NICE CITIZENS COUNCIL REPORT

ULTRA ORPHAN DRUGS

LONDON, NOVEMBER 2004

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PREFACE

The National Institute for Clinical Excellence (NICE) is part of the National Health Service (NHS). It exists to advise health professionals on how to provide NHS patients with the highest attainable standards of clinical care. In developing its guidance, the Institute has to take account of both the clinical effectiveness *and* cost effectiveness of the various interventions it considers.

The Institute and its advisory bodies base their conclusions on the best available evidence but they also have to make judgements. These fall into two categories. *Scientific* value judgements are concerned with interpreting the significance and relevance of the totality of the available scientific, technical and clinical data; and *social* value judgements that take account of societal aspirations, preferences and ethical principles that ought to underpin the manner and extent of the care provided to NHS patients.

The advisory groups who formulate the various forms of NICE guidance are well-qualified to make scientific judgements. Like the Institute's board, however, they have no particular legitimacy to impose their own social value judgements on the NHS and its patients. The Institute has therefore established a Citizens Council, drawn from the population of England and Wales, to help provide advice about the broad social values that NICE should adopt in preparing its guidance.

The 30 members of the Council reflect the age range, gender, socio-economic status, disability, geographical location and ethnicity of adults in England and Wales. Council members serve for a period of three years with one third retiring each year. And although they and their families have experience of the NHS as patients none are health professionals. Nor do they represent any particular section or sector of society; rather, they bring their own personal attitudes, preferences, beliefs and – sometimes – even prejudices! The Council meets twice a year.

At each meeting, the Council is asked for its views on an issue about which the Institute needs advice. Meetings are facilitated by an independent organisation (Vision 21) and members have the opportunity to hear, and cross-examine, expert witnesses as well as engage in discussion and deliberation in both plenary and small group sessions. The Council's conclusions are contained in a report that is presented to the Institute's board.

The issues about which the Institute seeks the Council's advice have been generally ones about which there are conflicts between fundamental bioethical principles. The board has made it clear to the Council that it does not expect members to necessarily reach a consensus. Rather, it wishes to learn of the reasons behind the divergent conclusions that may be reached.

This present report embodies the Council's conclusions about whether the NHS should be prepared to pay premium prices for drugs to treat very rare (so-called "ultra-orphan") diseases. The Institute sought the Council's views on this matter for the reasons described in the Council's briefing paper (Appendix 1). Once again, the board is extremely grateful to the Council for its continuing help in developing the Institute's social value judgements.

Professor Sir Michael Rawlins
Chairman, National Institute for Clinical Excellence

SECTION ONE – Executive summary - our key findings

The Citizens Council was asked to advise on whether or not the NHS should be prepared to pay premium prices for drugs to treat patients with very rare diseases. Twenty-seven members of the Citizens Council met to discuss this over the course of three days in November 2004.

"Everyone approached this discussion from the point of view of wanting to do what's fair – but we have different ideas on fairness. Twenty of us have taken a decision that we should use a different way of assessing value – sixteen give a qualified yes with conditions when it comes to paying for ultra orphan drugs, and four think that there shouldn't be conditions attached. Seven of us feel that rare diseases should not have a different decision making process applied to them."

In summary, our conclusions were as follows:

Just over half (16) of Council members thought that, with certain conditions, the NHS should consider paying premium prices for drugs to treat patients with very rare diseases.

A further four people thought that the NHS should pay whatever premium price is required for drugs to treat patients with very rare diseases.

Seven of us concluded that the NHS should not consider paying premium prices for drugs to treat patients with very rare diseases, but should decide whether or not to provide ultra orphan drugs using the same clinical and cost effectiveness appraisals as any other treatment.

The main criteria that the Citizens Council thinks the NHS should take into account when deciding to pay premium prices for ultra orphan drugs are, in descending order of importance[1]:

- The degree of severity of the disease
- If the treatment will provide health gain, rather than just stabilisation of the condition
- If the disease or condition is life-threatening

[1] Please see section 4 for a full list and an explanation of how these were arrived at.

A note on reading our report:
An account of our discussions, and some detail on the reasons behind our conclusions, is contained in sections two and three of this report. Because we were split in our recommendations as to what the NHS should do about funding ultra-orphan drugs, our report reflects this diversity of views.

In each section we try to explain clearly why some of us thought as we did: inevitably that means that others don't agree with those arguments. Wherever there was unanimous agreement on a point or a recommendation, we've indicated that this is the case. Unless it says so, therefore, readers should assume that some, and not all of the members of the Citizens Council hold the views expressed.

We've tried to make sure that the report reflects the spirit and the balance of our discussions, even though no individual member would subscribe to every view contained within it. On some points we took votes and so it's possible to say exactly how many people agreed or disagreed with a particular recommendation or viewpoint.

In order to give some depth to the report, and to give some context for our conclusions we have also included a flavour of the discussions we had over the three days. Therefore, there are occasions on which we say that 'some' or 'most' members held a particular view. This judgement about the strength of feeling is made on the basis of extensive notes taken over the three days. In these cases it isn't always possible to give numbers because, as well as containing our conclusions, the report contains a narrative describing the tone of small group and plenary discussions over three days.

We could have left this out and reported only on those statements we voted on – but we felt that readers would find it helpful not only to know what we concluded, but also to get some idea of the discussions we held and the reasons we had for coming to these conclusions.

SECTION TWO – The debate

"I've learned again that difficult decisions do have to be made within the NHS. Too often these decisions are made in secret. But they should know that we do support them and we know they have to keep within a budget. The NHS shouldn't be frightened of the public finding out about all this – they should discuss it more with the public. They'll only keep our confidence if they level with us about the difficult choices that have to be made."

OUR RATIONALE FOR OUR DECISIONS

The case for paying premium prices under certain circumstances …

The majority (20 out of 27) of Citizens Council members came to a conclusion that it is sometimes, or always, justified for the NHS to pay premium prices for ultra-orphan drugs. For twenty of us, the NHS should vary its normal assessment of cost effectiveness to allow expenditure on ultra orphan drugs where necessary. Sixteen of us thought that there should be some conditions attached to this: four of us thought that there shouldn't.

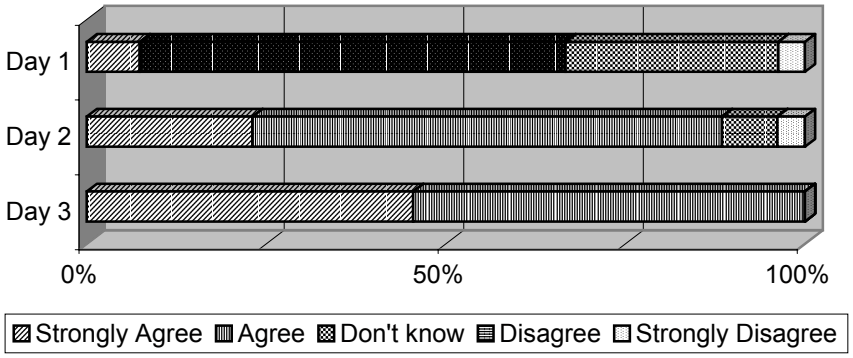
We accept the premise that the NHS needs to have a way of ensuring that the money it spends is used cost effectively, and is used to increase overall health gain in the population. We know that as a result of applying this principle, it is very unlikely that ultra-orphan drugs would ever be assessed as cost effective.

So there are a number of reasons why we felt that the NHS should treat ultra-orphan drugs differently. Most of us felt strongly that everyone should have fair and equally high standards of care – and in order to achieve this, it may be necessary to spend more on some people than on others. We don't feel that the minority should be penalised for the sake of the majority, and we were concerned that once we start to discriminate against people with rare conditions, who knows which group we may decide that we can't afford next.

The benefits to the individuals who suffer from rare diseases are obvious: improved quality of life, reduced pain and suffering, and their lives may be saved.

For sixteen of us, rarity on its own is not a factor – and the degree of severity must come into the picture. We would like to see more research done to recognise that the 'amount' of health gain may be the same in two cases, but is not always equally valued. For us, if someone starts from a position of having a very severe disease, then we would value their improved health more than someone who had something relatively minor wrong with them – even if they 'improved' to the same extent.

Rarity in itself should not be the reason for paying premium prices. Other factors - such as severity of the disease - may be more important



This concept gained increasing support over the three days. Those who did not think there was a case for treating ultra-orphan drugs for rare diseases differently thought that other factors might be more important to take into account when considering cost effectiveness. More people swung towards this view as the days went on. But even amongst those of us who agreed that there were grounds for paying premium prices for ultra orphan drugs, most people stressed that it was because these rare diseases are often so severe that it is justified. On its own, the rarity of a disease, would not give it special status.

But we think that there are also wider benefits to society that come from paying premium prices for ultra orphan drugs. Firstly, there is a possibility of other benefits that could help us treat more common illnesses being discovered as a consequence of this more specialised research. And secondly, we felt certain that the whole of society is made more humane and altruistic because of this social solidarity.

We think that investing public money, where necessary, into the discovery and manufacture of ultra orphan drugs will encourage and value research and development into the treatment of disease generally, as well as ultra orphan diseases in particular. We expect that the provision of these drugs, even though they may be at premium cost, may mean that fewer resources need to be used on symptomatic or palliative care – although we realise that there will probably always be increased costs involved in treating difficult and rare conditions.

"Is the economic modelling for rare diseases and their treatments good enough? Does it take all the wider costs into account, and does it prize the immediate benefits and costs more than the lifetime impact on a patient?"

We also wanted to distinguish between cost effectiveness and the potential budget impact. Although the individual treatments may be very expensive, because the number of people involved is small, it may have a small effect on the overall NHS budget.

For some of us, our ‘yes’ is also a way of buying some time, given that genetic engineering may play a part in the treatment of orphan and ultra-orphan conditions at some point in the future.

We would like there to be strict conditions attached to drugs being given the go-ahead, and we support moves to make sure that there are regular reviews of the effect of this public subsidy on the market. We are concerned that some unintended side effects of good-intentioned legislation may occur if a close eye is not kept on pharmaceutical companies. If the NHS is to invest to this extent in supporting the development and manufacture of ultra orphan drugs, then the wider public interest must be safeguarded.

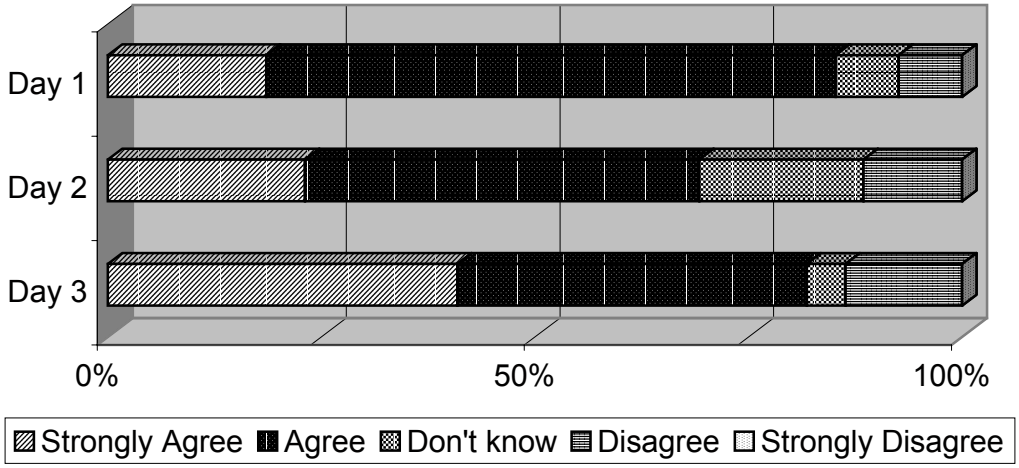
“I feel the way I do because I feel that equality should lie at the heart of our approach as a society to the provision of healthcare. However, that equality means that we should give an equal weighting to care for all severe conditions, regardless of the degree of rareness or commonness. My reservations exist because of the enormous growth of ultra orphan ‘subdivisions’ of disease - are we opening Pandora’s Box?”

“We need to back this and pay the prices we have to pay to use the drugs because we believe in scientific progress. The orphan drugs legislation means we back the discovery of new treatments. The logical step then is to pay so that they can be used on people who need them. Why invest in R&D and then not use the results? That would be the real waste of public money.”

“We need to educate society about the NHS not being an endless pot of money. We should encourage preventative medicines or better life style choices. Many people could improve their own health – which would mean that more money would be available for people who desperately need treatment through no fault of their own.”

“My conditions are firstly that the drug should have a proven record of success, and secondly, that the quality of life, however short, should be improved significantly.”

The treatment an individual receives from the NHS should not be affected in any way by the number of patients suffering or likely to suffer from their condition



A majority of Citizens Council members felt that the treatment an individual receives from the NHS should not be affected in any way by the number of other patients suffering or likely to suffer from their condition. At the start of the three days, just over 80% of us agreed with this. Although support for this position fell a little during the course of the debate, about three quarters of us agreed with this statement by the end of the meeting – and the proportion of us who felt strongly about it increased.

… and the case for not setting any conditions …

However, four of us didn't want to put conditions on this, and would be happy to pay whatever premium prices are required for ultra orphan drugs. For us it is an issue of principle – that if you need help, and we have a treatment that we know works, we should fund it.

We think that being rare does make the disease special, and these are often the less glamorous unheard conditions that should not be ignored. We felt that those who are unfortunate enough to have a rare and severe condition should not be put under more pressure than anyone else to justify why they 'deserve' whatever treatment they need.

As far as we were concerned, the phrase 'the NHS is not a bottomless pit' is a very emotive term – and society needs to re-prioritise what it values, and therefore what it pays for. If all else fails, the Government should increase taxation.

We felt that in a truly democratic society the wishes, together with the needs, of the majority are there to protect the minority. A small number of us felt most strongly that the NHS should pay for the cost of ultra orphan drugs. The cost of providing care for this tiny minority, when compared to the NHS budget as a whole, is infinitesimal and pales

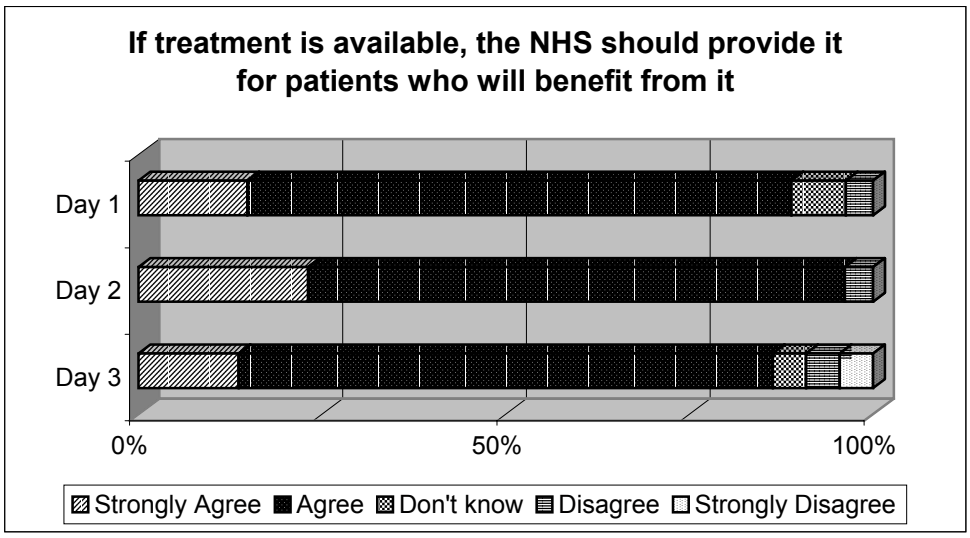
into insignificance. If the budget cannot be managed in such a way as to provide for this minority then something is seriously wrong.

"I have great difficulty in allowing someone to die if there is an effective treatment for a condition. If the NHS won't pay then rich people will live and poor people will die as some could afford their own treatment and others couldn't."

"Individuals should not be discriminated against because they have a rare disease. These are horrible diseases that we are talking about – if resources are limited then we should be prioritising treatments that people need – before we agree to spend on other treatments because people think they want them. There is no doubt that these people need the treatment. We should not deny it to them because they are in a minority – it would not be acceptable in other spheres of life."

"In a society that seems to aspire to equality of opportunity I find it obscene that this does not apply to health. To treat some people equally you need to treat them differently and to do this may well be extremely expensive."

"None of us know how often we will use the NHS when we are born – almost all of us either use it less or more than the average person. But people with rare diseases know in advance they will use it a lot more. It makes them feel guilty that they are using more resources than others. What about those who are accident prone, or drink a lot and have to keep getting their stomach pumped? They're expensive too – we just don't know that in advance. Are we putting unfair pressure on these people who have rare diseases, telling them that they are spending too much?"



The case against paying premium prices …

However, there was a minority who felt quite differently. Seven of us felt strongly that rarity in itself was not a sufficient reason for paying a premium price. If for the same price the NHS could get the same health gain from treating a big group of people, as it could from treating a small group, then why would we choose the small group over the large group? Paying premium prices for ultra orphan drugs can only be justified if you value rarity above all else. Our view was that we must have objective assessment

criteria to help to govern against 'those who shout loudest' getting the most. This also ensures the treatment for all conditions is judged fairly and without bias in any shape or form.

If there is to be any reason to override the normal assessment of what it is cost effective to provide, then it should be the degree of severity of the disease or condition, not the fact that a small number of people experience it. We were concerned that making 'rarity' the key criteria would result in larger numbers of people with severe and common conditions losing out. For us, the primary responsibility of the NHS is to ensure the greatest health gain.

We recognise a principle of the NHS is to facilitate treatment for all, but if it is not affordable there have to be compromises. Variation does occur but some form of threshold has to exist. If a treatment costs £1 million, £5 million, £20 million…. where do we stop?

"I feel that it is very important for NICE to be seen to be even handed when assessing treatments. I can't buy the concept that to be fair you have to treat people differently."

Budgets are a fact of life for any healthcare system anywhere in the world – no matter how much the budget is increased, needs and demands will always outstrip it. Our approach is an attempt to be fair and equitable, and recognises that unfortunately spending a lot of money on extremely expensive treatments for some would restrict treatment to many others. We are not inhumane and at an individual level we have compassion but budgets have to be worked to. This stance does not make us feel good but we feel it is an objective approach.

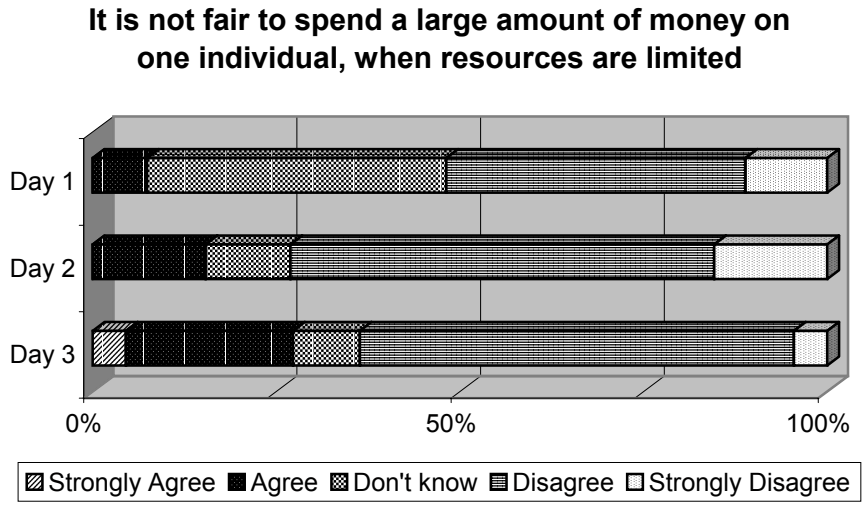
We recognise that there are some drawbacks to this approach – most likely that not everyone will be able to be treated on the NHS. We realise that some individuals may suffer, but this must be balanced against the larger group of those who will gain. We are also concerned that research into the treatment of rare diseases will be reduced, and that there is a risk of damaging British biotechnology business.

Deciding not to pay premium prices for ultra orphan drugs simply because a disease is rare may also lead to accusations of discrimination, and some high profile cases leading to adverse publicity, which could undermine Joe Public's confidence in the NHS. However, we feel that an open debate means that this policy would be open to scrutiny, and should be justified on the grounds of using NHS resources in a way that is as fair to as many people as possible.

"This is not easy. There's a danger that we are spending more taxes on healthcare and we may not see much change for ordinary people. The benefits of this will not be very visible – and yet we need the wider public to have faith in the NHS to continue to agree to fund it through taxes."

"Are we giving carte blanche to drugs companies to decide their own priorities?"

When we first considered whether it was fair to spend a large amount of money on expensive treatments for rare diseases, a lot of us weren't sure, and our views were rather polarised. By the Friday lunchtime, possibly as a result of having heard from the patient and carer representatives, most of us disagreed with this statement. By the end of the meeting, there were few of us who still weren't sure about this. Reflecting our final decision that it is justifiable to treat very rare diseases as a 'special case', most people still disagreed with this statement – although more people agreed. Again, this could have been due to the discussions we had on Friday afternoon with the professionals who have the responsibility for commissioning healthcare for the whole population in their area.



"In an ideal world we might want to fund all treatments. But being realistic we realise that resources are limited and we need to prioritise treatments according to severity and need."

"If the NHS just had to decide, one treatment at a time, whether or not to fund it on its own merits, it would be an easy decision. But society has to decide between many competing treatments. Each may do good, but we can't afford them all. That's when we need to work out which does most good to most people."

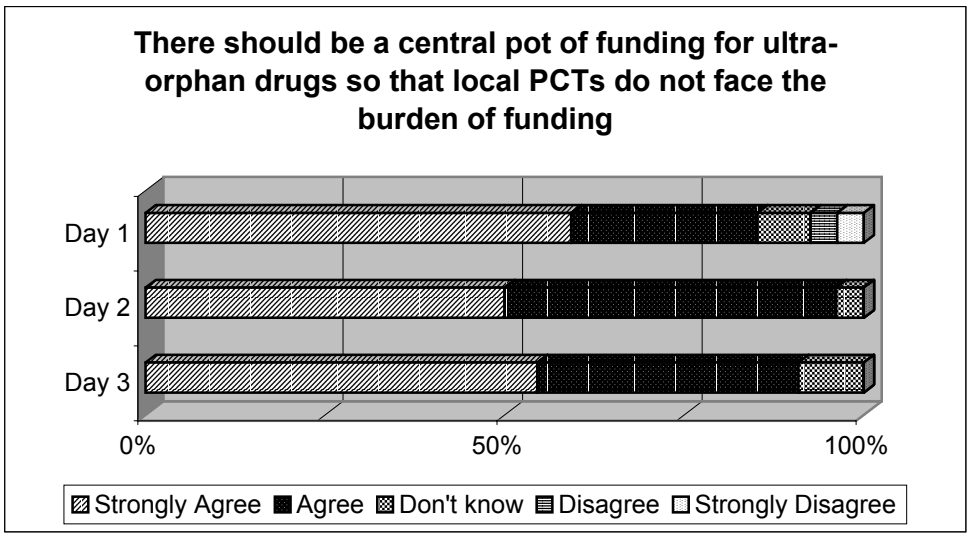
SECTION THREE – The implications – how do we do it?

Central funding

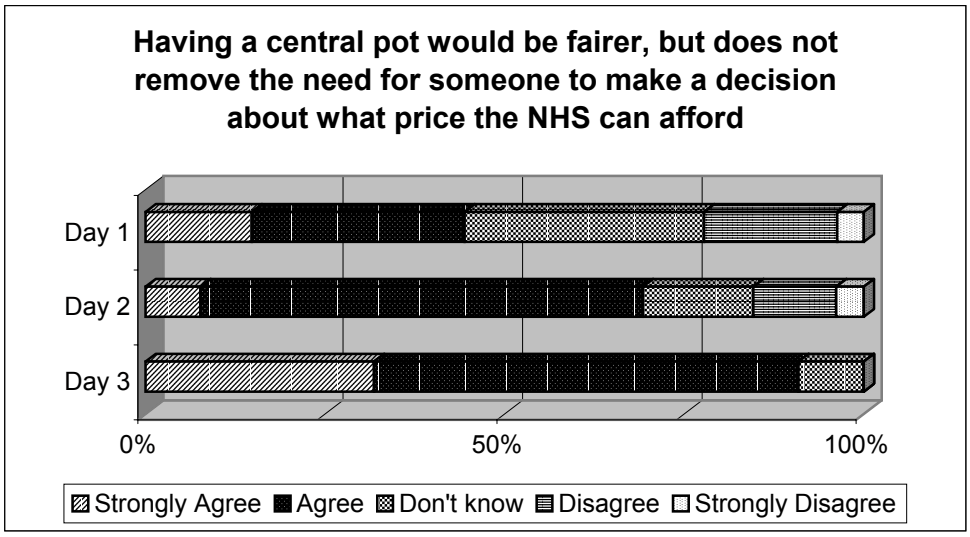
Many of us felt that it is unfair to ask individual Primary Care Trusts (PCTs) to find the funding for ultra orphan drugs. Because of the nature of many of the rare diseases, they are likely to be clustered in some areas and not others. This not only places a burden on the budget of the local PCT, but also is likely to lead to 'post code prescribing' with some patients receiving treatments while others are denied it as a result of different decisions taken by PCTs.

We would like to see a central pot of funding for the treatment of rare diseases.

"We need to nationalise the problem to rid ourselves of the distortions that can occur at a local level."



Does it take the problem away – or does it just move it? We felt there were at least two aspects to this question of a 'central pot'. The idea of removing the variations in decision-making – getting rid of post-code prescribing – was popular. Not only does the current system seem unfair to individual patients, but it also struck us as unfair on local PCTs, some of which might struggle more than others to balance the books. But although we supported central funding, we were under no illusions: we know that the difficult decisions have to be made somewhere. If we were a Citizens Council that was answerable to a single PCT, we may have said that there should be centralised funding and that would have been the end of it: problem sent elsewhere. But because we are NICE's Citizens Council, we know that they need our views on what the NHS overall should do. So for us, although an important measure to iron out local discrepancies, the concept of making decisions centrally about what is fair to fund is not the answer in itself – it's just the start of the debate.

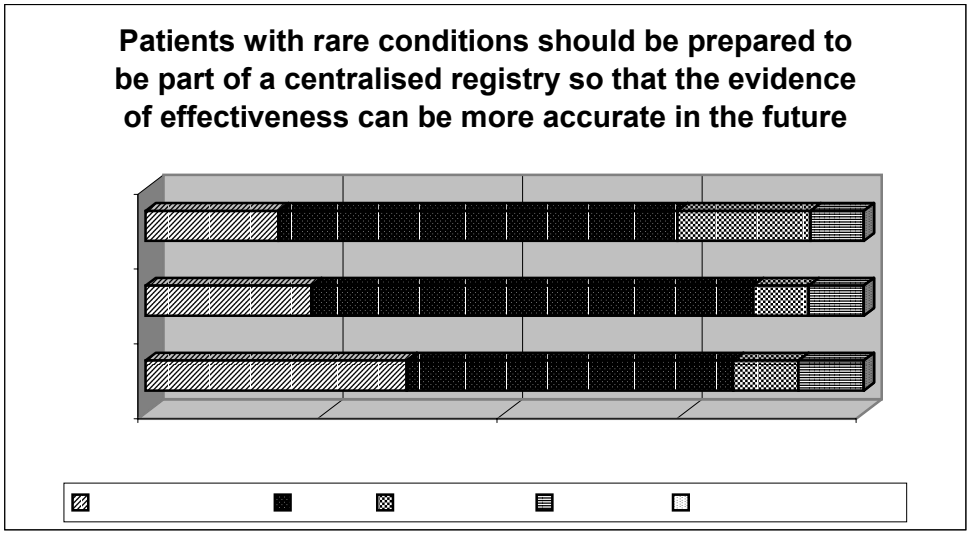


Centres of excellence
A 'top sliced' budget for treatments for rare diseases should also enable the development of centres of excellence and a small number of specialised care packages.

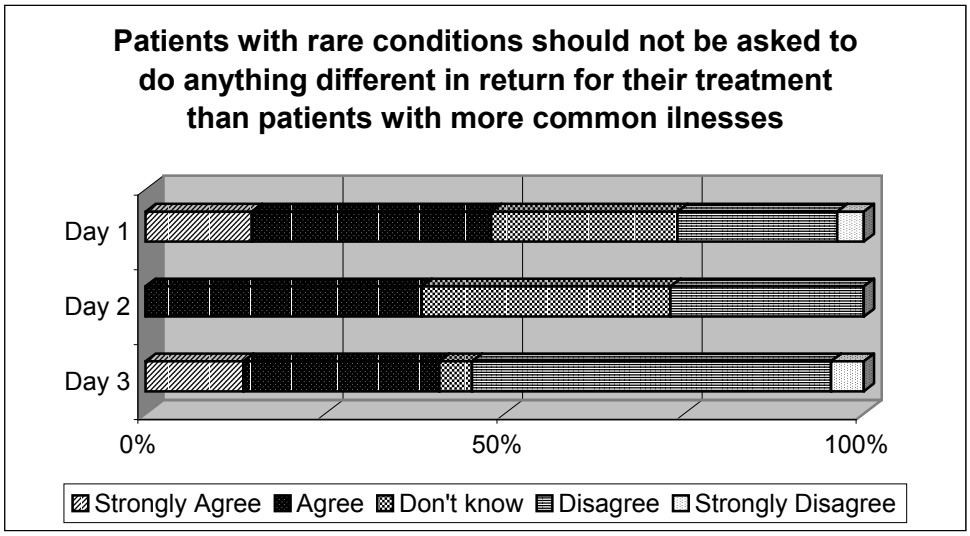
The quality of research
We heard about some of the difficulties in undertaking research into diseases and conditions that only affect a small number of people. Nonetheless, we felt that it is important that attempts are made to improve the quality of evidence available.

We would encourage there to be a national register of all patients who receive an ultra orphan drug, so that long-term research into the further clinical effectiveness of these treatments can be done.

"There seems to be enormous reliance on expert opinion, because there isn't the kind of robust evidence available. But all the experts are people who have an interest in that disease area – and so they would say that it works, wouldn't they - so more should be done to ensure long-term, valid studies."



Not everyone agreed with this, however. About a third of us, overall, thought that it wasn't right to ask patients with rare disease to be subject to special obligations not placed on the rest of the population. Having said that, it should be borne in mind that our previous Council discussions (in May 2004), when we were considering the use of confidential patient records by the NHS, showed that the vast majority of us felt strongly that we all owe a duty to the NHS to 'put something back' and allow the system to learn from us to the benefit of future patients. This time, too, most of us thought that patients should be prepared to be part of national registries *to "aid understanding", to "contribute to the knowledge available",* and *"to ensure that they and others in the future receive the best treatment".*



The effectiveness of the treatments

Another aspect of this question is that the effectiveness of rare and expensive treatments – although more likely to be questioned – may actually be better than the cheaper treatments that are more frequently given for common diseases. There is a natural desire to want to do something to help people who are sick, and so there may be a tendency to pay for cheap but not hugely effective treatments for common diseases, on the basis that it is better to do something than nothing at all for a large number of people who are suffering.

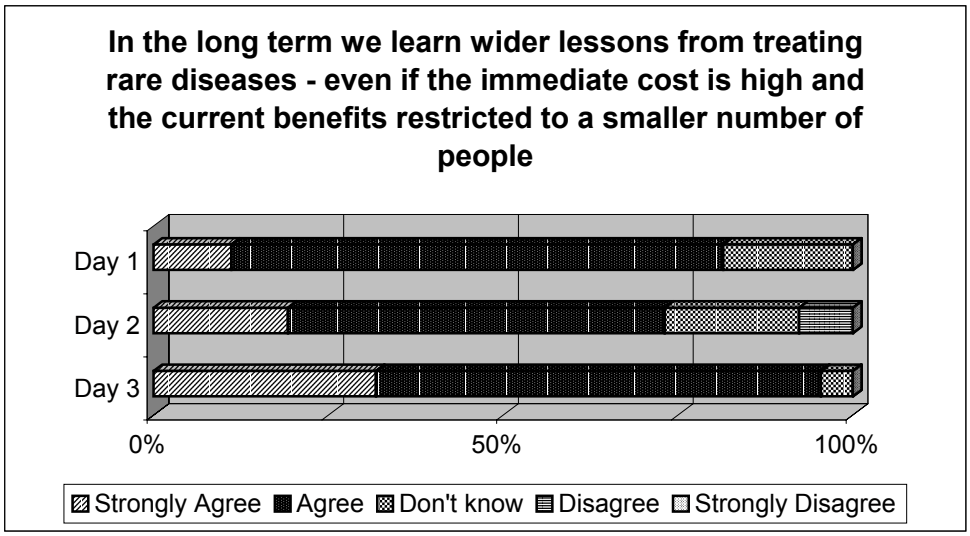
Money should not be wasted on drugs that are ineffective. The NHS should only administer treatment if it is found to be effective – and we would encourage NICE to make recommendations about what treatments should be discontinued, as well as recommendations about new treatments that should become available. This may allow resources to be spent on more effective – but more expensive per patient – drugs for rare diseases.

One Council member said: *"There seems to be a market for semi-effective treatments because of public demand to do something about common diseases. But why are resources being put into drugs that are not that effective? Money spent on endless similar and only slightly better treatments for these common conditions should be put into use of drugs that are effective and used for treating rare diseases."*

But another disagreed, and cautioned: *"While I disagree with paying for ineffective drugs, I can't remember being given any evidence of a widespread practice of such being done. There seems to be a tendency to accuse the NHS of major inefficiencies without any evidence. I think we need to be careful here. Is this all part of looking for an opt out, instead of taking a difficult decision?"*

Supporting research and development

A number of us were concerned that if the UK is not prepared to subsidise the development and supply of ultra orphan drugs, then pharmaceutical companies might stop doing research into these diseases. The market is a global one and the UK alone probably doesn't have the financial muscle to cause companies to withdraw from research programmes – so some of us acknowledged the more likely risk is that they could move their operations elsewhere.



We also thought that treatment of those with 'orphan' diseases could (in the long term) benefit society as a whole. One argument that a number of us found compelling was that despite the research in the 1980s into the gene that affects cystic fibrosis not yielding the desired results, what was learned about genes is now being used to develop very specific therapies for heart disease and cancer.

"An advanced society is one in which we fund progress. We don't know now what the future benefits will be of researching and providing drugs for rare conditions. But if we want to be going forwards, we need to be prepared to invest now. It's important for the few patients who will benefit in the short term, but who knows – maybe it will have wider benefits in the future that we can't possibly predict now? Short term thinking is rife in the UK but we'll never get anywhere with that attitude."

Keeping a close eye on the pharmaceutical industry

Many of us were very concerned about the unanticipated consequences of subsidising the market in this way – even if we felt that the reasons for doing so are very important.

We are worried that the pharmaceutical companies may be tempted to redefine some common diseases as a cluster of rarer diseases – or to find a new use for a profitable block-buster drug and thereby claim subsidies in a way that takes advantage of the letter rather than the spirit of the law.

"We're not advocating paying premium prices because we want to boost the pharmaceutical industry. We're advocating it because it's a public service to provide treatments to those who need them – if the market on its own won't ensure that. So there should be a tight system to make sure that the companies aren't making excess profits."

CONSEQUENCES OF SAYING YES

By Saturday morning, to help us with our decision-making, we had identified a number of arguments that held sway with us when considering saying yes to paying premium prices for ultra-orphan drugs. Of course, not everyone agreed with each of these, and the length of each list is simply indicative of the range of views that were held – not necessarily reflective of the strength of feeling for each position.

Possible POSITIVE consequences of saying yes

- It helps shape a more humane society
- Patients would benefit and be treated
- Lives of patients with rare diseases will be saved
- Possible eradication of some diseases – genetic hereditary disease could be eradicated due to better information & genetic screening (though some members objected to the idea of genetic screening)
- R&D would be encouraged with possible benefits for other diseases
- Possible to return to good health and employment – increased productivity
- It buys time for other developments
- The movement towards central funding for this kind of development will become even stronger
- The chances of more centres of excellence being established will be greater
- The development of ultra orphan drugs adds to the overall 'pot' of experience
- There might subsequently be some serious attention paid to waste in the NHS to compensate for the cost of drugs at premium prices
- Higher costs all round but a healthier population
- The health gain could be considerable – more than treating minor common diseases
- We already prioritise many conditions because they are cheaper or easier to treat

Possible NEGATIVE consequences of saying yes

- Resources would be limited for other treatments and services and could lead to other patients suffering or dying
- Less to spend elsewhere in the NHS
- Disinvestment in other worthwhile treatments to balance the books
- Drug companies could deliberately target rare diseases for commercial purposes reducing research in other areas
- The drug companies would not be pushed into making the drugs affordable – and may encourage inflated prices and profiteering by drugs companies
- The local PCT and the rest of the population have to bear the costs for one individual
- Some people with non life-threatening disorders may receive a lower level of care or wait longer
- Could be considered prioritising these conditions so making them higher status to others
- The health of the majority suffers
- Fewer lives overall could be saved
- More sufferers born as patients live longer and have children – and the demand for treatment increases
- There will be a rise in the drugs bill, compared to spending on other things in the NHS
- Once we've started we could never stop, and it could cause resentment amongst patient groups
- We will have to raise taxes
- It may undermine NICE's system of appraisal on grounds of clinical and cost effectiveness – which was introduced to bring fairness across the NHS

CONSEQUENCES OF SAYING NO

We also identified the following arguments that held most sway with us when considering saying no to paying premium prices for ultra-orphan drugs. Again, not everyone agreed with each of these, and the length of each list is simply indicative of the range of views that were held – not necessarily reflective of the strength of feeling for each position.

Possible POSITIVE consequences of saying no

- The frequency of the disease may reduce (in genetic or hereditary conditions) as sufferers die and genes are not passed on
- More resources would be available to spend on other treatments and services
- Society may catch up with providing the level of medical care already discovered before we develop anything new
- R&D into new treatments may not be slowed as the UK is a small player in the global market so it would depend on whether others followed our lead
- Those ill with common ailments would benefit, as more money to treat them is available

Possible NEGATIVE consequences of saying no

- Patients with rare diseases would suffer or even die
- The human rights of individuals could be breached
- The NHS would be standing by and watching people suffer unnecessarily
- Patients with severe rare diseases will still require care and resources
- Drug companies will only research and develop drugs for very common diseases
- Reduction in possible benefits from research spin-offs
- Adverse publicity leading to reduction in public confidence in the NHS
- Decision-makers may be open to criticism given that they might spend money on things that could be considered less worthwhile
- People with rare diseases will be discriminated against and it's not their fault
- The NHS would be seen to be moving away from caring according to need for all
- It may be the start of a slippery slope towards not spending money on more and more things
- Disincentive to do future research – why find a cure if you're not going to be able to use it?
- The UK biotechnology industry would shrink, as companies move to the US
- There could be a rich/poor divide – rich people could afford private treatment
- Public outcry as patients saw drugs being supplied in other countries

SECTION FOUR – Vision 21's description of how the Citizens Council came to their decisions

Social research and public consultation company Vision 21 recruited the members of the public who sit on the Citizens Council. We then organise and facilitate the six-monthly meetings.

The discussion paper for this topic was prepared by NICE's Citizens Council committee, a sub-committee of their Board, which Vision 21 attends. The first stage of the process, after deciding what topic to consult the Citizens Council on, is to draft a paper that scopes out the issue at stake for NICE. This also outlines what use will be made of the Citizens Council's answer, so they are aware of the context in which they are working.

The drafting of this paper was informed by other work being undertaken by NICE, including a joint conference on orphan drugs held in June 2004 with the Royal College of Physicians; and workshops over the summer with members of NICE's appraisal committee members which discussed how to incorporate the public's social value judgements into NICE's work.

Citizens Council was first sent the discussion paper (included in appendix one) in September 2004, and they were given the opportunity to comment on the scope of the question, and to make suggestions for speakers (biographies in appendix three) that they would like to hear from, or aspects of the debate that they would like to ensure were covered.

This draft paper was also circulated to many of NICE's stakeholders, including members of the Appraisal Committees, and some known experts in the field. They were asked to comment on clarity, balance, and the scope of the question and the background information that was being issued. We also consulted widely, asking for advice on how the discussions with the Citizens Council members should be structured, and Vision 21 incorporated these views into guidance for our facilitation staff.

In addition, Vision 21 tested the paper for clarity on 12 members of the public who are unrelated to the Citizens Council.

As a result of these processes, some changes were made to the topic paper, and a final version was sent to Citizens Council members a couple of weeks before the meeting.

Possible speakers were contacted throughout the summer to ensure a range of views would be represented, and the programme was finalised in the month before the Citizens Council meeting.

The Citizens Council then met for three days between 18-20 November, and had wide-ranging discussions as outlined in the programme below.

Throughout the meeting, the Council members' views were recorded in a number of ways. All plenary sessions were recorded on mini-discs, and the recordings were available to staff to listen to during the report-writing process. Two staff also typed (virtually) verbatim notes of all plenary sessions. In each small group session, a member of staff took notes of the course of the discussions and as many direct quotes as possible. In addition, Council members recorded their own flip-chart notes, and many also chose to submit an account of their own views at the end of the meeting.

In these ways, it was possible for Vision 21 staff to observe how Citizens Council members developed and articulated their thinking in a number of ways during the course of the meeting. Because people have different styles of contributing to meetings, it was also important to make sure there was a mixture of formal question and answer sessions, listening to a range of experts, discussion that was facilitated by external speakers and by Vision 21 staff, informal small group work, case studies, debate between those who held opposing views, work in small groups of like-minded people, and time for individual reflection.

On the Saturday morning, after the Council members established that the majority of them felt that there was a case for paying premium prices under certain circumstances, they listed as a group the following factors that they felt should be included as criteria when the NHS was deciding whether or not to pay premium prices for ultra orphan drugs.

Criteria	**Overall score**	No. of people who said it was most important	No. of people who said it was second most important	No. of people who said it was third most important
The degree of severity of the disease	**41**	10	4	3
If the treatment will provide health gain, rather than just stabilisation of the condition	**41**	5	11	4
If the disease or condition is life-threatening	**29**	7	3	2
The cost of other care, if the patient cannot have the drug	**18**	2	8	8
The robustness of evidence of effectiveness	**14**	2	1	6
Whether alternative treatments are available	**8**	0	3	2
What the impact might be on PCT budgets and therefore on the rest of the population's health	**7**	1	1	2
If there may be spin-off benefits from the research	**2**	0	1	0
The length of time it will need to be prescribed	**2**	0	1	0

The scores and therefore the order of importance was calculated as follows:

The Citizens Council listed as a group the factors they felt should be included as criteria when the NHS was deciding whether or not to pay premium prices for ultra orphan drugs. They then voted on each one, indicating whether or not they thought it was a valid criterion. They could vote yes, no or abstain.

They were then each asked to each list their personal first, second and third most important criteria. Each person's 'top' criteria got a score of three, the second most important got a score of two, and the third most important got a score of one. When these were ranked, the priorities were as listed above.

We then weighted the list, so that for each person who had voted against that criteria being valid at all, one point was removed. The order of the list remained the same. We weighted it further, so that each 'no' vote took two points away from the ranked criteria. Again, the order didn't change. At this stage, we were confident that the list reflected their priorities as a group.

As an additional way of seeing how their opinions developed, during the course of the meeting, a 'tracking survey' was issued to Council members on three occasions. They were asked to indicate the extent to which they agreed or disagreed with a range of statements - and where they could, to explain their reasons. These statements were compiled during the course of the research and discussions that Vision 21 had undertaken over the summer with a wide range of organisations and individuals. They were chosen because they provided a mixture of contrasting and overlapping views, and included a number of the frequently occurring statements that were put to us by people who had different perspectives on the topic.

Following the meeting, Vision 21 used this tracking survey to prepare graphs (included in the report) which show how the Citizens Council members' views changed during the course of their discussions.

Ruth Turner, Helen Bidwell, David Tyrer and Brendan Turner, Vision 21

PROGRAMME

Time	Session
Thursday 18 November	
9am 9.15pm	Welcome from Vision 21 Housekeeping, introductions, etc **First thoughts on Ultra Orphan Drugs** Group brainstorm on opinions, questions Council members have and want to ask, issues to discuss. An opportunity to hear and record instinctive thoughts. Issue the first of the 'opinion tracking polls'.
10.15am	**Andrew Dillon, Chief Executive, NICE** **a) Council business** - The Clinical Need and Age reports – what's happened? - Update on Confidential Enquiries - The evaluation and review of the Citizens Council - Retirement/Next year
10.45am	**BREAK**
11.15am	**Professor Sir Michael Rawlins, Chairman, NICE** **b) Ultra Orphan Drugs and NICE** - Why has NICE been asked to look at ultra orphan drugs? - What's so different about very rare diseases (children, hereditary, numbers involved)? - Why is this a dilemma for us? - What happens at the moment in the UK? (Europe/US)? - What other work is NICE doing to decide these issues? - What does NICE want to know from the Citizens Council?
12.00 noon	**The public and the industry perspectives: why does it all cost so much, and why does the public pay industry to develop these drugs?** **- Dr Rashmi Shah, UK representative, Committee for Orphan Medicinal Products – and Dr Frances MacDonald, Managing Director, Actelion Pharmaceuticals** - Why does it cost so much to develop these drugs? - Orphan drugs legislation and incentives
12.45pm	**LUNCH**
1.30pm	**Now we know some of the facts: what are the key ethical and economic issues at stake when these decisions are made? - Professor Carol Black, President, Royal College of Physicians, and Professor Stirling Bryan, Health Economics, University of Birmingham** Small group work using two case studies, and plenary discussion.
3.30pm – 4.00pm	**BREAK**
4.00pm – 5.00pm	**The national context – Dr Michael Gill, Chairman, National Specialist Commissioning Advisory Group**
5.00pm – 5.30pm	**Council members discussion – what do we think so far?**

5.30pm	**Tracking opinions** Give out second tracking survey End of Council sessions
Friday 19 November	
9am	Further thoughts? Council members all give a brief comment on what they think now; what issues they are struggling with; what else they need to know.
9.30am 10.15am	**Case study – Gaucher's Disease** **Professor David Barnett, Chair, NICE Appraisal Committee -** presenting the case study. PLENARY Case study discussions in small groups. What do they think? If they were there again, what would they do? Experts to be present during this session, each one to sit with one group, to listen and join in the discussions with Council members as appropriate. Experts available: **Dr Chris McCabe, Senior Lecturer in Health Economics, Sheffield University** **Linda Richfield, Senior Clinical Nurse Specialist at the Lysosomal Storage Disorders Unit of the Royal Free Hospital** **Dr David Meeker, President LSD Therapuetics/Genzyme** **Susan Lewis, co-founder, Gaucher's Association** **Susie Cohen, parent of a woman with Gaucher's disease**
11.15am	**BREAK**
11.45am	**Panel discussion with Council members**
1.00pm	**LUNCH** Issue third tracking survey form
2.00pm	**Council members – small groups** What do we think now?
3.00pm	**Public Health perspective:** **Dr Daphne Austin, Consultant in Public Health, West Midlands Specialised Services Agency and Paul Edmondson-Jones, Director of Improving Health & Quality, Portsmouth City Teaching PCT** The choices faced by PCTs and NHS Trusts: how do they decide what has to give when there are limited resources? Examples of different decisions taken: what did they do, and why did they do it?
5.00/5.15pm	Summing up, whole Council.
Saturday 20 November	
9.30am	**Answering the questions** Decision-making – what do the Council members think about the key issues and the supplementary questions?

	Using structured decision-making sheets, individually, then in small groups, then as whole Council, to make sure we have the detail needed – and the numbers/weighting/strength of feeling for each point.
12.30pm	**LUNCH**
1.15pm	Decision-making – confirm what recommendations should go in the report.
2.00pm	Final session – with Andrew Dillon
2.30pm	Finish

APPENDIX ONE – THE TOPIC PAPER

NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

CITIZENS COUNCIL

ULTRA ORPHAN DRUGS

Background

The discovery, development and manufacture of medicines is largely carried out by the pharmaceutical industry. Some potential new pharmaceutical products are initially discovered as a result of research in universities, research institutes or small venture capital companies. Their subsequent development and manufacture, is invariably undertaken by, or in partnership with, established pharmaceutical companies. The knowledge and expertise required to fulfil the requirements of national drug regulatory authorities, for the licensing a new medicine, is beyond the capacity of any university or healthcare system in the world.

The discovery and development of a new drug is now estimated to cost in excess of $800 million and may take more than to 12 years to complete. To recoup this investment, pharmaceutical companies seek peak annual global sales of $500million to $1 billion.

There is a strong tendency for the pharmaceutical industry to concentrate its research activities in areas where the return on its investment is likely to be high. Some of these common areas are shown in Table 1.

Table 1

Some common chronic conditions
(Affecting more than 25,000 persons in England and Wales)

Condition	Estimated numbers affected in the UK *	Drug costs (£) per person for a year's treatment
Asthma	5,100,000	~ 80
Indigestion**	2,392,000	~ 160
High blood pressure	16,000,000	~ 70
Angina	250,000	~ 15
Schizophrenia	260,000	~ 1,200
Parkinson's disease	106,000	~ 14

*The estimated numbers of people in the UK, with the condition, at any moment in time (known as the "point prevalence"). Note that not everyone with a condition will receive treatment – many may be unaware of their condition (for example, high blood pressure).
** Includes UK prevalence of gastric and duodenal ulcers, heartburn etc.

Orphan diseases and orphan drugs

Some diseases (known as "orphan diseases") occur so infrequently that under market conditions pharmaceutical companies would be disinclined to develop products for their treatment, due to lack of profit potential. In the US and (more recently) the EU, special

incentives are given to pharmaceutical companies to encourage investment in treatments (so-called "orphan drugs" for orphan diseases[2]). The preambles to the legislative instruments in both the US and the EU make similar points. The US Orphan Drugs Act (1983) states:

"It is in the public interest to provide incentives for the development of orphan drugs"

and the EU Orphan Drug Regulation (2000) states:

"Patients suffering from a rare condition should be entitled to the same quality of treatment as other patients".

An orphan drug is defined in America as one for which there are less than 200,000 patients with the disease; in the EU it is defined as one for which the frequency of the disease is less than 5 per 10,000 of the EU population[3]. Table 2 shows some examples of the more common orphan conditions.

Table 2

Some chronic orphan conditions
(affecting between 1,000 and 25,000 persons in the UK)

Condition	Numbers affected in the UK	Drug costs (£) per person per year's treatment
Haemophilia A (severe)	Less than 5,000	~ 35,000
Growth hormone deficiency (children)	2,900	~ 6,100
Chronic myeloid leukaemia	2,600	~ 25,000
Motor neurone disease	2,000	3,700

In both the US and the EU incentives are offered to pharmaceutical companies to develop orphan drugs. In both territories there is marketing exclusivity (for 10 years) which prevents *any* competitor gaining market access with the same medicine. In both territories the regulatory authorities offer assistance in the design of clinical trials; and they waiver their normal licensing fees. In the US (but not the EU) there is also tax relief and the possibility of access to ear-marked research grants fund. In the EU, tax relief is impossible, because decisions about taxation are made by individual member states; there is, however, the possibility of obtaining research grants from European Commission's research directorate, although their are no earmarked funds.

NICE has already appraised a number pharmaceutical products that have been granted "orphan drugs" status in the US or EU (or both). With one exception (beta interferon for multiple sclerosis) they were all considered "cost effective" (with a cost per QALY of around £30,000 to £35,000) even though the cost of their purchase was high (£5,000 per person per year or more).

[2] Orphan drug regulations have also been enacted in Australia, Japan and Singapore. Although they differ, in some respects, from the arrangements in the US and EU they are broadly similar in intent.
[3] The EU definition was expressed in this way, in 2000, so as to encompass the planned enlargement of the union

Ultra-orphan drugs

NICE has not, however, yet been asked to appraise medicines for very rare – ultra-orphan – diseases (so-called "ultra-orphan drugs"). Although there is no formal, or internationally agreed, definition of an ultra-orphan disease NICE uses the term for conditions occurring in less than 1000 people in the UK. In most instances there are just a few hundred sufferers in the UK. Table 3 shows some examples of these ultra-orphan diseases.

Table 3

Some chronic ultra-orphan conditions (affecting less than 1000 persons in the UK)

Condition	Product (type)	Numbers affected in the UK	Average drug costs (£) per person per year's treatment
Haemophilia B	Nonacog alfa (biotech)	380	35,000
Mucopolysaccharidosis Type 1 Hurler's syndrome Hurler-Scheie syndrome Scheie syndrome	Laronidase (biotech)	 68 39 22	 102,960 (child) 360,360 (adult)
Gaucher's disease (type 1)	Cerezyme (biotech) Miglustat (organic chemical)	270 (200 patients receiving treatment)	100,000 (average) Not available
Fabry's disease	Fabrazyme/Replagal (biotech) Miglustat (organic chemical)	80-200	36,249 (child) 126,880 (adult) Not available

Unlike "orphan drugs", "ultra-orphan drugs" pose particular problems:

1. Most are used to treat very rare, and very serious, hereditary disorders. Many appear in childhood.

2. The markets are very small and, to recoup the costs of the original research and subsequent manufacture, the purchase price is likely to be high.

3. Some of the drugs used to treat "ultra-orphan" diseases are biotechnology products involving complex, sophisticated (and very expensive) manufacturing techniques. Their purchase price will often be in excess of £100,000 per year per patient (see table 3). Although there may be compensatory savings as a result of the use of these treatments (because patients may not require symptomatic care) these do little to offset the costs of their purchase.

4. The evidence for the long-term effectiveness of ultra-orphan drugs will be limited at the time they are first launched.

Current NHS position

Primary Care Trusts, Health Authorities and Hospital Trusts currently make funding available for the majority of very expensive ultra-orphan drugs, though provision of the drugs across the country has sometimes been slow and variable. Not only are they expensive but, because these conditions are mainly hereditary, individual PCTs may have a cluster of affected patients in their area; whilst some specialist hospitals may carry a significant case-burden because of the expertise of individual members of their staff. This means that the cost of providing these drugs can fall unequally across the country, causing much greater strain on budgets in some areas compared to others.

This situation has recently changed for some ultra-orphan drugs. From April 2005, funding for some ultra-orphan drugs will be taken out of local budgets and these will instead be centrally funded for two years.

The dilemma

The dilemma facing policy makers is whether it is appropriate for the NHS to devote significant sums of money on the treatment of small numbers of patients.

On the one hand:

- Such people suffer two misfortunes. They not only suffer from a miserable disease; but it is so rare that either no-one will invest in finding cures or, if they do, society may not be prepared to pay for them.
- For such patients, these treatments may offer their only hope of leading reasonably normal lives;
- The total cost to the NHS will (for a single ultra-orphan disease) be about £20 million per annum. This represents less than 0.05% of the total NHS budget.
- With time, the price may fall as competitors enter the market.
- There is a real possibility, in the future, that “gene therapy” will make such treatments unnecessary. We may, therefore, be buying time: this will enable those currently receiving these expensive treatments to have the opportunity to benefit from future therapeutic advances. Gene therapy for Gaucher’s disease has started clinical trials (table 4).

On the other hand:

- Providing such expensive care to a small proportion of the population could reduce funding available to treat other diseases.
- Whilst the total sum spent in one ultra-orphan condition may be relatively small this will inevitably grow. Patients given these treatments will survive, instead of dying; and their number will grow as more children with these genetic defects are born.
- The number of ultra-orphan drugs, available to treat ultra-orphan diseases is likely to increase because of the current research programmes into finding effective therapies (see table 4).

Table 4

Ultra-orphan products in clinical development

Condition	Product (type)	Numbers affected in the UK	Stage of development
Hereditary tyrosinaemia (type 1)	Nitisinone (organic chemical)	34	Licence applied for
Congenital sucrase isomaltase deficiency	Sucraid (biotech)	35	
Pompe's disease	Pompase (biotech)	40-150	Late clinical trials
Maroteaux-Lamy syndrome	Aryplase (biotech)	12	Late clinical trials
Hunter syndrome	Idursulfas(biotech)	73	Early clinical trials
Nieman-Pick's disease Sandhoff's disease	OGT 923 (biotech) Miglustat (organic chemical)	Total = 150	Early clinical trials Late clinical trials
Gaucher's disease	GCR (gene therapy)	200	Early clinical trials

Question for the Citizens Council

The Council is asked to consider these issues and advise on whether or not the NHS should be prepared to pay premium prices for drugs to treat patients with very rare diseases.

Citizens Council Committee
September 2004

APPENDIX TWO - NICE CITIZENS COUNCIL MEMBERS 2004

- **John Baldwin** - an electrician who lives in Widnes, Cheshire.
- **Auriol Britton** - a singer who lives in Bristol.
- **Brian Brown** - an electrical engineer, from Chester-le-Street, County Durham.
- **Jennifer Brown** - a clerical officer who lives in Derby, Derbyshire.
- **Sylvia Brown** - a retired local government officer who lives in London.
- **Rod Crowshaw** - a store assistant who lives in Castle Bromwich, West Midlands.
- **Trevor Davison** - a supervisor scaffolder, who lives in Lincoln, Lincolnshire.
- **Geraldine Fost** - a retired careers guidance manager, who lives in Hungerford, Berkshire.
- **Marie Goorun** - a dressmaker and part-time French tutor who lives in Gillingham, Dorset.
- **Terry Hamer** - lives in Southampton. He works on the cruise ships at the terminal.
- **Mark Handley** - a project manager who lives in Kingston-upon-Thames, Surrey.
- **Susan Glendinning** – a part time actress and clerical assistant who lives in Cardiff, Glamorgan.
- **Lorna Girling** - lives in Norfolk, and is a part time literature student and a housewife and mother of two.
- **Robert Jones** - works as a warehouse operative and is a football referee in his spare time. He lives in Cwmbran, Wales.
- **Arun Jotangia** - lives in Bolton. Arun currently works in a post office, but used to be a hairdresser.
- **John Mahoney** - who lives in London, is a former foreign editor for the BBC and for ITN News at Ten.
- **Melanie McClure** - a mother of one who lives in Hebburn, Tyne and Wear.
- **Susan McNeill** - a secretary who lives in Market Harborough, Leicestershire.
- **Tony Messenger** - an insurance broker who lives in Windsor, Berkshire.
- **Sharon Morgan** - a milliner who lives in Birmingham, West Midlands.
- **Linda Moss** - currently unemployed, trained as a TEFL teacher and now lives in Todmorden, West Yorkshire.
- **Bob Osborne** - a retired former pilot who lives in Horsham, West Sussex.
- **Paul Pendlebury** - an assembly worker, who lives in Preston, Lancashire.
- **Lisa Spinks** - lives in Bradford, and is a communications operator for the police.
- **Heena Sabir** - worked for a while in human resources, and has recently moved to Huddersfield, where she is looking for suitable work.
- **Ian Simons** - a taxi driver, who lives in London.
- **Paddy Storrie** - a secondary school Deputy Headteacher, lives in Harpenden, Herts.
- **Fiona Taylor** - a legal assistant, who lives in Sidbury, Devon.
- **Peter Thomas** - a teacher, who lives in Rhondda, Cynon Taff.
- **Judith Ward** - a wood turner, who lives near Stoke on Trent, Staffordshire.

Arun Jotangia, Peter Thomas and Fiona Taylor were not able to be present at this meeting, and therefore the report cannot be said to represent their views.

APPENDIX THREE – SPEAKERS

The Citizens Council wishes to thank the speakers who gave generously of their time and expertise to help us in our discussions:

Dr Daphne Austin, BSc, MBChB, FFPHM
Dr Daphne Austin is a Consultant in Public Health working for the West Midlands Specialised Services Agency (WMSSA); a commissioning organisation funded by the 30 primary care trusts in the West Midlands area.

She undertook her medical training in New Zealand, having first completed a science degree. She trained as a public health doctor in the West Midlands region and has worked as a consultant in the region for the last 9 years, first in Worcestershire and more recently for the WMSSA.

For most of her public health career she has focused on hospital healthcare and specialised services in particular. She has expertise in the priority setting and the managed introduction of new treatments into the health service. She is one of a very small number of full time consultants in public health working in the area of specialised services.

Professor David Barnett, Chair of Appraisals Committee, National Institute for Clinical Excellence
Professor David Barnett is professor of Clinical Pharmacology at the University of Leicester Medical School. He is Honorary Consultant Physician at the University Hospital of Leicester NHS Trust with a special interest in cardiovascular medicine. He was previously a Non-Executive Director/Vice Chairman of the LRI NHS Trust and Chairman of the Specialist Advisory Committee for General Internal Medicine of the Royal College of Physicians (1996-2000) He has been Chairman of the Leicestershire District Research Ethics Committee and the Leicestershire District Prescribing Guide Committee. Professor Barnett is a member of the Medical Research Society and the Association of Physicians of Great Britain and Ireland.

Professor Carol Black, President, Royal College of Physicians
Carol Black first read history at Bristol University followed by a diploma in medical social work. During this year she was President of the Bristol Students Union. She entered medical school as a mature student in Bristol qualifying in 1970.

She trained in Bristol with Professor Alan Read, Professor of Medicine and soon found that rheumatology and Connective Tissue Disorders were to become her enduring interest. After Bristol she worked at Taplow with Barbara Ansell, and at the Postgraduate Medical School Hammersmith. Out of her clinical work sprang a research interest in systemic sclerosis, a disorder for which little could then be done. In time her unit at the Royal Free Hospital became the major centre for clinical care and research in Europe. In 2001 Professor Black was awarded the CBE for her work in this field.

In 1994 she became Professor of Rheumatology and was appointed Medical Director of the Royal Free Hampstead NHS Trust in 2000. Professor Black was elected to the Council of the Royal College of Physicians in 1996 and was elected Clinical Vice President in 1999. She is a Fellow of the Academy of Medical Science and a member of its Council. She is a member of the Modernisation Board, the Academic Board of the NHS University, the Imperial Cancer Research Fund Council, the National Specialist

Commissioning Advisory Group, the Scientific Co-ordinating Committee of the ARC, the Clinical Interest Group of the Wellcome Trust and the Postgraduate Medical Education and Training Board.. She has been Adviser to the Department of Health, and a member of the NICE Appraisal Committee. Professor Black has recently been elected Vice Chair of the Academy of Medical Royal Colleges.

Professor Black has lectured extensively abroad and has had particularly fruitful clinical and research collaborations with American colleagues. She has been given numerous Fellowships plus an Honorary DSc of the University of Bristol and a Companion of the Chartered Management Institute.

Professor Black enjoys long distance walking, running, music, especially opera, reading and renovating houses.

Professor Stirling Bryan
Stirling Bryan is a Professor in the Health Economics Facility within HSMC.

Other professional activities include:

- Director for the MSc in Health Economics and Health Policy.
- Co-Director of the University of Birmingham NHS SDO Programme Rapid Response Commissioning Group.
- External Examiner for the MSc in Economic Evaluation in Health Care
- Department of Economics, City University.
- External Examiner for the Health Economics Diploma, Centre for Health Planning and Management, Keele University.
- Peer reviewer for several academic journals, including Journal of Health Economics, Health Economics, Journal of Health Services Research & Policy and Social Science and Medicine.
- Peer reviewer for the monograph series, *Health Technology Assessment.*
- Peer reviewer for several research funding bodies, including, Medical Research Council, Economic and Social Research Council, NHS Health Technology Assessment Programme, NHS Service Delivery and Organisation Programme, NHS Research Methodology Programme, Department of Health Policy Research Programme, Wellcome Trust, and Health Foundation.

Susan Cohen
Susan is the mother of a young woman with Gaucher's Disease.

Andrew Dillon CBE, Chief Executive, National Institute for Clinical Excellence
Andrew Dillon joined the NHS in 1975. A period of time at The National Management Training Scheme was followed by a junior management post in Bolton and then a move to London in 1981. After a short period at Queen Elizabeth Hospital for Children, he spent three years at The Royal London Hospital before becoming Unit General Manager at The Royal Free Hospital in 1986. This was followed, in 1991, by his appointment as Chief Executive of St George's Healthcare, which became an NHS Trust in 1993. Andrew joined the National Institute for Clinical Excellence as Chief Executive on July 12th 1999.

Dr Paul Edmondson-Jones
Dr Paul Edmondson-Jones is a Consultant in Public Health Medicine and is the PCT's Director of Improving Health and Quality. Paul is responsible for the provision of public health leadership and support to the PCT and across the city. The responsibilities of his

Directorate are wide and include the lead for teaching PCT, clinical governance and GP education team as well as providing professional leadership on pharmaceutical and optometric issues. Paul gained wide experience in health service provision during his 21 years in the Army before joining the NHS locally in 2000, and has particular expertise around education.

Dr. Mike Gill
Mike has been a member of the National Specialist Commissioning Advisory Group since 1999, and its chairman since 2000.

He has been Regional Director of Public Health for the South East since 1999, having previously been Director of Public Health in Brent and Harrow and Riverside Health Authorities.

He is a member of the National Screening Committee, and chairs the group overseeing the rollout of the national newborn hearing screening programme.

He leads on initiatives to reduce excess winter and summer deaths, and was the main author of England's first Heatwave Plan, published this year.

He is a keen sailor, and has completed four transatlantic crossings, two with his wife and youngest son, then aged three.

Susan Lewis
Susan Lewis has Gaucher's disease and has suffered from the disorder since childhood. She helped start the UK Gauchers Association in 1991 and is a co-founder of the European Gaucher Alliance which includes membership of 24 European countries. Susan is also a Trustee of the Genetic Interest Group, an umbrella group for over 130 organisations representing a genetic condition in the UK.

Frances Macdonald
Frances graduated from Glasgow University, with a PhD in physiology, subsequently spending about 7 yrs in Scotland within Syntex's R&D site, in Clinical Pharmacology. Following a few years in European Regulatory Affairs, and as Pharmacoeconomics became more topical, Frances was asked to establish Syntex's European Health Economics group. After Roche acquired Syntex, she moved to Basel to initially head the European and subsequently the Global Health Economics group.

Moving back to the UK, in 2001, Frances established the UK/Ireland offices for Actelion, a small Swiss owned biopharmaceutical company, where she is now Managing Director. Actelion UK has a staff of about 20 people, and currently markets two orphan products.

Dr Chris McCabe
Chris McCabe is Senior Lecturer in Health Economics, Sheffield University. BA (CNAA), MSc (Newcastle upon Tyne)

Chris obtained his first degree in Economics from Middlesex Polytechnic followed by an MSc in Transport Operations from the University of Newcastle. He then worked for nine months in a commercial consultancy before joining the Health Economics Unit at the University of Liverpool, where he worked for three years. Chris joined ScHARR in April 1994. Whilst at ScHARR Chris has been responsible for leading the Trent Region

purchasing intelligence programme, the Working Group on Acute Purchasing. In addition, he has been responsible for a Health Technology Assessment of Neonatal Screening for Inborn Errors of Metabolism.

Chris is currently working on a national study of Neonatal Intensive Care provision, and a multi-centre trial of Nurse Practitioners and Junior Doctors in Pre-operative Assessment. He is also responsible for managing a number of pharmaco-economic studies.

Dr David P. Meeker, M.D., President, LSD Therapeutics
David Meeker joined Genzyme in 1994.

Dr. Meeker was medical director and then vice president, medical affairs, responsible for the development of therapeutic products including products in the current LSD portfolio prior to his promotion to senior vice president in 1998. In 2000 he assumed the position as business unit leader for Genzyme's lysosomal storage disease and Thyrogen® programs in Europe. In March 2003 he was promoted to president of the Global LSD Business unit.

Prior to joining Genzyme, Dr. Meeker was the director of the Pulmonary Critical Care Fellowship at the Cleveland Clinic Foundation.

He attended Dartmouth College and received his M.D. from the University of Vermont Medical School. Dr. Meeker completed an Internal Medicine residency at Beth Israel Hospital in Boston and a pulmonary/critical care fellowship at Boston University. He completed the Advanced Management Program at Harvard Business School in 2000.

Professor Sir Michael Rawlins, Chairman National Institute for Clinical Excellence
Professor Sir Michael Rawlins has been Professor of Clinical Pharmacology at the University of Newcastle since 1973. He is also Consultant Physician and Clinical Pharmacologist to the Newcastle Hospitals NHS Trust. He was Vice-Chairman (1987-1992) and Chairman (1993-1998) of the Committee on Safety of Medicines, and is currently Chairman of the Advisory Council on the Misuse of Drugs.

Linda Richfield, Senior Clinical Nurse Specialist at the Lysosomal Storage Disorders Unit of the Royal Free Hospital
The Royal Free Hospital is one of four national centres for the diagnosis and management of Gaucher's disease designated by the Department of Health through NSCAG (National Specialist Commissioning Advisory Group) from 1997. The Unit has recently received NSCAG designation for the diagnosis and management of Anderson-Fabrys disease and other lysosomal diseases for which there is treatment available.

The centre is primarily for adult patients. I lead a team of spedialist nurses working with Dr. Atul Mehta, Clinical Director of the service. I have worked within this sphere of metabolic haematology for over twenty years.

We manage the care of over 70 patients with Gaucher's disease, 57 of whom are treated with either Enzyme Replacement Therapy or Substrate Reduction Therapy. Not all patients with the condition require treatment however we still monitor them regularly to detect disease progression.

Our centre co-ordinates the care, assessment and follow up of over 100 patients with Anderson-Fabry's disease.

We also offer a screening and genetic counselling service.

In addition to our clinical services, an important role is in the education of both patients, their families and other health care professionals. We provide an annual three day R.C.P accredited course on Gaucher's disease for physicians from around the world.

Our service is audited on an annual basis. We contribute anonymised data to national and international databases on lysosomal storage disorders to increase the level of knowledge on the natural history of these rare conditions.

Dr Rashmi Shah
Dr Shah qualified in 1970 from the St Mary's Hospital Medical School in London and is a fellow of the Royal College of Physicians and a fellow of the Faculty of Pharmaceutical Medicine. He is also on the Examining Board of the Faculty.

He is a Senior Clinical Assessor at the Medicines and Healthcare products Regulatory Agency since June 1987. He has worked across a wide range of regulatory activities.

He is now the Principal Assessor to the government advisory committee responsible for approval of medicines and monitoring their safety. He also represents the UK interests at the Committee for Orphan Medicinal Products (COMP), Council for International Organisation of Medical Sciences and Organisation for Economic and Cultural Development.

He contributes extensively to drug regulatory activities at the European Union level. He also represents the EU at international level for specific drug safety issues.