

**APPRAISING THE VALUE OF INNOVATION  
AND OTHER BENEFITS**

**A SHORT STUDY FOR NICE**

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## **RECOMMENDATIONS**

### *RECOMMENDATION 1*

*NICE SHOULD BE MORE ACTIVE IN EXPLAINING ITS ROLE AND DECISIONS AND DEVELOP A STRATEGY TO ACHIEVE THIS*

### *RECOMMENDATION 2*

*NICE SHOULD WORK WITH PHARMA AND OTHERS TO IDENTIFY HOW THE COSTS OF RESEARCH AND DEVELOPMENT ARE DISTRIBUTED IN THE GLOBAL MARKET*

### *RECOMMENDATION 3*

*NICE'S APPRAISALS SHOULD CONTINUE TO BE BASED ON THE ICER/QALY APPROACH INTO WHICH IS INCORPORATED EXPLICIT CONSIDERATION OF RELEVANT BENEFITS. A TWO STAGE APPROACH SHOULD NOT BE ADOPTED*

### *RECOMMENDATION 4*

*NICE SHOULD CONSULT ALL RELEVANT PARTIES AND DRAW UP A LIST OF THOSE HEALTH-RELATED BENEFITS TO BE TAKEN INTO ACCOUNT IN ITS APPRAISALS. THE LIST SHOULD BE REVIEWED THROUGH AN APPROPRIATE MECHANISM FROM TIME TO TIME*

*NICE SHOULD SPONSOR (OR PARTICIPATE IN) RESEARCH TO DETERMINE WHETHER THE INSTRUMENTS USED TO CALCULATE QALYs AND CAPTURE HEALTH BENEFITS ARE ENTIRELY APPROPRIATE TO NICE'S NEEDS AND WHETHER THEY ARE APPLIED PROPERLY AND CONSISTENTLY*

### *RECOMMENDATION 5*

*NICE SHOULD BEGIN TO ADJUST ITS EVALUATION OF QALYs IN ADVANCE OF ANY RESEARCH FINDINGS ON METHODOLOGY, IN CONSULTATION WITH RELEVANT PARTIES, SO AS TO BEGIN TO TAKE ACCOUNT OF RELEVANT HEALTH-RELATED BENEFITS ONCE IDENTIFIED AND AGREED*

*RECOMMENDATION 6*

*THE PRESENCE OF BENEFITS OF THE SORT REFERRED TO IN PARA 3.8 SHOULD NOT RESULT IN AN INCREASE IN THE THRESHOLD USED BY NICE*

*RECOMMENDATION 7*

*SOCIAL BENEFITS OF THE SORT SET OUT IN PARA 3.11 SHOULD NOT CURRENTLY BE TAKEN ACCOUNT OF BY NICE IN ITS APPRAISALS, BUT NICE SHOULD COMMISSION OR PARTICIPATE IN RESEARCH TO DETERMINE WHETHER SUCH BENEFITS COULD FORM PART OF NICE'S APPROACH AND, IF SO, HOW*

*RECOMMENDATION 8*

*NICE SHOULD WORK CLOSELY WITH PHARMA TO ENSURE THAT NICE IS MADE AWARE AT THE EARLIEST POSSIBLE OPPORTUNITY OF ANY CLAIM BY PHARMA REGARDING BENEFITS AND THAT DATA RELEVANT TO NICE'S APPRAISALS IS GENERATED AS PART OF PHARMA'S RESEARCH*

*NICE'S SCOPING WORKSHOP AND SCOPING DOCUMENT SHOULD IDENTIFY ANY CLAIM OF BENEFITS DISCUSSED IN PARA 3.8 OR OF INNOVATION*

*RECOMMENDATION 9*

*NICE SHOULD INVITE MANUFACTURERS TO CONTRIBUTE TO PART I OF THE MEETING OF THE APPRAISAL COMMITTEE IN THE SAME WAY AS OTHERS WHO ARE CONSULTED*

*RECOMMENDATION 10*

*NICE SHOULD CONSIDER, IN CONSULTATION WITH INTERESTED PARTIES, WHETHER A VIDEO-RECORDING OF PART II OF THE APPRAISAL COMMITTEE'S MEETING COULD BE MADE AVAILABLE TO MANUFACTURERS AND OTHER INTERESTED PARTIES AFTER NICE'S GUIDANCE HAS BEEN PUBLISHED*

*RECOMMENDATION 11*

*NICE SHOULD ENHANCE ITS EFFORTS TO UNDERSTAND THE SPENDING BEHAVIOUR OF PCTs AND THE EFFECTS OF NICE'S DECISIONS ON PCTs' BUDGETARY PLANNING*

*RECOMMENDATION 12*

*NICE SHOULD WORK WITH OTHERS TO DEVELOP AN ACTIVE POLICY ON DISINVESTMENT BY THE NHS IN PRODUCTS WHICH DO NOT OFFER VALUE FOR MONEY*

*RECOMMENDATION 13*

*NICE SHOULD ESTABLISH AND KEEP UNDER REVIEW A MECHANISM WHEREBY UNSUCCESSFUL APPLICATIONS FOR APPROVAL CAN BE DISCUSSED WHEN THE FINAL APPRAISAL DETERMINATION HAS BEEN AGREED AND BEFORE GUIDANCE IS ISSUED*

*RECOMMENDATION 14*

*NICE SHOULD FORMULATE A DEFINITION OF “INNOVATION” ALONG THE LINES SET OUT IN PARA 4.10 AND CRITERIA ALONG THE LINES SET OUT IN PARA 4.11*

*SO THAT A JUDGEMENT CAN BE MADE THAT A PRODUCT MEETS THE NHS’ NEEDS, THE SECRETARY OF STATE FOR HEALTH SHOULD FROM TIME TO TIME MAKE EXPLICIT THE PRIORITIES OF THE NHS REGARDING INTERVENTION AND TREATMENT*

*RECOMMENDATION 15*

*NICE SHOULD ESTABLISH A MECHANISM WHEREBY PHARMA CAN SIGNAL AS EARLY AS POSSIBLE THAT A PRODUCT MAY CONSTITUTE AN “INNOVATION” AS DEFINED IN PARAS 4.10-11*

*NICE SHOULD WORK CLOSELY WITH PHARMA, USING FOR EXAMPLE ITS SCIENTIFIC ADVICE PROGRAMME, TO ENSURE THAT THE DATA REQUIRED BY NICE TO MAKE THIS JUDGEMENT IS GENERATED*

*NICE SHOULD OFFER ADVICE AND SUPPORT TO NEWER COMPANIES TO FACILITATE COMPETITION IN THE SECTOR*

*NICE SHOULD CONSIDER, AS INCENTIVES TO PHARMA, AGREEING A HIGHER THRESHOLD IN THE CASE OF “INNOVATION” (AS DEFINED) AND MAINTAINING IT FOR A FIXED PERIOD (eg FROM 3-5 YEARS) OR AGREEING THE USE OF A SCHEME UNDER THE REVISED PPRS (“FLEXIBLE PRICING” or “PATIENT ACCESS”)*

*NICE SHOULD REVISIT THE THRESHOLD TO BE USED IN THE APPRAISAL OF PRODUCTS WHICH DO NOT MEET THE CRITERIA OF INNOVATION IF A HIGHER THRESHOLD OR ONE OF THE SCHEMES UNDER THE PPRS IS USED AS AN INCENTIVE TO PROMOTE INNOVATION*

*RECOMMENDATION 16*

*NICE SHOULD ESTABLISH A MECHANISM WHEREBY THE NHS IS COMPENSATED FOR THE FINANCIAL LOSS WHICH WILL HAVE BEEN INCURRED UNDER PARA 4.12 IF A PRODUCT SUBSEQUENTLY PROVES NOT TO MEET INITIAL EXPECTATIONS*

*RECOMMENDATION 17*

*NICE SHOULD BUILD ON ITS REPUTATION AS LEADING THE WORLD IN THE APPRAISAL OF PRODUCTS TO ESTABLISH ITSELF ALSO AS A WORLD LEADER IN PROMOTING INNOVATION AND THE EARLY ADOPTION OF TREATMENTS*

*RECOMMENDATION 18*

*NICE SHOULD URGE GOVERNMENT TO MAKE APPROPRIATE ADJUSTMENTS TO THE SUPPLY SIDE, AS RECOMMENDED BY SIR DAVID COOKSEY AND THE OFFICE OF LIFE SCIENCES TO ENCOURAGE INNOVATION ON BEHALF OF THE NHS AND PATIENTS*

*RECOMMENDATION 19*

*NICE SHOULD ONLY OFFER INCENTIVES FOR INNOVATION WHEN IT IS REALISED*

*RECOMMENDATION 20*

*NICE SHOULD CONSIDER ESTABLISHING A FORMAL AND TRANSPARENT PROCESS, USING SUCH OPTIONS AVAILABLE TO IT AS ARE REFERRED TO IN PARA 4.19 TO OFFER INCENTIVES TO PHARMA WHEN A PRODUCT IS SAID TO HAVE THE PROMISE OF INNOVATION*

*NICE SHOULD PILOT THE PROCESS FOR A PERIOD OF (eg 3 YEARS) IF IT DECIDES TO ESTABLISH IT*

*RECOMMENDATION 21*

*NICE SHOULD MAKE URGENT REPRESENTATIONS TO GOVERNMENT, PARTICULARLY THE DEPARTMENT OF HEALTH, THAT ITS ABILITY EFFECTIVELY TO EVALUATE THE VALUE OF PRODUCTS DEPENDS ON THE EXISTENCE OF DATA AND INFORMATION FROM APPROPRIATE RESEARCH AND STUDY*

*NICE SHOULD URGE GOVERNMENT TO EXAMINE THE FUNDING OF RESEARCH AND FURTHER STUDY, WORKING WITH PHARMA AND ALL OTHER RELEVANT PARTIES, PARTICULARLY ACADEMIC HEALTH SCIENCE CENTRES, SO AS TO GENERATE DATA THEREBY ENABLING NICE TO EVALUATE PRODUCTS AS EFFECTIVELY AS POSSIBLE*

*NICE SHOULD URGE THE DEPARTMENT OF HEALTH TO SUPPORT, WITH OTHERS, THE FUNDING OF POST-MARKETING SURVEILLANCE OF PRODUCTS' EFFICACY AS WELL AS SAFETY*

*NICE SHOULD WORK WITH THE OFFICE OF LIFE SCIENCES TO ENSURE THAT THE PROPOSALS OF THE OFFICE RELATING TO RESEACH AND DATA COLLECTION ARE ACTED UPON PROMPTLY*

*RECOMMENDATION 22*

*NICE SHOULD CONSIDER WHETHER THE SAME OR A SIMILAR PACKAGE OF MEASURES AS THOSE SET OUT IN PARA 4.12 SHOULD BE USED TO GIVE INCENTIVES TO INNOVATION AND DEVELOPMENT OF PRODUCTS FOR RARE DISEASES*

*RECOMMENDATION 23*

*NICE SHOULD WORK WITH THE OFFICE OF LIFE SCIENCES SUCH THAT, IF AN "INNOVATION PASS" IS THOUGHT NECESSARY AND APPROPRIATE, CONDITIONS SUCH AS THOSE SET OUT IN PARA 4.26 APPLY*

*NICE SHOULD ESTABLISH A COMMITTEE OF EXPERTS TO ADVISE ON WHETHER THE CRITERIA FOR USE OF THE "INNOVATION PASS" ARE MET*

*NICE SHOULD SEEK TO ENSURE THAT FUNDING FOR THE PURCHASE OF THE PRODUCTS SUBJECT TO THE "INNOVATION PASS" COMES FROM A SPECIALLY CREATED FUND AND NOT FROM THE NHS*

*NICE SHOULD SEEK TO ENSURE THAT THE “INNOVATION PASS” DURING WHICH A PRODUCT IS NOT EVALUTED BY NICE SHOULD LAST FOR A FIXED PERIOD OF TIME (eg A MAXIMUM OF 3 YEARS)*

*NICE SHOULD SEEK TO ENSURE THAT AT THE EXPIRY OF THE FIXED PERIOD OF TIME THE PRODUCT IS APPRAISED BY NICE AND FALLS WITHIN THE THRESHOLD FOR APPROVAL*

*RECOMMENDATION 24*

*NICE THROUGH ITS MEDICAL TECHNOLOGY ADVISORY COMMITTEE SHOULD PLAY AN INCREASINGLY ACTIVE ROLE IN ENCOURAGING RESEARCH INTO MEDICAL TECHNOLOGIES TO BE CARRIED OUT IN THE UK*

*RECOMMENDATION 25*

*NICE SHOULD WORK WITH OTHERS, PARTICULARLY ACADEMIC HEALTH SCIENCE CENTRES, TO ENSURE THAT A SOUND INFRASTRUCTURE FOR RESEARCH INTO THE EFFECTIVENESS OF PSYCHOLOGICAL THERAPIES IS ESTABLISHED*

*NICE SHOULD WORK WITH OTHERS TO DEVELOP A SYSTEMATIC APPROACH TO EVIDENCE REGARDING PSYCHOLOGICAL THERAPIES, INCLUDING THE PLACE OF RCTs AND NON-EXPERIMENTAL EVIDENCE*

## 1 INTRODUCTION

1.1 I was asked by Sir Michael Rawlins, the Chairman of the National Institute for Health and Clinical Excellence, (NICE) in February 2009 to undertake a study in response to the views expressed by Sir David Cooksey in January 2009 in his *Review and Refresh of Bioscience 2015*<sup>1</sup>. Sir David wrote that “Currently, the perceived problem for UK industry is that NICE appraisals do not operate in a way that is supportive of innovation, or uptake and access to medicines and therefore dissuade companies from investing in the UK”<sup>2</sup>. As a response to this “perceived problem” Sir David offered Recommendation 16. This reads:

*“There should be an independent inquiry to assess NICE’s long term impact on cost, access to, and uptake of, medicines in the UK. There should also be an independent review of the way in which NICE values medicines so that the current economic evaluation is complemented by clinician, patient and research inputs on the value of innovation from their perspectives”*<sup>3</sup>.

1.2 The study that I was asked to undertake was intended to respond to the second of these recommendations. I take it as a condition of my study that there is a perceived problem concerning innovation. It is for others elsewhere to determine whether this is so<sup>4</sup>. Subsequently, in its response to Sir David’s review, the government rejected the first recommendation, that there be a root and branch inquiry into NICE, deeming it not “... the right way of addressing the specific issues his report raises.”<sup>5</sup>

1.3 The terms of reference that I was given were:

*to carry out a short study of valuing innovation aimed at addressing the following questions:*

- *What approach should be adopted by NICE to ensure that innovation is properly taken into account when establishing the value of new health technologies?*
- *Should particular forms of value be considered more important than others?*
- *How should innovation in health technologies be defined?*
- *What is the relationship between innovation and value?*

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<sup>1</sup> “A Report to Government by the Bioscience Innovation and Growth Team”, Department for Business, Enterprise and Regulatory Reform

<sup>2</sup> id p.43

<sup>3</sup> id p.51

<sup>4</sup> Two points can be made. First, rather than tinker with the NICE’s system to privilege innovation of a certain kind, it could be argued that there needs to be a fundamental re-examination of the what and how science should be pursued and of the business model adopted historically by the pharmaceutical industry, premised on the pipeline and the “blockbuster” drug. Second, it is important at all times to remember, as a matter of national policy, the importance to health and healthcare of health promotion and the prevention and avoidance of ill-health, and the myriad factors beyond the reach of the NHS which contribute to ill-health which should be addressed. It is, of course, a matter of balance, but this need for balance must never be overlooked, for shorter term considerations

<sup>5</sup> “Government response to review and refresh of bioscience 2015 report” May 7, 2009. It is worth saying that the role and performance of NICE has regularly been examined by a variety of bodies, not least the House of Commons Health Committee in 2001-02 and 2007-08

As I shall explain, these terms of reference subsequently became both more broad and more refined.

1.4 It was agreed that I would begin work on the study in mid-April. I was asked to prepare a report which could be considered by NICE's Board at its meeting scheduled for July 22, 2009. In keeping with Sir David Cooksey's recommendation, it was also agreed that I would conduct the study wholly independently of NICE. I was supported thereafter by NICE in terms of practical arrangements and access to individuals and meetings. I was also reimbursed by NICE. That said, I acted entirely independently. The views and recommendations are mine alone.

### **Submissions**

1.5 I chose to conduct the study in the following way. First, I asked that a call be made for expressions of view, in the form of written submissions, on a series of questions arising from the study's terms of reference. The questions were:

- What should be taken into account in establishing the value of new health technologies (health technologies are defined as drugs, medical devices, diagnostics and surgical procedures);
- Whether particular forms of "value" should be regarded as being more important than others;
- How "innovation" in health technologies should be defined and how should its relationship with "value" be described.

1.6 I was anxious that this call should reach a wide audience and not be limited to those organisations, groups and individuals close to NICE. In the event, 42 submissions were received. The time frame was tight and some felt unable to meet the stipulated deadline. I made it clear that I was content to receive late submissions, since the purpose was to allow me to become aware of the range of views which exist. This meant that I was still receiving expressions of view until mid-June. A breakdown of the submissions shows the following:

- healthcare industry - 23
- patients' groups - 9
- academics - 4
- professional groups - 2
- NHS Confederation - 1
- policy institute - 1
- healthcare professional - 1
- NICE - 1

In keeping with the principle of transparency, all of the submissions and subsequent correspondence were posted onto NICE's web-site.

1.7 It was disappointing that I received no formal submissions from commissioning bodies, medical practitioners or their representatives, (though I was pleased to receive a submission from the Royal College of Nursing), the Department of Health<sup>6</sup>, and opposition parties, despite, in the case of the last two, my invitation to contribute. I did receive a helpful short note from the NHS Confederation but would have been even more assisted by a fuller submission. I also had helpful meetings with Lord Drayson, the Minister responsible for the Office of Life Sciences, with Sir David Cooksey, and with Professor Sir John Bell, President of the Academy of Medical Sciences. Given that the bulk of the submissions that I received amounted to comments on NICE's approach to appraisals, I also asked officials at NICE to prepare a formal submission which could contain such responses to the points made as NICE might wish. My aim was to get as rounded a picture as possible. I received NICE's submission on June 15, 2009 and found it helpful.

### **Workshops**

1.8 Next, I asked that Workshops be organised so that those who had submitted papers and others could be brought together to explore in greater depth and in sufficient time the various themes on which I would value advice. The themes reflected in very broad terms the central arguments emerging from the submissions and my understanding of them. They were:

#### Workshop 1 – benefits/values in the assessment of technologies

1. What are the strengths and weaknesses of first a broad and then a more targeted approach to evaluating health technologies?
2. Has NICE missed any benefits in its current approach, particularly given Sir David Cooksey's reference to the perspectives of patients, clinicians and "research"? Should any be emphasized more?

#### Workshop 2 – the value of innovation

1. What is innovation? Can you agree a meaning?
2. Given that innovation may not always deliver on its initial promise, how should the various risks be shared amongst the various players?

#### Workshop 3 – methodology

1. Given that not everything in the assessment of health technologies can be quantified, what is the balance between "judgement" and "reproducible" process?

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<sup>6</sup> I also received a short paper from the Chief Medical Officer for Wales

2. There is pressure to minimize the time between licensing and subsequent approval by NICE. However, the closer they are together, the less likely the scrutiny will be exhaustive. How do you balance rigor of appraisal with timeliness?
3. If there is uncertainty particularly as regards the benefits which may accrue from innovation, how much uncertainty should be tolerated and whose responsibility is it to obtain further information?

The papers presented at the Workshops and the names of those attending appear on NICE's website.

1.9 The next stage was a meeting with Patients involved in NICE (PIN), from whom I received a helpful note, and then a meeting of NICE's Citizen's Council on May 28-30 at which a number of questions pertaining to the study were considered. The questions were:

1. What makes an innovation valuable to you?

2. If the innovation is more expensive than the cost per QALY gained threshold and DOES not demonstrate benefits at the moment, but there is a case that it may in the future, what should NICE do:

- Say NO for now and ask the developer to fund and do more research
- Say NO for now but fund some of the research for the developer on condition that the public gets a return proportionate to its investment
- Say YES – but on condition that
  - There is risk-sharing, eg NHS only pays in cases where the thing works
- Say Yes – but at how much above the threshold: £30K, £35K, £40K, £45K, £50K, £55K, £60K

3. Who should bear the costs and risks of research and development of health technologies?

The views expressed by the Council served further to inform the study.

1.10 Finally, I wrote my report which I now submit to the Board of NICE.

## 2. THE QUESTIONS

2.1 I start by recalling the poignant comment of a representative of a patients' group at one of the Workshops. She remarked that there had been a lot of talk about health economics and theoretical models, but not enough about what patients such as she wanted and needed. This captures the heart of the dilemma which NICE was established to address. The NHS exists to look after individuals (and those who care for them) when they need it. But, in the context of a limited level of resource, decisions have to be made as to how much of that resource may be spent in any particular set of circumstances. The claims of both those who make themselves heard and those who are not heard must all be weighed. And weighing means analysis, policy, (and health economics). It is not uncaring. Indeed, it is the only way of caring in an organised and accountable manner: caring for and about all. This may not mean, however, satisfying the claims of all.

2.2 It was clear from many of the submissions that the establishment of this study was seen by Pharma<sup>7</sup> and patients' groups, in particular, as an opportunity to raise a range of issues relating to NICE's technology appraisals. Innovation was discussed but so were other matters which, in the view of many, should be taken account of by NICE in its appraisals, but which, in their view, were not, either at all or adequately. I decided that I should include these matters in my study. They clearly reflected strongly held concerns of some. Moreover, it was apparent that a concern for innovation could not easily be separated off from a range of other considerations. As a consequence, I refocused the study to consider:

- whether, quite apart from any claim that a product constitutes an innovation in the sense in which I will use it in this study (see para 4.11), there are any benefits (or values) which NICE should take account of in its technology appraisal which it currently does not take account of, or takes account of only at the margins
- whether innovation as a benefit is properly taken account of?
- to the extent that innovation and other benefits should be taken account of, how should NICE do so?

2.3 I intend to follow this outline in what follows. I shall also offer some comments on proposals currently being considered to privilege some form of innovation, by excusing it from having to be appraised by NICE for an initial period of time.

2.4 In everything that I set out there is one factor which is forever in the background. This is the price proposed by manufacturers for the product being appraised. The system of appraisal, based as it is, on the cost-effectiveness of a product, once clinical effectiveness has been demonstrated, depends on the price proposed. To meet NICE's threshold, the price is crucial: in simple terms, the higher the price, the more difficult it will be to show that a product is cost-effective when compared with other forms of treatment. However, NICE has

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<sup>7</sup> This is the term commonly used to refer to the pharmaceutical industry. I shall refer to Pharma as a convenient shorthand. I do not overlook those who develop diagnostic tools, devices, and other forms of therapy. Indeed, at the end of this study, I ask whether a separate process of appraisal may be required for them.

no role in setting or even negotiating the price that a manufacture may propose. It simply works on the basis of what is put before it. And, for obvious commercial reasons, not least the fact that, although the UK market constitutes only about 3% of the global market for pharmaceutical products, about 25% of the global market reflects the price used in NICE's appraisal, the manufacturer will seek to maximise the return on the product. Whatever the justification for this arrangement, it seems to me that, even if NICE is not, I am entitled in this study to comment on the role that price has in the system. Consequently, I will do so when appropriate.

2.5 I also raise here, at the outset, a further consideration. It too is in the background and not explicitly acknowledged, but has played an important part in my thinking. It is that the focus has been placed on what can be called the demand side of the equation: how the approval and subsequent purchase of products are managed. But the supply side is equally significant, that is, the context in which manufacturers operate. I refer, for example, to

- the proposals in Sir David Cooksey's Review<sup>8</sup> that greater financial incentives be given to the sector
- the Statement from the Office of Life Sciences in response to Sir David's Review<sup>9</sup>, of such matters as incentives through the tax system for innovation the supply of finance to the life sciences industry, tax credits for research and development (R&D) and the regulatory procedures
- the cost of research, particularly of clinical trials and of surveillance of effectiveness after approval.

I will say something about these supply side issues as they arise. They are for government, not for NICE, but they affect the climate in which NICE operates. I make one further comment. Considerable emphasis was placed by a number of health economists, both in the Workshops and in submissions, on the desirability of altering the arrangements for patent protection and other features of the intellectual property regime, such as "market exclusivity". Of course, these are matters now firmly within the jurisdiction of the European Community and the World Trade Organisation. The government cannot act unilaterally.

### **Setting the scene**

2.6 Before I turn to the outline that I set out in para 2.2, it may be helpful to set the scene briefly. I do so, despite the Board's obvious familiarity with this scene, because my report will be read by others less familiar. Furthermore, it may be helpful for the Board to receive the views of an outsider.

2.7 NICE was established in 1999. Its explicit purpose, as regards what is relevant to this study, was to be a mechanism for allocating the scarce resources of the NHS. Health technologies in the form of medicines, devices, diagnostic tests, and other forms of intervention and therapy were to be appraised by NICE which would decide whether the NHS

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<sup>8</sup> note 1, chapter 2

<sup>9</sup> *Life Sciences Blueprint*, Office of Life Sciences, July, 2009

should pay for this or that particular drug or product. The basis of NICE's system of appraisal is simple: something will be approved for use by the NHS if the improvements to health offered to patients are expected to exceed the health that is inevitably foregone elsewhere in the NHS as a consequence of any associated costs, within a fixed budget. Behind this simplicity lies much complexity, and yards of books, learned articles, papers and other material.

2.8 I will have to explore some of the complexities of this system in due course. Before I do, I want to do more scene setting. In particular, I want to notice what I will call the culture of NICE on the one hand and of Pharma on the other. In doing so, I do not ignore other sectors of industry, such as bio-technology, bio-engineering, and diagnostics, nor those concerned with psychological therapies, nor professional groups, nor groups of patients brought together by a common cause or affliction. Indeed, perhaps a comment on professional and patients' groups is in order. Both are characterised by a special concern: professionals by a concern with their particular area of expertise, patients by a concern with their experience of disease and illness. Both are crucial to informing NICE's process and to enabling NICE to understand the possible impact of its decision. Patients' groups are, necessarily, advocates. They understand quite clearly that they may not succeed in their advocacy. But, they must always be heard. Professionals, however, come with a larger responsibility: not only to their patients, but to the patients of others and to the NHS. They need to recognise that they are part of a system. Sometimes, in the entirely understandable concern for the patients whom they treat, they seem to lose sight of that system. Those looking after patients with cancer, particularly patients whose disease is in a terminal phase, come to mind. In an important and powerful paper in the *Journal of the National Cancer Institute*<sup>10</sup>, the authors draw attention to the spiralling costs of cancer treatment and the need to rethink what counts as a benefit which society should pay for. They urge that "it is time to confront ... what counts as a benefit in cancer treatment" and that "the escalating price of cancer therapy" must be dealt with. "If we allow a survival advantage of 1.2 months to be worth \$80,000 and by extrapolation survival of 1 year to be valued at \$800,000, we would need \$440 billion annually ... to extend by 1 year the life of the 550,000 Americans who die of cancer annually. And no-one would be cured. ... The current situation cannot continue".

2.9 But, let me return to NICE and Pharma. I do so because they have been and are the central players. To this outsider, the impression is one of undeclared hostilities, if not war<sup>11</sup>. Pharma sees NICE as a barrier to its ambitions to bring products to patients. NICE sees itself as the guardian of the public purse and of all patients. It does not see itself as the guardian or advocate of particular groups of patients, nor of Pharma's aspirations, to the extent that they may be thought by NICE to be in conflict with NICE's wider responsibility.

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<sup>10</sup> "How much is Life Worth", JNCI Commentary, July 2009

<sup>11</sup> Referring to expressions of concern by Pharma (and patients' groups), the House of Commons Health Committee states that "We were surprised by the vehemence of the criticisms", House of Commons Health Committee, First Report of Session 2007-08, "National Institute for Health and Clinical Excellence", Volume 1 p.10. That said, NICE would say that working arrangements are such that the work gets done

2.10 One of the aims of this report is to suggest a way forward which meets the legitimate ambitions of both Pharma and NICE and (and it is an important ‘and’), maximises the opportunity of present and future users of the NHS to enjoy the best available therapies. If this can be achieved, it will represent a very significant opportunity for Pharma to develop and for NICE to become the world leader in encouraging and promoting the best for patients, particularly through innovation.

## NICE

2.11 Let me paint my picture of NICE first. It is an organisation which is highly respected across the world. It is seen by those charged with similar responsibilities as carrying out a challenging and difficult role with rigour and fairness. It sets the benchmark. It would also be the first to recognise, however, that there are a number of areas in which it could improve. They include the following:

- NICE is not well known beyond those inside the loop of health policy. For a body charged with such a responsible duty on behalf of the taxpayer and the public, this is unfortunate. NICE rarely appears to be on the front foot in terms of setting and discussing the agenda of resource allocation. Instead, it too frequently finds itself responding to the characterisations (and caricatures) of others. It does not seek energetically to communicate and explain what it does, particularly in high profile cases. So, it finds itself regarded as blocking patients’ access to drugs, rather than holding the ring between conflicting demands.
- NICE can appear complacent. It has the right approach and that’s that. In fact, in my experience, it is very open to debate and challenge, but this is not always obvious. Occasionally, there is a real sense of NICE’s frustration that its system of appraisal is not understood. The remedy largely lies in NICE’s hands.
- NICE needs to work ever more closely with Pharma and others, to respond to their legitimate needs and concerns, and with Primary Care Trusts, which must implement NICE’s decisions within three months. Efforts are being made. They need to be redoubled.
- NICE’s decisions are not always as transparent as it would claim and others might expect, particularly when it is urged that factors beyond the current calculation of QALY and ICER<sup>12</sup> be taken account of. This is largely a matter of communication and of the processes used in an appraisal. But it is also because the document (*Social Value Judgements: Principles for the development of NICE guidance*)<sup>13</sup> intended to guide the Appraisal Committee is not above criticism. The principles themselves are sound but of too high a level of abstraction to provide real guidance, and the reasoning underlying them is not always as rigorous as it could be.

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<sup>12</sup> I refer throughout to the ICER/QALY approach. ICER stands for incremental cost-effectiveness ratio and QALY for quality-adjusted life years. An explanation of the terms and how the system of appraisal works can be found in NICE’s *Guide to the methods of technology appraisal* (2008)

<sup>13</sup> *Principles of Social Value Judgements: Principles for the Development of NICE Guidance*, NICE

If NICE is to adapt in the ways that I will suggest in what follows, it must address these concerns, as a first step in adaptation.

### *RECOMMENDATION 1*

#### *NICE SHOULD BE MORE ACTIVE IN EXPLAINING ITS ROLE AND DECISIONS AND DEVELOP A STRATEGY TO ACHIEVE THIS*

## **Pharma**

### 2.12 What of Pharma?

- Pharma, whether intentionally or otherwise, creates the abiding impression that it does not engage with NICE on NICE's terms (and, by implication, the Government's terms, as expressed through the Department of Health). Fundamentally, there appears to be a lack of preparedness to accept the notion of a fixed sum of money available to the NHS which it is NICE's job to allocate in a fair manner<sup>14</sup>. For reasons which are understandable, from a commercial perspective, but make for what looks like a permanent state of guerrilla warfare, Pharma regularly adopts an approach based on the supremacy of the consumer/patient<sup>15</sup>. It is an approach based on individualism. What any individual wants/needs should be provided. NICE, however, is statutorily charged with preserving the interests of all patients, based on a principle of collective needs, in the context of a fixed amount of money. Thus, when Pharma refers to the value of a product to patients, NICE has to ask itself which patients, and whether other patients, for whom the product is not intended, will be adversely affected. In political theoretical terms, rather than leave the availability of care to the dynamics of the market, the government has created an agency charged with considering the interests of all, and allocating resources as fairly as possible. The NHS, funded from the public purse, was created on the principle of care being available free at the point of need. Both the dominance of those able to pay more and the tragedy of the commons<sup>16</sup>, must, therefore, be avoided. From an economic perspective, there is an imperfect market, since the consumer (the patient) and the agent (the prescriber) do not pay directly and are, therefore, unconcerned by cost. Somebody, or some body, however, has to be concerned, if costs are to stay within the overall amount available. Moreover, without such a body, there is an asymmetry of information, whereby, in effect, clinicians and patients are left to do their own appraisal without access to all the relevant evidence. Hence the creation of NICE. The dilemma for Pharma is

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<sup>14</sup> See, for example, the submissions of Johnson and Johnson and Bristol Meyers Squibb

<sup>15</sup> The submission of the BioIndustry Association puts it as follows: "the patient is the ultimate arbiter of a product's value ...", para 1.2

<sup>16</sup> Whereby, without any mechanism of regulation, the right of everyone to common land means that the land is exhausted through over-use

obvious. The UK represents a very small part of the global market (about 3%), but the standing of NICE means that around 25% of that global market will reflect the price set in the UK. And this price will need to be set in such a way as to meet NICE's criteria regarding the comparative cost-effectiveness of the particular product. It is hardly rocket science to assume that Pharma will seek the highest price and will complain if frustrated by NICE's insistence on comparative cost-effectiveness, as judged against a fixed sum of money available through the NHS.

- Pharma routinely and rightly refers to the cost of bringing a product to market. These costs, of course, are due to the regulatory systems in place, rather than to NICE, but they are still there. A significant element of those costs relate to research and development (R&D). But the R&D costs are global as are the costs of marketing. It is not clear how, in fixing a price for the UK market, the costs of R&D and marketing incurred globally are distributed among the various markets. Clearly, it is not in the UK taxpayers' interests, and, therefore, not in NICE's, to agree to prices which, in fact, subsidise research and marketing conducted elsewhere, the cost of which may also be recouped elsewhere, particularly in the US. Clearly, there would be some advantage in carrying out research into the global distribution of these costs.
- Pharma concentrates, it could be said too heavily, in its criticisms of the current approach to the approval of products, on what economists call the demand side, the behaviour of purchasers, and particularly NICE's actions. It may be, however, that, judged by reference to other markets, the demand side of the market in pharmaceuticals is both more certain, more stable and more predictable. The more important challenge for Pharma may lie on the supply side. Rather than regard NICE as "the fourth hurdle"<sup>17</sup>, Pharma's targets could more profitably be elements of the supply side such as those referred to in para 2.5, eg the cost of clinical trials, and of R&D more generally, and the extent to which the public purse could be involved in sharing some of this cost, and any possible adjustments to the tax regime and financial support.
- Pharma presses for greater access to the UK market, based on claims of innovation and consumer demand. Arguably, however, there is a need to address the difference in Pharma's investment as between marketing and R&D. There is a body of evidence that points to Pharma's developing variations on existing themes, rather than breaking new ground, with a consequently disproportionate effort spent on marketing to differentiate between broadly similar products<sup>18</sup>.

## *RECOMMENDATION 2*

### *NICE SHOULD WORK WITH PHARMA AND OTHERS TO IDENTIFY HOW THE COSTS OF RESEARCH AND DEVELOPMENT ARE DISTRIBUTED IN THE GLOBAL MARKET*

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<sup>17</sup> Having satisfied the regulator as to the safety, quality and efficacy of a drug, Pharma represents the need to demonstrate to NICE a product's cost-effectiveness as being a further barrier put between it and patients

<sup>18</sup> See, eg, Morgan and others, "Incentives for valued innovation in the pharmaceutical sector", University of British Columbia Health Services and Policy Research, November 2006, p.25

It may be thought that, in making these comments about Pharma, I am straying from my brief. The answer is that the points are of central relevance. NICE must assess the cost-effectiveness of a product. Central to that assessment is the price set by Pharma. The more expensive it is to produce the product, the higher the price, the more effective the product has to be and, therefore, the more Pharma has to do to justify approval by NICE.

2.13 In the light of these views, the challenge is to establish a system of incentives, including the formal appraisal and approval of products, that will meet Pharma's need to remain profitable, while ensuring that the focus is really on innovation and on products that are effective and make a real difference to patients. I will explore a range of measures which might achieve this in due course. The goal must be to bring about a detente between NICE and Pharma. NICE's process of appraisal must be sensitive to some of the claims made by Pharma and patients' groups that some matters of importance to them are currently only obscurely taken account of, if at all. Pharma must accept the rules of engagement consequent on a fixed budget allocated through a statutorily established mechanism. It must also recognise the need for genuine innovation. The taxpayer must value Pharma and find ways to facilitate innovation and research.

2.14 Before addressing the first question that I posed in para 2.2, and those that follow, I adopt as a starting point my firm conviction that the approach adopted by NICE is fundamentally sound. Indeed, I would go further and describe the ICER/QALY approach as quite simply the best tool available to do the job which NICE has been set<sup>19</sup>. It focuses on two central issues: is the product clinically effective? and is the product cost-effective? It is explicitly endorsed in the Office of Life Sciences' "Blueprint": "...it is vital that the NHS values and uses cost-effective innovations".<sup>20</sup> The approach is, as one commentator described it, "a great leveller".<sup>21</sup> While it does not exclusively determine whether a product will be approved, it is at the centre of the process of deliberation. It is the classic device to allow apples to be compared fairly and effectively with pears. It is neither patient-specific nor disease-specific. I accept immediately that, as NICE frequently says, the ICER/QALY approach is by no means perfect and that much more research is needed to underpin it. Moreover, notice that I refer to the job that NICE has been set. NICE does not exist as an arm of government's industrial policy. It exists for other purposes. But, as I shall suggest later, it has a central role in encouraging, indeed driving innovation, thereby furthering the interests both of patients and the contribution of Pharma to the national economy. Notice also that I do not say that NICE's current approach is beyond improvement. Indeed, I shall suggest some improvements. But, the improvements that I will propose should be incorporated into NICE's overall approach rather than serve as an alternative way of doing things.

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<sup>19</sup> Interestingly, in laying on Strategic Health Authorities a legal duty to promote innovation, the Department of Health asks itself in its Guidance "How could innovation be measured?" and suggests a number of metrics, including, as regards a measure of value to patients, the QALY. "Creating an innovative culture", Department of Health 2009

<sup>20</sup> note 9, para 2.1. It is not entirely easy to square this commitment with the Blueprint's notion of an "innovation pass", discussed at para 4.25 onwards

<sup>21</sup> Dr. Tim Crayford, referred to in the Health Committee's Report note 11, p.36

### **3. TAKING ACCOUNT OF BENEFITS OTHER THAN INNOVATION**

3.1 I now turn to the first of the questions that I identified in para 2.2:

*whether, quite apart from any claim that a product constitutes an innovation in the sense in which I will use it (para 4.11), there are any benefits (or values) which NICE should take account of in its technology appraisal which it currently does not take account of, or takes account of only at the margins*

In responding to this question, I will largely focus on pharmaceutical products. In doing so, I do not ignore the circumstances of those developing devices or diagnostic tools, nor of those concerned with psychological therapies. Given that they seem to pose somewhat different questions, I shall deal with them later.

#### **Which Benefits?**

3.2 Are there benefits/values which products could bring which are not currently taken account of by NICE, or only taken account of at the margin (and, some would say, unclearly)? Many submissions claimed that there were such benefits and said that they should be taken account of either because they are relevant to the ICER/QALY analysis on which the approval, or otherwise, of a product largely depends, or because they should supplement the analysis in one way or another. The benefits cited range from those which touch on the health of the particular intended recipient, on the one hand, to those which involve something which will redound to the benefit of society as a whole, such as increased productivity through joining or returning to the workforce. NICE's response is to state that many of the benefits which, it is said fall outside its approach, are in fact taken account of, either through the calculation of the ICER/QALY, or through resort to the principles set out in the guidance on "Social Value Judgements". These are intended to ensure that the ICER/QALY approach is appropriately moderated when certain grounds exist. The process is, NICE states, a deliberative process: factors other than the ICER/QALY analysis are considered and taken account of.

3.3 The perceived difficulty is that the way in which these factors are taken account of, or Social Value Judgements made, is not entirely clear: the extent to which an Appraisal Committee does, in fact, refer to them to moderate the ICER/QALY approach is, it is said, often less than transparent. The claim is that the process may be described as "deliberative", but what goes into the deliberation and how it is deliberated is hard to see or know.

3.4 It may be better to start from a different point. This would be to identify those benefits which it is thought should be factored into an appraisal and signal how this is to be done. Equally, those benefits which should not be factored in should also be identified. NICE should make it clear that they will not be taken account of and explain why. As regards the inevitable grey area which will remain, NICE should devise a way of considering whether to take account of things that fall into it or not and make clear the criteria on which this consideration is to take place and the process to be employed. Pharma will know where it stands. In all cases, it will remain the case that a judgement is called for. That cannot be

escaped. But, the process leading up to the judgement should be understood by all. I will discuss what this may involve more fully in what follows. But, the initial starting point for analysis must be clear. The system of appraisal must make explicit what type of analysis needs to be made (and how to do it) to determine the relative importance of the various benefits as between each other, and how important they are when set against what would be displaced. In view of what I argue later in para 3.11, this analysis must be based on clear criteria, but cannot be reduced to some formulaic prescription. Ultimately, it must be based on informed judgement.

### **Benefits to be taken account of**

3.5 Let me therefore turn to those benefits which should explicitly be taken account of. An initial question is whether they should be incorporated into the existing ICER/QALY approach or whether, as is advocated by some, constitute a second stage of formal analysis, once the initial ICER/QALY approach had been completed. I take the view that to contemplate a two-stage process would be to undermine fatally the centrality of the ICER/QALY approach: it would suggest that QALYs were only a stage (indeed, to some, a preliminary stage) in the system of appraisal, rather than a central feature of the system. Given my unequivocal conviction that the ICER/QALY approach is both right and essential, a two-stage process of appraisal would not be appropriate.

3.6 It follows that the benefits to be taken account of should be incorporated into the existing deliberative approach centred around the ICER/QALY analysis. NICE might argue that, in one way or another, they already are. What I am saying here is that this taking account must be explicit, not least so that Pharma and patients' groups can bring their views to NICE's attention and have them factored into the relevant calculations and analysis. As I have said, such analysis will not entail any specific conclusion. Rather, it will form the basis of the judgement that must ultimately be made.

### *RECOMMENDATION 3*

*NICE'S APPRAISALS SHOULD CONTINUE TO BE BASED ON THE ICER/QALY APPROACH INTO WHICH IS INCORPORATED EXPLICIT CONSIDERATION OF RELEVANT BENEFITS. A TWO STAGE APPROACH SHOULD NOT BE ADOPTED*

3.7 Three matters then need to be addressed:

- the benefits
- their weight
- implications for the threshold

3.8 What are these benefits, or more carefully put, what is the distinguishing feature of these benefits which calls for them to be factored in, so as to affect the QALY arrived at<sup>22</sup>? The answer must lie in explicitly adopting a somewhat wider view than appears currently to be the case of what, in the language of NICE, is a gain to the health of the individual receiving the therapy and thus, a gain for the NHS<sup>23</sup>. Such a wider view would involve avoiding where possible the somewhat tenuous distinction between health gains and “social convenience”. I set out below some examples of benefits which should be taken into account. Clearly, this is not intended to be an exhaustive list. I would propose that NICE seeks the views of all relevant parties and then agrees a range of benefits, which can be revisited from time to time. Examples could be divided into two groups: those that relate to how patients may value their health (broadly) and, thus, what should be incorporated into the definition of benefit, and those that relate to how the health of different groups of patients is valued by society. The distinction is important because evidence to establish the weight that ought to be ascribed to a benefit, as between the two groups, may be different. Examples of the first group that were put forward in the submissions that I received include:

- a different mode of administering a drug, for example, a tablet rather than an injection, or one daily injection rather than several
- the opportunity to be treated at home rather than attend a hospital or clinic<sup>24</sup>
- a reduction in unwanted/side effects
- improvements in quality of life (the difference is drawn by some between health related and non-health related quality of life, but arguably they are all on a continuum of wellbeing and health)
- enjoyment of greater dignity
- enjoyment of greater independence
- minimising the social visibility of disease or care

Examples of the second group include:

- the status of the patient: children, the disadvantaged and those affected by inequalities in health and healthcare
- patients at the end of life

A benefit which can belong in both groups is:

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<sup>22</sup> The fear that there may be “double counting” because it is said that NICE already takes account of some of the factors/benefits under consideration, is met by the insistence that the system be entirely transparent, such that all relevant factors are considered, but not considered twice

<sup>23</sup> On a few occasions, after agreement by the Department of Health, NICE has adopted a wider perspective of costs and benefits to be assessed in the cost-utility analysis. But, these are exceptions to the general rule

<sup>24</sup> It is claimed by advisers to NICE that this and the benefit set out in the previous bullet point are already captured in NICE’s appraisal: “... convenience and improved administration is [sic] commonly included in appraisals by modelling the impact of administration on NHS resource use and modelling the impact of convenience through adherence to health outcomes and costs”. The point that I am making here is whether what is claimed is explicit in the system, or only known to those operating the system (which seems more likely, given the opaque nature of the last few words). This point is recognised, “... Despite this there remains a distinct concern that inadequate consideration is given by the Committees to these issues [social values]”. Decision Support Unit, “The Value of Innovation”, NICE 2009 p.31,33

- the severity of the condition

It is important to understand here that, as I have said, NICE might argue that the benefits set out are already taken account of in any good ICER/QALY analysis. My response is that apart from this not being transparently so, there are some elements of these benefits which currently may not be taken account of. There may be at least two reasons. The current ICER/QALY analysis may simply not capture them. Or, while the system is right in principle, there may be a problem in the way in which the various instruments used in the ICER/QALY analysis, are being applied, or they may be in need of revision. This latter point suggests that NICE should commission a study to enquire into whether the measures used are entirely apposite and are applied correctly, and take appropriate action in the light of the findings.

#### *RECOMMENDATION 4*

*NICE SHOULD CONSULT ALL RELEVANT PARTIES AND DRAW UP A LIST OF THOSE HEALTH-RELATED BENEFITS TO BE TAKEN INTO ACCOUNT IN ITS APPRAISALS. THE LIST SHOULD BE REVIEWED THROUGH AN APPROPRIATE MECHANISM FROM TIME TO TIME*

*NICE SHOULD SPONSOR (OR PARTICIPATE IN) RESEARCH TO DETERMINE WHETHER THE INSTRUMENTS USED TO CALCULATE QALYs AND CAPTURE HEALTH BENEFITS ARE ENTIRELY APPROPRIATE TO NICE'S NEEDS AND WHETHER THEY ARE APPLIED PROPERLY AND CONSISTENTLY*

3.9 Next, what weight should be given to these benefits, or health gains? The answer in broad terms is that adjustments need to be made to the way in which ICER/QALYs are assessed so as explicitly to incorporate them. As I understand it, a claim for this or that benefit of the kind discussed would mean that the product would attract more QALYs or would otherwise be transparently factored into the judgements made. This, in turn, would mean that a higher price than might otherwise have been the case, may be available to the manufacturer. (I do not see it as my role here to set out the techniques whereby these adjustments should be made. I am aware that research may be necessary, but would urge that the need for research is not used as a reason not to proceed. It would be better to proceed experientially.). Such adjustments, being part of the ICER/QALY calculation, would keep faith with the principle underlying NICE's approach: that a gain for one patient represents a loss for another, such that the gain should, after the calculation has been done, fall within the established threshold. The process would remain deliberative in the way in which NICE uses the expression, namely the superimposing of judgements on formula-driven calculations. The Appraisal Committee will still have to come to a judgement. But, it would be a judgement based on an assessment of the relative merits of clearly identified benefits, made according to clearly identified criteria.

*RECOMMENDATION 5*

*NICE SHOULD BEGIN TO ADJUST ITS EVALUATION OF QALYs IN ADVANCE OF ANY RESEARCH FINDINGS ON METHODOLOGY, IN CONSULTATION WITH RELEVANT PARTIES, SO AS TO BEGIN TO TAKE ACCOUNT OF RELEVANT HEALTH-RELATED BENEFITS ONCE IDENTIFIED AND AGREED*

3.10 The third matter raised in para 3.7 is somewhat different. It challenges what I have just said (in para 3.9). It is pressed by Pharma and by patients' groups. It asks whether NICE should contemplate a higher threshold (ie price), beyond the accepted threshold, if there is appears to be a particular benefit, of the type under discussion, for patients or a particular group of them. The traditional response is that "the cost-effectiveness threshold [should not be] determined by the characteristics of the patient, technology or disease under consideration in any specific appraisal".<sup>25</sup> Put another way, as attributed to Culyer and his colleagues, "... in the presence of a fixed budget, which cannot be changed by the decision-maker, the cost effectiveness threshold is not a measure of willingness to pay for health. It is an estimate of the opportunity cost (health foregone by others) of substituting a new technology into the portfolio of technologies provided".<sup>26</sup> I agree with this response. Thus, I do not accept the proposition that, because a product brings benefits of the sort set out earlier (in para 3.8), the threshold should be higher.

*RECOMMENDATION 6*

*THE PRESENCE OF BENEFITS OF THE SORT REFERRED TO IN PARA 3.8 SHOULD NOT RESULT IN AN INCREASE IN THE THRESHOLD USED BY NICE*

**Benefits not to be taken into account**

3.11 The next group of benefits which some say that NICE should include in its appraisal are what may be described as social benefits. Currently, NICE is not entitled to take account of factors other than those resulting in gains and losses (or costs and benefits) to the NHS (and personal social services). But, if an argument could be made for NICE's taking account of them, the argument could also be made to change NICE's statutory remit. So, what are these benefits? They fall into two broad classes: reductions in those costs of care which do not fall on the NHS, and benefits to the wider society. Examples include:

- carers are able to lead a more independent life

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<sup>25</sup> id p.34

<sup>26</sup> Id p.33

- patients can join the workforce
- increased tax revenue
- reduction in social costs
- reduction in absenteeism from work

They largely relate to benefits to the economy, through increases in productivity attendant on having access to a particular therapy, and thus being able to work, or the freeing of carers to enter employment, or benefits to particular groups of patients who have particular needs currently not met or not adequately met<sup>27</sup>. In my view, even if NICE were to have the power to do so, subject to my later proviso, these benefits should not find their way into NICE's system of appraisal.<sup>28</sup> There are very great difficulties in calculating any such benefits, so as to set them against any losses that others might suffer in no longer having access to certain treatment. There is a hard-to-justify bias in favour of those capable of working and being productive, as against children and the elderly<sup>29</sup>. There is the privileging of those who are heard as against those who are not: NICE exists to weigh the interests of all patients, not merely those who make their cause known. But, perhaps most telling is the point that goes to the core of NICE's approach and is central to the arguments advanced here. The social values or benefits which would be enjoyed if a particular therapy were approved, are currently enjoyed by others, who would, in the zero sum game which is resource allocation in the NHS, lose them if others gained. Thus, it is not enough to claim that a new technology has effects which are valued by society. It must also be shown that the new technology produces more benefit for patients and the NHS than the technology that will be replaced if it is approved. To make the point concrete: if a treatment were approved because it allows X to be productive, another treatment would have to be foregone which currently allows Y to be productive, or Z or A to enjoy some other social value. The only way to ensure that Y does not lose, would be to set the price of the product at a level which brought it within NICE's current threshold. And, given the uncertainty of the calculations to be made to determine the product's cost-effectiveness in terms of what are claimed as the broader benefits to society and the economy, this would be an exceedingly difficult task<sup>30</sup>. But, now for my proviso: there are distinguished commentators<sup>31</sup> who argue that social values (or at least some) could be accommodated in NICE's appraisal, without undermining NICE's fundamental approach. Clearly, it is important that the relevant research be carried out.

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<sup>27</sup> It needs to be pointed out that while there are benefits, there are also costs. A more grisly feature of the analysis here would demonstrate that an older population will subsequently consume more than it produces and will increase the burden on the NHS' resources through increased recourse to carers and healthcare. The Department of Health has commissioned research into how appraisals may take account of social values and their costs and benefits which is due to be published at the same time as this study. Clearly, NICE's Board will need to consider anything that I may recommend in the light of this research.

<sup>28</sup> I recognise that there is a counter-view, which has it that if a model could be produced, consistent with the overall notion of health losses not exceeding gains, it could be adopted. My difficulty is that any model, even if possible, would inevitably involve weighing the NHS and its resource against other claims on the public purse. Arguably, the NHS has historically been underfunded and will face a crisis of funding in less than two years, such that any further threat to its funds ought to be resisted

<sup>29</sup> And, of course, the claim that entry to the labour market is itself a benefit, assumes full employment

<sup>30</sup> See "The Value of Innovation", note 24 p.35-6

<sup>31</sup> Such as Professor Peter Smith of Imperial College, London

## RECOMMENDATION 7

*SOCIAL BENEFITS OF THE SORT SET OUT IN PARA 3.11 SHOULD NOT CURRENTLY BE TAKEN ACCOUNT OF BY NICE IN ITS APPRAISALS, BUT NICE SHOULD COMMISSION OR PARTICIPATE IN RESEARCH TO DETERMINE WHETHER SUCH BENEFITS COULD FORM PART OF NICE'S APPROACH AND, IF SO, HOW*

3.12 There will be occasions on which the benefit claimed does not fit clearly into either of the categories just set out (those to be taken account of and those not to be). It will lie between them. A choice will then have to be made whether to take account of it in the system of appraisal or not. As I will make clear later (para 3.18), I contemplate the earliest possible engagement between Pharma and NICE to determine what may be claimed as benefits and what evidence NICE would need to consider the claim (and see para 3.17). Two fundamental questions would need to be addressed. Can the benefits claimed be described as health gains to patients and the NHS, using a more flexible definition of health gain than hitherto? And, secondly, can they be calculated to a sufficient degree of plausibility to figure in the assessment of the product's cost-effectiveness? If the answer to both questions is yes, then they should be considered.

3.13 To set out my conclusions so far, in exploring the case for including a consideration of benefits not currently taken account of (or not sufficiently explicitly), I have concluded that there are some benefits which should be considered. I have also concluded that, if they are to be considered, this should be within, rather than outside and in addition to, the deliberative approach (para 3.6) with the ICER/QALY analysis at its centre.

3.14 I have also considered the arguments made in favour of raising (and, by some, of lowering) the threshold for approval across the board, rather than in special cases. I am not persuaded that the case has been made. I have seen a draft report of the Workshop held by NICE in April, 2009. It is clear that opinions were very varied: some arguing that it be raised, some that it be lowered, and some preferring the *status quo*. No agreement was reached. A report from the Workshop will go to NICE's Board in July, 2009. The Board will then decide what if any action to take. I just add one point. In my consideration of NICE's response to innovation, I make a recommendation in para 4.12 about a possible raising of the threshold. Any such increase would have implications for the NHS as a whole, given that the funding available is fixed and likely to fall in the coming years in line with other reductions in what is available to the public purse. The Board will need to take account of this recommendation in its deliberations on the current threshold.

### **How should NICE take account of the various benefits?**

3.15 I need now to address the question of how NICE in its appraisals should take account of the benefits which I have concluded that it should consider. There are two elements to the answer. The first can be described as methodological, the second as a matter of process.

## Methodology

3.16 As regards methodology, it was suggested by those who advocated a two stage approach, first ICER/QALY and then other benefits<sup>32</sup>, that the various other benefits could each be given a score and added together. The total would then serve to qualify the ICER/QALY (what is known as “equity weighting”) to produce the final assessment of value. This, it is said would make the system more transparent, and, it is added as a rider, reduce the levels of dissatisfaction and challenge by Pharma. I have already indicated that adding a separate set of calculations to the ICER/QALY approach would completely undermine the very basis of that approach. To that extent, I do not need to consider the argument further. But, I make the following points, in any event. First, the claim of greater transparency is illusory. What it would introduce is some entirely mechanistic process, in which benefits are arbitrarily given the same weight *inter se* and over time. But, what is at stake is a set of judgements, which, while they must be based on clear criteria, should not be reduced to some exercise in spurious numerical certainty simply through adding them up. Indeed, there is no validated mechanism for doing so. Rather, the Committee must reach a judgement as to how the ICER/QALY approach should deal with the evidence before it, taking account of any special circumstances which have been put before it and the general good<sup>33</sup>. Calls are frequently made for more research and analysis to be carried out, so as to ground the approach ever more firmly in some empirical foundation. It may well be, however, that there must be a point at which reductionism can go no further. A judgement, based on clear criteria, is all that can be expected. It may not give the degree of predictability sought by some, but it may be the price to be paid for casting the net of factors to be considered as wide as some would wish. As regards the claim that challenges would be fewer, it is at least arguable that such a system, so far from preventing challenges, would in fact promote them, as arguments over weighting and scoring went back and forth.

3.17 Because I have concluded that those benefits which I say should be taken account of should be incorporated into NICE’s estimation of health gains as against health losses, the appraisal system should make it clear how this is to be done. This would allow Pharma and patients’ groups to ensure that NICE was made aware of any claims being made. It would also mean that, once the criteria were clear, Pharma and NICE could work together to ensure that the relevant data was collected during the research, so that NICE could factor it into its appraisal. NICE could still turn to its document on making social judgements. As I have said, the principles set out are sound. But it must do so in a way that does not perpetuate the unfortunate idea, which could currently be entertained, that there is a methodology based on ICER/QALY and then there is some set of afterthoughts. If indeed social judgements, values or benefits do form part of NICE’s appraisal as NICE claims and it is a “deliberative process”, then they should overtly be identified as part of that deliberative approach and

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<sup>32</sup> Various approaches were suggested, eg Multiple Criteria Decision Analysis (MCDA) and Comprehensive Benefits and Value (CBV)

<sup>33</sup> Professor Andrew Stevens, at the Workshop on the threshold in April 2009 described the deliberations of Appraisal Committee as partly “cortical” and partly “gut”. The submission of GlaxoSmithKline argues against an increasingly mechanistic approach and calls for “pragmatism” and deliberations which “would capture the bigger picture”

reflected in the ICER/QALY analysis. This is what I have recommended. The detailed working through of how to do this should be taken forward by NICE with all due speed, in consultation with Pharma, patients’ groups, the Department of Health and relevant others.

## **Process**

3.18 I turn now to the process by which NICE might take account of the benefits of the type referred to in para 3.8. As regards the process to be followed by NICE in its appraisal of products, I have noted the need for greater co-operation between NICE and Pharma, from an early stage in the development of a product, so that there is the greatest possible alignment between what Pharma needs, eg for the purpose of licensing, and what NICE needs for its appraisal<sup>34</sup>. While it is for NICE to determine the particular mechanism that it should use to achieve the recommended objective, it may help if I try to relate what I am proposing here to the way in which NICE currently proceeds. Topics for appraisal by NICE are recommended by NICE to the Department of Health. NICE first organises what it calls a “Scoping Workshop”, in which the scope of the proposed appraisal is examined with all interested parties. A number of matters are addressed, including: the clinical problem and population(s) to be served; relevant comparators; the principal outcomes sought (eg survival, quality of life); what evidence exists; and what the evidence demonstrates regarding outcomes. A Scoping Document is then produced. What I am proposing here is that there would be added to this list of factors to be considered in the Scoping Workshop any claim made by Pharma or others, either that the product brings benefits (as set out in paras 3.8 and 3.12) or that the product constitutes an innovation (as set out below in para 4.11)<sup>35</sup>. The claim would be assessed by the Workshop and a view reached on the evidence adduced. The normal process would then be followed in that the scoping document would go to the Department of Health, flagging up, for example, the claim of innovation. The Minister would then refer the topic to NICE, to examine the clinical and cost-effectiveness of what is proposed, in accordance with the scoping document. The effect of this would be the identification at the earliest possible stage of claims of innovation and other benefits, so that Pharma and NICE could work together to ensure that the relevant evidence to support the claim is generated, and that the incentives for innovation (set out in para 4.12) are considered.

## *RECOMMENDATION 8*

*NICE SHOULD WORK CLOSELY WITH PHARMA TO ENSURE THAT NICE IS MADE AWARE AT THE EARLIEST POSSIBLE OPPORTUNITY OF ANY CLAIM BY PHARMA*

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<sup>34</sup> I notice also and welcome the reference in the Pharmaceutical Prices Regulation Scheme (PPRS) 2009 to a single unified horizon-scanning process to identify new technologies in development. The point is that the earlier the engagement between NICE and Pharma the greater the prospect of early identification of potential benefits (including innovation)

<sup>35</sup> NICE’s *Guide to the methods of technology appraisal* (2008) in para 2.14 allows for this in principle when it states that a draft scope may include “... special considerations and issues that are likely to affect the appraisal”. NICE and Pharma may, of course, disagree on occasions as to whether the case is made. But, if the collaboration between NICE and Pharma contemplated here has taken place, these occasions should not be numerous. When they arise, NICE’s decision will be final

*REGARDING BENEFITS AND THAT DATA RELEVANT TO NICE'S APPRAISALS IS GENERATED AS PART OF PHARMA'S RESEARCH*

*NICE'S SCOPING WORKSHOP AND SCOPING DOCUMENT SHOULD IDENTIFY ANY CLAIM OF BENEFITS DISCUSSED IN PARA 3.8 OR OF INNOVATION*

**Procedure**

3.19 There are also three minor changes in its procedure which would have real and symbolic importance and should be adopted by NICE. First, manufacturers cannot understand why they are not able to attend meetings to help the Appraisal Committee on matters touching on their application. Having observed an Appraisal Committee in action, I am convinced that the Committee would benefit from their attendance and that they should routinely be invited to attend. My understanding is that informal discussions have already begun to enable manufacturers to attend at least the first part of meetings of Appraisal Committees, to answer questions and draw the Committee's attention to matters of fact needing clarification or correction. This would be a useful development in promoting better understanding and working relationships, as would the opportunity for manufacturers to meet officials of NICE if a product has not been approved, despite an appeal<sup>36</sup>.

*RECOMMENDATION 9*

*NICE SHOULD INVITE MANUFACTURERS TO CONTRIBUTE TO PART 1 OF THE MEETING OF THE APPRAISAL COMMITTEE IN THE SAME WAY AS OTHERS WHO ARE CONSULTED*

3.20 Secondly, as I have said, Pharma complains that factors of relevance to the outcome of an appraisal, but not clearly part of the ICER/QALY analysis, are not properly taken account of, or if they are, the process is opaque at best. This is a complaint about the current system, which, as I shall suggest, may fall away if my proposed approach is adopted. One of the reasons for the complaint is that the Appraisal Committee goes into private session for part 2 of its deliberations on cost-effectiveness. It is at this point that it was acknowledged by NICE that the process could be more transparent. It is at this point that all the wider benefits which could qualify as health gains are aired, not least by reference to NICE's document on Social Value Judgements, referred to earlier. The reason for proceeding in this way is prosaic. I found no evidence of a desire to be secretive or unaccountable. Rather, it is because the final decision will gradually begin to emerge from the discussion. The decision can obviously be very important to the share price of a manufacturer. So, to avoid attempts to take advantage of early information, the decision is taken in private and conveyed to all relevant parties in a

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<sup>36</sup> The Office of Life Sciences' "Blueprint" indicates that these two measures will be put in place by NICE (note 9, para 2.6), which I welcome.

managed way. There seems no easy way around this difficulty of the need to respect commercial confidentiality. What I would expect, however, is that, if the approach to identifying and then incorporating consideration of the range of benefits within the ICER/QALY analysis as discussed earlier, were adopted, these benefits would have been put forward by Pharma for consideration, analysed by NICE and discussed by the Appraisal Committee, with the manufacturer(s) present (see para 3.18). This is about as transparent a process as is compatible with commercial considerations. There is, however, one suggestion that I think warrants further consideration. Part 2 of the Appraisal Committee's deliberations could be recorded (eg video-recorded). It could then be shown to those interested after the relevant guidance is made public. The problem of commercial sensitivity would have disappeared, and transparency would have been enhanced<sup>37</sup>.

#### *RECOMMENDATION 10*

*NICE SHOULD CONSIDER, IN CONSULTATION WITH INTERESTED PARTIES, WHETHER A VIDEO-RECORDING OF PART II OF THE APPRAISAL COMMITTEE'S MEETING COULD BE MADE AVAILABLE TO MANUFACTURERS AND OTHER INTERESTED PARTIES AFTER NICE'S GUIDANCE HAS BEEN PUBLISHED*

3.21 Thirdly, it has long been a concern that NICE's appraisals take a long time. In part, this is often inevitable given the complexity of the issues involved, the lengthy nature of the process of consultation, and the need for rigorous analysis. NICE has responded to the concern by introducing the system of STA (Single Technology Appraisal) which has led to more prompt decisions. The need for timely decisions is that much more pressing in the context of innovations which I discuss below. The sooner that innovative products can reach patients the better, (all things being equal in terms of the increased benefit to patients and the NHS). Thus, the closer to the launch of a product that NICE can carry out its appraisal, the sooner the product can be available. The way forward, in my view, lies in closer understanding and co-operation between manufacturers and NICE, of the kind I have already referred to and will mention again later. I have seen that this need is recognised by NICE<sup>38</sup>. They are making strides in reaching out to manufacturers, not least regarding information that will be needed for appraisals. Manufacturers need to do the same. They must work with NICE. Many know the rules and seek to work within them. But even as they do, they are driven by other imperatives which may not assist them in dealing with NICE eg considerations of pricing in a global market. They need to square that particular circle and enable NICE to do its job. Some manufacturers do not seem to know the rules. They cannot complain if they encounter problems. They need to learn.

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<sup>37</sup> I recognise that some data which may be regarded as "commercial in confidence" may be discussed on occasions and that some patients or members of patients' groups may not wish personal details to be aired publicly. I regard these as challenges to be overcome rather than reasons for rejecting consideration of the proposal

<sup>38</sup> See the evidence of Sir Michael Rawlins to the House of Commons Health Committee, note11 p. 41

## **PCTs and the threshold**

3.22 I also had brought to my attention a number of other claims suggesting flaws or weaknesses in NICE’s approach, for example, what were said to be the limitations of the EQ-5D questionnaire<sup>39</sup>. While I understand the points made, they did not persuade me that NICE’s system should be radically changed. (That said, the Medical Research Council is setting aside £2 million to address methodological issues, not least any shortcomings in the EQ-5D tool and the calculation of the cost-effectiveness threshold. In addition, NICE is working with the EuroQol group to identify possible ways of improving the EQ-5D tool: it is accepted that this tool does not capture well, for example, diminution in quality of life consequent on sensory loss or impairment of cognition. It follows that anything I say here must be read in the context of these other studies when the results are known). Two points, however, do warrant mention, albeit that the first was not raised by others. I refer to the symmetry entailed in the ICER/QALY approach: the assumption of a loss of health commensurate with the gain to be achieved. This symmetry in calculation may be thought by some to reflect an assumption by NICE that there is also a symmetry in action: that the purchaser of care (the PCT, for example) makes the same rigorous calculations as does NICE, so that the threshold and any cost above the threshold will be as sensitively identified by the PCT as NICE assumes. NICE’s approach, however, recognises that PCTs are somewhat more “rough and ready” in their calculations. NICE needs to know, on average, and given the current state of decision-making by PCTs at local level, what gets displaced when something is recommended. The more NICE has information on behaviour, through, for example, emerging programme budget data, the more the threshold can be calculated with greater confidence that it properly reflects reality. I would be anxious to see this point explored further.<sup>40</sup> Research into the best estimates of the behaviour of PCTs as purchasers of care is crucial given the need for alignment between the decisions of NICE and the responsibilities of PCTs.

### *RECOMMENDATION 11*

*NICE SHOULD ENHANCE ITS EFFORTS TO UNDERSTAND THE SPENDING BEHAVIOUR OF PCTs AND THE EFFECTS OF NICE’S DECISIONS ON PCTs’ BUDGETARY PLANNING*

## **Disinvestment**

3.23 A further point follows on. It relates to disinvestment. If NICE, through its system of appraisal seeks to maximise the value for money that the NHS can obtain, there is clearly a

<sup>39</sup> The standard questionnaire used to assess responses to a particular product

<sup>40</sup> I am conscious of the views expressed in the report of the House of Commons Health Committee, note 11, p. 60-61, which raise the point but do not indicate what, if anything should be done, except more research. Certainly, the notion of “implementation consultants” (p 68) drawn from NICE and working with PCTs to assist in managing NICE’s guidance within their constrained budgets, seems a helpful move

need to ensure that scarce resources are not expended on products that have little or no value or are much less cost-effective than others. NICE would appear to have a positive obligation to keep products under review with a view to issuing guidance that PCTs should no longer purchase a particular product. The exchanges between NICE and the Health Select Committee, set out in the Committee's report<sup>41</sup>, suggest that there is more work to be done. It is important that it be done<sup>42</sup>.

## *RECOMMENDATION 12*

*NICE SHOULD WORK WITH OTHERS TO DEVELOP AN ACTIVE POLICY ON DISINVESTMENT BY THE NHS IN PRODUCTS WHICH DO NOT OFFER VALUE FOR MONEY*

### **Appeals**

3.24 Finally, although perhaps not entirely within the scope of my study, I comment on one further point made by Pharma about NICE's process. I refer to appeals. With so much hanging on NICE's decisions and with the obvious desire to pursue an appeal on occasions, it is clear that Pharma should feel at the end of the process that they have had a fair crack at gaining approval, whatever the outcome. I was struck by Pharma's discontent with appeals, despite NICE's clear delineation of the rules of engagement. I cannot find any justification for Pharma's discontent. The Guidance made available by NICE for appellants explains in appropriate detail the steps to be taken by those contemplating an appeal and what the nature of the process consists of. It is, perhaps, the latter which needs to be clearly understood: the decision of the Appraisal Committee, constitutes a recommendation to NICE's Board. In the case of an appeal, the Board asks the designated Appeal Panel to determine the appeal. The grounds are clearly set out, as is the fact that the appeal will not entertain new evidence (since all relevant evidence should have been before the Appraisal Committee), and that the appeal "is not an opportunity to reopen arguments" and that the Panel "will not substitute its own judgement for that of the Appraisal Committee".<sup>43</sup> That said, there is a level of discontent. Clearly, much of it arises from a sense of disappointment,<sup>44</sup> but some may arise from the need to understand and comment on what is called the Final Appraisal Determination (FAD). This is the final guidance which, subject to any appeal, will be issued. The inability to comment at this stage means that there is a temptation to appeal and try to introduce points that the manufacturer may wish to make, even though the procedure on appeal does not allow for this. In such circumstances, there is much to be gained from NICE's holding a meeting with the manufacturer after the issue of the FAD, rather in the way of a post-mortem. Such a meeting would not amount to a re-hearing: the manufacturer would still have to go to the

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<sup>41</sup> note 11, p. 31-2

<sup>42</sup> A view echoed in the submission of the NHS Confederation

<sup>43</sup> *Technology Appraisals Process: Guidance for Appellants*, NICE. 2004

<sup>44</sup> Around 9% of applications for approval are rejected in whole

back of the queue if it wanted the product to be appraised again. But, it would give the manufacturer an opportunity to be heard and on occasions cause NICE to reconsider. I welcome the fact that this idea is currently under consideration by NICE and recommend that it be adopted. While it may seem to extend the time taken in appraising products, which is to be avoided, it could well, in fact, expedite the process by eliminating inappropriate but, perhaps, understandable appeals.

### *RECOMMENDATION 13*

*NICE SHOULD ESTABLISH AND KEEP UNDER REVIEW A MECHANISM WHEREBY UNSUCCESSFUL APPLICATIONS FOR APPROVAL CAN BE DISCUSSED WHEN THE FINAL APPRAISAL DETERMINATION HAS BEEN AGREED AND BEFORE GUIDANCE IS ISSUED*

### **Care at the end of life**

3.25 I end this section by wondering aloud what effect the recent changes in NICE's appraisals in the case of "end of life" treatments will have. I do so because of my previously expressed opinion about the importance and centrality of the ICER/QALY approach. On the one hand, it could be said that all that NICE has done is value, in terms of QALYs, the last few months of life more than any other period of life. This may well accord with popular sentiment and certainly accords with the views of campaigning groups. On the other hand, however, it could be said that it is a Trojan Horse introduced into NICE's system, which will make it increasingly difficult for NICE to withhold approval. The argument could be taken further by saying that NICE has effectively undermined the system on which its credibility and sustainability depends. Because, while patients with terminal cancer will be able to require their PCT to purchase the expensive drug approved by NICE, a whole raft of patients, unknown, unsung, unrepresented and undistinguished by any particular condition, will lose out on aspects of health and healthcare that they might otherwise have received, and thus be at risk of further ill-health. The ICER/QALY system was developed just so as to be able to ensure that the interests of the unknown were not neglected. Thus, if treated as anything other than a rare exception, the "end of life" category could threaten the very existence of a rational system of resource allocation in which the interests of all are weighed<sup>45</sup>.

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<sup>45</sup> Morgan, note 18, points to the danger of a "captive" market of inelastic demand, given the seriousness of the condition, in which a very high price may be charged without losing sales. He concludes that "to reduce this possibility, policy interventions may be required to set reasonable limits on prices charged for treatments that aim to improve or prolong the health of vulnerable patients", p.16. An internal analysis prepared for the last meeting of NICE's Board suggests that currently only a minority of applications under the "end of life" category have been approved

## 4. INNOVATION

4.1 I turn now to innovation. It was the importance of promoting innovation throughout the NHS and the perception that NICE did not do so as effectively as it could, but rather serves as a check to innovation, that prompted the setting up of this study. As I have explained, the questions raised have extended beyond innovation, but it remains a central concern. In the original Directions to NICE, the Secretary of State specifically requires NICE to take into account in its appraisals “...the potential for long term benefits to the NHS of innovation”<sup>46</sup>. Furthermore, NICE in its own Guidance enjoins its Appraisal Committees to take account of the “innovative nature of the technology, specifically if the innovation adds demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the QALY measure”<sup>47</sup>. Thus, it is clear that NICE formally recognises the need to consider innovation, and is under a duty to do so. The question is what happens in practice.

4.2 To be clear, what is said as regards innovation is that it brings a particular benefit or value which should qualify a product demonstrating innovation for some special treatment by NICE. In other words that it is a social value, but of a different order from those discussed in para 3.11. The difference lies not only in the duty laid on NICE to take specific account of it, but also in its importance as representing the constant pursuit of the frontiers of real excellence on behalf of patients and the NHS.

4.3 Before exploring in greater detail what we should mean when we talk of innovation, there is a prior question of great importance and some complexity. The answer to it calls for a grasp of both policy as applied to health and the economy, and a detailed understanding of the model used by health economists in the ICER/QALY analysis. The question at its most general is: to what extent should any special treatment given to innovation be achieved by changes in the supply side, in the demand side, or both. Changes in the supply side are not part of NICE’s brief. They are a matter of government policy and action. Changes in the demand side are, in part, within NICE’s powers to effect. There is a view that the current ICER/QALY system should not be adjusted (more than it currently is in exceptional cases) to accommodate innovation. Indeed, the view goes further and holds that if a product does constitute real innovation, it will be seen as bringing more benefits, therefore attracting more QALYs and thereby capable of having a higher price. In other words, the demand side already does enough to promote innovation, and any further promotion should rest with government. Furthermore, to make inroads into the ICER/QALY approach, which I have said previously is at the heart of NICE’s approach, would be to put in jeopardy the system of predictable (within limits) and consistently applied resource allocation which works to the benefit of all, not some.

4.4 These are powerful arguments. But, I suspect that they are too purist. I have no doubt that changes to the supply side are required. I also have no doubt that, if carefully orchestrated, (to avoid such well-known problems in government plans as perverse incentives or gaming) such

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<sup>46</sup> Hansard does not record any definition of “innovation” being offered by the government in the debate on the Order establishing NICE, 3<sup>rd</sup> Standing Committee on Delegated Legislation, March 10, 1999

<sup>47</sup> note 35, para 6.2.23

changes could provide Pharma with significant incentives to aim for innovation. But, I am sure at the same time that some adjustment to the approach adopted by NICE is possible, without undermining its fundamental purpose and rationale.

4.5 In what follows, therefore, I will make some proposals as to how NICE's system of appraisal might be adjusted to take account of innovation. In doing so, I will seek to identify the challenges that these proposals represent to NICE and how they may be met. I will then suggest changes in the supply side.

4.6 In para 4.2, I said that the claim is that innovation should attract some special treatment from NICE. That special treatment could, for example, take the form of approving the product at a price which would otherwise take it beyond NICE's threshold, even after taking account of the QALYs awarded because of the increased benefits achieved. (If the price was such as to mean that the product fell within the threshold, there would be no need for any special concern for innovation, save for speedy approval. And, if the basis of the claimed innovation is that it brings benefits of the sort that I have already discussed in paras 3.8 onwards, then it can be dealt with in the way that I have proposed there). Clearly, the view of Pharma is that innovation warrants special treatment of this kind and if it is not granted, deleterious consequences for the industry (in the UK) and for patients and the NHS will follow. This is the issue for the demand side.

### **The meaning of innovation**

4.7 In addressing it, my first challenge was to establish what was meant by innovation in the particular context of pharmaceutical products, (recognising again the somewhat different circumstances of devices, diagnostics and psychological therapies, which I will consider later). It will come as no surprise that, while everyone was content to use the word, and everyone agreed that it was a good thing,<sup>48</sup> it was not easy to identify what was being discussed. In fact, as is common in policy-making, the absence of any hard centre of meaning allows people from all quarters to appear to be in agreement, without the need to nail down what it is that they were agreed on.

4.8 There is no shortage of definitions of innovation<sup>49</sup>. Their very number suggests an amorphous concept. It is clear to me that the notion of innovation has a range of connotations which are, to a degree, context-specific. And, the world of pharmaceutical products is one such context. As a first step, it may help to know what Sir David Cooksey had in mind when he called for this study. When I spoke to him he referred to innovation as connoting "different ways of doing things which bring improved outcomes". This helps. There is the

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<sup>48</sup> See, for example, Lord Darzi's endorsement of the key importance of innovation in *High Quality Care for All: NHS Next Stage Review Final Report*, Department of Health, 2008 and the very recent *Life Sciences Blueprint*, note 9

<sup>49</sup> Examples include: "the successful exploitation of ideas", DTI (2003); "the adoption of new-to-the-organisation or new-to-the-NHS technology products and/or service delivery processes, comprising incremental or disruptive change, and resulting in a significant improvement in patient outcomes, experiences, safety and potentially cost effectiveness" NHS National Innovation Centre (long on words but short on comprehensibility); "when new drugs provide medical breakthroughs or significantly improve on standards of care delivered by existing treatments", Office of Fair Trading (2007)

idea of difference, or newness, and the idea that it represents an improvement on what went before. But, before going further, I remind myself what is being considered. The case being put is that a claim that a product represents an innovation entitles it to special treatment in the form of a higher price, or put another way, that the ICER/QALY threshold should be raised to accommodate a calculation of cost-effectiveness that exceeds NICE's normal range<sup>50</sup>.

4.9 If this is what is being urged, then it should be clear that something more than newness (or difference) plus some degree of improvement in effectiveness may be necessary to qualify as innovation in this specific context. This is because, in essence, what is at stake here is the effective use of incentives. The question is: should any incentives relating to innovation be put in place to make Pharma successful in its own right and in meeting the needs of patients, and what will enable NICE to get the best out of Pharma by way of a constant pursuit of innovation for patients and the NHS? The NHS needs the best, most up-to-date and effective products. NICE's system of appraisal and approval should reflect this need. NICE's system should serve to encourage Pharma to meet the NHS' needs. It should be so designed as to give Pharma an incentive to concentrate on products that are truly innovative, highly effective, and, critically, are valuable to the NHS. There should be no incentive to innovate in products which, for whatever reason, are not of any, or only very limited value to the NHS in meeting its responsibilities. Products that offer a limited variation on already-existing products will, of course, still be developed, (and some incremental improvement in such products is desirable<sup>51</sup>). But, they will not warrant any special treatment. Only if they are priced in a way that meets NICE's established approach, will they warrant approval. Such products may be described as innovative, but the claim alone will cut no ice, nor bring any special treatment.

4.10 Where innovation becomes important, therefore, is when Pharma states that a product meets three initial criteria, in that the product:

- is new
- constitutes an improvement on existing products
- offers something more: a step-change in terms of outcomes for patients<sup>52</sup>.

As I have said, I am conscious that some would argue that the ICER/QALY analysis, properly conducted, would capture all of these features and leave no justification for a price taking the product over the threshold. What I argue for here challenges that view. It calls both

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<sup>50</sup> It is worth noting that of the countries studied by NICE's Decision Support Unit, few gave any particular weight to "innovation" per se. Exceptionally, in Belgium the distinction is specifically drawn between "innovation" and "adaptation" and "alternative", compared with existing products, but there are no procedures set out to reflect and give effect to this distinction

<sup>51</sup> I discuss the notion of incremental innovation in para 4.18

<sup>52</sup> Arguing that neither newness nor effectiveness separately or together constitute innovation, Morgan and others may set the bar too high when they state that "Pharmaceutical innovation requires novelty of effectiveness. Pharmaceutical innovations create value for society by making it possible to generate improvements in patient [sic] health ... that were previously unattainable. It is the uniqueness of such health improvements that defines ... innovation". Morgan, Lopert, Greyson. *Open Medicine* 2008; (1):E4-7

for a recognition of the increased social value of innovation<sup>53</sup>, and of the need for properly articulated criteria to recognise this value.

4.11 As a consequence, NICE’s system of appraisal could adopt a variation on its usual approach, to recognise innovation (as defined) in a particular case and, thereby, give a more general signal of this recognition. I realise that the term “step-change” is question-begging to a degree. Pharma can rightly say that some guidance is needed. For my part, I would suggest that NICE consider the following as being possible criteria of a “step-change”<sup>54</sup>:

- the product significantly and substantially improves the way that a current need (including supportive care) is met<sup>55</sup>
- the need met is one which the NHS has identified as being important
- where appropriate, research on stratification (as referred to in Sir David Cooksey’s review) has identified the population(s) in which the product is effective<sup>56</sup>. This may be all of the population with the condition or just a subset
- the product has been shown to have an appropriate level of effectiveness - for example, benefiting 70% of the intended target group,  
and
- the product has marketing authorisation for the particular indication.

#### *RECOMMENDATION 14*

*NICE SHOULD FORMULATE A DEFINITION OF “INNOVATION” ALONG THE LINES SET OUT IN PARA 4.10 AND CRITERIA ALONG THE LINES SET OUT IN PARA 4.11*

*SO THAT A JUDGEMENT CAN BE MADE THAT A PRODUCT MEETS THE NHS’ NEEDS, THE SECRETARY OF STATE FOR HEALTH SHOULD FROM TIME TO TIME MAKE EXPLICIT THE PRIORITIES OF THE NHS REGARDING INTERVENTION AND TREATMENT*

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<sup>53</sup> Health economists might argue that the value is not to the NHS but to the manufacturer in being able to operate in a more favourable (for the manufacturer) economic environment. But this is the point here: that there is a value to the wider economy in having Pharma working in the UK’s economy and contributing to it, and the trick is to ensure that a quid is gained for the quo.

<sup>54</sup> What is sometimes called “disruptive” innovation, Morgan, “Innovative Health Technologies” Presentation to NICE’s Citizen’s Council, May 2009.

<sup>55</sup> When asked to rank the innovations they regarded as most valuable, NICE’s Citizen’s Council at its meeting in May 2009 ranked most highly an innovation which increases the quality of life

<sup>56</sup> It is high time that agreement was reached on the pooling, with appropriate safeguards, of NHS data for the purposes of stratification and bio-marking. The data is unique in the world. Using it wisely and carefully can produce a sea-change in the treatments on offer to patients and the care that they receive, as well as enabling manufacturers to succeed

## Process for responding to innovation

4.12 If NICE were to adopt a special approach to innovation as defined, how should it proceed? The following process could serve as a basis:

- Pharma would need to signal as early as possible in the process of development that its product could well amount to an innovation as defined (see para 3.18 on the use of the process of scoping).
- NICE would then need to work much more effectively with manufacturers and patients' groups to align the data to be produced from research not only with the needs of the regulator, but also with NICE's requirement for information to appraise and approve the product, with particular regard to what makes the product an innovation. A welcome start has recently been made by NICE in its creation of its Scientific Advice Programme. This is a key development in improving links generally between Pharma and NICE and is crucial in the case of innovation. Given the importance laid on stratification, such alignment should ordinarily begin from at least the point at which Phase III trials are embarked upon.
- To encourage competition within Pharma, (the key defining feature after all of a market), NICE could seek to ensure that sufficient advice and support (for example regarding data collection, see para 4.21) was made available to newer companies, so as to enable them to compete on level ground.
- As an incentive to Pharma, in the case of innovation, a higher price could be accepted for some patients or indications, or even across the board, taking the cost-effectiveness of the product beyond the normal threshold. There could be an agreed higher threshold, determined by NICE. The price could then be maintained for a set period of time, eg 3-5 years, after which it must be adjusted to bring the product within the normal threshold. NICE could achieve this by establishing a special protocol for innovation. Or, NICE could undertake the appraisal using one of the new schemes established through the recent revision of the Pharmaceutical Prices Regulation Scheme (PPRS) (2009), the "flexible pricing" scheme, or the "patient access" scheme<sup>57</sup>. It would be inherent in this approach to innovation that health losses would exceed health gains in the particular case. The justification lies in the incentives it offers to Pharma to strive for innovation and the consequent long-term benefit to the NHS and patients. Putting it another way, the health gain for the NHS though less than the health loss has an enhanced and beneficial value in that it amounts to an innovation, as defined. Also, it can be justified by the fact that it is only for a short and fixed time<sup>58</sup>.
- The fact that the NHS would lose in the short term means that, in this context, the ICER/QALY system and the consistency of approach that it represents are, to an

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<sup>57</sup> These schemes are complex. I see it as my role here to offer the challenge that they be employed to best advantage. The operational details are for NICE and others

<sup>58</sup> Moreover, there are already a number of precedents for NICE's approving a product despite its exceeding the cost-effectiveness threshold, Submission from NICE, "Value of Innovation", para 2.12

extent, undermined. It follows that the criteria would need to be applied with extreme rigour.

- Agreeing a higher threshold, or using one of the schemes under the PPRS in the case of products which constitute an innovation (as defined), will inevitably lead to a reduction in the funding available to the NHS to purchase other products. Given that the total sum available is fixed, and is likely to fall as public expenditure is cut over the next several years, the consequence might be that the threshold for a product which is not an innovation will have to be reduced.

#### *RECOMMENDATION 15*

*NICE SHOULD ESTABLISH A MECHANISM WHEREBY PHARMA CAN SIGNAL AS EARLY AS POSSIBLE THAT A PRODUCT MAY CONSTITUTE AN “INNOVATION” AS DEFINED IN PARAS 4.10-11*

*NICE SHOULD WORK CLOSELY WITH PHARMA, USING FOR EXAMPLE ITS SCIENTIFIC ADVICE PROGRAMME, TO ENSURE THAT THE DATA REQUIRED BY NICE TO MAKE THIS JUDGEMENT IS GENERATED*

*NICE SHOULD OFFER ADVICE AND SUPPORT TO NEWER COMPANIES TO FACILITATE COMPETITION IN THE SECTOR*

*NICE SHOULD CONSIDER, AS INCENTIVES TO PHARMA, AGREEING A HIGHER THRESHOLD IN THE CASE OF “INNOVATION” (AS DEFINED) AND MAINTAINING IT FOR A FIXED PERIOD (eg FROM 3-5 YEARS) OR AGREEING THE USE OF A SCHEME UNDER THE REVISED PPRS (“FLEXIBLE PRICING” or “PATIENT ACCESS”)*

*NICE SHOULD REVISIT THE THRESHOLD TO BE USED IN THE APPRAISAL OF PRODUCTS WHICH DO NOT MEET THE CRITERIA OF INNOVATION IF A HIGHER THRESHOLD OR ONE OF THE SCHEMES UNDER THE PPRS IS USED AS AN INCENTIVE TO PROMOTE INNOVATION*

4.13 Clearly, if the Board regards such inroads into the ICER/QALY approach as unjustified, then, if it wants to recognise the special case of innovation, as it is obliged to do, it must either demonstrate in the clearest possible way how innovation as I have defined it is already encouraged within the current approach, including within the threshold. Alternatively, it must press for changes in the supply side to achieve similar results (see para 2.5). For my part, I am persuaded that, if operated vigilantly and with constant attention to the extent of any gain to the NHS when set against the loss of life expectancy of others, an approach of the sort I have suggested in para 4.12 warrants adoption.

4.14 There is always the danger that the product fails in time to live up to expectations, despite the best efforts of those who originally evaluated it. The concern is clear. The

manufacturers will have enjoyed a higher price, and the NHS suffered a commensurate loss, until this failure is discovered. Subject to its continued effectiveness it would remain something that PCTs would be obliged to purchase, but at a reduced price to bring it within the established threshold. But, how will the NHS' loss be recouped? The most pessimistic answer is that it could not be, such that this problem means that the approach that I am suggesting in para 4.12 is not viable and should not be contemplated. But, there are other responses. The first is that, if the scrutiny of the claim of innovation is sufficiently rigorous, the problem is unlikely to occur, such that it is a risk worth taking in pursuit of incentives for Pharma and the best therapies for patients. Secondly, whether by Regulation or by agreement, NICE could have the power re-appraise the product at a lower cost, as being an effective but not innovative (as defined) product. This might, of course, persuade the manufacturer to cease to produce it if it is no longer profitable (and if the later price has knock-on effects globally). Thus, a third option could be a straightforward system of reimbursement of the NHS, in a manner to be established by agreement between NICE, the NHS and Pharma, once it has been agreed by relevant experts that the product has not met expectations.

#### *RECOMMENDATION 16*

*NICE SHOULD ESTABLISH A MECHANISM WHEREBY THE NHS IS COMPENSATED FOR THE FINANCIAL LOSS WHICH WILL HAVE BEEN INCURRED UNDER PARA 4.12 IF A PRODUCT SUBSEQUENTLY PROVES NOT TO MEET INITIAL EXPECTATIONS*

4.15 Of course, to be able to come to a view about whether the product is actually continuing to deliver the effective therapy which caused it to be treated as a special case as an innovation depends on continued surveillance of the product's performance. I will set out below (in paras. 4.21 - 4.22) ways in which this need could be addressed. They too raise fundamental questions about the relative burden of cost to be borne by Pharma and others, including the NHS.

4.16 If the approach set out in para 4.12 were adopted, the NHS would get products to meet needs identified as important priorities. NICE would be able to meet the Secretary of State's direction that it takes account of the value of innovation to the NHS, and provide incentives to Pharma to do so. Pharma would receive clear signals as to what areas of development would be most rewarded, would be able to collaborate effectively with NICE, and be rewarded for success. The aim would be to realise the vision of Sir David Cooksey in his report that NICE, working with manufacturers, could not only ensure that patients receive early access to the best possible products, but, also give the UK a competitive advantage, by providing early assessments of the economic impact of products, so that manufacturers could understand and predict the market for their products with greater certainty. Indeed, NICE, having already established the reputation as a world leader in appraising products, could acquire the further reputation of leading the world in developing a system of appraisal which

relentlessly looks for and drives innovation in the treatment of patients. The UK could become the crucible for the early adoption of treatments which constitute a real step-change in treatment for patients.

#### *RECOMMENDATION 17*

*NICE SHOULD BUILD ON ITS REPUTATION AS LEADING THE WORLD IN THE APPRAISAL OF PRODUCTS TO ESTABLISH ITSELF ALSO AS A WORLD LEADER IN PROMOTING INNOVATION AND THE EARLY ADOPTION OF TREATMENTS*

4.17 NICE cannot do this alone. It can affect the demand side. It can and should bring together the various elements of this side of the equation into a coherent whole, in which it plays the role of both agent and sponsor of change. Pharma, as has been said, need to be engaged and know what is expected of them on the demand side. But, as I have said repeatedly, the supply side, whether additionally or alternatively, must also be addressed<sup>59</sup>. The Department of Health, through its various agencies must facilitate research and the gaining of data<sup>60</sup> before and after licensing, including through some properly controlled form of co-funding. The recently created Academic Health Science Centres must be brought into the picture, given their links with Pharma and their obligation to translate research into treatment in the NHS locally and more widely, even globally. And Whitehall, from the Treasury to the Department of Business, Innovation and Skills, must play its part in making necessary adjustments to the supply side in such areas as financial support, incentives and taxation. The “Blueprint” for the Life Sciences<sup>61</sup>, emanating from the Office of Life Sciences and endorsed by the Department of Health, is an indication of the government’s intention to adopt a cross-government strategy. It brings together proposals to “give patients faster access to cutting-edge medicines”<sup>62</sup>, to build “a more integrated life sciences industry”, to facilitate access to finance and to improve incentives through the tax system. All must be mutually reinforcing<sup>63</sup>. All must be done in the name of innovation – real innovation as I have suggested that it be understood<sup>64</sup>.

#### *RECOMMENDATION 18*

*NICE SHOULD URGE GOVERNMENT TO MAKE APPROPRIATE ADJUSTMENTS TO THE SUPPLY SIDE, AS RECOMMENDED BY SIR DAVID COOKSEY AND THE OFFICE*

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<sup>59</sup> See para 2.5

<sup>60</sup> It is worth saying here that the data to be collected must be the best obtainable to give the most robust evidence. Thus, regardless of what might satisfy the regulator, products coming to NICE for approval against the background of seeking to maximise innovation, should be compared in trials with the best existing therapy, rather than the least effective or with placebos

<sup>61</sup> note 9

<sup>62</sup> On which see para 4.25 onwards

<sup>63</sup> Sometimes referred to as the “innovation ecosystem”, Sainsbury “The race to the top. A review of government’s science and innovation policies”. 2007

<sup>64</sup> As Lord Drayson put it to me “we must be mercilessly clear that we mean real innovation”

*OF LIFE SCIENCES TO ENCOURAGE INNOVATION ON BEHALF OF THE NHS AND PATIENTS*

**The promise of innovation**

4.18 So far, I have considered the situation in which the manufacturer claims that a product amounts, here and now, to an innovation. What of the claim that the product holds out the promise of being an innovation, although currently it barely differs from existing products? It was put to me strongly that innovation is often incremental, and examples were cited. I accept the point. But, of course, this still leaves open the question of what to do when there is only the promise of something. It was suggested to me that the mere promise<sup>65</sup> of something amounting to an innovation at some time in the future should be enough to warrant a higher price now, and thus a higher cost-effectiveness ratio, going beyond the threshold. I find the argument unconvincing<sup>66</sup>. It really is a question of risk: who bears the risk of failure in the future and who profits from success? It is not clear to me why Pharma should be insulated from the normal winds of commerce. The makers of Betamax held out the promise of their machine as the future for video-recording. They got it wrong and lost out. There was no question of being able to charge a higher price as insurance against failure. The makers of VHS took the risk. They got it right and profited accordingly. Given that the market for medicines is much more stable and predictable, it seems to me that Pharma should bear this particular risk.

*RECOMMENDATION 19*

*NICE SHOULD ONLY OFFER INCENTIVES FOR INNOVATION WHEN IT IS REALISED.*

4.19 But, that said, in keeping with my aim of seeking some incentives for Pharma to maximise the benefits to the NHS through innovation, this should not be the end of the story. I propose the following way forward as regards products which, it is claimed, hold the promise of innovation. Provided that the product in its current state is cost-effective within the threshold, as judged by NICE, and that the promise is of innovation of the nature previously described, the process of appraisal and approval could be adjusted to take account of this promise. There are several options already available to NICE. They are:

- approval on the basis that further research is carried out, sometimes referred to as “in the context of a well-designed programme of research” (ie “only in research”), or as “approval with evidence development” (I discuss in para 4.21 how to ensure that the work is done and how the cost should be borne)

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<sup>65</sup> The ABPI’s submission argues that “the failure to recognise or reward innovation in one area *may* compromise an entire pathway of ... follow-on developments” (my emphasis); AstraZeneca in its submission talks of “*possible* innovations” being lost to patients (my emphasis)

<sup>66</sup> As did NICE’s Citizen’s Council at its meeting in May 2009. And see the report of the Office of Fair Trading, *The Pharmaceutical Prices Regulation Scheme: an OFT market study*. 2007

- approval for a particular sub-group of patients
- approval through a “patient access” or “flexible pricing” scheme

NICE may argue that it already acts, or is beginning to act in this way. My point here is that what is needed is a formal and transparent process, triggered by a claim of the promise of innovation.

4.20 Two comments by way of further explanation are needed. First, use of the “patient access” or “flexible pricing” schemes may be the most attractive both to NICE and Pharma. For example, the “flexible pricing” scheme could be operated in such a way that the product would be approved at a price which brought it within the current threshold, since it currently offers little by way of change. If the contemplated promise materialises, (and even allowing for the fact that an adjustment of the assessment of QALYs could, in fact, result in its remaining within the threshold), Pharma could receive, from the time that the increased benefit accrued to the NHS and patients, a higher price for a period of time, on the same basis as that which I have already suggested in para 4.12 for immediate innovation. Again, this would constitute a departure from the ICER/QALY approach. This, in turn, would again mean that the consistency in principle and practice which currently underpins NICE’s appraisals, would in this context, be at risk. And, it would represent a net health loss to the NHS. It is a matter for the Board to weigh this risk. For my part, I am persuaded that it is a risk which could well be taken, provided NICE remains vigilant that the rules of engagement, as set out, are observed and that Pharma commits themselves to staying within them. As a precautionary measure, NICE could pilot the approach for a period of time, eg three years, with the clear message that it will not be continued if the gain (real and projected) to the NHS do not justify its continued use.

#### *RECOMMENDATION 20*

*NICE SHOULD CONSIDER ESTABLISHING A FORMAL AND TRANSPARENT PROCESS, USING SUCH OPTIONS AVAILABLE TO IT AS ARE REFERRED TO IN PARA 4.19 TO OFFER INCENTIVES TO PHARMA WHEN A PRODUCT IS SAID TO HAVE THE PROMISE OF INNOVATION*

*NICE SHOULD PILOT THE PROCESS FOR A PERIOD OF (eg 3 YEARS) IF IT DECIDES TO ESTABLISH IT*

#### **Evidence of continuing effectiveness – sharing costs**

4.21 Secondly, in all cases, further research or surveillance of the product’s effectiveness and performance is called for. This is expensive. Moreover, Pharma would have little interest in conducting research, if it carries the risk of proving in some cases that a product is not what it was thought to be. Thus, some kind of arrangement to share the costs of further

research and collection of data between the Department of Health, on behalf of the NHS, and Pharma may be necessary. The arrangement would stipulate that the product would only be made available to that number of patients necessary to conduct the required research or data collection, and that continued approval of the product would be contingent on the necessary research being carried out within a specified time-frame<sup>67</sup>. Any arrangement must, of course, avoid the situation in which Pharma gains while the product is being purchased and again through a subsidy of its research, while the NHS loses in paying the higher price for the product and also paying in part for the research which establishes the product's effectiveness. Support for the costs of R&D, in the form, for example of cost-sharing, is not, however, a matter for NICE. It requires an adjustment to the supply side. If a way can be found to ensure that the costs of research are shared in such a way as to avoid the problems just referred to, Pharma and the NHS will gain if a product is, indeed, an innovation. The NHS will gain, through saving resources, if the product proves disappointing in due course.

4.22 This idea of sharing the cost of further research is one of the ways in which, as I have indicated, modifications can be made to the supply side. A parallel can be drawn with the support by way of public funding given in the USA and the UK to research in the form of Phase III clinical trials. Such trials are a very large component of the cost of developing a new product. Publicly funded support for them has been advocated by the Nobel Laureate in economics, Joseph Stiglitz<sup>68</sup>. In the U.S. over \$4 billion is spent by the NIH, and thus the federal taxpayer, on supporting clinical trials. In the UK, by contrast, government spends very considerably less. The principle can also be applied to other research, the aim of which is to gain further evidence about a product's effectiveness and performance. A way needs to be found whereby funds, from government, from the MRC, and from the major charities which support research, and from Pharma, can be applied to carry out both the research and collection of data contemplated here. Great care must be exercised so that, on the one hand, Pharma does not gain undue reward, while also enjoying the incentives entailed in what is being proposed, and, on the other, that the nation's strategic focus regarding research is not skewed by an overemphasis on research into pharmaceutical products, important as it is. The need for a system of joint funding was, of course, recognised by Sir David Cooksey in his review of publicly funded research in healthcare: "funding [should] be identified and formal arrangements be established between the NHS HTA Programme, NHS SDO Programme and NICE"<sup>69</sup>. I am aware that NICE, through the Medical Research Council, has commissioned research to take full advantage of the "only in research" option. But, funding through the Department of Health remains a sticking point<sup>70</sup>. If government is serious about supporting

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<sup>67</sup> I recognise that it is difficult to withdraw approval of a product once patients are receiving it, albeit that the number of patients may be limited to those involved in the gaining of further evidence

<sup>68</sup> Jayadev A., Stiglitz J. "Two ideas to increase innovation and reduce pharmaceutical costs and prices". *Health Affairs* 2009;28(1): 165-168

<sup>69</sup> Cooksey, *Review of UK Health Research Funding* (2006). The Health Select Committee was somewhat lukewarm in its support of the idea

<sup>70</sup> I am aware of tensions in the Department of Health over funding, whereby quasi – semantic distinctions between eg types of "research" (experimental and observational) and "post-market surveillance" or "audit" (as a general term) to determine the real effectiveness of a product, are drawn to protect funds. While understandable, a way through has to be found

innovation, this state of affairs, with all its complexity regarding the relationship between private enterprise and the public purse, needs to be addressed as a matter of urgency. The Office of Life Sciences’ “Blueprint recognises the need to “provide[s] an excellent environment for clinical trials and investigations”<sup>71</sup>, but the proof of the pudding will be the ability to make collaboration between government departments and between government and industry really work.

4.23 It might be thought that my references to the supply side take me beyond my brief which is to consider the role of NICE. But, as I have already said, NICE operates in a larger context. The context is one in which NICE needs evidence and data so as to carry out the best possible evaluation of a product. It is crucial, therefore, for NICE that appropriate research is carried out. Currently, for reasons beyond NICE’s control, research of the sort which would assist both NICE and Pharma is not always being carried out. This state of affairs operates against NICE’s interests (and, therefore, those of patients, the NHS and Pharma). It should be addressed.

*RECOMMENDATION 21*

*NICE SHOULD MAKE URGENT REPRESENTATIONS TO GOVERNMENT, PARTICULARLY THE DEPARTMENT OF HEALTH, THAT ITS ABILITY EFFECTIVELY TO EVALUATE THE VALUE OF PRODUCTS DEPENDS ON THE EXISTENCE OF DATA AND INFORMATION FROM APPROPRIATE RESEARCH AND STUDY*

*NICE SHOULD URGE GOVERNMENT TO EXAMINE THE FUNDING OF RESEARCH AND FURTHER STUDY, WORKING WITH PHARMA AND ALL OTHER RELEVANT PARTIES, PARTICULARLY ACADEMIC HEALTH SCIENCE CENTRES, SO AS TO GENERATE DATA THEREBY ENABLING NICE TO EVALUATE PRODUCTS AS EFFECTIVELY AS POSSIBLE*

*NICE SHOULD URGE THE DEPARTMENT OF HEALTH TO SUPPORT, WITH OTHERS, THE FUNDING OF POST-MARKETING SURVEILLANCE OF PRODUCTS’ EFFICACY AS WELL AS SAFETY*

*NICE SHOULD WORK WITH THE OFFICE OF LIFE SCIENCES TO ENSURE THAT THE PROPOSALS OF THE OFFICE RELATING TO RESEACH AND DATA COLLECTION ARE ACTED UPON PROMPTLY*

4.24 The same arguments can be made concerning the development of products for rare diseases. Currently, based on NICE’s aim of maximising the gain in health from limited

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<sup>71</sup> note 9 para 2.1 and 2.10 onwards

resources, rare diseases, affecting small populations, have not attracted the same expenditure on R&D and, thus, on development. Incentives of the sort already discussed could, therefore, be offered to Pharma to promote development and innovation in this area. The R&D costs could be subsidised, through involvement of the public purse, the enjoyment of “market exclusivity” could be pursued, or, for an agreed period of time, the ICER/QALY threshold could be raised.

#### *RECOMMENDATION 22*

*NICE SHOULD CONSIDER WHETHER THE SAME OR A SIMILAR PACKAGE OF MEASURES AS THOSE SET OUT IN PARA 4.12 SHOULD BE USED TO GIVE INCENTIVES TO INNOVATION AND DEVELOPMENT OF PRODUCTS FOR RARE DISEASES*

#### **Fast track “innovation pass”**

4.25 Before leaving this discussion of innovation, I offer some comments on the proposed creation of a “fast track” for certain products. The idea, as set out in the Office of Life Sciences’ “Blueprint”, is that in certain limited cases, a product would be made available through funding from public sources without undergoing appraisal by NICE. Primary Care Trusts would not, therefore, be under a duty to purchase the product for patients, but it would be available for purchase. The proposal is that the “innovation pass” should be piloted for one year (2010-2011).

4.26 This notion of an “innovation pass” clearly has implications for what I have been asked to look at. I begin by suggesting that if what I have already proposed regarding innovation is accepted, the need for a “fast track” will be less strong. If, however, the idea is to be adopted nonetheless, there are a number of matters to be addressed. First, what products is this procedure intended for? Arguably, it should be limited to a product:

- which currently may only have “conditional marketing authorisation”
- which, in the view of a Committee of experts is very innovative,<sup>72</sup> such as constituting, for example, a new mechanism for action, or reaching a new target
- which, where relevant, is accompanied by evidence relating to stratification
- where the body of evidence is still relatively limited and immature, but, in the view of the Committee of experts, is strong enough to suggest a high degree of effectiveness<sup>73</sup>
- which is intended for a relatively small population of patients

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<sup>72</sup> For the reasons already set out in para 4.18, I do not think that it is enough to have the “promise of innovation”, because it takes us from the realm of incentive to the realm of subsidy

<sup>73</sup> The Committee would need to be alert to the dangers that if new products are diffused too early and without a proper assessment of their cost-effectiveness, it will be difficult (eg for reasons of ethics) to generate the necessary evidence as to efficacy, and that once a product is available, it will be more difficult to remove it through non-approval. This condition must not be used as a back-door to approval by NICE

- which will not cost a great amount of money<sup>74</sup>.

When I refer to a Committee of experts, I contemplate the establishment of an expert advisory group, preferably by NICE as guardian of the system for approving products, to receive proposals and to determine whether they qualify. The process of decision-making must, of course, be clear and transparent, although, as ever, the decision will constitute a judgement by the experts. The Committee's decision should take the form of a recommendation to NICE, which would, in turn, advise the Department of Health.

4.27 The second question is, who will pay for products approved under the proposed innovation path? Even though not approved by NICE, Primary Care Trusts could well come under pressure to purchase a particular product as a result, for example, of some campaign. The moment that products begin to be purchased without being exposed to analysis by NICE as to their cost-effectiveness, the whole system of rational resource allocation within the NHS would be threatened. Thus, if there is to be any "fast track", the money to support it and allow for the products to be purchased, which will not be a large amount (ie in the tens of millions of pounds), must not come from the NHS, and thus not be part of the accounts of PCTs. It must be provided through some central government mechanism. The Office of Life Sciences' "Blueprint" talks of £25 million from a "new ring-fenced budget" for the one year pilot. (This might be thought to be rather too modest a sum to have any real impact).

4.28 Thirdly, there should be a fixed time for which the product enjoys freedom from appraisal by NICE, perhaps up to 3 years. During this time, the further research necessary to confirm its value should be carried out. There may be a case, in keeping with what I have said previously, that the research could be funded jointly by Pharma and government, through some appropriate mechanism. Arguably, such funding should not come from the NHS, given that until NICE carries out an appraisal, the ratio of health gain to loss will not be known and the resources of the NHS might be already inappropriately depleted given what it is getting in return, without also funding research to see whether this is so. Moreover, Pharma has an incentive to conduct the necessary research, given the reward of approval by NICE and consequent requirement on PCTs to purchase the product. Finally, to advance the interests of what may be called UK plc, it would be appropriate to require that the research be carried out in the UK.

4.29 At the end of the period of freedom from appraisal, the product must be subject to NICE's established system of appraisal. In that appraisal it must be shown to be cost-effective within NICE's threshold. If it is not, or put another way, the manufacturer seeks a price that takes it beyond the threshold, it will not be approved. The 3 years of grace is a significant incentive to concentrate on innovation. Should the product not be approved by NICE at the end of the period, patients already receiving it should continue to do so, if it is deemed clinically appropriate, at the manufacturer's expense.

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<sup>74</sup> These criteria are more detailed than the general statement of intent set out in para 2.5 of the "Blueprint", note 9. They constitute my recommendations to NICE, given that the "Blueprint" states that NICE "will play a key role in developing and applying eligibility criteria for the Pass", para 2.5

*RECOMMENDATION 23*

*NICE SHOULD WORK WITH THE OFFICE OF LIFE SCIENCES SUCH THAT, IF AN “INNOVATION PASS” IS THOUGHT NECESSARY AND APPROPRIATE, CONDITIONS SUCH AS THOSE SET OUT IN PARA 4.26 APPLY*

*NICE SHOULD ESTABLISH A COMMITTEE OF EXPERTS TO ADVISE ON WHETHER THE CRITERIA FOR USE OF THE “INNOVATION PASS” ARE MET*

*NICE SHOULD SEEK TO ENSURE THAT FUNDING FOR THE PURCHASE OF THE PRODUCTS SUBJECT TO THE “INNOVATION PASS” COMES FROM A SPECIALLY CREATED FUND AND NOT FROM THE NHS*

*NICE SHOULD SEEK TO ENSURE THAT THE “INNOVATION PASS” DURING WHICH A PRODUCT IS NOT EVALUTED BY NICE SHOULD LAST FOR A FIXED PERIOD OF TIME (eg A MAXIMUM OF 3 YEARS)*

*NICE SHOULD SEEK TO ENSURE THAT AT THE EXPIRY OF THE FIXED PERIOD OF TIME THE PRODUCT IS APPRAISED BY NICE AND FALLS WITHIN THE THRESHOLD FOR APPROVAL*

## **5. DIAGNOSTIC TOOLS, DEVICES AND OTHER THERAPIES**

5.1 It was clear from various submissions and other comments that those involved in the development of diagnostic tools, devices and other therapies, particularly psychological therapies, felt that they were “poor relations” as regards NICE’s system of appraisal. The view expressed was that the paradigm for appraisal was the submission of evidence generated from randomised clinical trials (RCT) typically by Pharma. This approach, it was said, was often not appropriate, whether because, as in the case of diagnostic tools and devices, change is often experiential and continuous, and RCTs are difficult and expensive to organise and might even slow up development. In the case of psychological therapies, similar comments were made about the appropriateness of RCTs as well as the expense of conducting them. NICE, it was urged, should rely on other, different forms of evidence<sup>75</sup>.

5.2 I am aware that NICE recognises the different circumstances of those who develop these various technologies, such as diagnostic tools and devices, and has embarked on an examination of how best it can appraise such products.<sup>76</sup> Manufacturers, patients’ groups and healthcare professionals have much to offer in such an examination and I am confident that their views will be sought. Clearly, the key lies in what constitutes evidence on the basis of which NICE may confidently make a decision. I welcome NICE’s decision to establish the Medical Technology Advisory Committee as a way forward in dealing with claims of innovation in the evaluation of diagnostic tools and devices. NICE will now be able to engage with manufacturers regarding the evidence required and how such evidence can be developed and synthesised, so as to make it possible to undertake a proper cost-effectiveness analysis. It is envisaged, as I understand it, that the Committee will decide which products require evaluation, and then, either direct the evaluation to one of NICE’s programmes of evaluation or itself appraise the product and advise the Board, or call for more research and encourage the research to be done, even through co-operation with the NHS. In doing so, NICE will be reflecting the agreement of the House of Lords’ Committee on Science and Technology with Professor Sir John Bell’s view that there is a “need to identify a new agency that can handle the clinical utility evaluation of diagnostics.” The Committee recommended that NICE take on this role.<sup>77</sup>

### *RECOMMENDATION 24*

*NICE THROUGH ITS MEDICAL TECHNOLOGY ADVISORY COMMITTEE SHOULD PLAY AN INCREASINGLY ACTIVE ROLE IN ENCOURAGING RESEARCH INTO MEDICAL TECHNOLOGIES TO BE CARRIED OUT IN THE UK*

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<sup>75</sup> I am grateful to the submission of Schering Plough for pointing out that reliance on RCTs also presents problems in the area of paediatric care

<sup>76</sup> The submission of the Association of British Healthcare Industries was helpful in this regard

<sup>77</sup> <http://www.publications.parliament.uk/pa/ld200809/ldselect/ldsctech/107/107i.pdf> p. 32

## **Psychological therapies**

5.3 As regards psychological therapies, there are clearly differences, as against pharmacological therapies, in what might constitute evidence of clinical effectiveness and how such evidence might be generated. The RCT is most suited to establishing the effectiveness of drugs, not least because the trial can be properly “blinded” and the role of the therapist in the effectiveness or otherwise of the therapy is less significant, compared with psychological therapies. That said, NICE cannot issue guidance without having some sound basis on which to proceed. Moreover, it is unlikely that a real understanding of the comparable effectiveness of a psychological therapy can be established without some form of trial. CBT (Cognitive Behaviour Therapy) has led the way in this acceptance of the value of trials and other forms of psychological therapy need to follow. NICE is conscious of the need not to privilege one form of therapy, simply because it can produce evidence from RCTs. What is needed is a systematic approach to evidence which is appropriately flexible and combines “observed practice” with valid trials, moving from the former to the latter and then back to observed practice as further validation. Critical to the success of such an approach is both the need to collect data from practice and bring it together with data from other centres in the NHS, and the need to organise trials. NICE needs to emphasise the need for the development of evidence of effectiveness and work with others to ensure that a proper research infrastructure is put in place. NICE might well seek to work with the newly established Academic Health Science Centres (AHSCs), or Collaborations for Leadership in Applied Health Research and Care (CLAHRCs) to make psychological therapies one of their research priorities, given the AHSCs’ mission both to conduct research and to take the fruits of that research into the NHS locally and beyond. I am aware also that NICE is working with the Medical Research Council on research into the use of different types of evidence in its appraisals, such as “colloquial” evidence and non-experimental evidence from disease registers.

### *RECOMMENDATION 25*

*NICE SHOULD WORK WITH OTHERS, PARTICULARLY ACADEMIC HEALTH SCIENCE CENTRES, TO ENSURE THAT A SOUND INFRASTRUCTURE FOR RESEARCH INTO THE EFFECTIVENESS OF PSYCHOLOGICAL THERAPIES IS ESTABLISHED*

*NICE SHOULD WORK WITH OTHERS TO DEVELOP A SYSTEMATIC APPROACH TO EVIDENCE REGARDING PSYCHOLOGICAL THERAPIES, INCLUDING THE PLACE OF RCTs AND NON-EXPERIMENTAL EVIDENCE*