitive collaboration within industry. Public-private partnerships have been effective in correcting market failures in producing drugs for neglected and orphan diseases of the developing world.
- Industry is particularly interested in collaborating with the large research networks to undertake phase III clinical trials.
- Academic-industrial collaboration should not only be with the pharmaceutical industry. There are opportunities to work with the food, insurance, diagnostics, biotechnology and device industries, amongst others. For example, the food industry is currently looking for guidance on how to help address obesity.
- At the moment, there are few incentives for those in the NHS to conduct research or collaborate with academia. Current financial pressures act as a further disincentive for the NHS to conduct research. Collaborative research between the NHS and academia needs to be seamless. Activity at the University of Edinburgh, discussed by Professor Savill, offers a good example of collaborative research.
- The NHS should be seen as a partner in, rather than a receptacle for, research activity. NHS managers should be actively involved in research collaboration. There are opportunities for all types of health trust (acute, primary care, mental health etc.) to form research collaborations with

universities. However, there are often tensions between academic and non-academic consultants, particularly at the local level within the NHS. To permit more research collaborations with academia, a cultural change is needed in the NHS, as many Primary Care Trusts (PCTs) are too small and inward looking. It is likely that there will be greater opportunities for research collaborations as the current PCTs merge.

- Many universities are organised into traditional vertical structures that impede interdisciplinary research. This issue is exacerbated by the Research Assessment Exercise, which rewards this 'traditional' approach. However, it is research focused on specific diseases or questions that provides opportunities for multidisciplinary collaboration.
- Multidisciplinary teams with clear shared goals are key for both industry and academia in the future. Collaboration with industry and the NHS needs to begin early in any research endeavour. Many universities do not have strong business development units. Universities and academics need to be better educated in business development as they often over-estimate the value of their ideas.
- Given the number of stakeholders, it is important that conflicts of interests are well managed.

11. Evaluation

- Metrics should be specific, measurable, achievable, realistic and time-related. A key problem is that metrics are often activity rather than value-based. They should generally be based on outputs rather than inputs, although the cancer networks have successfully used patient enrolment to evaluate clinical trials.
- Metrics are an effective tool for changing behaviour. The purpose for using research metrics to evaluate an area should be defined at the outset. Whatever system is put in place, the metrics must be agreed and owned by the relevant community.
- However, to be useful, metrics can only be assessed by experts. Simple metrics, blindly applied, can be counter-productive. Research evaluation is a long-term process. The Report, *Medical research: assessing the benefits*

to society (AMS/MRC/Wellcome Trust, May 2006), is a valuable contribution to this debate. It suggests useful methodologies for assessing public impact of research, including case study and narrative case study methods.

- Metrics to assess knowledge transfer, as opposed to knowledge generation, are also needed.
- For metrics related to translation, there needs to be much better understanding of the conditions for success in translating research. Bibliometrics are less useful for applied research. Here, influence on clinical practice is more important. The speed at which research is translated into practice is a useful metric, providing quality is maintained. Other ways to evaluate translation might be for institutions or funding applicants to state the clear translational objectives, describe the translational portfolio, assess the 'translational culture' (e.g. stakeholder analysis) and declare measures of success including financial and product metrics. Despite some limitations, Quality Adjusted Life Years (QALYs) are useful metrics for mortality and morbidity. QALYs help indicate which diseases cause greatest harm, and so can be used to determine research priorities.
- With the increasing importance of team work in biomedical science, there is a case for greater use of metrics at the institutional rather than individual level. Institutional metrics will encourage organisations to ensure some of the best people move into areas like knowledge transfer that are often currently less well populated. Rather than listing the number of spin-out companies, success would be better measured by counting the number of people employed by each company. However, to prevent the elimination of all high risk research, there needs to be increased institutional autonomy which could allow groups to take risks. Any increase in risk will increase the number of 'failed projects,' but this should be an acceptable part of the research system with the necessary support in place.
- Benchmarking is useful to help guide expectations. Broadly speaking, industry tends to be more metric-based than academia. For instance, the

pharmaceutical industry uses new molecular entities as a metric to measure the success of its basic research.