Response ID ANON-G4DK-5RRX-U

Submitted to **Cancer Drugs Fund Consultation**
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Cancer Drug Fund Consultation: Page 1

1 Do you agree with the proposal that the CDF should become a 'managed access' fund for new cancer drugs, with clear entry and exit criteria?

Agree

Please provide comments to support your response::
1. Whilst we agree with the proposal set out in the question, we do not agree that the current CDF is not a 'managed access' fund.

1.1 We would argue it qualifies as a member, albeit a less mature member, of that class since the current fund shares the features of the fund proposed for the new model.

1.1.1 These are set out in the current (May 2015) Standard Operating Procedures (SOP) and are (the references below are not exhaustive):

(i) Entry criteria to access the fund: section B.4.5 of the SOP

(ii) A data gathering machinery: the Systemic Anti Cancer Therapy (SACT) dataset which since April 2014 has collected Real World (chemotherapy) Data (RWD) from all providers in England. Following the July 2015 NHSE:PHE agreement, this data is now able to be shared. The database currently contains data for 63,000 patients reimbursed via the CDF (Peter Clark, Chair of the CDF, in response to Q 62 at the Public Accounts Committee (PAC): 'Oral evidence: CDF' 30th November 2015).

(iii) An evaluation machinery: to assess the performance of drugs reimbursed via the fund using the data gathered (Appendix D: National CDF Prioritisation Tool)

(iv) A process to manage an exit from the fund: either into baseline commissioning or from future routine use in the NHS (SOP: section C.6.7)

1.1.2 As section 1 of the consultation notes, the various iterations of the CDF have managed entry into the fund and permitted more than 72,000 patients access to treatment.

1.2 The concern has been with whether management has been competent and use of the fund efficient joined at a later stage with a worries about whether its design was appropriate given nearly two years have been allowed to elapse since the expiry date (March 2014) envisaged for the fund.

1.2.1 The September 2015 National Audit Office (NAO) report of its investigation into the CDF was critical of the failure to gather data from the 2011 launch of the fund onwards despite the DH recognising this was necessary (NAO section 12).

The report was also critical of the failure of NHSE to activate any regular evaluation of drug:indication pairings reimbursed via the fund even though there has always been provision to do so throughout the fund's lifetime (NAO section 15 and section 4 p.5 CDF Consultation Guide May 2015).

Setting aside the two relatively recent exercises in late 2014 and 2015, the only re-evaluation that has occurred over the last five years was the precursor like exercise carried out to generate a single national list from the regional lists ready for the April 2013 launch of NHS England (the public facing name for the NHS Commissioning Board).

1.2.2 The 2015 Independent Cancer Taskforce report also concluded by implication that defects in its design and operation had resulted in the fund becoming a refuge that '...enabled some pharmaceutical companies to bypass NICE cost effectiveness arrangements' (section 5.3.3.1)

1.2.3 What the Taskforce appeared not to notice were the attempts made to address these and other emerging problems in the two recent (2014 & 2015) revisions of the SOP (for example: section B.3.1 of the 2014 SOP and section B.6.16 of the current SOP)

1.3 The consultation proposals seek to develop a more sophisticated model (and SOP design) in response with the NICE TA process introduced into, and integrated within, the model rather than running in parallel to it. Its role mirrors its traditional evaluation function and we welcome the introduction of a more developed approach than that embedded in the current SOP.

1.3.1 However the entry, evaluation (of real world data with reimbursement via a fixed, annual fund) and exit features of the current model remain in place. As with the other features, the funding element is simply a much more developed version of its predecessors.

1.3.2 Significant concerns remain about the capability, capacity and operational effectiveness of the SACT to fulfil the purpose intended for it.

Concerns are:

(i) It remains unclear if all chemotherapy providers in England will populate all the data fields in the SACT, in particular the Section 6 outcome fields (numbers: 37 - 42) and, even if this were to occur, doubts remain about the quality of the data submitted (see Peter Clark's reference to remaining 'problems' in his response to Q 62 at the November 30th PAC CDF oral evidence session)

(ii) Since Homecare medicines (and data associated with them) are not included in the SACT, coverage is not comprehensive.

Drugs for Chronic Myeloid Leukaemia (CML) fall within this category, including three of the five drugs available for the treatment of CML that are resident in the CDF, with increasing numbers of CML patients being covered by Homecare programmes.

(iii) The publication of SACT derived outcomes data will not include all the RWD data required by the Appraisal Committees in an Shortened TA since there are no fields that elicit vital data on adverse events and/or side effects.

(iv) In addition, the design of the SACT reflects, very understandably, traditional chemotherapy agents and treatment regimes. Here the focus is on cycles of treatment.

In contrast, the design of CML treatment regimes is built around daily usage over a patient's lifetime where there is a reasonable expectation that those patients obtaining an optimal response will survive to average or near average life expectancy. In most cases treatment duration is measured in decades not weeks or months.

(v) For an increasing number of CML patients, treatment regimes now involve a de-escalation of dose at some stage assuming an optimal response has been obtained and maintained over the long term. Although there is a SACT 'Regime Modification - dose reduction' data field (number 38), its design is not appropriate since the assumption is that dose reduction is an entirely toxicity, rather than efficacy, driven strategy. This is not to deny this applies to some CML patients but it certainly does not to all.

1.4 What puzzles us is that there is no mention of the fund being available for categories other than 'new cancer drugs' and that our agreement, or otherwise, is not being sought on the use of a fund for drugs in these categories.

1.4.1 Some qualifying patient populations for reimbursement via the fund include those for whom the fund functions in a manner that does not accord with the features of a managed access fund.

For example, the patient population that continues to have their drugs reimbursed even though these drugs have been removed from the fund following a re-evaluation exercise where these drugs are no longer available for routine use in the NHS.

1.5 It should not be forgotten that a fixed budget fund is not a member of a class of 'necessary and sufficient conditions' for the development of a managed access or managed entry agreement (MAA and MEA respectively) scheme. Its quite possible for an MAA/MEA to operate without a dedicated fund and operate successfully as for example with the time limited MEAs operative in Italy.

1.6 Finally, the deployment of a fund with a fixed annual budget in its design carries inbuilt demand driven tensions which require high levels of accurate prediction to be available for use in mitigation together with a commitment to flex to meet demand.

1.6.1 We remain unconvinced that these conditions are present within the new model as our answers to other consultation questions will detail.

2 Do you agree with the proposal that all new cancer drugs and significant new licensed cancer indications will be referred to NICE for appraisal?

Disagree

Please provide comments to support your response::
2. The category 'new cancer drugs' clearly refers to cancer drugs that have yet to emerge from the licensing process with a positive CHMP opinion but it remains entirely unclear which drugs would qualify as being members of the class 'significant new licensed cancer indications'.

2.1. The lack of clarity is magnified by slight differences in the wording in two sections of the consultation. Section 18 is as above and accords with the proposed NICE Process guide amendment (section 2.3.3 of the guide) yet section 22 refers to 'significant license extensions for existing drugs'.

2.2. Ten weeks after the consultation document's publication date and three weeks before consultation closure, a Q & A document was jointly published by NHS England & NICE and contains, in an answer to Q6, this sentence:

'It may be that NICE does not consider that an indication requires a full Technology Appraisal, and might channel it through another part of NICE.'

As with so much of the wording in the consultation it remains dazzlingly unclear what this phrase might mean.

2.3. One possibility could be that entry into the other NICE appraisal route, the High Specialised Technologies (HST) Programme, would be possible for cancer products.

Currently there is an informal bar on cancer products entering HST confirmed by NICE representatives at the 'Topic Selection Stakeholder Event: Orphan Drugs & Rare Diseases' meeting held, and hosted by NICE, on 15th October 2014.

If the reference in the same Answer to 'arrangements for this are still to be developed' refers to both the lifting of the bar and the long delayed consultation on what are interim arrangements for HST, we would warmly welcome both being brought forward at speed.

2.4. However the Q 6 Answer phrase 'another part of NICE' might also refer to the NICE evidence summaries programme.

Although we think this programme has merit we have reservations about the possibility of any of its outputs being regularly adopted for routine use in the NHS.

Evidence summaries do not have the status of formal NICE guidance and more pertinently do not carry any statutory support to enforce commissioning.

They are, as their title indicates, simply evidence summaries with an overwhelming focus on an analysis of the available clinical evidence that would support a product's use in the NHS.

The programme currently lacks provision for economic analysis.

Although of course establishing the cost of a medicine, rather than gathering and analysing evidence for its cost effectiveness, is included.

2.5. We are therefore unable to agree with the proposal because, at present, its scope remains unclear as to which drug:indication pairs would, and would not, be appraised.

2.6. However we would stress that we agree with the proposal that all new cancer drugs that have yet to emerge from the licensing process with a positive CHMP opinion should be referred to NICE for a technology appraisal.

3 Do you agree with the proposal that the NICE Technology Appraisal Process, appropriately modified, will be used to evaluate all new licensed cancer drugs and significant licence extensions for existing drugs?

Agree

Please provide comments to support your response::
3. We agree with the proposal about what the NICE TA process should evaluate although 3.6. below adds a caveat to our decision.

3.1. However we do not agree that the revisions to the Process and Methods guides set out in the consultation document amount to an appropriate (modificatory) response to meet the challenge which is briefly described in section 2 of the consultation document and more pertinently and fully explored by Prof. Sir John Bell in his (Annex A) contribution to the 'Accelerated Access Review: Interim Report'.

In essence, the argument is that advances in the life sciences driven by genomics and digitalisation represent a paradigmatic shift for drug research and development that requires an at scale, government supported, response across the full 'bench to bedside' spectrum.

An example of the perils of a lack of a co-ordinated response is set out in last summer's influential Scott Ramsey's Health Affairs paper 'How State And Federal Policies As Well As Advances In Genome Science Contribute To The High Cost Of Cancer Drugs' Health Affairs: 34, no.4 (2015):571-575

If a sustainable solution to access to cancer drugs, and indeed all drugs, is to be developed fundamental reforms will have to be introduced to both regulatory and evaluation processes that render them both more flexible in their operation and pragmatic in their evaluation.

3.1.1 Currently the commitment to reform appears much more evident in the regulatory than evaluation sphere. The MHRA's Chairing and involvement in the 'Expert Group on innovation in the regulation of healthcare' is one broad based example with the agency's development of the Early Access to Medicines Scheme (EAMS) being a specific example of a related process output.

3.1.2 The relevant Minister, George Freeman, has also repeatedly referenced the need for change as the two Hansard entries below demonstrate:

'However, the rapid development of breakthroughs in genomics, informatics and new diagnostics means that NICE's processes will have to adapt' (Adjournment debate on NICE Technology Appraisals 1st September 2014 Col 142)

'The genomic and informatics revolution will require NICE to change how it works. The explosion of progress in this field is what has put so much pressure on the CDF.' (Westminster Hall debate on cancer drugs 20th October 2015 Col 286WH)

3.2 An indication of the particular issues facing anti cancer agents within the NICE TA process is the higher percentage of negative recommendation decisions awarded by appraisal committees (32%) in the period March 1st 2000 to December 31st 2015 relative the percentage of negative recommendations for all appraisal decisions (15%) over the same period https://www.nice.org.uk/news/nice-statistics

Commenting on this phenomenon Andrew Dillon observed (his response to Q 103 at the November 30th PAC CDF oral evidence session): 'There is clearly something about cancer drugs at the time we were appraising them that separated them out from other treatments'.

Our argument is 'that something' was not that these drugs, which incidentally had all been judged clinically effective enough by the EMA to obtain a market authorisation, had somehow, and suddenly, proved clinically ineffective but rather it was 'that something' must be related to the methods and processes deployed by NICE to evaluate anti cancer drugs.

3.3 NICE to date has made no substantive move to adapt to these changes beyond offering warm words on a willingness to reform and some strictly exploratory activity that covers the relevant issues, often on a cooperative basis.

Examples include: (i) membership of the Technology Strategy Board (now Innovate UK) hosted 'Stratified Medicine Innovation Platform' programme (ii) involvement in the MIT NEWDIGS programme (iii) the Janus programme (a NEWDIGS offshoot) (iv) the EU funded Get Real project (iv) their decision to set up an Innovation Office.

3.4 In particular there has been no suggestion or proposal made to revise (the evidence) section 3 of the Methods guide especially the hierarchy of evidence tree which places a classically designed randomised control clinical trial (RCT) at its apex.

3.4.1 Appraisal committees remain the ultimate decision makers. Committees working with the arrangements proposed would still be considered exemplary in their conduct if they argued that data from the clinical trial evidence remained the most plausible form of evidence on which to base their decision making assuming there was an absence of any key corrupting design issues.

3.4.2 We are not suggesting RCTs should be disregarded but rather there should a more contemporaneous approach taken which recognises the need for the evaluation machinery to keep pace with scientific development by periodically making the necessary adjustments required.

3.5 Our concerns are encapsulated in, and better championed by, Professor Sir Michael Rawlins in his 'What Constitutes Credible Evidence of Effectiveness' 2012 lecture to the OHE .

In particular he called for rigid evidence hierarchies to be replaced with a more pragmatic approach.

Even though some three and a half years have elapsed since the lecture, the topics he addressed are even more pertinent today than they were then.

3.5.1 We would argue a particular focus point should be the relentless fragmentation of what are/were once tightly (ICD) defined patient populations into ever smaller sub groups of patients often biomarker identified.

This renders traditional differentiation of the cancers into the 'Big Four' (or 'more common') and rare ('less common') increasingly meaningless whilst also posing difficulties, methodological and otherwise, for regulators and evaluators to accommodate to.

3.5.2 The evaluation body in Scotland (SMC) has recognised the need for a response to ensure it remains fit for purpose. They have adjusted their approach and have done so by offering what amounts to different access routes for the evaluation of non orphan, orphan, ultra orphan products whilst also making an accommodation for End of Life, unmet need and Burden of Illness.

This approach is markedly different from the current NICE response offer of more comprehensive coverage (all new cancer drugs) and an additional recommendation category (recommended for use within the CDF).

The SMC is accepting of greater uncertainty being present as the target patient populations for the different classes of drugs decrease in size. Just as it accepting of a higher cost per QALY, although not one without limit, for a much expanded set of criteria than those operative in England.

3.6. The wording in the question does not include 'significant new licensed cancer indications' and instead refers more restrictively to 'significant license extensions for existing drugs'.

As noted in our response to Q2 the former is the wording that appears in the amendment to the NICE Process Guide.

What is and is not to be subject to evaluation by a NICE TA requires clarification rather than obfuscation.

Unfortunately the latter seems to be approach taken and we are surprised an organisation like NICE, who pride themselves on their attention to detail and rigorous approach, have agreed to be a party to a publication where the pursuit of a lack of clarity seems to have been granted an almost objective like status.

4 Do you agree with the proposal that a new category of NICE recommendations for cancer drugs is introduced, meaning that the outcome of the NICE Technology Appraisal Committee's evaluation would be a set of recommendations falling into one of the following three categories:

Agree

Please provide comments to support your response::
4. We welcome the addition of the proposed new category of NICE recommendations for cancer drugs.

4.1 However we think it reasonable to expect that the consultation document would include a comment on the relationship between the four types of decision recommendation that can currently be made by Committees and the proposed new category.

4.2 In particular the recommendation 'for use only in the context of a research study' which, although little used by Committees (5% of anti cancer agent appraisal decisions between March 1st 2000 & December 31st 2015 https://www.nice.org.uk/news/nice-statistics), nevertheless has an obvious and close affinity with the new category.

4.3 It remains uncertain if there is an expectation that a similarly small percentage of decisions will be made by Committee use of the new category. It also remains unclear, although the question seems to imply, if the restriction to three rather than five categories would replace those decisions for whom an 'only in research' decision might have previously been made.

4.4 Set against this view is NHSE thinking which seems to be that the new category '...will be where quite a number of these new drugs will end up' (Simons Stevens' Q 84 response at the November 30th PAC CDF oral evidence session).

4.5 A more nagging worry concerns the factors to be considered for the award of the new recommendation category (section 31)

4.5.1 Two of the three factors are clinical and cost effectiveness related.

The former would, assuming a grant of marketing authorization was forthcoming and the CHMP opinion published remains congruent with the indication submitted by the company, be sufficient to warrant a status of ‘clinical promise’ being ascribed which would in turn provide a parameter within which ‘the extent and nature’ (section 31) of uncertainty could be discussed.

Similarly, discussions of the modeling developed by both the company and ERG or assessment group would presumably, although perhaps more contentiously, establish if the emerging ICER value had the ‘potential to lie within‘ (section 31) whichever threshold range was applicable.

There is a developed history, and even a culture, that is available to inform and assist those involved in navigation on these issues.

4.5.2 However, this is not present for the (section 31) data gathering component. This criteria seems to posit that the only pertinent issue for discussion concerns the feasibility of delivering the data required within the (24th month) timeframe imposed.

We would argue there are other issues in play which should be the subject of discussion and therefore be incorporated either as additional factors or through the expansion of the existing factors. These are:

(a) The availability of patient numbers in England to meet the requirement defined by the Appraisal Committee as sufficient for data gathering.

For drug:indication pairings for lines of treatment distant from first for cancers that themselves fall within informal definitions of rare cancers, recruiting the number of patients required would present a major, if not impossible, challenge
to meet.

For ponatinib, for example, the total qualifying patient population for ALL its licensed CML indications is estimated to be 84 (NICE Batch 33 Block Scoping Report. Item 5.4
https://www.nice.org.uk/media/default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/Block-scoping-reports/Batch-33-block-scoping-report.pdf)

For bosutinib the total annual qualifying patient population for ALL its licensed CML indications is estimated to be 75 (the NICE 2013 Costing Statement https://www.nice.org.uk/guidance/ta299/resources/costing-statement-426809053).

(b) The design of the data gathering exercise:

We assume the most accurate description available would be that this would be an audit like activity.

We assume that the nearest technical equivalent to what is proposed would be a some variant of a longitudinal observational study rather than a clinical trial.

It therefore follows that comparator treatments would/might not be available or considered including those that fall within the Best Supportive Care category.

We remain unsure how a Committee would deliberate faced with a proposal akin to an observational study that was sophisticated in its design but included a (not unusual) duration of considerably more than 24 months where a reduction of its duration to 24 months would introduce a corrupting factor into its design.

(c) We also note in the Answer to Q 5 in the Q & A that it now seems proposed that other, and diverse, sources of data would be accepted for consideration at the process endpoint, the Shortened TA.

It remains unclear how Committee decision making would proceed should a company argue that other evidence gathering activity elsewhere that fell within the categories described in the Answer to Q5 obviated the requirement to engage in the same or similar data gathering activity in England.

(d) The emergence of another recommendation ‘gap’ due to the over rigid application of the (section 31) three factors.

The exclusion of drugs that demonstrate clinical effectiveness yet meet neither of the three factors nor carry sufficiently low levels of uncertainty to enable committees to settle on a ‘recommended for routine use’ decision.

Using the CML drug:indication pairings currently resident in the CDF as an example, we remain unsure if any would qualify for the ‘recommendation for use within the CDF‘

* Ponatinib, in particular, might be refused entry because sufficient numbers of patients might not be able to recruited to meet the population size set by the Appraisal Committee.

* The same applies for bosutinib although a carry over of pre-existing TA difficulties with ICER values may also result in disqualification on ‘potential to lie‘ within the standard range grounds.

* With dasatinib, as with the other two drugs discussed above, 24 months may not prove sufficient to permit the accumulation of data on intolerance based adverse events.

This is an area where data quality issues are acknowledged to be present especially amongst chemotherapy providers lacking specialist experience in the treatment of CML.

5 Do you agree with the proposal that “patient population of 7000 or less within the accumulated population of patients described in the marketing authorisation” be removed from the criteria for the higher cost effectiveness threshold to apply?

Disagree

Please provide comments to support your response::
5. We disagree unless the higher cost effectiveness thresholds mentioned in the question are made available, on the same population neutral basis as the proposal, to other populations that were the target of the ‘new approach’ noted in section 3 of the consultation document.

5.1. To withdraw a commitment to develop methodologies that would address issues that were the focus of ‘value based pricing‘ simply because difficulties were encountered speaks more to the absence of political will rather than the presence of insuperable problems.

5.1.2. There is no overt commitment in the consultation proposals to address unmet need, burden of illness, the non health benefits of a treatment or the award of breakthrough (innovation) status.

We find this complacent, defeatist and, despite protestations to the contrary, at variance with what section 8 of the consultation document refers to as ‘the emerging conclusions of the AAR.‘

5.1.3 Focusing on the area considered to be the most difficult by evaluators; the non health benefits of a treatment (rendered in the last half decade as Wider Societal Benefit or Impact) are being propelled forward as worthy of attention and evaluation because of the steady increase in (over ten years) survival enjoyed by ever more cancer patients.

Unlike the SMC, NICE lacks a mechanism to accommodate this factor and seems disinclined to introduce one.

5.2. Setting that to one side; we can understand the ‘redundancy’ logic deployed in the proposal but we are surprised our views have not been solicited about the other End of Life amendments mentioned in section 29 of the consultation document which grossly describe the changes to sections of the Methods guide set out in Appendix of the consultation document.

5.3. More generally, we remain concerned at the perverse incentive offered to pharmaceutical companies by this modulating factor when considering their drug development strategies.

5.3.1. Rational economic decision making on their part would surely lead them to conclude that they should focus their efforts on developing drugs capable of extending life at the end of life by a minimum of three months to meet (and trigger the pricing opportunities made available by) the very significant increase (the maximum available weight is 1.7) in the ICER threshold on offer.

5.3.2. This does not seem to align with the core proposition underpinning the new five year strategy for cancer which is that the strategic focus should be on the earliest rather than latest (end) disease stage since this is the stage where intervention is most likely to result in the most beneficial outcomes (as traditionally measured).

5.4. All three CML drugs with drug:indication pairings resident in the current CDF are capable of conferring an extension of life to near average life expectancy. It seems to us, and to many specialist CML clinicians, the current situation is truly bizarre since it amounts to a price paid penalty for companies developing life saving, as opposed to life extending at the end of life, drugs.

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6 Do you agree with the proposal for draft NICE cancer drug guidance to be published before a drug receives its marketing authorisation?

Agree

Please provide comments to support your response::
6. Yes, we do agree with the proposal that draft guidance be developed before marketing authorization is granted.

6.1. However the proposals set out in the consultation document (section 19) and Process guide (section 2.3.3) make it clear that publication of the draft guidance would occur after, not before, a drug receives its marketing authorization.

6.2. In addition it remains unclear who would be party to a decision to initiate ‘further Appraisal Committee discussion‘ should the CHMP opinion be ‘substantially different from the indication provided in the company submission‘ (both 2.3.3 Process guide) or indeed what ‘substantially‘ might amount to.

6.3. As elsewhere, and repeatedly, in this consultation, the provision of more detail would have allowed us to pronounce our agreement with more certainty and with less use of caveats.

7 Do you agree with the process changes that NICE will need to put in place in order for guidance to be issued within 90 days of marketing authorisation, for cancer drugs going through the normal European Medicines Agency licensing process?

Agree

Please provide comments to support your response:
7. Yes, we agree with the process changes but we do not think the timeline put forward feasible.

7.1. The NICE Process guide time lines set out for scoping followed by either an STA or MTA to a point equivalent to that proposed in the question would involve very significant levels of compression.

This, even after allowing for the bypass of process elements that the commitment to automatically refer, minimally, all new cancer drugs for appraisal removes.

7.2. Section 3.1.4 of the Process guide notes the various time lines, set out in Figs 4 and 5 for the STA and MTA process respectively, represent the '..minimum number of weeks for each stage of the appraisal process'.

7.3. The number of weeks cited for the development of the scope and assembly of the block scoping report is 18 (Fig 2 of the Process guide). Assuming each week amounted to five working days, the total number of days would be 90.

7.4. The number of weeks taken to pass through the various stages of the STA & MTA processes to reach the point where the appraisal committee meeting to develop the ACD (or FAD) had been completed is 21 and 37 weeks respectively. Making the same assumption as the scope, this would amount to 105 and 185 days respectively.

7.5. Even when an allowance is made for a reduction in the number of working days allocated to scoping to accommodate for the redundancy of some elements because of the amendment introduced in section 2.3.3. of the Process guide, we would argue these minimum time lines would be highly demanding to meet for an STA and impossible to meet were an MTA initiated given the 90 day allocation proposed for completion of the equivalent stages.

7.5.1 MTAs should not be considered some occasional NICE activity. Statistics published by NICE for anti cancer drug TAs for the period 1st March 2000 to December 31st 2015 note MTAs (at 89) were in the majority compared to STAs (at 76) https://www.nice.org.uk/news/nice-statistics

7.6. The consultation document is silent on this issue. It should not be.

8 Do you agree with the proposal that all drugs that receive a draft NICE recommendation for routine use, or for conditional use within the CDF, receive interim funding from the point of marketing authorisation until the final appraisal decision, normally within 90 days of marketing authorisation?

Agree

Please provide comments to support your response:
8. Yes, we agree with the proposal.

8.1. We also agree with the commitment set out in section 52 of the consultation document that all patients:

'...receiving treatment funded through the CDF on 31st March 2016 will continue to receive treatment until the point that they and their consultant agree that it is appropriate to stop'

8.2. We assume, to ensure the maintenance of a rational approach and equity of access, this commitment would extend to any application made on behalf of a patient that meets the relevant criteria during the period between 1st April 2016 and the conclusion of the transition process for a current list CDF drug:indication pairing.

8.3. For the avoidance of doubt we assume that, should the appraisal recommendation be negative, these patients would continue to receive treatment on the same basis as that set out in section 52.

8.4. To argue that any comment on the transition arrangements be excluded from this consultation makes little sense given their effect on the fund's budget after 1st April 2016.

8.5. We also note that some answers to questions posed in the consultation Q & A cover the re-consideration of drugs in the current CDF (Q: 1, 6, 9, 18). We think it fair that, since NHSE & NICE have granted themselves permission to comment on the transition, this should be extended to respondents.

8.6 Finally we assume the wording in the row, 'Recommended for routine commissioning', and column, 'Effect for new patients', in the 'Guidance within 90 days of grant of Marketing Authorisation' table, in Appendix A of the consultation document, will be adhered to.

9 What are your views on the alternative scenario set out at paragraph 38, to provide interim funding for drugs from the point of marketing authorisation if a NICE draft recommendation has not yet been produced, given that this would imply lower funding for other drugs in the CDF that have actually been assessed by NICE as worthwhile for CDF funding?

What are your views on the alternative scenario set out at paragraph 38, to provide interim funding for drugs from the point of marketing authorisation if a NICE draft recommendation has not yet been produced, given that this would imply lower funding for other drugs in the CDF that have actually been assessed by NICE as worthwhile for CDF funding:
9. We have already expressed doubt in our response to Q 7 that the commitment to complete the stages of the initial appraisal process as set out within 90 days is feasible.

We believe this to be an ambition aspired to rather than a likely reality described.

9.1. It follows that the alternative scenario amounts to a default scenario unless it is proposed that access between the time marketing authorization is granted and the initial appraisal stage being completed be unfunded.

9.2. However the 'lower funding' implication referred to is already present in cases where a 'draft recommendation for routine commissioning' eventually becomes a 'not recommended' decision within 90 days of market authorization being granted.

In this case, the funding would represent a scenario where it emerged that resources had, after all, been wasted whereas, in the scenario described in the

question, this possibility would yet to have become apparent.

9.3. That said, we agree that the alternative scenario would amount to an additional pressure on the fund's budget to those that already exist including the scenario described in 9.2 above.

9.4. An additional concern here is that there is a possibility that the delay referred to could be the result of process inefficiencies.

9.4.1 The consultation document makes it clear, for example in section 21, that failure to meet deadlines will result in the application of penalties to non compliant companies. There appear, however, to be no similar proposals should the evaluator fail to meet a process deadline.

9.4.2 We accept the difficulties present that would enable a distinction to be made between non compliance that was volume driven as opposed to that which is a consequence of organizational inefficiencies but this does not devalue the point made.

9.4.3. One solution would be for an annual allocation above that detailed in the August 2015 DH:ABPI ' Addendum to the 2014 PPRS' to be available as a resource to relieve this particular budget pressure.

This would surely act as an incentive for the public bodies involved to purge any inefficiencies from the process.

The precedent for an increase in budget allocation is already established, even though no rationale has been offered, in the additional £20M allocation to the 2016/17 CDF budget (Annex section 2.3 : DH 'Government's Mandate to NHSE for 2016/17).

9.5. The 'lower funding' reference to drugs already possessing a recommendation that permits access to the fund for their reimbursement would already be operative were the budget to either ignore demand, underestimate it or be otherwise constrained.

Deployment of the investment control mechanisms represents the real time delivery of 'lower funding' yet leaves unaddressed these other issues.

10 Do you have any comments on when and how it might be appropriate for the CDF in due course to take account of off-label drugs, and how this might be addressed?

Do you have any comments on when and how it might be appropriate for the CDF in due course to take account of off-label drugs, and how this might be addressed:
10. We would advocate that the CDF be made available as a reimbursement resource for off label drugs once a suitable machinery is designed to achieve this goal.

10.1. There are currently a significant number (9 of the 48 national list members) of off label drug: indication pairings reimbursed via the CDF.

10.1.2. To date no plans have been published that include them in the transition process and we can only assume funding through the CDF will no longer be available to new applicants after 1st April 2016.

10.1.3. We recognize the provisions set out in section 52 of the consultation document extends to patients being treated with off label drugs.

10.4 We accept the exclusion of non licensed products (and therefore off label usage) from the NICE TA process.

10.5 NICE already has a set of procedures in place to provide an evidence base for off label usage (described in NICE paper 'Evidence Summaries:unlicensed and off label medicines - integrated process statements'). The end product is the publication of an 'Evidence Summary: unlicensed & off label medicine' (ESUOM).

10.6 However, a ESUOM is not supported by any funding requirement of which the most compliance inducing is the statutory support given to positive NICE TA recommendations neither does a ESUOM qualify for formal NICE guidance status.

The most appropriate description of their status would be that ESUOM's are available as an evidence based information resource should an NHS organization wish to make use of them as an aid to inform decision making.

It would be an understatement to say this falls some way short of the status accorded to current off label CDF members.

10.7. We would advocate that, in the interests of equity with other list members, current CDF off label national list members be channelled down this alternative NICE route with process completion matching the 2016/17 deadline set in section 51.

10.7.1. Those emerging with a positive ESUOM would move to baseline commissioning joining the many other off label class members already in routine use in the NHS, many of which lack a ESUOM.

10.8. Regarding proposals for new candidates for this class, we would advocate the same route be made available but this process be linked to revisions to the relevant Generic Commissioning Policy which would be 'Experimental & Unproven Treatments'.

10.8.1. Consultation for the suite of interim Generic Commissioning Policies has been subject to persistent delay since the initial autumn 2013 date set and we would advocate for an across the board consultation on all these policies rather than this be confined to the policy mentioned above.

10.8.1.1 In particular, we would want a consultation on Individual Funding Requests (IFR) brought forward since we are concerned that only passing reference is made to CDF IFRs in the consultation document. No indication is given if they will remain semi detached from the mainstream IFR policy and process in an

environment where integration underpins most revising efforts.

10.8.2 We would also advocate that a similar allocation to that set out in 9.4.3 of our Q9 response be made to fund movement through whatever machinery was devised to support the generation of a ESUOM via a twinning arrangement with the commissioning policy named in 10.8.

10.8.3 Any positive ESUOM output from the process would move to baseline commissioning only after discussion with the manufacturer about an appropriate discount that would reflect its lack of a license and the unanticipated revenue source that had potentially become available.

10.8.4. The NHSE negotiating position would be enhanced by its near monopoly of purchasing in England and would be further finessed once the relevant pharmacy and procurement reforms advocated by Lord Carter were implemented.

Cancer Drug Fund Consultation: Page 3

11 Do you agree with the proposal to fix the CDF annual budget allocation and apply investment control mechanisms within the fixed budget as set out in this consultation document?

Agree

Please provide comments to support your response::
11. Yes, we agree that an annual budget be fixed for the CDF and we agree that, as with the prudent management of all budgets, consideration should be given to appropriate measures to control budgets before they are made available for expenditure to be set against them.

11.1 However, there is a default requirement that any particular budget set should reflect the likely demand placed upon it. To secure operational effectiveness, there should also be a commitment to a companion exercise to establish the level confidence in the forecast that a particular allocation would meet anticipated demand.

Finessing current horizon scanning arrangements, particularly through using data generated as a result of the roll out of digital technology throughout the NHS, should result in forecasts which enjoy higher levels of confidence than exist at present.

11.1.2 One, but not the only, consequence of not undertaking the exercises listed in 11.1 is a loss of public and stakeholder confidence in the process with the end-result being the devaluation of the status of the public bodies involved.

11.2. Since no details are provided in the consultation document it remains unclear if relating likely demand to an annual budget is to be considered. We note, in contrast, the attention given to relating demand to the capacity of the evaluation process to meet it is considerable (see for example: sections 21,33,38 of the consultation document)

11.2.1 As our 9.4.3 response to Q9 indicates we are aware of the maximum CDF expenditure figures over each of the remaining 2014 PPRS years set out in the main body of the Addendum text as we are of the additional allocation agreed for the 2016/17 CDF budget.

11.2.2 Should a decision be made that no consideration be given to matching budgets to demand with subsequent adjusting allocations being agreed, then the investment control mechanism would be exercised to whatever degree it was judged was necessary to remain in budget.

It is therefore entirely possible that the reimbursement price for the data gathering population might be very considerably, and negatively so, distant from that agreed in the Commercial Access Arrangement (CAA).

It would be hard not to disagree with the conclusion that this might deter companies from entering the evaluation process given they would be unable to establish, pre entry, if their product would be recommended for entry into the fund for the data gathering period.

11.3. As with our comment on the Q9 ‘alternative scenario’ proposal, the assumption seems to be of an NHSE budgetary machinery functioning at 100% efficiency.

11.3.1. We would propose that the historical record suggests this to be a wildly optimistic assumption. The NAO report of its investigation into the CDF supports our view.

11.3.2. An example:

Simon Stevens NHSE CEO in response to a question (Q 116) at the PAC 30th November 2015 CDF oral evidence session gave a ‘run rate budget position of about £340 million going into 2016/17’ for 2015/16 CDF expenditure.

The January 2016 NHSE board finance paper set out a 2015/16 Month 8 CDF overspend figure of £81 million which accounted for the vast bulk of the £95.4 million specialised services overspend at that point.

The NHSE forecast expenditure overspend for 2015/16 for specialised services, which includes the CDF, is £81.5 million.

Its entirely reasonable to conclude that a majority of the £81.5 million overspend would be CDF related, which given the annual CDF budget figure of £340 million, makes Mr Stephens run rate projection of £340 million for 2015/16 wildly optimistic.

11.4 Given the situation described in 11.3.2, we would argue that the £340 million budget for 2016/17 is grossly inadequate to meet the likely demand placed on it when consideration is given to the scale of reimbursement for various classes of drug:indication pairings involved.

Given also the determination to remain in budget, we remain perplexed as to how the fund will be managed in the 2016/17 financial year.

12 Do you consider that the investment control arrangements suggested are appropriate for achieving transparency, equity of access, fair treatment for manufacturers and operational effectiveness, while also containing the budget? Are there any alternative mechanisms which you consider would be more effective in achieving those aims?

Do you consider that the investment control arrangements suggested are appropriate for achieving transparency, equity of access, fair treatment for manufacturers and operational effectiveness, while also containing the budget? Are there any alternative mechanisms which you consider would be more effective in achieving those aims:
As worded, this places a numerous in number and diverse in focus burden of remits on the investment control arrangements whose more routine and core function is budget containment. Taken individually, the achievement of:

Transparency:

As with so much of this consultation, there is no detail provided and no draft of the SOP to refer to allow what is to be made publicly available and what will remain confidential to be established (in contrast, current SOP examples are Appendix G: 4.1 & 9.3).

This is a bewildering question to pose given the almost complete lack of detail of much of what is proposed.

Equity of access:

As we have noted in our answer to Q 1, a time limited, fixed fund is only one approach to managed entry models. As with any approach, its design inevitably introduces tensions that require management and mitigation rather than resolution.

We would argue (see the next section below) small manufacturers will be disadvantaged by the process set out. Once operational, that disadvantage may be translated into disengagement and a refusal to enter the process.

Instead small manufacturers may turn to other markets, like Scotland and Wales, where operating processes offer greater certainty they will be reimbursed quickly with agreed prices that remain firm.

This will be to the detriment of patient populations in England with indications their products are licensed for.

This describes the situation confronting those CML patients with indications for which ponatinib has been granted a license and whose clinicians recommend its use as a treatment.

Its manufacturer, Ariad, is a small, relatively new, company with a small portfolio.

Patients living in Wales and Scotland are able to access ponatinib across all its licensed indications yet this is restricted to a single indication in England accessible only via an application to the current CDF.

The rationale offered in the Answer to the relevant question (Q10) in the Q&A is understandable when applied to global corporations but much less so for smaller companies.

Government policy elsewhere recognises not only the differences operative here (SME vs global corporation) but also the necessity of sensitive adjustment to avoid the development of oligopoly and its effect on the efficient operation of markets.

Fair treatment of manufactures:

The very brief detail provided would lead us to conclude that SME manufacturers, who lack the deep pockets of the global companies, will be disadvantaged in a number of ways by these proposals:

(a) It seems, although as ever the wording lacks clarity, a manufacturer would be unaware, at the CAA discussion stage, of the (%) degree of retention planned in the Prospective Contingency Provision which we assume would vary depending on forecasts of demand on the fund.

If however the term ‘consistent‘ refers to a fixed (%) figure for a year, it remains unclear how this would be calculated with any precision. Instead we would argue it would tend to generate a figure with a very significant safety margin built in which would be to the disadvantage of SME companies given this represents the only reimbursement stream on offer.

(b) A manufacturer would also be unable to establish, at the CAA discussion stage, the likelihood of the magnitude of any across the board price cut that might be levied or the likelihood of its occurrence.

(c) The same applies to attempting to estimate, at the Managed Access Agreement (MAA) stage, the size of the data generating patient population since this would presumably only be definitively decided at the final guidance stage.

Notwithstanding the above, an SME company would then be required to supply, at zero cost to the NHS, their drug to all patients outside the data gathering population for

(i) The two years allocated for data gathering

(ii) Over the time taken to conduct and publish the Shortened Appraisal
(iii) Assuming the recommendation was positive, for 90 days thereafter.

The above, near three year timeline, assumes a perfect working of the process which, as we have noted elsewhere, is an assumption that lacks plausibility.

However, if the recommendation was negative, the post Shortened TA period would involve supplying at zero cost not only data gathering population but also those patients outside the data gathering population.

For CML drugs, like ponatinib, that demonstrate the potential to secure long term survival with a duration measured in decades this represents a significant financial burden for an SME and, we would argue, would amount to an equally significant deterrent against entry into a MAA.

Operational effectiveness:

We have already commented on the consultation's lack of proposals for any incentives that would stimulate the introduction of efficiencies into the day to day operating procedures of the new model which would, in turn, act to secure optimal operational effectiveness.

We have read the NAO report which lays out the lack of operational effectiveness of the current machinery over the lifetime of the CDF through its failure to systematically evaluate drugs on the national list or to undertake any corrective action to prevent forecastable, ever escalating budget breaches once the fund passed its 2014 expiry date.

An assumption that a fund whose budget is controlled is, de facto, a well managed fund is one that is flawed.

13 Are there any other issues that you regard as important considerations in designing the future arrangements for the CDF?

Are there any other issues that you regard as important considerations in designing the future arrangements for the CDF:
Yes, these are:

1. As we have noted elsewhere in our consultation response we believe what is proposed does not amount to a sustainable solution to access to cancer drugs and instead amounts to yet another 'bridge'.

Stakeholders, who include patient groups, have witnessed five years of prevarication, delay, failure to make long term decisions and short term responses to a point where it is reasonable to ask if a destination is envisaged at all. In short are we forever to be presented with bridges to nowhere?

1.1 We would ask that work on the destination's design should begin on April 1st and should be especially sensitive to the development of features that accommodate unmet need, burden of illness, non health benefits of treatments and the award of breakthrough status within an operating framework.

Careful study of relevant recommendations in Accelerated Access Review's final report will obviously be necessary.

1.2 As will the output of the current review of the Patient and Clinician Engagement (PACE) initiative in Scotland.

The development of measures to improve the quality and status of the much neglected third pillar of evidence (patient experience) is essential. The more so as 'living with cancer' takes on a long term dimension for ever more patients.

In this context PACE should be regarded as a first rather than final step in the engagement part of the process.

1.3 The rather odd retrieval of a section of the 2007 Cancer Reform Strategy that appears in section 17 of the consultation document includes this phrase when discussing NICE TAs:

'....there is not a more appropriate alternative mechanism for appraisal'

This is treated as if it carried a warrant of biblical certainty when it is completely incorrect.

There is a post 2007 alternative mechanism and its called a NICE HST.

The HST programme has much to offer given its explicit orientation to and attempted capture of elements currently at the margin of the TA process.

Particular focus should be given to the criteria set out in section 37 in the 'Methods for the evaluation of highly specialised technologies' which forms the second part of the 'Interim Process and Methods of the Highly Specialised Technologies Programme' (May 2013).

2. Timely consultation and its link to subsequent events:

The July 2015 NHSE Board paper on the future delivery of the CDF noted:

'Public consultation is required to take place at the latest in September to allow sufficient time for responses to be analysed, orderly transition from the existing scheme to be implemented and the new CDF to be operational from 1 April 2016.'

The consultation was not published until seven weeks after the end of September with a resulting loss of 25% of the minimum time judged necessary for a 1st April launch date to be adhered to.

The current situation says much about the lack of readiness for an April 1st launch date with NHSE and NICE having to issue a Q&A three weeks before, and significantly later than initially committed to, the consultation closes due to the extreme lack of clarity and outright omissions in the consultation document.

3. The need for a serious consultation:

A draft SOP was not published alongside the consultation document in marked contrast to the 2014 and 2015 CDF consultations.

The effect has been of ever changing interpretations of what the new arrangements might involve accompanied by a series of webinars, workshops, documents and meetings that have attempted to add clarity but have sometimes appeared to contradict statements in the consultation document or provided no further clarity.

For example:

(i) Its now clear that the commitment to appraising all drugs in the current CDF in line with the new criteria 'during the course of 2016/17' has already been breached for drugs NICE classifies as Group 3 drugs.

(ii) The off label CDF drugs cannot be appraised 'in line with the new criteria' because they are unable to enter NICE but there are no arrangements in place to evaluate them over 2016/17.

(iii) Other evidence than that generated from the data gathering exercise will now be considered in the Shortened TA which does not accord with the wording in the consultation document.

(iv) Although it is clear that companies will be required to fund the data gathering process, the identity of the 'organisation which is performing the data collection' (Answer to Q12 of the Q&A) remains vanishingly unclear.

For us an illustrative non-healthcare equivalent would be attempting to conduct a consultation on a road traffic management scheme without providing those consulted with maps and instead relying on a short description of what was involved.

The SOP is a formal description of a set of procedures. We cannot understand how a serious consultation can be expected to take place with only a short description offered of what is proposed

We strongly support the approach adopted by NICE to consultations where a draft of the relevant document is published with deletions and amendments clearly indicated.

We also admire the rigour brought to the NICE consultation process which includes a detailed and considered post submission response.

We note NICE, in contrast to NHSE, has provided the exact wording of changes it proposes be made to the Methods and Process guides.

14 Do you agree that, on balance, the new CDF arrangements are preferable to existing arrangements, given the current pressures the CDF is facing?

Agree

Please provide comments to support your response::
The current pressures the CDF is facing are self induced by NHSE.

The NAO report demonstrates conclusively that the budget allocations up to the expiry date originally intended for the fund (end of March 2014) were consistently underspent.

In that sense, given the history of overspend on fixed budget projects across Departments, the CDF enjoyed outstanding success in achieving the objectives set for it.

Over the lifetime of the financial years completed (that is years for which data does not include an element that is forecasted) the fund has only been overspent by 4% if all allocations and expenditures are aggregated. We would argue, again given the historical factor mentioned above, this hardly constitutes a failure of epic proportions.

Our view is that the (new approach) destination for the bridge (that is the CDF) remains undecided in design. The new proposals are, as described in the consultation title, simply a new CDF operating model.

We take the view that, whatever the intentions of the Institute, NICE Appraisal Committees will more likely than not, and increasingly so, to issue 'recommended for treatments within the CDF' decisions over the duration of the current arrangements which we believe will be relatively short.

We will therefore have to wait until 2020 or thereabouts to discover if the 'something about cancer drugs' Andrew Dillon refers to becomes 'nothing about cancer drugs' because Appraisal Committees recommendations for anti cancer drugs will become unremarkable compared to all drugs appraised.

In that sense alone, we offer a highly cautious welcome to the new model as an improvement on the old.

About you

15 Are you responding:

on behalf of an organisation

About you

17 If you are responding as a health or social care professional, or on behalf of an organisation, please indicate your primary area of work or the nature of the organisation you represent.

Other

If you selected 'Other', please give details.:
Patient lead registered charity: The Chronic Myeloid Leukaemia Support Group

About you

18 'Sunshine' provision/conflict of interest disclosures: have you or your organisation received any payments, grants or other funding from the pharmaceutical industry in the last three years?

Yes

If you selected 'Yes', please specify the source of funding and sums involved in each of the last three years::
1. Details are set out below but we find it perplexing that this question is restricted to the pharmaceutical industry and not other industries that are competitors for resources for cancer healthcare.

For example, a respondent who falls in the category NHS Acute but also has, or has had, some financial transaction(s) as, for example, a researcher, advisor etc or involvement as, for example, a Director, shareholder etc with the medical devices industry is not required to disclose such relationships.

In this context we, and others, have noted that 67% of the responses to the autumn 2014 consultation were from either the NHS or NHSE yet there is no data available on the percentage falling in the category mentioned in the example.

2. As you will also discern from the details below, we are assiduous in our efforts to secure support from all the companies with targeted therapies for the treatment of CML.

Our reasons for doing so is to remove any implication of bias towards one particular company's therapy over any others and to ensure each company fulfils their corporate social responsibility role towards the patient population and those that support them.

3. Finally and to reiterate the obvious, we have yet to meet any patient who displays any brand loyalty towards any particular product.

As a patient lead group, we share the prime objective of all patients which is to secure access to effective treatments. What that might amount to differs from patient to patient as section 2 of the consultation notes.

We call that self interest not conflict of interest.

Funding support (£):

2013:
Novartis 16,500.00
Bristol Myers Squibb 10,000.00
Pfizer 11,500.00

2014:
Novartis 16,500.00
Pfizer 3,500.00
Ariad 10,000.00

2015:
Novartis 9,250.00
Bristol Myers Squibb 10,300.00
Pfizer 15,000.00
Ariad 10,000.00

Equality Monitoring

19 How old are you?

How old are you?:
Over 55

20 What gender do you identify yourself as?

What is your sex?:
Male

21 Do you consider yourself as a person with a disability?

Do you consider yourself as a person with a disability?:
No

22 What is your ethnic group?

What is your ethnic group?:
White and Black Caribbean

If you selected 'Other', please specify.:

23 What is your religion or belief?

What is your religion or belief?:
None

If you selected 'Other', please specify.:

24 Which of the following best describes your sexual orientation?

Which of the following best describes your sexual orientation?:
Heterosexual / Straight