NHS
Blood and Transplant

NHSBT Board
31 January 2019

Clinical Biotechnology Centre – progress update

1. Status - Official

2. Executive Summary

Over the last few years there has been a significant increase in the development and adoption of clinical therapies that require gene therapy products. The demand on NHSBT's Clinical Biotechnology Centre (CBC) has, as a result, outstripped its manufacturing capacity at the current facility in Langford.

In January 2018 the NHSBT Board approved a £7.4M investment to construct a dedicated facility for the CBC at Filton. The investment included:

- Capital funding of £6.0M to build and fit-out based on an Affordability Cost (i.e. estimate) and a Concept Design[1]
- Capital funding of £0.75M for equipment
- Non-recurring revenue funding of £0.6M.

This proposal supports the Government strategy for establishing the UK as a global hub for manufacturing advanced cell and gene therapies. It also delivers benefits to NHSBT that include:

- Increasing income to over £5M per annum by 2022/23
- More than doubling manufacturing capacity for clinical-grade DNA plasmids
- Increasing the number of products and services offered from 3 to 7.

Following submission of a business case, the Department of Health and Social Care (DHSC) confirmed their approval in May 2018, stating that £6.75M should represent the maximum capital envelope for the project. A further submission would be required in the event NHSBT expected to breach this limit.

Since approval, the project has focussed on the detailed design[2] for the two-storey extension. Additional support has been provided by eXmoor Pharma Concepts Ltd who are specialists in designing facilities for cell and gene therapy manufacture. This stage of the project is now nearing completion. The project has been in receipt of updated Affordability Costs as the detailed design has developed and the scale of change has been significant with each iteration. An update to the NHSBT Board was considered appropriate when an Affordability Cost was based on a stabilised design.

The latest Affordability Cost to construct and fit-out is £1.75M more than stated in the Detailed Business Case (DBC) in Appendix 1. Despite the reduced NPV (Net Present Value) and extended payback period (Table 1) the project remains financially viable.

[1] Concept Design is an early stage of design that identifies spaces, adjacencies and process flows.
[2] Detailed Design is the stage where the design is refined and plans, specifications and cost estimates are created.

Table 1: Summary of Cost Movement

	Build & Fit-out	Contingency (10%)	Net VAT	Total	10 year NPV	Payback
DBC Affordability Cost	£5.25M	£0.53M	£0.23M	£6.0M	£3M	2yrs 10mths
Latest Affordability Cost	£7.0M	£0.7M	£0.31M	£8.0M	£1M	4yrs 7mths
Movement	£1.75M	£0.17M	£0.08M	£2.0M		

Note: NPV and Payback are based on the same income projections as per DBC. Income projections will be reviewed again when the DBC is updated for submission in May.

The project team wish to continue to work with Kier Construction, the principal supply chain partner (PSCP), to derive a Guaranteed Maximum Price (GMP) for the build and fit-out. This is expected in April 2019. The additional funding required to develop the GMP is £0.63M bringing the total project expenditure to date to £1.26M.

3. Action Requested

The NHSBT Board are asked to support the continuation of the project to GMP at a further cost of £0.63M.

There is a reasonable expectation that the GMP will not increase significantly beyond the Affordability Cost of £7.0M shown in Table 1. On receipt of the GMP in April 2019 a revised DBC will be presented to the NHSBT Board in May 2019. It is worth noting that the build and fit-out costs would need to increase to around £7.7M to generate a negative NPV. Under these circumstances, the project would no longer be viable and NHSBT would have incurred £1.26M in aborted costs.

4. Background

4.1. The CBC produces clinical-grade gene therapy products. These are components used to genetically modify cells or for administration to patients as vaccines.

4.2. The CBC's current facility at Langford, 20 miles from Filton, is limited with respect to space and flexibility to manufacture different product types. In a rapidly growing gene therapy market the CBC is declining more work than it can accept. In 2018/19, it is estimated that the CBC has declined work valued at £2M.

4.3. A number of options were considered during the development of the DBC and included:

- Building an extension at Langford
- Leasing manufacturing space
- Re-locating to the new NHSBT facility at Barnsley.

These were dismissed because:

- The option failed to meet the specification for manufacturing capacity and flexibility
- The option still incurred significant expenditure at a site with poor infrastructure
- Of the risk of losing highly trained and experienced staff.

4.4. The option to build an extension at Filton provides the CBC with much greater manufacturing capacity and the flexibility to manufacture different product types without the risk of losing critical personnel.

4.5. The only plausible alternative, should this project not proceed, would be to undertake a controlled cessation of CBC's activities to achieve complete closure. Consideration would need to be given to:

- Honouring current contracts
- Redeploying CBC staff where possible or making redundant
- Minimal maintenance of an ageing facility until closure
- Decommissioning and dilapidation works at Langford
- Potential reputational damage to NHSBT as this option would not be aligned with the UK's Life Sciences Industrial Strategy.

5. Project Progress

5.1. Since receiving DHSC approval the project has been developing the detailed design of the two-storey extension. The extension will total 940m^2 of space over 2 floors and include:

- Suites of clean rooms designed for parallel manufacture of clinical-grade DNA plasmids, recombinant proteins and viral vectors
- Laboratories equipped to undertake preclinical manufacture, development and Quality Control (QC) testing activities
- Agile offices.

5.2. It has become evident during detailed design that additional costs will be incurred and these can be broadly attributed to 2 key areas summarised in Table 2.

Table 2: Summary of Cost Increases

Area	Increase	Reason
Unknown at Concept Design	£0.98M	• Existing foundations will not support additional load • Higher fire rating specification required for floors, ceilings and partitions • Additional ground works required for flood attenuation • Additional steel required to reinforce roof to accommodate plant • Increased mechanical and electrical works due to heat load of equipment and the required number of air changes to meet specification
Additional fees	£0.77M	• Additional support required from eXmoor Pharma to address internal knowledge and skills gap • Increased Kier fees as levied at 7.2% of overall project value • Increased risk allowance as this is applied at 2.5% of design development

5.3. The latest Affordability Cost from Kier represents a 33% increase on the cost included in the DBC. The DBC was submitted when the project was at an early stage of design and the cost to build and fit-out was estimated based upon an informed estimate at that time. In hindsight, the project could have staged the approval process as follows:

- Presented an Outline Business Case (OBC) that sought funding to progress the early concept design to detailed design and derive a GMP.
- Presented the DBC only when a qualified design was available with a GMP.

5.4. A GMP for the construction and fit-out will be provided in April 2019. This is 9 months later than stated in the DBC. The delay in the provision of the GMP can be explained as follows:

- The DBC underestimated the time required to undertake detailed design to exacting regulatory standards and qualify the design
- The Project Team assumed that internal knowledge and experience of operating and maintaining clean rooms would be sufficient to support

elements of the detailed design. This was not the case and additional support from eXmoor Pharma Concepts Ltd was required
- There was limited Kier project management support for the project at the time detailed design commenced. This meant that design process, planning, roles and responsibilities were not sufficiently well defined
- "Value engineering" the design added to the overall detailed design timeline.

5.5. The impact of a 9-month delay on the project timeline can be reduced to 4 months, as a number of activities can be undertaken in parallel. This is subject to more detailed planning and the receipt of Kier's final programme in April 2019.

5.6. The CBC's customers are aware of its intention to relocate to Filton and the timeline to completion. Some have indicated that their ambitious growth plans require a second (overseas) manufacturer of plasmid DNA. The CBC will remain the preferred supplier.

6. Next steps

6.1. Assuming NHSBT Board support, the project will continue to work with Kier and other key suppliers to complete the Design Qualification (DQ) – a stage that verifies that the design meets the requirements as outlined in the original building specification.

6.2. Once DQ is complete, Kier will seek prices for individual packages of work via competitive tender exercises to inform the GMP for the build and fit-out. Forecast expenditure from January 2019 to achieve GMP in April 2019 is £0.63M.

6.3. A revised DBC will be presented to the Transformation Programme Board, NHSBT Board and DHSC in May 2019.

Appendix 1

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