

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

NICE submission to Cooksey review

1 Executive Summary

- 1.1 The National Institute for Health and Clinical Excellence (NICE) aims, amongst its other objectives to encourage innovation and facilitate access to promising treatments while ensuring the efficient use of healthcare (NHS) resources. To fulfil this function, NICE depends on high quality relevant evidence, much of which originates from UK-based health research. NICE is therefore especially interested in this review and is pleased that question 8 of the review specifically invites comments on “how UK health research funding can most effectively be used to support the work of NICE...”
- 1.2 As part of its guidance development process, NICE routinely identifies priorities for research that reflect important gaps in the evidence base. We believe it is important that the new institutional and funding arrangements in UK health research should help fill these evidence gaps in a timely and effective way. To help achieve this, the Institute suggests five specific developments:
 - 1.1.1 The new R&D structure should contain a designated NICE liaison team which would work closely with NICE and its support units to ensure that its primary research requirements are met.
 - 1.1.2 Current contractual arrangements for the commissioning of secondary research through the HTA programme should be reviewed in light of the new structure to establish the most efficient commissioning model.
 - 1.1.3 A designated budget line and implementation system should be established to facilitate the initiation of studies in the NHS and other health environments when NICE issues “in the context of research” recommendations (see 10.1). This should include formalised arrangements between the Institute, research funders, the NHS and industry.
 - 1.1.4 A designated budget line and implementation system is put in place (including a coordinating and support centre) to collect and analyse clinical data outside specific randomised controlled trials (disease registries) to support the introduction of innovative interventional procedures into the NHS. This should also have the capacity to support other NICE programmes when required.
 - 1.1.5 A designated budget line and implementation system should be established to facilitate methodological studies including the assessment of the impact of NICE guidance

2 Background

- 2.1 NICE has responsibility for providing NHS professional staff with guidance on achieving the highest attainable standards of care for their patients. Since 2005, NICE has also had analogous responsibilities to the wider public health community and has now started to provide guidance on preventing ill health and maintaining good health for the population as a whole. In undertaking both functions above, NICE has actively engaged with patients and the public through a number of initiatives, including the NICE-based Patient and Public Involvement programme, lay membership in all NICE Committees and Advisory Bodies, the Citizens' Council and through encouraging patient and public participation in the NICE consultation processes.
- 2.2 NICE's own interests in health R&D are fourfold:
 - 2.2.1 In developing both its clinical and public health guidance, NICE uses the best available evidence in order to ensure that its conclusions and recommendations are robust. The Institute is therefore a consumer of primary research.
 - 2.2.2 NICE has a particular interest in secondary research (i.e. systematic reviews, research synthesis, meta-analysis) which underpins all its development processes. For NICE, the quality and relevance of secondary research is no less significant, in ensuring the robustness of its guidance, as the quality and relevance of primary research upon which it is based. Secondary research to support the Institute's guidance products is undertaken by NICE's own staff, by its Collaborating Centres, and by the NHS R&D's Health Technology Assessment Centres.
 - 2.2.3 The Institute, itself, has methodological research needs especially in health economics and, more recently, implementation. NICE does not, itself, have resources to undertake such research but the NHS Research Methodology programme has been able to commission, and fund, some of those most important to its work.
 - 2.2.4 During the development of its guidance NICE's advisory bodies invariably identify gaps in knowledge (i.e. research priorities) which, if filled, would enable its advice to be improved when the topic is revisited (usually after three to four years). These are listed in a separate "research recommendations" section in all NICE guidance. In the past, both manufacturers, and the NHS R&D Programmes (see section 8), have played an important role in undertaking (or commissioning) appropriate studies addressing the Institute's research needs.
 - 2.2.5 The Institute also uses another way for articulating its research needs, of particular relevance to new promising innovative technologies for which the evidence base is relatively weak: it sometimes issues recommendations for the use of these technologies only "in the context of research".

2.3 The Institute has critical interactions with both the MRC and the NHS R&D programmes. NICE's interactions with the MRC, itself, have largely been as a consumer of its primary research. Individual members of the MRC staff also make important contributions to the work of the Institute as members of its advisory bodies. NICE's interactions with the NHS R&D programmes have also been extensive. The Institute relies on the HTA programme to undertake the production of assessment reports for the technology appraisals programme which is co-ordinated by the National Collaborating Centre for Health Technology Assessment (NCCHTA) and funded by DH R&D. The HTA and NHS Service and Delivery (SDO) programmes have also been able to commission research addressing some of the evidence gaps identified during the development of NICE guidance (see point 2.2.4 above).

Responses to the review questions

3 Strengths and weaknesses of the MRC and NHS R&D Programmes

Question 1 - What are the strengths and weaknesses of the MRC and NHS R&D programmes at present? How do each of these support the research and training needs of the NHS, social care, industry and academia? Does more need to be done?

3.1 Strengths of the MRC:

- The MRC is a long established organisation with an international reputation for its successful support of both basic and clinical research. In particular the Council's support for basic biomedical research has been extremely productive and successful.
- In the clinical field the Council, and its predecessor body (the Medical Research Committee), were instrumental in developing the methodology that underpins the modern evaluation of therapeutic interventions. Over many years the Council has continued its support of numerous clinical trials which have had a major impact on clinical practice. These have not only been in respect of pharmaceuticals (e.g. its HIV/AIDS and leukaemia trials) but also devices (e.g. aortic stents) and complex technologies (e.g. physical therapy in the management of back-ache).
- The Council's Clinical Trials Unit (CTU) has been particularly successful in undertaking important and innovative research in the evaluation of therapeutic interventions; as well as helping others to design and execute clinical trials. The close involvement of the MRC's CTU with the UKCRC is an encouraging development.

3.2 Strengths of the NHS R&D Programme:

- This funding programme is of more recent origins but, in a relatively short time, has made very important contributions.
- The R&D Programme has been of central importance in establishing the Health Technology Assessment programme as well as the Cochrane Collaboration and the

Centre for Reviews and Dissemination in York. As these initiatives are now internationally respected, the NHS R&D Programme can take credit for having brought about a recognition of just how important research synthesis is as a foundation for policies and guidelines.

- Furthermore, the NHS R&D programme has been pro-active in seeking applications for research support to resolve specific questions of practical importance. The HTA programme has supported clinical trials in areas where there are pressing needs to identify optimal care for patients, but which have not been considered a priority by the research charities and the MRC. In addition, the NHS R&D Programme has funded an extensive programme of methodological research.

3.3 Weaknesses of the MRC:

- There is a perception, widely held by clinical scientists, that the Council's priorities are directed towards basic – rather than clinical – research which has had the effect of directing young clinical scientists towards basic research rather than utilising their knowledge and skills in developing translational and clinical research programmes.
- The Council's support for translational research, health services research and public health has been particularly weak.
- At least part of the problem arises from the fact that the Council largely operates in response mode, seeking applications for support from investigator-led initiatives rather than taking a more strategic approach that targets areas of special importance. When it has considered applications for support for clinical and public health projects and they have not been methodologically robust there has been a tendency to reject them rather than investing in methodological developments that might enhance their scientific utility.

3.4 Weaknesses of the NHS R&D programme:

- The NHS nominally invests around £650 million per annum in health R&D. Much of this (£400 million per annum) supports NHS providers (predominantly university hospitals) with infrastructural costs to offset their clinical research initiatives, although it is often difficult to distinguish between the application of funds for clinical and research purposes.. The clearly identifiable resources available for R&D, in the NHS, are around £130 million per annum. This latter sum funds the HTA, CRD, Cochrane work in the UK, SDO, NEAT and Policy Research programmes.
- There will be a need for the future Health R&D structure to identify the “real” funds” available for research within the NHS infra-structure
- With some exceptions, such as NHS R&D SDO, the NHS R&D programme has done little to engage with NHS management. This is beginning to change, particularly with the emergence of the UKCRC.
- A major weakness of the NHS R&D programmes and, in particular HTA, has been their inability to set strategic research priorities in a systematic and transparent way.

As a result, the unique potential of this publicly-funded, priority-led research organisation to address the needs of the decision-makers and the broader NHS, has never been fully realised.

4 Key challenges

Question 2 - . What do you believe are the key scientific and organisational challenges facing health research, and underpinning training, in the UK over the next decade? How might the UK Government best help address those challenges? What do you believe should be the Government's objectives for health research, and why?

4.1 Health research in the UK should aim to support and promote the overall health of the population. In doing so, health research should also encourage innovation and foster high quality academic research activity.

The key scientific and organisational challenges facing UK health research are:

- the need to develop the organisational structures bringing together the research community, health service and private sector; and providing the right incentives for innovation that adds value to the economy and the health of the UK population;
- the need to support evidence-based health policy and, thus, promote the efficient use of health resources;
- the need to nurture, within the NHS and UK universities, a culture that supports, promotes and encourages basic, translational, clinical and public health research; and that helps develop a cadre of young people with expertise in, and enthusiasm for, clinical and public health research;
- the need to foster the notion, amongst clinicians and managers, that clinical research is part of their routine practice.

5 Government priorities for research

Question 3 - What should be the Government's priorities for health research? Is there anything it should stop doing or funding? What is it not doing or funding that it should do, and, in the absence of further sources of support, what can it lower in order to release the necessary funds?

5.1 The primary government objective for health research should be to support basic and applied research in a manner that is designed – in the broadest sense – to promote and sustain health. In doing so, government needs to:

- ensure the strategic research agenda supports the efficient use of healthcare resources through evidence based decision-making;
- identify the appropriate balance between publicly-funded basic and applied research;
- provide opportunities for, and encouragement of, research training in basic, clinical and public health research;
- make special efforts to support clinical and public health research;
- identify the appropriate balance between nurturing publicly funded, and commercially funded, translational and clinical research.

5.2 There are several approaches to releasing funds to re-invest in cutting edge areas of research. It is important to note, however, that disinvestment in specific areas will be difficult.

- Merging the MRC and NHS R&D programmes would produce some savings in “back-room” functions.
- The use of that proportion of the NHS R&D budget, nominally used to provide an institutional research infrastructure, to support clinical and public health research would have substantial benefits.
- There needs to be a careful scrutiny of the research portfolios of both the MRC and the NHS R&D programmes. Those activities that do not fall within the scope of the priorities indicated above should be given special scrutiny. And even for those that do so, the government should ensure that UK research in the area is internationally competitive.

5.3 The merged MRC and NHS R&D programme should be expected to work much more closely with the commercial biosciences sector than has hitherto been the case. In doing so, a new relationship needs to emerge.

5.4 Considerable savings, and substantial gains, could be made by creating “virtual” units and centres rather than the conventional geographically constrained

arrangements. This, to some extent, has already started with the establishment of clinical research networks but could be much more extensively undertaken.

6 Getting the balance right

Question 4 - How should decisions be taken on the balance between the long-term economic and social benefits of a high quality biomedical research base; and the needs for research to improve healthcare and other public services? What is the appropriate balance between public funding for investigator-led and priorities led research? How do we balance funding for basic science, translational science and applied science? Is this something that should vary over time? What mechanisms should be used to make judgements about this balance?

- 6.1 The economic and social benefits of high quality biomedical research, and the needs for research to improve health and healthcare, are not mutually exclusive. Indeed, they are mutually supportive and a high quality biomedical research base is essential for both forms of research.
- 6.2 The need for any new organisation to provide for both investigator-led and priorities-led research will be critically important. Historically the MRC has tended to be pre-occupied with the former and the NHS with the latter; but the public interest is likely to demand that the balance varies over time.
- 6.3 Balancing basic, translational and clinical/public health research is likely to be more difficult. The knowledge and skills are very different for each; and individuals will not be able to move easily from one area to another.

7 Research to promote advances in science and medicine

Question 5 - In your experience, how have the results of publicly-funded health research in the UK been used, both in the development of new treatments and to influence / change wider policy and healthcare practices? What lessons can usefully be learned to improve the uptake of advances in science and medicine?

- 7.1 Evidence shows that, for a number of reasons, the UK is traditionally slow to adopt new treatments. NICE has a special interest in ensuring that the results of health research are used for the benefit of the population. Furthermore, as an evidence-based policy-maker, NICE is in a unique position to support, through its guidance, the introduction of innovative technologies in everyday practice across the NHS.

- 7.2 Since its establishment in 1999, NICE has accelerated the uptake of new technologies¹ while providing appropriate incentives for innovation that adds value. However, the Institute depends on good quality, relevant evidence to underpin its recommendations on the use of new and existing technologies and practices.
- 7.3 A more flexible, responsive relationship with the research community is necessary to support timely evidence based decisions on the clinical and cost effectiveness of health interventions. Such a relationship would ensure the seamless utilisation of research outputs in the development of NICE guidance to the NHS and the broader public sector.
- 7.4 There is no single approach that can be universally adopted. Nevertheless, the involvement of clinicians in research as part of their clinical practice not only enhances a research culture but also encourages the adoption of new approaches and techniques.

8 Building multidisciplinary research capacity

Review question - 6. How might better links be forged between 'basic', translational and applied researchers, working across the whole field of health research, from the laboratory bench to the front line of the NHS? How might better links be forged across disciplines, e.g. with engineers, physicists, and social scientists?

- 8.1 Effective communication is essential in ensuring multidisciplinary collaboration. Virtual networks can ensure research initiatives and findings are disseminated encourage a more integrated approach across different sites and stages of the research and development process.
- 8.2 Appropriate training schemes and providing the right incentives for collaboration through research grants can also help forge links across different disciplines and sites.

9 Fostering entrepreneurship and innovation

Question 7 - How can the Government encourage translation, entrepreneurship and innovation in health research to improve public services in the UK?

- 9.1 A number of academic research centres in the UK carry out high quality health research. However, most of these centres of excellence lack the means and motivation for introducing innovation in everyday practice. The government could

¹ Tracking guidance implementation, NICE website: <http://www.nice.org.uk/page.aspx?o=266844> (accessed June 2006)

encourage translation and innovation in health research with the aim of improving the health of the population by:

- 9.1.1 engaging with all key stakeholders, including patients and the public, industry, professionals and decision-makers, to identify and articulate the UK health research *priorities* in an explicit and transparent way;
- 9.1.2 encouraging *collaborations* between academic centres of excellence, the NHS, and the commercial sector, in high priority areas to meet these priorities;
- 9.1.3 providing the right *incentives* for these collaborations to meet the above priorities. Examples of relevant incentives include:
 - the successor of the Research Assessment Exercise should reward research that contributes to improving the health of the population in addition to prestigious scientific publications;
 - academic health research funding;
 - the Healthcare Commission assessment of NHS Trusts;
 - the Clinical Excellence Awards scheme should aim to reward involvement in research that addresses strategic UK priorities and aims to improve the health of the population.

10 Health Research Funding; supporting NICE

Question 8 - How can UK health research funding be most effectively used to provide the appropriate infrastructure for basic, translational and applied research, whether funded by the UK public sector or other sectors? How can UK health research funding be most effectively used to support the work of NICE, facilitate innovation and collaboration with industry, and address market failures in the application of healthcare?

There are a number of ways that NICE's current approach to supporting innovation can be enhanced

- 10.1 **The role of NICE in supporting the introduction of innovative technologies - recommending the use of a technology in the context of research:** Reliable evidence is necessary to improve health outcomes and ensure the efficient use of resources. NICE sits at the interface between health research and clinical practice. Based on the best available evidence, it issues guidance on the clinical and cost-effective use of technologies in the NHS and the broader public sector. However, NICE increasingly reviews technologies closer to the licensing stage when there is often only preliminary evidence of costs or effectiveness. This particularly applies to specific indications and subgroups. In these cases NICE can recommend that a technology is used in the context of clinical research so that the necessary evidence is generated to inform a future decision on its use.

Recommending the use of a technology in the context of research is an effective way of achieving the dual goal of innovation, and efficiency, in the face of uncertainty. It can: enable patients to gain access to a promising innovation within a controlled environment, support industry in its efforts to improve health outcomes when more evidence is required, and ensure that definitive decisions are only made based on robust evidence of clinical and cost-effectiveness. For this model to deliver, the new national arrangements for research should ensure that NICE priorities in research, articulated as recommendations for the use of technology or intervention in the context of research, are addressed in a timely manner. To do so requires:

- Designated resources to support this type of research
- Formal arrangements between NICE, industry and the NHS (including patients and professionals) to be established to take such research priorities forward
- That the research outputs feed into the NICE review process and inform future NICE recommendations

10.1.1 Recommendations for the use of technology in the context of research are a means of containing costs while rewarding health outcomes that produce real health gains. In an environment where the pressures on the health service to support expensive new technologies are increasing, evidence-based decisions provide the right incentives for innovation. When the evidence base is weak, positive decisions can result in waste, unresolved uncertainty, and perverse incentives for commercial R&D. On the other hand, negative decisions for promising technologies can stifle innovation and compromise health outcomes. Recommendations for the use of a technology in the context of research are, on certain occasions, the most appropriate alternative for the decision maker.

10.1.2 NICE has issued recommendations for the use of a technology in the context of research on a limited number of occasions in the past (approximately 5.4% of Technology Appraisal recommendations between 1999-2006). For example, NICE recommended (in 2000) that laparoscopic resection for colorectal cancer should only be undertaken in the context of a clinical trial². This decision encouraged recruitment to the then ongoing UK-based MRC trial (CLASICC) which has since provided the necessary evidence to support the introduction of this intervention in routine NHS practice³. NICE's advice on the use of liquid based cytology is another similar instance⁴ where the Institute recommended further research before issuing

² Guidance on the Use of Laparoscopic Surgery for Colorectal Cancer, Technology Appraisal Guidance No. 17, NICE, December 2000

³ Laparoscopic surgery for the treatment of colorectal cancer (appraisal consultation document), NICE, March 2006

⁴ Guidance on the use of liquid-based cytology for cervical screening, Technology Appraisal Guidance No. 69, NICE, October 2003

a positive recommendation for the adoption of a new technology across the NHS. (also see Appendix B – OIR)

10.1.3 Unfortunately, there are no formal arrangements between NICE, industry and the clinical research community (including NHS Trusts and PCTs and patient organisations) to pursue the research necessary to resolve the uncertainty and put NICE in a position to issue definitive guidance. This contrasts with the active arrangements for promoting the uptake of positive NICE recommendations. In fact, NICE recommendations for the use of a technology in the context of research are perceived to be negative recommendations. For example, in a recent BMJ paper⁵ reviewing NICE recommendations between 1999 and 2005, Raftery classifies recommendations for the use of a technology in the context of research as “no” decisions. Out of the 22 ‘negative’ recommendations identified, nine are actually recommendations for the use in the context of research. Out of those, four are now positive recommendations following additional research having been undertaken, while the remaining five are still recommendations for use in the context of research. If relevant supportive evidence becomes available then the “in the context of research” recommendations will become positive recommendations when the Institute reviews its guidance.

10.1.4 In 2003 NICE recommended the use of photodynamic treatment in a specific subgroup of patients with macular degeneration, only in the context of a trial⁶. Despite the initial positive response by PCTs and industry, such trials have proved to be extremely hard to organise given the lack of formal support by national research funding organisations. Prospective studies are currently underway, almost 3 years after the issuing of NICE recommendations, but are unlikely to inform the forthcoming review of the guidance.

10.1.5 The absence of formal arrangements to take such pressing research needs forward in a timely manner can result in:

- local commissioners of services interpreting recommendations for the use of a technology in the context of research as negative decisions.
- patients being denied access to promising technologies
- delays in building the evidence base in key areas with a negative overall impact on health outcomes
- research funders often downgrading these priorities as it is argued that the burden of proof should be borne by the technology sponsor
- NICE Committees moving away from making these types of decisions

⁵ James Raftery, “Review of NICE’s recommendations, 1999-2005”, BMJ 2006;332:1266–8

⁶ Guidance on the Use of Photodynamic Therapy for Age-related Macular Degeneration, Technology Appraisal Guidance No 68, NICE, September 2003

- removing any incentives for innovation and private investment in R&D

10.1.6 Innovation and timely access to new technologies need not be at odds with efficient use of resources and evidence based practice. With UKCRC and the developing IT infrastructure, there is a unique opportunity for UK research to support NICE in promoting innovation that adds value.

10.2 **The role of NICE in public health research:** Another area where the Institute's committees have issued recommendations for the use of an intervention in the context of research is that of Public Health. As highlighted in the recent UK Health Research Analysis by UKCRC⁷ only 2.5% of health research funding supports prevention-related research.

10.2.1 In its recent guidance on interventions to encourage physical activity, NICE recommended the use of pedometers and exercise referral schemes only in the context of well designed trials. The guidance describes the type of research needed to assess these interventions that already take place within the NHS and the broader public sector. The Institute is in discussions with the Department of Health on how to co-ordinate the necessary research retrospectively. This is an example demonstrating the need for a streamlined approach to addressing the research needs of decision makers.

10.3 **The role of NICE in expanding the evidence base around new and established treatments - research recommendations:** In the process of guidance development, NICE identifies evidence gaps that will need to be addressed to inform the guidance review. These gaps are identified in a systematic way, with the involvement of key stakeholders and are subject to public consultation, as is the case for all sections of NICE guidance (see Appendix A – RR). As highlighted in the WHO review of the NICE Technology Appraisal programme⁸, "...the Research Recommendation section [of NICE guidance] can assist in generating new information on the effectiveness of medicines under appraisal as well as in targeting the medicine to those patients most likely to benefit". Having acknowledged the importance of promoting its research agenda, NICE has set up a Research and Development programme to improve the quality of and promote these research priorities to research funders. As it has no funds to support its research needs, NICE relies entirely on research funders, such as NHS R&D, research councils, charities and industry to support its research priorities.

10.3.1 NHS R&D HTA has been particularly sensitive to NICE's research recommendations. A "direct access" process was set up in 2004/05 to take forward 2-3 essential NICE research priorities per year and a number of joint NICE/NHS R&D prioritisation panels have taken place as part of an ongoing collaboration, to prioritise and promote research in relevant to the Institute areas. We have so far,

⁷ UK Health Research Analysis, UKCRC, May 2006

⁸ Technology Appraisal Programme of the National Institute for Clinical Excellence, A review by WHO, June-July 2003

with the help of NHS R&D HTA and SDO, taken forward a total of four research proposals on: non-pharmacological treatments for childhood depression (HTA), pre-operative testing for elective surgery (HTA), fallers' clinics in the elderly (SDO), and rehabilitation interventions for MS (SDO). Most of these initiatives are still in the commissioning stage. Trying to co-ordinate guidance production with the timelines of different research funders has proved to be a challenging task for the Institute. More responsive arrangements are required if the Institute is to play its part in meeting the NHS's research needs in a timely and effective manner. The ongoing review of research funding in the UK can help establish a streamlined process for securing financial and technical support for the NICE research priorities. This will in turn ensure the research outputs inform policy decisions in a consistent and systematic way.

10.3.2 NICE is in a unique position, particularly through its clinical guideline and public health programmes, systematically to review and assess established practice across care pathways, from prevention to treatment. NICE can highlight areas of uncertainty around the effects of established practices and encourage further research to determine their true clinical and economic benefits and risks. When important evidence gaps are identified, NICE needs the support of the research community to generate evidence of effectiveness and cost effectiveness. This will ensure:

- Patient safety: established treatments are often based on weak evidence. In some cases, medical interventions can do more harm than good⁹
- Efficient use of resources: with a finite budget, it is important that only clinical and cost-effective interventions are encouraged. NICE needs evidence of effectiveness (or lack of it) for existing interventions in order to decide whether an intervention should be offered by the NHS or discontinued

10.4 **Methodological research to support NICE:** The Institute has an international reputation for introducing robust scientific methods of critical appraisal and cost-effectiveness analysis in developing evidence based guidance. It is continuously faced with new challenges and has a need for methodological research to address these. Areas where there is urgent need for methodological research include economic evaluation in public health, appraisal of non-RCT evidence, disinvestment methods, indirect comparisons between treatment options, implementation and behavioural research methods. These methodological requirements are not unique to NICE and the new national research infrastructure could ensure that there is a co-ordinated approach to meeting them.

10.5 **NCCHTA:** NICE develops evidence based guidance on the clinical and cost effectiveness of mostly new, but also established, technologies through its

⁹ Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage, Lancet 2004;364:1321-28 and Lancet 2005;365:1957-59

Technology Appraisals programme. The decisions of the NICE Advisory Committees are informed by assessment reports and reviews prepared by academic centres of excellence across the country. Once the technologies to be appraised have been identified, these centres are commissioned, for NICE, by the National Co-ordinating Centre for HTA (NCCHTA)¹⁰. This additional administrative layer between the Institute and the academic centres has a historical justification, as HTA and NCCHTA preceded the establishment of NICE. However, with the experience gained over the last 6 years it is now appropriate to re-assess this model and to test it to see if it is the most efficient and effective approach to meeting the Institute's needs. Issues of timeliness, overall costs and methodological consistency across the different academic centres should also be considered.

10.5.1 NICE already commissions, directly, the academic centres involved in the development of guidance in its public health and clinical guidelines programmes. We propose that this model is tested against the current arrangements between NICE and NCCHTA. The need for a rapid and interactive relationship is even more pressing with the recent establishment of the Single Technology Appraisal process and the Institute's commitment to a timely guidance production mechanism.

10.6 **Registers:** Both the technology appraisals and the interventional procedures programmes often recommend, as part of their guidance, the use of a technology or intervention in parallel with prospective collection of important information on side-effects, efficacy or costs. Sometimes a recommendation encourages the use of existing registers or clinical databases while on other occasions, the establishment of a new register or clinical database is proposed (e.g. hip prostheses database). Post-licensing monitoring of a technology or intervention can be a valuable source of information for NICE guidance, as highlighted in the recent HTA report¹¹.

10.6.1 The Institute has convened a group with representation from professional organisations, academia and internal NICE experts to direct its efforts in expanding the evidence base underpinning NICE guidance, through the establishment of new or the improved usage of existing registers / databases, with an initial focus on Interventional Procedures guidance. Furthermore, NICE is working with the Agency for Healthcare Research and Quality (AHRQ), to set out clear methodological quality criteria for the collection of clinical data while exploring the possibility of establishing joint Anglo-American registers / databases with the Centre for Medicare/Medicaid Services (CMS) in areas of mutual interest.

10.7 In his recent report on "Spending on healthcare; how much is enough?", the Chief Economist of the King's Fund recommends that the "role of NICE is strengthened and the publicly funded research programme supports this strengthened role by

¹⁰ The Principles Underlying the Work of the National Coordinating Centre for Health Technology Assessment, <http://www.hta.nhsweb.nhs.uk/sundry/probity.pdf> (accessed June 2006)

¹¹ Potential use of routine databases in health technology assessment; HTA 9(20); 2005

providing the evidence needed for comparative evaluation of treatment options¹². We feel that NICE has an important role to play in realising both economic and health benefits of health research.

11 International Influences

Question 9 - what lessons should the UK learn from other countries in making the proposed changes to the institutional arrangements for the funding of health research?

11.1 In April 2005 the Centers for Medicare and Medicaid Services (CMS) in the USA launched a consultation on a new policy called “Coverage with Evidence Development” (CED). This policy is an attempt to link coverage decisions to acquiring evidence of effectiveness of the technology provided by CMS and, more than a year later, it is currently in a second round of public consultation¹³. Before articulating this new initiative, CMS had on a number of occasions made provisional coverage decisions with the requirement that beneficiaries participate in a disease register or clinical trial. Examples include:

- Lung Volume Reduction Surgery and the National Emphysema Treatment Trial¹⁴
- Percutaneous Transluminal Angioplasty for carotid stenting
- FDG (18- Fluorodeoxyglucose) – Positron Emission Tomography for dementia^{15, 16}
- Prophylactic use of Implantable Cardioverter

11.2 Some of these trials were funded either solely by NIH or jointly by NIH and CMS. The main lesson learned from the US experience, as described by the then CMO of CMS, is the detrimental effects of the lack of co-ordination between NIH, the major public funders of research in the US, industry and CMS^{17, 18}. The CMS administration has found it remarkably difficult to establish the new CED policy.

¹² Spending on health care – how much is enough?; John Appleby and Anthony Harrison; King’s Fund; 2006

¹³ National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development, July 2006, https://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8 (accessed July 2006)

¹⁴ Carino *et al.*, Using clinical trials as a condition of coverage: lessons from the National Emphysema Treatment Trial, *Clinical Trials* 2004; 1:108-121

¹⁵ CMS decision memo, <http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=104> (accessed June 2006)

¹⁶ Kulasingam *et al.*, Linking dementia research to policy: an example using fluorodeoxyglucose positron emission tomography for the diagnosis of Alzheimer's dementia and mild cognitive impairment. *Am J Alzheimers Dis Other Demen.* 2006 Mar-Apr;21(2):73-8

¹⁷ Tunis *et al.*, Practical clinical trials: Increasing the value of clinical research for decision making in clinical and health policy, *JAMA*, September 2003, 290;12: 1624-1632

¹⁸ Tunis S, A clinical research strategy to support shared decision making, *Health Affairs*, 24; 1: 180-184

Despite considering it¹⁹ Australia's Pharmaceuticals Benefit Scheme never introduced a similar policy in Australia.

11.3 In an attempt to base coverage decisions on evidence of effectiveness, US health insurers including organisations such as Blue Shield²⁰ are providing financial support for groups evaluating the effectiveness of new medical technologies. In the current US climate, there is consensus on the importance of basing coverage decisions on evidence of "value" (as opposed to costs). Both private and public insurers are now working on producing this evidence through provisional coverage decisions and post-market surveillance mechanisms. The review of the institutional arrangements for research funding in the UK can make sure the mistakes of fragmentation, and the lack of communication and collaboration between decision makers and research funders, are not repeated in the UK setting.

11.4 The US AHRQ²¹ is a federally funded body responsible for carrying out research on medical effectiveness and evaluation. In the new UK health research setting, AHRQ-type research into methods and evaluation should form an integral part of the broader national health research priorities. Areas of research undertaken by AHRQ that would be of particular relevance to NICE and the NHS in general are around:

- Implementation research and impact evaluation
- Quality research and benchmarking of services

12 Bringing MRC and NHS R&D together

Question 10 - In implementing the single fund for health research, to what extent should the MRC and DH / NHS R&D be merged or brought together? And to whom should the single, ring-fenced fund be accountable? Please provide reasons and any supporting evidence for your response.

12.1 Health research is a continuum extending from the laboratory, to the clinic, and to the population as a whole. NICE has no doubt that a single organisation covering basic, translational, clinical and public health research should be created in order to allow a seamless approach and ensure that prioritisation of the research agenda is made more explicit.

¹⁹ Glasziou P, Support for trials of promising medications through the Pharmaceutical Benefits Scheme. *The Medical Journal of Australia*, January 1995, 162; 33-36

²⁰ <http://eastbay.bizjournals.com/eastbay/stories/2006/05/15/daily26.html?surround=lfm>, press release, May 2006 (accessed June 2006); also see: Garber A., Evidence-based coverage policy, *Health Affairs*, Sep/Oct 2001; 20, 5: 62-82

²¹ <http://www.ahcpr.gov/>

12.2 The most appropriate structure would be to establish a new organisation by primary legislation. The new body would, ultimately, be responsible to parliament for its use of the merged (MRC and NHS R&D) funds. By analogy with the Food Standards Agency, however, the new health research organisation would inevitably need to be sensitive to the needs of individual government departments (especially DH and DTI). Safeguards could be built into the legislative arrangements so that the wider public interest was protected.

13 Connecting for Health

Question 11 - To what extent does the success of recent innovations in health research (e.g. Clinical Research Networks) and the proposed structures rely on the new Connecting for Health NHS IT system, and to what extent should it do so?

13.1 Connecting for Health (CfH) is a very important development in the NHS setting. However, we feel that pressing needs, such as the establishment of disease registers and post-marketing surveillance tools have so far been linked to the progress of CfH and, therefore, postponed until CfH becomes fully operational.

13.2 Connecting for Health can be used as a means of identifying and tracking patients. But we must start building supplementary systems that will, to a degree, need to be independent from (albeit compatible with) CfH. We feel that there is a need for a national strategy on registers for surgical interventions and medical technologies. NICE is currently working with CMS and AHRQ on the development of a methodology for setting up registers and also on sharing information between the two countries. However, we need support to take these initiatives forward independently of CfH.

14 Devolved administrations

Question 12 - Given that NHS R&D is currently devolved, but that the work of Research Councils is not, how can these functions work best together to maximise the health and economic benefits to the UK?

14.1 The creation, under primary legislation, of a merged body (see above) could provide – with appropriate safeguards – the devolved administrations with a research base that is substantially more effective than at present.

Peter Littlejohns, Kalipso Chalkidou

Appendix A

NICE Research Recommendations: 1999-present

Since its establishment NICE has issued approximately 600 research recommendations across all different types of guidance products, including Clinical Guidelines, Cancer Service Guidelines, Public Health guidance and Technology Appraisal guidance. In addition to the above, NICE Interventional Procedures guidance often recommends further audit or the establishment of a registry for a specific intervention in order to better monitor the use of a particular procedure. Examples of research recommendations from different types of NICE guidance products are given below:

Clinical guidelines (CG)

- From **CG023**, *Depression* (Dec 2004): "The efficacy of organisational interventions, such as chronic disease management programmes or other programmes of enhanced care for depression should be tested in large-scale multicentre trials in the NHS."
- From **CG024**, *Lung cancer* (Feb 2005): "The management of common problems such as cachexia, anorexia, fatigue and breathlessness experienced by patients with lung cancer needs further research. Specifically, research is required into clinically meaningful outcome measures for the treatment of the cachexia-anorexia syndrome. For example, does the level of physical activity as measured by an activity meter relate to performance status, quality of life and use of health and social care services?"
- From **CG026**, *Post-traumatic stress disorder* (Mar 2005): "A randomised controlled trial, using newly developed guided self-help (GSH) materials based on trauma-focused psychological interventions, should be conducted to assess the efficacy and cost effectiveness of guided self-help compared with trauma-focused psychological interventions for mild and moderate PTSD."
- From **CG032**, *Nutrition support in adults* (Feb 2006): "What are the benefits of enteral tube feeding to patients compared with no enteral tube feeding in people with dysphagia and early to mid-stage dementia in terms of reduced complications associated with swallowing, improved nutritional status, delayed onset of advanced stage dementia, hospital admissions, cost effectiveness and survival?"

Cancer Service Guidelines (CSG)

- From **CSG001**, *Breast* (Aug 2002): "The research on social support for patients is generally poor. There is a need for methodologically sound studies which focus on the effects of simple supporting strategies for breast cancer patients."
- From **CSG004**, *Haemato-oncology* (Oct 2003): "Positron emission tomography (PET) scanning may be considered, if available, for discriminating between residual lymphoma and fibrotic tissue after chemotherapy, but further research is necessary to determine its cost and utility in relation to other forms of imaging."
- From **CSG007**, *Skin tumours including melanoma* (Feb 2006): "Research should continue to evaluate new agents for the treatment of cutaneous lymphoma."
- From **CSG008**, *Supportive and palliative care* (Mar 2004): "Research is needed to determine cost-effective ways of providing specialist palliative care to patients and families outside the hours of 09.00-17.00, Monday-Friday."

Public Health Intervention guidance (PHI)

- From **PHI001**, *Smoking cessation* (Mar 2006): "Has the impact of brief interventions changed as a result of increased investment in tobacco control activities, including development of the NHS smoking cessation services?"
- From **PHI002**, *Physical activity* (Mar 2006): "What is the effectiveness and cost effectiveness of the DH/Countryside Agency national pedometer programme on the long-term (over 1 year) physical activity levels of previously inactive adults?"
- From **PHI002**, *Physical activity* (Mar 2006): "An immediate priority is to establish the best validated measure(s) to assess baseline and subsequent changes in physical activity levels, following an intervention. A basic minimum data set also needs to be established to assess levels of physical activity in the population. This might include related physiological and psychological measures."

Technology Appraisals (TA)

- From **TA061**, *Colorectal cancer - capecitabine and tegafur uracil* (May 2003): "Further research is required to determine the place of capecitabine and tegafur with uracil in the treatment of metastatic colorectal cancer. In particular, RCTs are needed to assess the use of these oral treatments compared with infusional 5-FU/FA regimens. Such studies should include evaluations of quality of life, acceptability and cost effectiveness."
- From **TA070**, *Leukaemia (chronic myeloid) – imatinib* (Oct 2003): "Further good-quality studies are also needed to investigate:
 - ⇒ the efficacy of imatinib in combination with other treatment options or the clinical and cost effectiveness of dose escalation (within licensed indications)
 - ⇒ the need for, and duration of, long-term imatinib therapy in those who respond to initial treatment
 - ⇒ the definition of inadequate response to imatinib treatment."
- From **TA072**, *Rheumatoid arthritis – anakinra* (Nov 2003): "Longitudinal data on the quality of life of people with RA, and the impact of anakinra and other interventions on quality of life are required to improve the reliability of economic analyses."
- From **TA084**, *Sepsis (severe) – drotrecogin* (Sep 2004): "Further research is required on the longer-term impact of drotrecogin alfa (activated) on mortality, morbidity, health-related quality of life and resource use among UK patients with severe sepsis and multiple organ failure. Survivors of severe sepsis may have a low health-related quality of life and an increased risk of death, at least in the initial few years following the septic episode. The potential of drotrecogin alfa (activated) to offset this burden of illness has yet to be adequately defined. In addition, little is known about the long-term costs incurred when patients survive sepsis. The longer-term impact of drotrecogin alfa (activated) could be assessed by means of case-control studies, observational research and clinical audit using high-quality databases."
- From **TA098**, *Attention deficit hyperactivity disorder (ADHD) - methylphenidate, atomoxetine and dexamfetamine* (Mar 2006): "Further research is required to determine the utility values associated with ADHD and different treatment strategies, including drug therapy and the associated adverse event profiles of different drugs. Ideally, utilities should be obtained with the use of a generic health valuation measure, valued with public preferences."

Appendix B

NICE clinical and public health recommendations for the use of a technology in the context of research: 1999-present

Below are examples of “*in the context of research*” recommendations from Technology Appraisals and Public Health interventions guidance.

The Institute has, so far, issued 16 recommendations for the use of a new technology only in the context of research, as part of its Technology Appraisal guidance. Positive guidance has been or is in the process of being issued for a quarter of these recommendations, in all those cases where the relevant research was undertaken and the required data successfully collected (see Table 1). For the remaining ones, the recommendations for further research remain to be taken up by relevant research bodies or sponsors of the technologies. In no occasion has the Institute reversed a recommendation for use in the context of research into a negative or restrictive recommendation, so far. A number of recommendations for the establishment of a registry or requirements for prospective data collection have also been made in a number of Technology Appraisal guidance (approx 5 in total).

Recommendations for the use of a technology in the context of research have also been made by the Institute’s Public Health Advisory Committee in the recently published public health guidance on physical activity; the interventions considered there are established ones with a very limited evidence base. This type of intervention usually has no sponsor.

Examples of “in the context of research” and register-type recommendations are given below:

Technology Appraisals

- From **TA068**, *Macular degeneration (age related) - photodynamic therapy* (Sep 2003): "PDT is not recommended for the treatment of people with predominantly classic subfoveal CNV (that is, 50% or more of the entire area of the lesion is classic CNV but some occult CNV is present) associated with wet age-related macular degeneration, except as part of ongoing or new clinical studies that are designed to generate robust and relevant outcome data, including data on optimum treatment regimens, long-term outcomes, quality of life and costs."
- From **TA072**, *Rheumatoid arthritis – anakinra* (Nov 2003): "On the balance of its clinical benefits and cost effectiveness, anakinra is not recommended for the treatment of rheumatoid arthritis, except in the context of a controlled, long-term clinical study."
- From **TA092**, *Tooth decay – HealOzone* (Jul 2005): "HealOzone is not recommended for the treatment of tooth decay (occlusal pit and fissure caries and root caries), except in well-designed randomised controlled trials."
- From **TA093**, *Colorectal cancer (advanced) - irinotecan, oxaliplatin and raltitrexed* (Aug 2005): "Raltitrexed is not recommended for the treatment of patients with advanced colorectal cancer. Its use for this patient group should be confined to appropriately designed clinical studies."

Public Health Intervention guidance (PHI)

- From **PHI002**, *Physical activity* (Mar 06): "Practitioners, policy makers and commissioners should only endorse pedometers and walking and cycling schemes to promote physical activity that are part of a properly designed and controlled research study to determine effectiveness. Measures should

include intermediate outcomes such as knowledge, attitude and skills, as well as measures of physical activity levels.”

- From **PHI002**, *Physical activity* (Mar 06): “Practitioners, policy makers and commissioners should only endorse exercise referral schemes to promote physical activity that are part of a properly designed and controlled research study to determine effectiveness. Measures should include intermediate outcomes such as knowledge, attitudes and skills, as well as measures of physical activity levels. Individuals should only be referred to schemes that are part of such a study.”

Table 1: NICE recommendations for the use of a technology on the context of research that have been turned into positive recommendations following review of the guidance.

Guidance	NICE recommendation (original guidance)	NICE recommendation (review)	Comments
Cervical cancer – cervical screening	Whilst liquid-based cytology (LBC) could provide significant and important benefits.... [The] quality of the evidence is variable and... there is insufficient evidence to justify the nationwide introduction of LBC technology at this time. The Committee recommends the undertaking of a series of pilot studies to investigate the feasibility of liquid-based cytology in terms of workload, productivity and detection rates. (TA005 - 2003)	Liquid-based cytology should be used as the main way of preparing samples of cervical cells for cervical screening. (TA069 - 2003)	The evaluation of the introduction of liquid-based cytology at these pilot sites informed important sections of the systematic review and modelling analysis underpinning the cost-effectiveness analysis of liquid based cytology. As a result, this technology was recommended by NICE in 2003.
Colorectal Cancer – laparoscopic surgery	People with colorectal cancer should have ordinary (open) surgery rather than laparoscopic surgery to remove their cancer. People should only have laparoscopic surgery as part of a clinical trial. (TA017 - 2000)	Laparoscopic (including laparoscopically assisted) resection is recommended as an alternative to open resection for individuals with colorectal cancer in whom both laparoscopic and open surgery are considered suitable. (<i>In preparation</i> - 2006)	The NICE guidance of 2000 accelerated recruitment into relevant trials; the new data generated by these studies were reviewed by the Committee and a positive (draft) recommendation for the use of this technology was issued in 2006.
Depression and anxiety - Computerised Cognitive Behavioural Therapy (CCBT)	Current research shows that Computerised Cognitive Behavioural Therapy (CCBT) may be of value in the management of anxiety and depression, but this evidence is not strong enough to recommend CCBT for general use in the NHS. The NHS should consider supporting an independent programme of research into CCBT. This research should include looking at how CCBT could fit into a 'stepped care' approach to treating anxiety and depression and the setting up of carefully monitored pilot projects. It should also include	NICE recommends using: <ul style="list-style-type: none"> • Beating the Blues for people with mild and moderate depression. • FearFighter for people with panic and phobia. There is not enough evidence to recommend COPE and Overcoming Depression for managing depression. But people can use them specifically as part	Given the uncertainty surrounding the various CCBT interventions, the Institute recommended independent research in order to gather more evidence on how the NHS might use this technology in the future. Based on The Committee considered the evidence base on Beating the Blues and FearFighter which had improved since the previous appraisal. On the basis of the new evidence, the Committee recommended the use of the above two interventions.

	<p>pilot projects. It should also include investigations into what users prefer, what their needs are, and what makes people suitable or unsuitable for treatment with CCBT - for example, does cultural background or level of education affect whether CCBT is an appropriate treatment. (TA051 - 2002)</p>	<p>of ongoing or new clinical trials. (TA097 - 2006)</p>	
<p>Advanced colorectal cancer – irinotecan, raltitrexed</p>	<p>Irinotecan combination treatments with 5FU/FA are not recommended as routine first-line treatment, on the basis of insufficiently robust evidence of their clinical and cost effectiveness.</p> <p>Raltitrexed is not recommended for use outside appropriately designed clinical studies (TA033 - 2002).</p>	<p>Irinotecan within its licensed indication, is recommended for people with advanced colorectal cancer in combination with 5FU/FA as first-line therapy</p> <p>Raltitrexed is not recommended for the treatment of patients with advanced colorectal cancer unless in the context of appropriately designed clinical studies. (TA093 - 2005)</p>	<p>In 2003, the available data did not support widespread use of irinotecan or raltitrexed. At the same time, the Medical Research Council (MRC) established the FOCUS trial to address the uncertainties surrounding the value of irinotecan as a first line therapy. NICE guidance actively encouraged oncologists to enrol the patient (following discussion and consent) in this trial to ensure that patients are treated appropriately and data is collected to determine the true value of these treatments. The MRC FOCUS trial reported in 2004, and NICE guidance was reviewed in 2005. Both the FOCUS and other studies were used to inform the review and support a positive recommendation for irinotecan. The evidence base had not developed for raltitrexed so the “in the context of research” recommendation remained in the 2005 review.</p>

