

# MSD Response to the Cooksey Review of UK Health Research July 2006

Merck Sharp & Dohme Limited (MSD) is the UK subsidiary of Merck & Co., Inc., of Whitehouse Station, New Jersey, USA, a leading research-based pharmaceutical company that discovers, develops, manufactures and markets a wide range of innovative pharmaceutical products to improve human health.

The company believes that substantial investment in the UK will enable its talented scientists and technicians to remain at the forefront of pharmaceutical research and manufacturing. MSD committed £290 million between 2002-2005, towards the redevelopment of its UK facilities to ensure that it has up-to-date technology and can develop medicines with optimal efficiency.

MSD employs approximately 1600 staff across its three UK sites, which include its company headquarters and pharmaceutical research and development laboratories in Hoddesdon, Hertfordshire, its state-of-the-art pharmaceutical manufacturing and supply centre at Cramlington in Northumberland and a chemical manufacturing plant at Ponders End in Middlesex.

MSD welcomes the Government's commitment to R&D in the UK and its continued partnership with the pharmaceutical industry through the Ministerial Industry Strategy Group (MISG). We believe however that there is a place for an increased Government drive to help the industry conduct successful research in the UK. MSD is therefore very pleased to have this opportunity to comment on the design and institutional arrangements for public funding of health research in the UK.

## Executive Summary

*MSD believes that fundamental to the long-term success of the Government's new strategy for NHS R&D in England, is **the need to foster a research-driven culture in the NHS**. It is our view that the current overwhelming focus on service delivery is creating a barrier to progress and improvement in NHS R&D.*

***Performance measures at individual and institutional levels should be used to create an environment in which research is viewed as meritorious and protected time needs to be created in order for doctors to be enabled to conduct research.** Incentives should be provided to encourage more ancillary staff to train as specialist research nurses, pharmacists etc.*

*To date the NHS has not provided a fertile bed for clinical research, and despite Government and industry's collaboration since the Pharmaceutical Industry Competitiveness Task Force was set up in 2000 to improve matters, it continues to get increasingly difficult to conduct clinical research in the UK.*

*MSD welcomes the introduction of the UK Clinical Research Collaboration (UKCRC) but is concerned that the potential for primary care settings to be harnessed is being overlooked. At present PCTs do not get any benefit from conducting trials. Consideration should be given to incentivising GPs to support trials through the Quality and Outcomes Framework. It is our view that the **introduction of metrics which will contribute to NHS Trusts' performance ratings** would be a constructive step to take and would have knock-on benefits for the physical and human infrastructure needed to improve NHS R&D. If the research incentives are effective it is likely, for example, that science education would benefit in the longer term.*

*Funding streams in the NHS also create barriers to research. If a GP refers a patient to a Centre for Excellence in a different trust, the cost of care follows the patient into that trust. MSD believes the **introduction of a cross funding system for clinical trial work could transform the ability of industry to run successful trials in the UK.***

*MSD believes Connecting for Health, when it goes live, will provide the UK with an enormous competitive advantage as a location for clinical trials. MSD recommends that Connecting for Health should be connected to Biobank to facilitate provision of samples for research. Care should be taken to **avoid layers of bureaucracy which will undermine the potential for Connecting for Health to be an effective tool in research.***

*MSD believes that it is important to **retain a ring-fenced national fund for R&D.** Our view is that a regional funding approach risks dilution and duplication of bureaucracy. MSD further recommends that a **Chief Executive post is created to oversee the joint MRC/NIH fund.***

*It is MSD's view that research funding from the MRC and the medical research charities is overly biased towards basic and very late stage research where endpoints can easily be identified. There is a significant gap in between which is under serviced and MSD believes the NHS R&D strategy should seek to tackle this 'middle ground'. At present much of this developmental research is pharmaceutical industry funded. However, the NHS could attract more of this if the **facilities needed to run clinical research were improved. There is presently inadequate supply of both expensive technology, such as scanners, and basic infrastructure,** such as dedicated rooms in which clinical trials can be run. A central, combined R&D fund should address this.*

*MSD is concerned that £300m seems to have gone missing in the Government statements on the size of the joint annual funding - ie £1billion compared with the current joint spend of £1.3billion. Overall funding needs to be enhanced, not reduced, to see the benefit of a merger.*

MSD's views on the specific questions set out in the Consultation are given below:

## **1a. Strengths and weaknesses of the MRC**

### *Strengths*

- The MRC has international standing for its cutting edge basic research: examples of major contributions to translational research include monoclonal antibodies and the confocal microscope.
  - The MRC has also made important contributions to clinical research through funding major programmes on clinical trial design.
  - MRC tends to take a long term view and looks at the 'big issues' such as Biobank
- ### *Weaknesses*
- Although MRC makes a significant contribution to biomedical research response mode funding in the University sector, it has recently suffered from resource constraints meaning that only 20% of applications were funded in 2004 / 5.
  - There is an imbalance in the resource provided to basic and clinical research, with a significant bias in favour of the former.
  - The MRC decision making process is slow.
  - MRC's decision-making process heavily favours scientific content at the expense of adequate attention to delivery of results.

## **1b. Strengths and weaknesses of NHS R&D**

### *Strengths*

- The NHS provides a 'real world' setting for research
- The structure of the NHS (in terms of consolidation) offers great potential
- Access to patients in the NHS is good.

### *Weaknesses*

- Funds earmarked for research infrastructure have been diverted to support direct patient care.
- The lack of incentives for NHS Trusts to support research has created a culture in which research is not valued.
- Infrastructure, outside the specialist centres, is inadequate: lack of finance to set up basic laboratory provision has impeded the use of research funds provided by charities. Support services are often poor.
- Training opportunities are limited
- NHS Research Governance concentrates on process not delivery
- Absence of shared care between acute and primary care

## **1c Research and Training Needs**

MSD believes that dedicated research time needs to be created for practitioners. Specialist research centres are in short supply and tend to be oversubscribed (often prompting industry to take studies overseas).

## **2. Key scientific and organisational challenges**

MSD believes the key *scientific* issue is likely to be ensuring that all areas of the broad remit of the new body are given appropriate priority. It would be counter-productive if more areas were funded yet none or few of them were able to achieve the critical mass to ensure success. In the clinical context there would need to be a balance between regional 'seed corn' funding and centralised centres of excellence.

Recognition and success in research is judged too heavily by publication. MSD believes there is a need for broader measurement and recognition for other types of research.

As already mentioned there are no metrics for benchmarking quality and volume of research in NHS organisations. MSD believes other organisational challenges that need to be addressed are:-

- How to distribute funding in the optimum way to support research;
- Whether to have priority areas for funding or to rely on curiosity-driven research proposals;
- How to select the best scientists and clinicians to receive funding and how to institute metrics to ensure that the money is being spent in a way that makes a difference;
- The increasing cost of indemnity in a litigious society;
- Competition from Eastern Europe and the Far East which benefit from low costs, good scientists, and custom built facilities;
- Grants for young scientists are too short term and act as a disincentive because of a lack of security and confidence in future funding;
- How to encourage an entrepreneurial culture within NHS R&D;
- Developing mechanisms that ensure advances are rapidly translated to everyday use;

- MSD believes that Connecting for Health has huge potential. If it works as hoped it could allow patients to be followed throughout the system. Data such as this would be hugely valuable to industry. However there are currently huge overhead costs for GPs running GPRD and an additional system will be unwelcome. Data ownership will be a significant challenge. In the application of information technology (the database opportunity in Connecting for Health) how do we get consent from the public in a way that facilitates research?

### **3. What should be the Government's priorities for health research?**

- MSD believes the Government should strive to maintain a powerful and competitive research base. As part of this, appropriate capacity building is needed, together with support for outstanding individuals (gifted scientists or clinicians).
- MSD believes there is a need for a greater emphasis on developmental research, ie the efficient translation of experimental research for the benefit of patients and society.
- The bureaucracy associated with the Research Governance Framework needs to be reduced with Trusts being given stricter guidance so that variability is reduced.
- MSD recommends that Government discuss its priorities with industry on an annual basis and should be prepared to be flexible.

### **4. How should decisions be taken on the balance between long term and short term needs?**

- MSD believes the key drivers for decision making should be the availability of creative ideas, talented researchers and advances in enabling technology;
- Any top-down prioritisation must take into account scientific feasibility and the input of innovative ideas from the scientific community;
- The NHS is currently driven (out of necessity) by short term priorities but would benefit from a longer term perspective;
- An integrated approach should be adopted, with broadly equal funding for scientific and pragmatic research;
- Closer involvement with industry in translational research is needed and development of partnerships should be encouraged at the early stages i.e. using public funding as "seed corn".

### **5. How have the results of publicly-funded health research been used?**

- MSD believes that one of the best examples of practical benefit from publicly-funded research is the monoclonal antibody therapies developed from the work of Milstein et al and Winter et al at the Laboratory for Molecular Biology. Much research does not have direct deliverables in terms of health care benefit but will be part of a body of work that eventually transforms the way we think about a field or disease. It is important to remember that some research has a very long gestation period before healthcare benefits are seen;
- Many of the mechanisms which the pharmaceutical industry has used to discover new drugs have come from publicly funded research done in the Universities and again, the benefit of this is sometimes seen many years after the initial scientific discovery (e.g work done at the Royal College of Surgeons in the 1960s and 1970s on a slow reacting substance associated with anaphylaxis led to discovery of the leukotrienes which in turn led to the introduction of the use of leukotriene receptor antagonists for asthma in the 1990s);

- Screening is a good example where public funding has been effective: cervical cytology, colon cancer screening and UK PDS;
- However, overall, the record is not great when viewed in the context of the amount of investment that has been put forward;
- Plans for exploitation of discoveries should be developed in parallel with experimental studies. For example the MRI scanner was invented in the UK but practical uptake was so low that development of the technology was taken elsewhere;
- Public funding should also be used to improve the effectiveness of NICE. Recommendations by NICE are too heavily influenced by health economists and require more input from clinicians.

## **6. How might better links be forged between basic, translational and applied researchers and across disciplines?**

- MSD is in favour of improved links but believes new bodies that simply act as 'talking shops' should be avoided.
- A single health care fund should be able to better support research that crosses traditional boundaries and this should include some research currently funded by BSRC.

## **7. How can the Government encourage translation, entrepreneurship and innovation?**

- MSD believes that developing a strong culture of healthcare R&D, together with constructive interaction with industry is the best way to achieve this. This has already been done successfully by the technology transfer groups of Cancer Research UK and the MRC.
- Government should encourage a focus on pre-competitive areas of research such as predictive toxicology. A greater willingness to put public money together with investment from industrial consortia would act as a valuable stimulus;
- Government must critically appraise the governance processes and seek to remove unnecessary bureaucracy;
- Consolidation of the regulatory process from bench to clinic would make it easier to follow research through;
- Improve access to start-up funding and rewards based on late stage output (i.e new drug / new process)
- Government must ensure a responsible drug reimbursement scheme continues to be in place in the UK. The OFT enquiry into the PPRS will bring this issue to the fore and MSD would like to draw attention to the ramifications of a purely cost-driven procurement approach. The effects of such an attitude are clearly seen in the case of vaccines where large-scale government purchases of vaccines at heavily discounted rates has left the industry with narrowing profit margins in an environment of increasing costs and risks. Many companies were forced to withdraw from this important area because it simply became so un-economic, the number of companies now making vaccines has decreased from twenty-six in 1967 to five in 2004 (GlaxoSmithKline, Sanofi-Aventis, Merck, Wyeth, and Chiron). Drug pricing must provide fair returns for R&D and take into account the wider environmental context, especially patient and public health.

The "lessons" from the vaccine case seem clear and the evidence solid. Pricing systems that encourage research-oriented firms to leave the industry or to spend less on innovation will have a negative impact over the long-term on the ability of the private sector to develop new preventive or therapeutic medicines.

**8. How can UK health research funding be most efficiently used to provide infrastructure, support the work of NICE, facilitate innovation and collaboration with industry?**

- MSD believes that the provision of local 'seed corn' funding would be helpful providing it could be done without diluting the amount of funding elsewhere;
- An infrastructure (eg the 'well-found' laboratory) needs to be built that allows full advantage to be taken of charity funds. Interfacing the new NHS IT network with research initiatives would maximise the value of this investment;
- Pharmacogenetic studies to identify responding patients could improve treatment options with both new and existing drugs, could combine basic and applied objectives and could interface with NICE;
- The Clinical Research Networks could be used to harness the work of NICE and other decision making organisations/agencies;
- Invest in custom built facilities;
- Tie these to the Topic Research Networks.

**9. What lessons should the UK learn from other countries?**

- The US Government has spent most and as a result its research has been most productive - although not all initiatives have been successful. Most European countries have been much less successful than the UK and many of them have top heavy, very traditional systems that make it hard for young researchers to get funded;
- However MSD believes complacency in the UK is a big problem. The UK is only a small part of the world's research base and this is often a hard message to communicate to the scientific community. There is an unrealistic view of the UK's importance and its relative competitiveness;
- Rising stars of the moment include Singapore which has less regulation, a good pool of scientists and helpful tax breaks;
- "Transfer Units" in Germany have proved to be quite effective. These are projects designed to transfer basic science to application. In Germany there is also more direct support given to young scientists in terms of career progression;
- The Scandinavians' use of medical record data bases and registries enables them to conduct large scale, population-based studies. Their relatively liberal laws also give them a competitive advantage in the area of stem cell research;
- MSD would also recommend that the Government review models from within the UK that have been most successful as examples of best practice.

**10. In implementing the single fund, to what extent should the MRC and DH / NHS R&D be merged and to whom should the single fund be accountable?**

- MSD believes that a merger has the potential to create a system that will continue to support world-class basic research, will be able to facilitate experimental medicine and satisfy the needs of industry for epidemiology and post-experience studies.
- A merger would also allow investigator-led research to be complemented by designated research initiatives in areas of unmet medical need.
- MSD is concerned that £300m seems to have gone missing in the Government statements on the size of the joint annual funding - ie £1billion compared with the current joint spend of £1.3billion. Overall funding needs to be enhanced not reduced to see the benefit of a merger.

- A suitable over-arching board or council with strong leadership is needed and should be put in place. Relationships with the DTI and the DH should be preserved in the organisation to ensure 'interdisciplinarity', to recognise the essential nature of the links with the pharmaceutical industry and ensure a degree of ownership by the NHS Trusts.

**11. To what extent does the success of recent innovation (e.g. CRN) and the proposed structures rely on the CfH NHS IT system?**

- MSD believes that the Clinical Research Networks do not need Connecting for Health to work but could benefit from it;
- It is our view that Connecting for Health should be a development goal of the Clinical Research Network: it will aid hypothesis generation, feasibility testing, patient identification and outcomes tracking;
- MSD believes Connecting for Health is a unique opportunity but one that has not yet been shown to be successful (or even to work!). However the potential benefits and the competitive advantage it could confer on the UK are unquestionable.

**12. Given that NHS R&D is devolved and the MRC is not, how can the functions work together?**

- MSD believes this to be a significant challenge and there is no easy solution outside England. It may be necessary to integrate healthcare research in Scotland and Wales at some point in the future but regional prioritisation will always be appropriate in some cases.

**Addendum: HTA in the UK**

In conversation with the Cooksey Review team, MSD was also invited to submit its comments on NICE, the process of drug development, research and innovation.

**1. NICE and clinical innovation**

- One of the reasons why NICE was set up was to support clinical innovation and the rapid uptake of effective, new medicines by the NHS. It is MSD's view that has not happened. Instead, it appears that there is an increasing trend towards NICE recommending drugs with the lowest acquisition cost rather than branded medicines which are more expensive (but, crucially, which have still been deemed to be both clinically and 'cost-effective' i.e. value for money).
- MSD believes a proposed "disinvestment strategy" is relevant here and that a necessary corollary of NICE supporting innovation should be that it also eliminates bad practices and bad medicines from the NHS.

## **2. Comparators in NICE appraisals**

- Recently, NICE has issued a series of negative recommendations about new medicines (e.g. for certain cancer drugs) in which one of the grounds for refusal appears to have been that the comparator drug used by the manufacturer has not been one which is commonly used in UK clinical practice. This has serious implications for all UK manufacturers, meaning that manufacturers will have a much tougher time getting through NICE if the comparator drug is not one that is routinely used in England and Wales. Placebo-controlled trials are becoming less and less acceptable to NICE - and to other health technology organisations. The difficulty here, of course, is that clinical trials tend to be global, or at least cover several countries and it is unrealistic to expect a global trial to be designed around NICE's requirements. As mentioned in section 9 of MSD's response above, the UK represents only a small part of the global research base.

## **3. The new Single Technology Appraisal ('fast-track') process**

- MSD would like to use this opportunity to highlight its concerns about the new STA process. In theory, one could argue that a new fast-track process is good for innovation. It ensures that the NICE appraisal is conducted much more efficiently and quickly, with NICE guidance being issued very soon after the product has been launched in the UK.
- In practice, however, MSD is concerned that NICE is looking to review products very early in their lifecycle, when there will be no data on clinical outcomes, no post-marketing studies, no data on actual usage in a particular country, etc i.e. the concern is that NICE will be making decisions on a very limited dataset. In this context MSD is concerned that NICE does not fully understand the drug development process, nor the limitations of the evidence that is available at product launch, and therefore will not be sufficiently competent to make pragmatic decisions about the use of new medicine at such an early stage in the product lifecycle.
- Historically, MSD has been somewhat reluctant to embrace this trend towards appraising new medicines close to launch because of the concern that HTA could start to become submerged into the regulatory process and/or pricing and reimbursement decisions. At the moment, HTA in the UK is entirely separate from the regulatory, pricing and reimbursement processes and MSD firmly believes that the regulatory and HTA processes should remain entirely separate and distinct.

### **In response to direct questions raised by the Review team, MSD comments are as follows:**

- MSD does not believe it would be desirable for NICE to be involved in the drug development process. We would not support any change in function that would impact current regulatory processes, pricing or reimbursement decisions.
- MSD believes all stakeholders have an interest in NICE making its decisions more quickly, but only if this does not compromise the quality of assessments and if the recommendations that are issued result in a universal and rapid uptake of new medicines. MSD's experience to date is that NICE recommendations are not having this effect.

- The data generated during the drug development process (eg on drug safety) do not determine whether a medicine is cost-effective or not. This is not part of the licensing/regulatory process. Cost-effectiveness/health economic data is a good example of data which is generated once a product has been launched in the market-place. Only then is it possible to see how that medicine is being used/prescribed and how effective it is being.