Consultation on proposals for a new Cancer Drugs Fund Operating Model: Pfizer Submission

Executive Summary

Pfizer are pleased to contribute to the consultation on the future of the Cancer Drugs Fund (CDF).

Since even before the inception of the CDF, there has existed a need to define a single, sustainable solution to the concerns surrounding patient access to new cancer drugs in the UK. At its heart, this solution must ensure that UK patients are afforded similar access and achieve similar outcomes as observed across other EU countries. The CDF itself was conceived as a temporary measure to improve access to cancer medicines while proposals were developed to reform HTA more broadly. Six years on, this reform has yet to materialise. In our view, the proposals put forward in the consultation risk setting back UK patients’ access to new cancer medicines to a position possibly worse, and even more uncertain, than that which existed at the inception of the CDF. This is neither the ambition of Government, the NHS, patients, nor Industry.

There are a number of elements within the proposed CDF process of which we are broadly supportive, at least in principle. These include the new process being NICE-led; the availability of new managed entry agreements to support earlier patient access; and the addition of a new conditional recommendation from NICE to support additional evidence generation, at least where particular uncertainties in the current data prevent an immediate recommendation into baseline commissioning.

However, we have significant concerns that in reality the current proposals will not expand access to cancer medicines, and we believe that if the current proposals are left unchanged, there would be a decrease in patients being able to access new innovative medicines in the future, thereby stymieing any ability to drive an improvement in patient outcomes. The single most important issue not addressed in the proposed CDF operating model is the fundamental reform of NICE methods and processes. Without a firm commitment to progress with this and to clarity regarding the timelines for implementation, we are unable to support the current proposals.

We would consider successful reform of NICE to include the introduction of a revised decision making framework which permits a broader, pragmatic and flexible assessment of value for new cancer medicines, especially with respect to end-of-life medicines, medicines for rare and ultra-rare conditions, and those signalled as breakthrough treatments by the regulators, to enable faster access to patients.
To address the most pressing issues, Pfizer offers the following principles for the development of a sustainable solution for the CDF. These are noted below, and expanded upon in subsequent questions:

- **Fewer restrictions on the format of commercial access agreements** (i.e., allowing for more flexible reimbursement arrangements and multi-year agreements, as specified in the Accelerated Access Review interim report);
- **Flexible value assessment timelines**, dovetailed to global launch timelines;
- **A structured, multi-criteria decision-making framework**, to allow for a broader value assessment, including modifications to the current End-of-Life Criteria (extending the criterion on expected survival from 24- to 36-months) and **cost-effectiveness thresholds** (increased thresholds for breakthrough medicines, and medicines for rare- and ultra-rare conditions);
- **Prioritisation of breakthrough medicines**, including consideration of FDA breakthrough status, MHRA-designated PIM (Promising Innovative Medicine) or the EMA’s Adaptive Licencing Programme, both with respect to access to CDF monies and to the cost-effectiveness threshold used for value assessment;
- **Rapid approval mechanisms for managed entry agreements**, and greater flexibility around the evidence generation requirements for these, including the acceptance of data maturation from clinical trials, as well as real world evidence from European/global registries;
- **A CDF budget able to adapt to fluctuating launch patterns and to allow for multi-year access agreements**, informed by enhanced horizon scanning, and with overspend appropriately managed through a contingency fund (rather than through iterative re-negotiations with manufacturers); and
- **Appropriate management of the transition of medicines currently funded by the CDF.**

Separate to the above, an immediate concern raised by the consultation itself is the notable lack of detail contained therein. The absence of a published impact assessment to accompany the consultation does little to mitigate this concern. In the response to the consultation comments, Pfizer request that details of any impact assessment are made available.
Core Questions: Consultation Response Form

**Question 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? **Disagree**

Pfizer are broadly supportive, at least in principle, of the CDF becoming a managed access fund; however, in order for this to be an acceptable solution, the entry and exit criteria need to be redefined. In the absence of these changes, the proposal cannot be supported.

We propose that the entry criteria to the fund are broadened to include cancer medicines with breakthrough designation from regulatory bodies. The entry criteria also require further specification to accommodate other avenues of data generation (including the acceptance of data maturation from clinical trials, as well as real world evidence from European/global registries). Ongoing data collection exercises should be frequently reviewed, at appropriate time points, to determine whether data collection has completed early, or to consider extending data collection beyond the initial time frame, perhaps due to patient recruitment. We suggest that the exit criteria are also broadened to provide greater flexibility regarding the duration of funding to reflect the specific evidence requirements for each individual medicine/cancer type, as necessary. A two-year time period is arbitrary, and may only be relevant for a small number of medicines.

Lastly, Pfizer cannot support a fund for which the budget is fixed into the long-term, and for which the onus of all variable costs is placed the manufacturer. Details of our particular objections, alongside suggested solutions, are provided in the response to question 11 below.

**Question 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? **Unsure**

Pfizer will only support this proposal if broader NICE reform is included as part of the solution, in order to ensure that there is a positive change in patient access to cancer medicines. We are not satisfied that the current proposals will improve access to cancer medicines for patients in England and Wales. Evidence from a recent ABPI analysis (and which will accompany the ABPI response to the consultation) shows that under the current proposals, only a handful of medicines would likely enter into routine baseline commissioning. The risks to access, and consequently to patient outcomes, are particularly acute for medicines used to treat rare and ultra-rare conditions, both of which are highly unlikely to be approved under the current arrangements.

The CDF proposal sets out welcome changes to the End-of-Life Criteria. However, as acknowledged by NICE in the consultation document, the removal of the patient population criterion will have little effect, as this has only applied to a very small number of medicines since introduction of the Criteria in 2009. That no more substantive reforms have been put forward is concerning, as medicines failing to meet the current End-of-Life Criteria are unlikely to be afforded access in an otherwise unchanged system. Indeed, the current proposals could unintentionally create an imbalance in the drugs recommended for routine or conditional use,
favouring those indicated for End-of-Life conditions, at the expense of other cancers. It is clear from past appraisals that if a medicine does not satisfy the End-of-Life Criteria, it is extremely unlikely to be recommended as a treatment option.

Looking beyond the scope of the End-of-Life Criteria themselves, the assessment of cancer medicines should be further reviewed with respect to the wider value that cancer medicines offer. A structured, multi-criteria decision-making framework should be introduced by NICE which permits all aspects of value to be taken into account alongside the cost per QALY, and applied in a more pragmatic and flexible manner. There is a need to recognise higher cost-effectiveness thresholds for particular medicines, such as those treating end-of-life, and/or rare or ultra-rare conditions, and as a means of prioritising ‘breakthrough’ medicines, as signalled by the regulators.

Recognising that wider reforms may necessitate longer implementation timelines, in the short-term Pfizer suggest the following changes are made to the assessment process:

- Extending the current End-of-Life criterion on expected survival from 24- to 36-months;
- Implementing a higher cost-effectiveness threshold (£50,000/QALY) for all medicines deemed breakthrough therapies by either the EMA, MHRA or FDA; and
- Implementing a higher cost-effectiveness threshold for medicines for rare and ultra-rare conditions.

There is also a need to bring forward swift solutions to issues currently subject to discussion between NICE and the ABPI, including medicines that are not cost-effective at zero price, and the challenges associated with the use of generic comparators in the assessment of new medicines.

**Question 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? **Disagree**

We would only support NICE appraising all cancer medicines if the calls for fundamental reform to current NICE methods are satisfied. As stated above, a structured decision-making framework should be introduced by NICE which permits all aspects of value to be taken into account alongside the cost per QALY, and applied in a more pragmatic and flexible manner. There is a need to recognise higher cost-effectiveness thresholds for particular medicines, such as those treating end-of-life, and/or rare or ultra-rare conditions, and as a means of prioritising ‘breakthrough’ medicines, as signalled by the regulators.
**Question 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: **Disagree**

1. Recommended for routine use;
2. Recommended for use within the Cancer Drugs Fund;
3. Not recommended.

Pfizer welcome the opportunity for a medicine to be given a recommendation for conditional use, subject in the short term to the modification of the entry and exit criteria outlined in our response to question one, and in the long-term to wider NICE reform. These modifications should allow for a higher cost-effectiveness threshold for breakthrough medicines in the same manner that has been adopted for end-of-life medicines, and for such breakthrough medicines to be made available within the CDF from launch until NICE guidance is published. However, **without these modifications, the current proposals cannot be supported**. If the proposals go ahead as written, very few patients will be better off than prior to the introduction of the original CDF. The current proposals require demonstration of – or the potential for demonstration of – cost-effectiveness against current NICE criteria. Medicines for many types of cancers, such as metastatic breast cancer, have been unable to surmount these hurdles for years.

We must confront the short-sightedness of the proposal with respect to its reliance on real world data alone to solve to problems of access to cancer medicines created by the current NICE methods. Indeed, as acknowledged by NHSE itself in the consultation Q&A document released 27 Jan 2016, “data collection […] in England alone for the period of two years will probably not resolve all of the relevant uncertainty in the clinical effectiveness.” By way of example, the uncertainty which currently prevents the Appraisal Committees from making a recommendation for routine use often concerns the overall survival estimates of the comparator treatment(s). Such uncertainty cannot be addressed by real world data collection for the intervention being appraised. Similarly, the dependence on real world data to resolve uncertainty poses problems for rare conditions, where small patient numbers will necessarily make it difficult to collect substantial additional data. Furthermore, some uncertainty may be associated with outcomes for which data may need to be collected over a longer period than two years. For these and many other reasons, data collection in the UK is presently challenging, and so the true ability to generate relevant, robust results needs to acknowledged and appropriately accounted for.

For those few instances in which uncertainty may be truly resolvable with the collection of real world data, **more detail is needed on the mechanisms and methodology for gathering and assessing these data**. The new CDF process should be able to accommodate the maturation of randomised clinical trial data, data from existing registries, and/or data from new international studies, rather than focus solely on the collection of new data within England and Wales. Whilst this may be appropriate for some medicines, it should not be prioritised at the expense or to the exclusion of larger, more robust study designs.

A point separate to those above, but nonetheless relevant for consideration, is how NHS patients in Wales will be dealt with under the ‘recommended for use within the CDF’ category.
As the CDF is currently for England only, patients in Wales will not have access to the CDF, until such time as NICE recommends the medicine for routine use. This issue needs to be resolved urgently.

**Question 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? **Agree**

Population size is not linked to the underlying rationale of the End-of-Life Criteria. The removal of the population size criterion for consideration as an End-of-Life medicine is therefore welcomed. However, it is important to note that it is nevertheless a nominal change; analyses of past appraisals indicate that only one medicine rejected by NICE on the basis that they did not meet the End-of-Life Criteria would have been recommended if this population restriction was removed.

As highlighted in the responses to previous questions, the value assessment for cancer medicines should be reviewed with respect to the wider value that cancer medicines offer. As a minimum, and in the short-term, additional modification should be made to the current End-of-Life Criteria, as access is unlikely for any medicines not able to meet the current Criteria. Indeed, of all the patient populations covered by medicines that have failed to meet End-of-Life Criteria (until Dec 2015), only a small percentage have access to a NICE-approved treatment. These proposed modifications are described in our response to question two above.

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

Pfizer welcome the move towards earlier access for patients, and are fully supportive of minimising as far as is possible the time between the granting of a marketing authorisation and the publication of final NICE guidance to the NHS.

We would support NICE guidance being made available after CHMP Positive Opinion has been granted; NICE should not publish any data in advance of the regulator.

As described in our response to question seven below, flexibility in the process is encouraged, and we would not wish for a system that penalises companies unable to submit early, provided this has been discussed and agreed among all relevant parties in advance.
**Question 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? **Disagree**

As described above, Pfizer welcome the move towards earlier access for patients, and are fully supportive of minimising as far as is possible the time between the granting of a marketing authorisation and the publication of final NICE guidance to the NHS.

However, owing to obvious difficulties in producing estimates of cost-effectiveness in parallel to analyses of clinical data required for regulatory approval, companies should have the option for early evaluation of medicines, but should not be penalised if they cannot submit early, so long as the submission timelines have been agreed with NICE and NHSE well in advance. To allow for such planning and requisite early dialogue, the process needs to include clear timelines for enhanced horizon scanning and scoping that align more closely with global pharmaceutical company launch preparation timelines. Ultimately, the need to afford NICE sufficient control over the planning of the Appraisals Programme workload should be balanced against the availability of data to support a meaningful appraisal.

Pfizer have additional concerns relating to the timelines associated with Patient Access Schemes, and the requisite approval by the Patient Access Scheme Liaison Unit (PASLU) and the Department of Health (DH), whose current timelines often extend beyond the suggested periods needed for review. This issue will further complicate any inherent difficulties in producing early guidance. Indeed, the current DH/PASLU timelines for reviewing complex schemes, and the current mind set for approving such schemes, are incompatible with the aspirations of a faster and more responsive appraisals process, and with the flexibility called for in the Accelerated Access Review. This needs to be addressed urgently.

**Question 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**

Pfizer support the proposal for earlier access to innovative cancer medicines for patients. That said, we would want to ensure that specific arrangements are in place for managing patients exiting the fund, as well as clear implementation guidelines to guarantee access for patients to medicines which have received a positive recommendation.

In addition, as described below in our response to question nine, it would beneficial to introduce a system of prioritisation, such that access to particular medicines (those deemed to be breakthrough treatments by the regulatory bodies) can be available from launch, provide the timelines for subsequent NICE appraisal have been discussed and agreed among NICE, NHSE and the manufacturer.
**Question 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?

Pfizer do not support this scenario when applied to all medicines. However, as the original objective of the CDF was to increase patient access to innovative cancer medicines in the UK, it would be appropriate to designate a proportion of the fund to provide interim access to those medicines deemed by the regulatory bodies to be breakthrough treatments.

**Question 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?

Pfizer suggest that off-label medicines currently available through funding from the CDF should continue to be made available, and the evaluation of future off-label treatments should be deprioritised in preference to the evaluation of licensed cancer medicines. Other routes available to support clinical decision making (e.g., NICE evidence summaries) may be appropriate for the consideration of off-label drugs, and resources should be marshalled to allow for their timely use.

**Question 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? **Disagree**

Pfizer cannot support the proposal of a fixed annual budget; the present proposals around investment control arrangements will need to be significantly changed. We do not believe that it makes sense to set a fixed budget for the CDF which does not take account of the particular launch patterns of new cancer medicines in any given year. Pfizer suggest a budget is set whereby it is flexible, not constrained to an annual cycle (i.e., is able to account for investments in one year that may reap savings in future years), and is more accurately forecast through enhanced horizon-scanning and early dialogue with manufacturers. Based on this, there is a need to develop a plan to transition the CDF from a fixed budget to a more flexible budget, which should also outline the vision for more sophisticated horizon scanning mechanisms. This would enable NHSE to improve, as far as is needed, their financial- and service-planning for new cancer medicines.

As proposed by the Accelerated Access Review interim report, the managed access fund should facilitate “agreements between companies and the health system that both specify requirements for access, and control financial risk.” The implication was that this risk would be shared by both companies and the health system in a way that prioritises patient access. By contrast, the proposal places a disproportionate financial risk on manufacturers. Fixed costs are proposed for the NHS, and in contrast companies bear the full risk of any variable costs.
the NHS overspends on the CDF budget. The proposal that Industry bear all the risk of managing the budget of the new CDF fund is unacceptable. While Pfizer understand the budgetary pressures faced by the NHS, and are playing an active role in cost-containment via the current Pharmaceutical Price Regulation Scheme (PPRS) agreement (pursuant to which Industry already underwrites all expenditure on branded medicines over and above agreed limits), we do not agree with the proposed complete shift of financial risk onto manufacturers. Indeed, there are significant disincentives for research companies to enter into agreements with outcomes which they have little control.

Further to the above, Pfizer cannot agree to the proposal that funding within a managed entry agreement will be based only on minimum data collection needs. Patient numbers within any managed entry agreements should be jointly agreed on an individual basis.

To shift the onus of budget management back into balance, Pfizer propose that NHSE should set aside its own contingency fund, taken from the existing CDF budget, if it considers that there is a risk that the CDF Investment Control Group will be unable to succeed in the task of managing the available CDF budget, for which it is ultimately accountable.

**Question 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?

No, we do not believe the current proposals will facilitate fair and equitable access for patients.

As stated above, Pfizer do not support the proposed mechanism for investment control which is based on the manufacturer underwriting 100% of any over expenditure in the fund. We would propose instead that NHSE set aside its own contingency fund, taken from the existing CDF budget. Additionally, we suggest the set budget is sufficiently flexible to account for fluctuating launch timelines, not constrained to an annual cycle, and more accurately forecasted through enhanced horizon-scanning and early dialogue with manufacturers. Without these changes to the way the budget is defined, patients eligible for treatment with medicines launching later in the year will be necessarily disadvantaged.
Question 13
Are there any other issues that you regard as important considerations in designing the future arrangements for the CDF?

Yes. Pfizer view the following considerations, outlined below, as important in designing future arrangements for the CDF:

1. **Alignment with the Accelerated Access Review (AAR):** It is extremely important to seize the opportunity to align ongoing initiatives in order to ensure a clear, consistent and joined-up system is in place for the launch of all new medicines in the UK, including (but not limited to) those in cancer. This will avoid the creation of potentially duplicative and overlapping structures. Indeed, it must be acknowledged that if the changes implemented within this initiative (the CDF consultation) are to form any sort of blueprint for the way forward with the AAR, the current CDF proposals create an unacceptable platform from which to roll-out a wider programme of assessment for all new medicines.

2. **Interim funding & implementation:** Interim funding should be provided for CDF listed medicines until the publication of updated NICE guidance. Interim funding will provide stability and continuity of patient access during the transition process, and is absolutely necessary if we are to avoid yet further destabilisation of patient access to cancer medicines which has been seen as a result of the previous two delisting exercises undertaken by NHSE.

   Development of a clear implementation plan with milestones and detailed timelines for the entire transition period is required, including timelines for broader NICE reform, as requested above.

3. **Enhanced focus on acknowledging and rewarding innovation:** In the current proposal, no specific consideration has been given to acknowledging and valuing medicines with an MHRA-designated PIM (Promising Innovative Medicine) status, FDA Breakthrough status, or which have undergone, or are planned to undertake, the EMA’s Adaptive Licencing Programme.

4. **Considerations for medicines for rare indications:** As mentioned previously, the dependence on real world data to resolve uncertainty poses problems for rare conditions where small numbers of patients make it difficult to collect substantial additional data. Pfizer propose that consideration be given to allowing for flexibility in the economic evidence and considerations for medicines for rare indications.
Question 14
Do you agree that, on balance, the new CDF arrangements are preferable to existing arrangements, given the current pressures the CDF is facing? **Disagree**

Pfizer support the ambitions of the proposal to move towards earlier access for patients, and are fully supportive of minimising as far as is possible the time between the granting of a marketing authorisation and the publication of final NICE guidance to the NHS. However, as stated throughout our responses to the earlier questions, Pfizer do not consider the current proposal to contain the required significant fundamental changes. The CDF was originally created as a bridge to value based pricing in recognition that current NICE methodology was not fit for purpose for cancer medications. By 2015, the CDF had created a continuously evolving access landscape which didn’t allow clinicians or patients to plan for their next therapy with any certainty. The proposed minimal changes to the NICE methods are indeed necessary, but certainly not sufficient.