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Biomedical Catalyst Evaluation

Process Evaluation and Baseline Impact Evaluation - Annexes

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Annex A: Impact Evaluation Framework

This Annex sets out an overarching framework for the evaluation of the Biomedical Catalyst programme. This framework specifies the policy objectives for the programme, the rationale for intervention, and defines a 'theory of change' outlining the causal process by which the Biomedical Catalyst is expected to deliver its outputs, outcomes and impacts. This understanding is formalised in the definition of a 'logic model' and a set of key outcomes that will need to be explored through the evaluation. Finally, this section sets out a range of contextual issues that will need to be considered with the potential to influence the outcomes of the programme.

A.1 Policy Objectives

The Biomedical Catalyst programme was created in 2012 as part of a wider package of measures to support the growth of the life sciences sector under the Industrial Strategy[1]. The policy objectives of the Biomedical Catalyst are to:

- Deliver growth to the UK life sciences sector;
- Deliver innovative life sciences products and services more quickly and effectively into healthcare;
- Provide support to both academically and commercially led research and development in a seamless, effective, and efficient manner.

The Biomedical Catalyst involves £240m (originally £180m) of grant funding for Early and Late Stage R&D projects and is delivered jointly by the Medical Research Council and Innovate UK (with the two organisations responsible for administering £120m of research grants to academic institutions and SMEs respectively). The Biomedical Catalyst builds on the earlier Development Pathway Funding Scheme created by the Medical Research Council in 2008 to fund translation research in the biomedical sector.

The scheme involves four distinct types of grant awards targeted at projects at different stages of technical and commercial development: Confidence-In-Concept awards for portfolios of small projects at the earliest stages of technical development by academic institutions, feasibility awards (comparable in focus to the Confidence-In-Concept awards, but awarded on a firm-by-firm basis by Innovate UK), Early Stage Awards (funding for pre-clinical activity), and late-stage awards (funding up to a Phase II clinical trial or equivalent[2]).

A.2 Rationale for Intervention

The rationale for public investment in the Biomedical Catalyst programme can be broadly split into two key elements: a strategic case relating to both the scale of the economic opportunity presented by growth in the life sciences sector, the opportunities for improving human health through more rapid commercialisation of basic and applied research, and the strengths and weaknesses of UK based firms and academic institutions in terms of their ability to exploit this opportunity, and an economic case relating to the presence of specific market failures inhibiting investment in research and development in the sector.

A.2.1 Strategic Case

The strategic case for the Biomedical Catalyst programme can be summarised as follows:

[1] Industrial strategy: government and industry in partnership, BIS, 2013
[2] Note that Innovate UK has funded one project involving a Phase III clinical trial.

- **Global market:** The global market for the products of the life sciences industry (broadly encompassing pharmaceuticals, biotechnology and medical technologies) is projected to grow rapidly, as a consequence of both an aging population and increasing per-capita health spending. For example, research sponsored by HM Government[3] suggested the global medical technology market was estimated at £150-170bn in 2010 and projected to grow to £300bn by 2015. Equally, the value of the medical biotechnology market was estimated at £45-48bn, growing at a rate of 20 percent per annum. As indicated in the Industrial Strategy, the course of biomedical research and development is also increasingly focused on the development of medicines that are tailored to individual characteristics or genetics (and associated diagnostic technologies), which have the potential to allow health conditions to be treated more effectively[4].

- **Industry strengths:** The UK has traditionally been internationally competitive in the life sciences sector, which accounted for eight percent of UK manufacturing GVA, and 28 percent of business R&D expenditure, in 2011 when the scheme was announced. The pharmaceutical, medical biotechnology and medical technology sectors comprise 4,500 firms, employing 165,000 staff, with an annual turnover of £50bn. This level of expertise would initially appear to suggest that the UK is well placed to exploit the opportunities presented by global growth in healthcare expenditure.

- **Academic infrastructure:** The quality of academic research in life sciences undertaken in the UK is also generally regarded as internationally competitive. For example, a report prepared for the Department for Business, Innovation and Skills[5] indicated that UK publication output and citation impacts in the field of Regenerative Medicine were comparable, if not ahead, of most EU-27 nations and economies in South East Asia, though slightly behind the US. The high quality of academic research has the potential to support the life sciences industry through a range of processes, including provision of contract research services, supplying highly skilled scientific personnel as well as opportunities for collaboration and knowledge exchange between academia and business.

- **Disinvestment in R&D:** However, despite the strengths of the life sciences industry in the UK, research and development investment in the pharmaceutical sector peaked at £4.9bn in 2011 (after 30 years of almost uninterrupted growth[6]) before falling to just £4.0bn in 2013 (albeit still accounting for over 22 percent of the UK total). While R&D is often suggested to be pro-cyclical[7] (as activities tended to be funded from cash rather than debt), the life sciences sector has traditionally been less exposed to normal business cycles as revenues and profits are typically dependent on the expenditures of national healthcare systems (the budgets of which tend to be preserved during recessionary periods). Two important factors have contributed to disinvestment by large pharmaceutical firms. Firstly, the widely publicised 'patent cliff' in which expiration of patents on a large number of highly profitable drugs has eroded revenues, leading to consolidation in the sector. Secondly, the cost of the research and development process itself has increased substantially, which has been attributed in part to the rising cost of the clinical trials required for regulatory approval and the failure of those drugs in trials[8]. However, a recent paper published in Nature by AstraZeneca[9] suggested that drug failure rates were often high due to weaknesses in the underlying understanding of how new compounds would affect patients. Safety concerns driven by off-target effects were cited as amongst the primary reasons for project failure,

[3] Strength and Opportunity, The Landscape of the Medical Technology, Medical Biotechnology, and Industrial Biotechnology Sectors in the UK, HM Government, 2010
[4] Strategy for UK Life Sciences, Department for Business, Innovation and Skills, 2011
[5] A Bibliometric Analysis of Regenerative Medicines, Department for Business, Innovation and Skills, 2011
[6] Business Enterprise Research and Development 2013, Office for National Statistics, November 2013
[7] The Impact of R&D Subsidies During The Crisis, Martin Hud and Katrin Hessinger, Centre for European Economic Performance, 2014
[8] Stifling New Cures: The True Cost of Lengthy Clinical Trials, Avik Roy, Manhattan Institute for Policy Research, 2012
[9] Lessons Learned from The Fate of AstraZeneca's Drug Pipeline: A Five Dimensional Framework, David Cook, Dearg Brown, Robert Alexander, Ruth March, Paul Morgan, Gemma Satterwaite, and Menelas Pangalos, Nature, June 2014

though the study suggested that the firm would often pursue R&D projects where there were high concerns with the safety profile of the compounds emerging from pre-clinical research.

- **Changing industrial structure:** The disinvestment by large vertically integrated pharmaceutical firms has been in part been compensated by a growth in small businesses. For example, the number of micro-businesses (zero to 10 employees) operating in the pharmaceutical sector rose by 25 percent between 2010 and 2014 (with little growth observed in the number of larger firms). These smaller firms will typically be involved in R&D activities focused on a single, or small number of, target products, and reliant on equity investment (rather than profits) to fund their activities. These trends have been accompanied by greater vertical disintegration: small firms do not typically have the manufacturing capabilities to produce the compounds they are exploring, or the ability to deliver the large scale clinical research trials needed to reach regulatory approval, and the growth of Contract Research and Manufacturing Organisations (CROs and CMOs) supplying these services is a symptom of the greater fragmentation of the sector.

- **Barriers to translational research:** Finally, a range of barriers to translation research (the translation of basic scientific findings observed in laboratories into clinical application in humans) have been identified in the literature[10] (and may lead to missed opportunities to raise R&D productivity). In particular, the medical research landscape has become increasingly fragmented since the 1970s, with basic and clinical researchers becoming increasingly specialised in their respective fields. This has created parallel challenges, driven on the one hand by falling knowledge of patient needs amongst basic researchers, and difficulties in processing the large volumes of increasingly complex findings[11] amongst biomedical researchers (with the collaboration between the two often failing to emerge). Issues are exacerbated by weak incentives for basic researchers to engage in translation research: such research does not tend to be published in the highest profile journals, which in turn can damage career prospects[12].

- **Health impacts:** The disinvestment in R&D and barriers to translation research will ultimately have negative social effects through failures to realise technological advances made possible by the increased understanding of the underlying biology associated with disease as rapidly as might be feasible through public intervention.

As such, in order to exploit the commercial opportunities presented by growth in global demand for healthcare, it will be critical that there is a sufficient supply of finance to the growing number of smaller firms that will likely drive growth and technological progress in the sector as well as support the commercialisation or translation of knowledge generated within academic institutions. However, close collaborative working between academics and industry (or clinicians) is also needed to ensure that (1) the process of research and development is based on a sound understanding of underlying basic research, and (2) the process of translation draws in sufficient understanding of both patient need and the regulatory frameworks involved.

A.2.2 Economic Case

The central market failure rationale justifying public investment in the Biomedical Catalyst relates to imperfections in capital markets inhibiting the flow of finance into the life sciences sector to fund projects that would deliver a (risk-weighted) rate of return higher than the risk-free rate of return (in perfect financial markets, all such projects

[10] For example, see Translational Research: Crossing the Valley of Death, Nature, 2008 (News Feature)
[11] See Translational Research and Context in Health Monitoring Systems, Ashford, Moore, Hu, Jackson, and Wan, Birmingham City University, paper prepared for the 2010 International Conference on Complex, Intelligent and Software Intensive Systems.
[12] See, for example, Translating Research Into Clinical Practice, Deliberations from the American Association for Cancer Research, Clinical Cancer Research, 2005

would be funded, assuming zero transaction costs and risk neutrality). Such imperfections are caused by information asymmetries by which the investee has substantially greater knowledge of the risks associated with the project than the investor (and may be able to mask known deficiencies, for example, in the underpinning science). In these circumstances, the investor is forced to approximate the risks involved on the basis of market wide returns, offering funds at too high a cost for some potentially profitable projects. There are a range of features of the life sciences sector that exacerbate these issues: the cost of the R&D process is typically high, as is the risk of failure, while the highly complex nature of the underlying science will make it challenging for non-specialists to appraise those risks without incurring substantial transaction costs to acquire the needed technical information.

These issues in part explain why R&D activities (where the returns are often highly uncertain and long term in nature) are funded from cash rather than debt. This was not problematic for large pharmaceutical firms while profits remained high: however, the combination of the patent cliff and falling R&D productivity has caused consolidation and disinvestment amongst these firms. The smaller firms (or academics seeking to commercialise innovation developed in academic institutions) now driving R&D investment in the life sciences sector will typically have less in the way of assets or borrowing capacity to fund such activity (and are more dependent on equity investment to fund the costs involved).

Venture capitalists are the typical suppliers of this type of finance, though further market failures inhibit supply. In particular, there is a moral hazard problem in which the investee has an incentive to pursue less risky commercial objectives after the finance is secured. This problem is often solved through introduction of strict monitoring obligations (for example, the venture capitalist taking a seat on the firms' board). However, these types of transaction costs mean that it is only efficient for the firm to make relatively large scale investments, inhibiting supply of finance for projects at the earlier stages of technical development. Business Angels can fill the gap for very small investments (suitable for the first stages of the R&D process, though there is an issue as to the proportions able to assess the risks involved) though it is generally acknowledged that there is a gap between the finance offered by Business Angels and venture capital providers. With respect to the life sciences sectors, there is also anecdotal evidence that there has been a loss of skilled financial analysts specialising in the industry as a consequence of the recession (which would exacerbate the information asymmetry issues highlighted above, reducing willingness to invest in the life sciences industry). As such, subsidies for R&D expenditure have the potential to both address financial market constraints directly (through providing direct funding for the research and development process), as well as through 'de-risking' projects (though provision of equity or subsidies for the transaction costs involved could achieve a similar result).

Clearly, other market failures may also be present: in particular, the possibility of spill-over effects may also act to restrain investment in research and development at sub-optimal levels (effects by which the innovating firm cannot internalise the full benefits of their activities). Life sciences firms typically publish the results of clinical trials as means of increasing consumer confidence and encouraging adoption by national health systems, knowledge that can potentially be exploited by competitors in the development of competing treatments. Additionally, while patenting may offer protection, patent registrations are in the public domain, giving competitors insight into the compounds or devices being explored (it is clear from applications to the Biomedical Catalyst that applicants have a strong awareness of the potential competing treatments currently under development and their efficacy). This ability to free-ride on the investment made by competitors provides a supplementary economic rationale for the Biomedical Catalyst (as subsidies will to some extent compensate for the inability of applicants to fully internalise the returns of R&D activity).

Finally, and again peculiar to the life sciences sector, is that the primary consumer of biomedical products are national health systems. The risk averse, monopsonistic, and budget constrained nature of these buyers may

distort rates of return to investment to biomedical research (again, inhibiting uptake of new technologies and causing sub-optimal levels of investment).

A.3 Theory of Change

This section articulates the expected causal process by which the Biomedical Catalyst programme will deliver its intended results. While this framework largely defines the range of outcomes and uncertainties that will need to be explored through the impact evaluation, a number of issues are highlighted that will also require attention through the process evaluation.

A.3.1 Application Process

Applicants to the Biomedical Catalyst are required to provide detailed project plans and an assessment of the commercial potential of the product under development. While it is anticipated that such a process will be in many respects familiar to the SMEs applying for R&D subsidies, there may be effects on applicants from academia. In particular, it is expected that going through this process will help improve skills relating to the commercial planning of translation research projects, as well as encouraging closer links with industrial partners (who may be able to offer relative strengths in this critical area needed to make a successful application to the programme).

Such effects may have longer term benefits that will need to be explored in the evaluation. For the applicants themselves, this may increase the likelihood the project is successfully brought to market through a variety of mechanisms (particularly if they respond positively to the feedback received). However, the scheme may also leverage broader changes in behaviour amongst universities: for example, the scheme may give confidence that sufficient funding is available to support translation research to justify investment in internal teams focused on identifying and developing proposals or research areas with the potential for clinical application and later commercial exploitation. The evaluation will also need to be alert to the potential hazard associated with encouraging applications from those that may not possess the necessary skills to develop a translation research project of the highest quality (the process evaluation will need to examine the scale of transaction costs incurred by applicants to explore how far waste is a possible issue).

A.3.2 Project Selection Processes

The various appraisal, review, and project selection processes employed in the delivery of the Biomedical Catalyst have been designed to give rigorous scrutiny to both the scientific and commercial case for investment of public funds. These processes might be expected to lead to a wide range of effects on the overall success of the programme (providing these processes function sufficiently effectively).

Firstly, these processes might be expected to ensure that public investment is levered into those projects where the scientific rationale is strongest. If this is the case, then this might be expected to be observed in lower than average failure rates between stages of technical development. However, the scrutiny of applications and provision of feedback throughout the process may also help applicants improve the design of the research and development process, again serving to improve success rates (and it will be important to establish the perceived value of this feedback through the process evaluation).

However, the fact that successful applicants have been exposed to, and passed, a rigorous assessment of their project plans, may also go some way to reducing the impacts of information asymmetries on their ability to secure the necessary finance to progress R&D projects to the next phases (effectively providing a potentially significant market signalling mechanism). Clearly, the emergence of such effects will be contingent on awareness of the

Biomedical Catalyst amongst the relevant investor community, and confidence in the mechanisms employed in project selection (which will be important elements to test in the process evaluation).

Another aspect that will need consideration through the process evaluation is issues with the speed of project funding decisions. Many applicants (particularly those at later stages of technical development) will have already protected intellectual property through patents at the point of application. The time limited nature of patent protection means that any time lost in securing funding from the public or private sectors will reduce the commercial potential of the products ultimately developed. As such, there is an important trade-off between a rigorous scientific appraisal (which absorbs time) and the need to make rapid decisions (from a strictly commercial perspective), which may be more important for some categories of product that are quicker to market with shorter lifespans (such as medical devices).

A.3.3 Unsuccessful Applications

It should be acknowledged that given the hypothesised nature of the market failures justifying the scheme, failure to secure funding through the programme may have a substantial effect on unsuccessful applicants. They may struggle to raise finance privately, and for those projects at a later stage of development where intellectual property has already been protected, delays due to difficulties in funding in R&D activity will begin to erode the commercial potential of the project. As such, and particularly where SMEs have no scope in revenues, it would appear likely that many unsuccessful applicants would be forced to close (potentially ending development of the technology concerned). For academic-led projects, being rejected for funding may bring the translation research effort to an end (unless alternative sources of academic funding can be obtained), though there is the possibility that the research team is forced to commercialise before they are ready.

This prospect raises a number of problematic issues that will need to be addressed in the evaluation. Firstly, it may be difficult to undertake primary survey research with SMEs that have dissolved since their failed funding application (it is not anticipated that this issue will be significant for academic applicants). However, the exclusion of such firms in analysis will lead to a form of attrition bias in which those firms least able to secure funding are dropped from the comparison sample (leading to understatement of the impact of the Biomedical Catalyst). This issue can be resolved by assuming that R&D expenditure falls to zero following the dissolution of the SME (with similar strategies adopted for other key variables), where this outcome is known (this can potentially be identified from Companies House records). However, the possibility that the entrepreneurs concerned reappear at a later stage (and under a different name) cannot be discounted, and it will be highly challenging, if not infeasible, to establish such outcomes.

A.3.4 R&D expenditure and Leverage

The hypothesised economic rationale for the Biomedical Catalyst is that there are market failures (largely information asymmetries) in capital markets that inhibit the flow of finance into translation and other R&D projects in the life sciences sector. As such, if the Biomedical Catalyst is effective in meeting its objectives, it is anticipated that one of the key outcomes that would be observed would be an increase in research and development expenditure amongst successful firms.

However, in order to achieve these aims, R&D subsidy programmes need to be targeted at infra-marginal projects (i.e. those that would not have been taken forward without the grants). The academic evidence broadly suggests that R&D subsidies lead to an increase in research and development expenditure when it is targeted at small and

medium sized firms. A study examining the impacts of R&D incentives[13] on firms in Northern Italy (in which resources were allocated using a broadly similar process to that employed in the delivery of the Biomedical Catalyst) found that amongst small firms, R&D expenditure rose in line with the subsidies offered (though no impact was observed across the population of grant recipients overall). A Finnish study[14] examining the impact of EU subsidies for R&D found that subsidies caused increases in expenditure in excess of grants offered (implying that the scheme levered in additional private spending). Other patterns that emerge from the broader evidence are that subsidies (at least for capital investment[15] and R&D) are less effective where they reach large firms (an issue that has been designed out of the Biomedical Catalyst through eligibility restrictions). Differences between the effectiveness of individual programmes are likely to be at least partly attributable to the effectiveness of the processes adopted to judge how far a project is 'infra-marginal,' and close attention to these elements of the resource allocation process are required as part of the study.

A similar, though more complex, pattern of effects would potentially be anticipated in academic institutions. One study examining the effectiveness of research grants in raising research output (an area that has received limited attention) at universities in the US suggested that the impacts of such grants (on publications and citations) were limited[16]. This finding was in part explained by the competitive and fragmented nature of academic funding (as those rejected may be able to find funding from other sources, an issue that will need to be examined in depth in the study). Additionally, the grants available through the Confidence-In-Concept, Early and Late Stage awards may increase the level of resource expended in *translation* research projects, there is also a possibility that this comes at the expense of reduced focus on other research activities (and such trade-offs will need to be explored).

The cost of the R&D process (particularly for the development of new medical therapies) are high, largely driven by the need for large scale clinical trials to either demonstrate the safety or efficacy of the new product. While these costs may in some cases be lower for low risk (Class I) medical devices or digital health projects that might be sold directly to the consumer, investment in clinical trials would still be needed to provide the evidence needed for adoption by national health services. A recent US study[17] examining the costs of bringing a range of new drugs to market provides some indication of the total cost associated with the R&D process in the life sciences industry: the range of costs of phase I, II, III trials associated with three obesity drugs were estimated at between $185m and $409m, between $78.4m and $333.2m for four GLP-1 inhibitors (a treatment for diabetes), and between $2.9bn and $3.1bn for two factor Xa inhibitors (a treatment for cardiovascular disease). The costs involved were driven largely by the cost of Phase III trials which accounted for over 90 percent of the R&D cost in all cases (in which the drug is tested in thousands of patients to reach the levels of statistical precision required to demonstrate superior efficacy relative to existing treatments, and isolate any side-effects that may be present for small percentages of the population). There are lower costs associated with the R&D process associated with developing treatments for rare diseases (as Phase III trials typically involve smaller numbers of patients).

The high cost of Phase III clinical trials has important implications for the evaluation as subsidies are (in general) only available up to a Phase II clinical trial (in which the effectiveness and safety of the new product might be tested on 100 to 300 patients). As such, it is anticipated that applicants will need to raise substantial additional investment from the public or private sector in order to progress projects once they have reached the limit of what can be subsidised through the Biomedical Catalyst. As noted above, the Biomedical Catalyst has the potential to

[13] Are Incentives for R&D Effective? Evidence from A Regression Discontinuity Approach, Raffaelo Bronzini and Eleonora Iachini, 2009
[14] The Impact of TEKES' Direct Support on Business R&D, Elias Einiö, 2013
[15] Causal Effects of an Industrial Policy, Ciara Criscuolo, Ralph Martin, Henry Overman, and John Van Reenan, Centre for Economic Performance, 2012
[16] The Impact of Research Grant Funding on Scientific Productivity, Journal of Public Economics, Jacob and Lefrgen, 2011
[17] Stifling New Cures: The True Cost of Lengthy Clinical Trials, Avik Roy, Manhattan Institute for Policy Research, 2012

have a substantial effect on the ability of applicants to secure this finance: while progress through different phases of the product development process will reduce risks to new investors, the assessment of the scientific and commercial merits of each application may also help reduce the information asymmetries involved. A key outcome for the evaluation (alongside R&D expenditure) will be the level of private investment attracted by applicants (including beyond the lifetime of the project): and if the programme is effective in tackling the market failures identified, the treatment effects involved could be anticipated to be of a substantial magnitude (notwithstanding the issues identified above relating to additionality), though equally resources may be wasted where projects fail to secure follow-on funding.

A.3.5 Employment and GVA effects associated with the R&D process

Initial employment and Gross Value Added[18] effects associated with the programme will be those associated with the additional R&D expenditure levered by the programme (though it is important to understand these as a social cost of the project, rather than as a benefit[19]). To some degree, these effects may be observed within the applicant organisations themselves (for example, if implementation of the project requires recruitment of additional scientific or other personnel). Such effects may be present both within academic and SME led bids: although employment effects may be less significant for academic bids if the staff involved can be redeployed easily on other research projects, or may visible in other metrics.

However, the R&D projects funded through the Biomedical Catalyst often involve the outsourcing of various elements. For both therapeutics and medical device projects, the applicant will often subcontract the delivery of clinical trials to a Contract Research Organisation (CRO), or the manufacture or synthesis of the clinical products under investigation to a Contract Manufacturing Organisation (CMO). Additionally, the applicant may contract out other elements such as specific pieces of analysis or consultancy advice or regulatory advice. Other costs may include fees for MHRA approval. For SME projects, typically only a small share of the project cost is retained by the firm to fund internal posts, or the purchase and installation of capital equipment. As such, the majority of these initial employment and GVA effects would be expected to be observed in organisations external to the applicants.

This raises a range of potential issues that will need to be explored through the evaluation:

- **Input additionality:** If it is difficult to collect longitudinal data on the R&D expenditure of applicants, it may be feasible to establish input additionality of the scheme through an examination of the turnover of sub-contractors. As sub-contractors are identified within applications for funding, a data-linking exercise aiming at establishing the longitudinal records of employment and turnover required for such an analysis may well be feasible (and the issues associated with implementing this will be provided at a later stage).

- **General equilibrium effects:** Any additional demand for the services of the CMOs, CROs and other suppliers will place pressure on their capacity. If the additional demand cannot be accommodated within existing capacity, firms may either raise prices, or recruit additional workers (leading to price growth through pressure on earnings). As such, pressure on prices may dampen demand for these services elsewhere in the economy (unless investment is made in capacity). As such, estimates of the net impact of the scheme on the turnover of sub-contractors may be a superior indicator of the net effect of the programme on R&D expenditure at the level of the economy, though it is unlikely this complication could be fully addressed through the study.

[18] Gross Value Added is the value added to raw materials in the process of production, and can be estimated as the sum of profits and wages, or the value of turnover less expenditures on intermediate goods and services.
[19] Additional R&D expenditure represents an investment cost that will only produce social benefits if it leads to the commercialisation of a new technology or process (the benefits of which will include both private and social returns to that investment).

- **Academic projects:** Utilisation of the CMOs and CROs are also present in academic projects, so investigation of this issue will need to cut across both arms of the Biomedical Catalyst.

Additionally, in order to assess the net impact associated with the project (in economic terms) it will also be important to consider the strength of any leakage effects in which the delivery of contracted services (and associated profits and employment) is provided by overseas suppliers.

A.3.6 Collaboration

The Biomedical Catalyst was created with a specific objective of stimulating greater levels of collaboration between academia and industry in the life sciences sector (with the wider aim of achieving greater pull-through of academic research into the commercial sector). Such collaborative effects might be catalysed in a number of ways. As noted above, the process of preparing an application may foster collaboration through highlighting the need for academics to secure industrial partners (or vice versa). Additionally, the publicity associated with Biomedical Catalyst may act to generate interest in collaborative working between academics and industry through raising wider awareness. Finally, technical progress achieved through Biomedical Catalyst projects may also help lever collaboration: for example, showing proof of concept in animal studies may be required to secure the commitment and investment of industrial partners. In turn, this collaboration could bring important direct improvements to the quality or commercial potential of the project, as well as more indirect effects through mutual learning, skills exchange, or movement of workers between academia and industry.

However, the processes that have been adopted in the delivery of the Biomedical Catalyst programme that have been designed to produce a collaboration effect (e.g. MRC co-funding of academic components of SME led bids creates financial incentives to collaborate) are primarily passive in nature. There are often substantial market failures inhibiting collaborative research and development projects (such as transactional frictions driven by the unevenness of returns to collaboration, incomplete contracts and free-riding). As such, while it will be important to explore these types of effects through the evaluation, some caution over the strength of the causal effects that might be observed is needed.

A.3.7 Technical Progress

A key aim of the Biomedical Catalyst is to accelerate the commercialisation of new products originating either in academia or the private sector (and over the timescale of the evaluation, this will be a fundamental measure of the overall success of the programme). Provided that firstly, Biomedical Catalyst funding is reaching infra-marginal projects, and secondly, the scientific merits of project proposals are adequately assessed through the project review and selection process, then the resources invested in research and development should produce an effect in terms of bringing the products concerned closer or more quickly to market (if not to market). Such an effect may not be limited to the duration for which subsidies are available (as noted before, if the Biomedical Catalyst levers private investment into projects through de-risking projects then effects on technical progress could be observed well beyond the lifetime of funding), though clearly it will be important to establish any stages at which product development is being held-up.

There are a number of ways in which technical progress might be understood and measured for the purposes of the evaluation which are discussed in more detail in Section 4. Medicines, medical devices and medical technologies need to pass through various stages of regulatory approval before launch to market (which reflect the stages of technical development). However, these stages vary by type of product (the regulatory requirements involved in bringing a Class I medical device to market are currently substantially less onerous and costly than those associated with new medicines). Additionally, the investment cost and time associated with reaching the next stage of technical progress will broadly grow exponentially as the product get closer to market. As such, it is

anticipated that there will be substantial variation in the treatment effects both across different product types and levels of technical development at the point of application).

Given industry wide failure rates at various stages of the regulatory approval process (at least for new medicines), it can be anticipated that some projects will either fail to reach regulatory approval, or will be aborted due to concerns with safety or efficacy (and these outcomes will also need to be tracked through the evaluation). However, it may also be helpful to benchmark failure rates against industry averages to establish some measure of how far the Biomedical Catalyst is effective in 'de-risking' projects through the processes in place to judge the scientific merits of applications (though care will be needed to separate such effects from any possible tendency for project selection panels to favour lower risk projects).

A.3.8 Patenting

Alongside technological progress, if the projects lead to knowledge that can be exploited commercially, then a patenting effect might also be anticipated. The level of patenting will also depend on baseline levels of technical development: for late stage awards, it is not anticipated that applicants will register new intellectual property, though such effects might plausibly be observed for projects at earlier stages of technical development. Additionally, the commercial value of patents will be potentially priced into company accounts and may provide an early indication of the potential economic impacts of the project (as discussed below), though the act of valuing intangible assets tends to be correlated with acquisitions (and as such would not provide reliable measure as it could be anticipated that it would be unobserved in many cases). Collaboration effects may also be visible through patenting activity (through joint registration of patents).

A.3.9 Publication Effects

Both academic and industry-led projects have the potential to lead to research publications in academic journals. R&D projects will lead to new knowledge (for example, into the action of new compounds in humans). While academics may have wider incentives to publish the results of their research, the publication of the results of clinical trials also acts to encourage the adoption or consumption of any new products developed (as national health systems will typically require evidence that the treatments involved are both effective and cost-effective). As with patenting, publications may also provide indirect evidence of any collaboration effects (where academic and industrial partners co-author publications). However, though publication effects might plausibly be observed, they may be not be visible over the duration of this evaluation owing to the duration of the peer review process associated with academic publishing.

A.3.10 Exit Strategies

The review of project application forms highlights a number of exit strategies may potentially be pursued applicants with distinct implications for the character of the outcomes that might be observed:

- **Spin-out activity:** For academic bids, a key indicator of progress towards commercialisation will be the propensity for the researchers involved to 'spin-out' or create a new entity with the objective of commercially exploiting the intellectual property generated. However, there is some ambiguity as to the possible direction of the impacts that may be observed in this area: one possibility is that the availability of MRC funding for translation research helps protect the researchers from the need to commercialise too rapidly (with possibly damaging effects on the commercial prospects of the project under development), which could lead to a reduction in the propensity to spin-out in the short term (though the spin-outs themselves may ultimately prove more sustainable).

- **Commercial production:** Applicants may ultimately seek to adopt an exploitation model based on the full scale commercial production and sale of the products developed. Such a commercial strategy would likely lead to the greatest pay-offs for the applicant (as the value added as a consequence of marketing, logistics, and so forth would be retained by the company), though this would involve deferring those returns to such a point at which the product could be launched to market. Additionally, the applicant would also need to find resource (through equity investment or an IPO) to complete the research and development process.

- **Licensing:** The marketing and logistical costs associated with commercial production may also be externalised through licensing agreements with other firms assuming responsibility for manufacturing, logistics and marketing (Technology Transfer Offices will be tasked with facilitating this in the case of academic led projects). Such a strategy may deliver lower pay-offs for applicants, but would also externalise the risks associated with managing a complex set of commercial operations (an area in which those responsible for leading the R&D process may not have the necessary/appropriate level of experience or skill).

- **Selling out:** An applicant may also be able to exploit the value of the IP generated by selling their intangible assets (for example, after demonstrating proof of concept) to a larger pharmaceutical firm with the resources required to take the product through Phase III trials, regulatory approval, and marketing.

These possibilities raise the strong risk that the effects of interest will ultimately not be observed within the applicant organisation, but in new commercial entities or other firms. As such, it will be critical to track R&D projects across these organisational boundaries to develop estimates of the overall impact of the Biomedical Catalyst.

A.3.11 Economic Impacts

The policy objectives for the Biomedical Catalyst centre on the potential economic impacts of translation and commercial research and development processes:

- **Sales:** Following regulatory approval and any post-marketing activities, initial economic impacts might be expected to be observed in the form of either product sales or licensing fees (where the commercial strategy primarily rests on licensing the intellectual property generated through the project). A review of project application forms suggests that many applicants expect to maximise the returns on their R&D investment by marketing their products globally (a sequential strategy, by which the applicant focuses on domestic markets in the first year, before rapidly expanding to European and then US markets – with internationalisation often driven by licensing agreements - is fairly typical of commercial plans[20]). In line with the high costs of the R&D process, revenues are typically expected to be substantial (£bns per year would be not atypical) once peak sales have been reached (though clearly there may be a degree of optimism bias associated with such financial projections). For firms successfully taking R&D projects to market, the prior expectation would be a long period in which observed turnover would be zero before growing rapidly following successful introduction to the market (notwithstanding the possibility that firms generate revenues from the sale of other products).

- **Profits:** One of the key economic benefits associated with successful projects will clearly be the profits associated with the sale or licensing of new products. However, given the high volumes of equity or private investment needed to bring these products to market, it is anticipated that only a share of profits will be retained by the applicant (with the remainder being shared by investors). As such, it will be important to

[20] For medical devices, the pattern can sometimes run the other way, where it is feasible to secure national approval in EU member states (whereas in the UK, adoption will need to be secured individually with each Clinical Commissioning Group).

capture the scope of any effects by which the main economic benefits of the programme 'leak' outside of the UK to foreign investors (and to some extent, such leakage effects might be anticipated on the basis of the current or future geographical profile of commercial investors in supported projects or firms). Those entering licensing agreements with applicants would also be expected to earn a profit on product sales (and again, it will be important to track the international distribution of such organisations to determine how far such profits are accruing to individuals resident in the UK).

- **Direct employment impacts:** While sales and profitability effects are expected to be significant (contingent on a successful product launch), direct employment (and associated wages[21]) impacts are expected to be modest. A review of application forms received by Innovate UK suggested that the manufacturing of new products (both therapies and medical devices) is often expected to be undertaken by an external manufacturer on a contract basis (discussed under multiplier effects below). While applicants expect to create new jobs (often in not unsubstantial volumes), these are often jobs associated with marketing or logistics rather than manufacturing. The creation of manufacturing is possible in some scenarios (for example, some SMEs may have manufacturing operations, or the applicant may ultimately be acquired by larger vertically-integrated pharmaceutical firms), though again, this job creation activity will only benefit the UK if the facilities involved are also based in the UK.

- **Displacement:** Clearly, the introduction of new medical therapies and devices has the potential to lead to displacement effects in the product market. Where medical therapies and devices are introduced in competition with existing technologies available for treatment or diagnosis within the disease area of interest, sale of the new products will likely cause a reduction in the sales (and associated employment and profits) amongst competitors. However, even where there are currently no competing treatments, displacement could occur through diversion of resources from other types of treatment, or from the sales of products currently being developed by other firms. Such displacement effects will offset the economic impacts described above (to the extent that the profits and wages associated with the production of the products displaced would have otherwise accrued to residents of the UK). However, as regulatory approval or adoption by national health systems will often (though not always) require that the product is more effective than treatments already available, it can be anticipated that any displacement effects be accompanied by an improvement in social welfare through human health effects or reduced costs to the NHS (in effect, an improvement in productivity).

- **Multiplier effects:** As highlighted above, the manufacture of the medical products developed through the programme will typically be undertaken by CMOs, and if the Biomedical Catalyst leads to the creation of new (or protection of existing) manufacturing jobs this will likely be observed amongst CMOs rather than the applicants themselves (though the possibility that the applicant firm is acquired by a large pharmaceutical firm with its own manufacturing facilities cannot be ruled out). Equally, the potential for licensing agreements may mean that jobs associated with marketing and logistics are also observed in other firms. The extent to which these multiplier effects lead to employment and GVA effects within the UK will again depend on the geographical distribution of the relevant CMOs.

As is clear above, the scale of economic impacts (and therefore value for money) associated with the Biomedical Catalyst programme will be sensitive not just to the technical progress achieved but also on the level of leakage of benefits to territories. As well as being a key issue for exploration in the impact evaluation, it will also be important to consider whether appraisal processes work towards the Biomedical Catalyst's stated objective of supporting the long term growth of the life sciences in the UK as part of the process evaluation.

[21] As set out above, GVA can be represented as the sum of profits and wages.

A.3.12 Human Health

The main social welfare benefit associated with the Biomedical Catalyst will be the impacts on human health resulting from the introduction of new products, enabling diseases to be treated, prevented or diagnosed more effectively (or cost-effectively). This will create benefits both for patients (through enhanced quantity/quality of life) and for national health systems (through efficiency gains), potentially on a global basis (though for the purposes of a CBA in line with HM Treasury guidance, only those benefits accruing to residents of the UK should be included[22]). Clearly, the scale of these benefits will be dependent on the following factors:

- the relative prevalence of the disease or condition targeted by the product
- the impact of the disease or condition on quantity/quality of life
- the size of the patient population for which the treatment is suitable
- the effectiveness of the new compound or device relative to existing treatments and,
- the extent to which the new product displaces existing or competing treatments or technologies (which in turn will in part depend on the price of the product relative to competitors)

While the bulk of these effects will not accrue until products have been brought to market (which will most likely be beyond the lifetime of this evaluation), there is a possibility that those patients involved in clinical trials will derive a health benefit from their participation (obviously this is based on the presumption that the products will be effective in treating the condition concerned, and any gains in quality of life are not offset by unwanted side-effects). Such effects amongst patients receiving a placebo are also likely to be limited.

A.3.13 Spill-over Effects

As highlighted above under the economic case for intervention, there is a possibility of spill-over effects by which the knowledge developed through the project can be exploited by others. The mechanism by which such an effect may occur in the case of the Biomedical Catalysts is via the tendency for the results of R&D projects to enter the public domain (as described above) as a consequence of the need to secure acceptance from either the public or national health systems. This will allow other firms or researchers to freeride on those investments by building on those results (published findings may offer lessons that are helpful, for example, in guiding the firm's own R&D efforts). The possibility of spill-over effects will be strengthened where R&D projects are focused on platform technologies.

A.3.14 Demonstration Effects

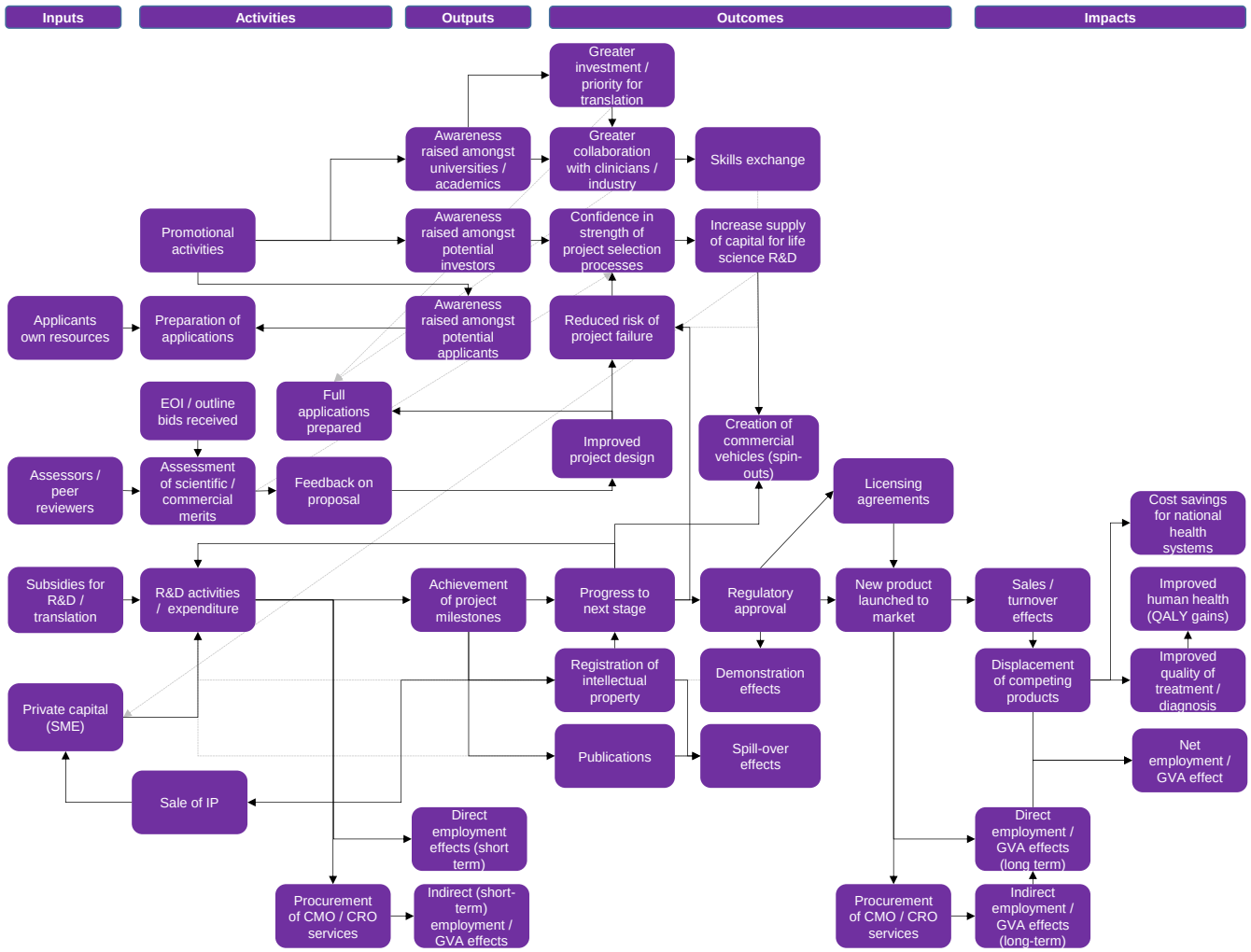
The Biomedical Catalyst (through 'de-risking' innovative or novel research and development projects) also has the potential to deliver supplementary benefits through demonstration effects. As an example, for wholly new types of treatment (such as cell therapy) that have never reached regulatory approval, commercial investment may be constrained by the substantial risks and uncertainties involved. If the projects subsidised through the Biomedical Catalyst are able to reach regulatory approval for novel products, this may act as a signal to the market that the further investment in these areas may generate commercial returns (which in turn, may improve the supply of finance for SMEs or spin-out activity). If more resource is directed at these areas, a range of effects could be observed (such as increased levels of publications, patenting activity, regulatory approval for additional new products, and further economic impacts of the nature specified above).

[22] This aspect is potentially highly complex in the case of the diseases presenting a global problem. For example, the development of vaccines or treatments for diseases originating overseas (e.g. Ebola) may have no immediate benefit for patients in the UK, but generate benefits for the UK through the limiting the spread of the disease.

A.4 Logic Model

The preceding discussion around the anticipated impacts of the Biomedical Catalyst are summarised in the logic model presented below.

Figure A.1 – Logic Model



A.5 Key Outcomes

Proposed indicators for the key outcomes identified above are summarised in the table below (and breaking them down as to how far they would be relevant to commercial applicants or academic institutions.

Table A.1 – Key Outcomes

	Commercial Entities	Academic Institutions / Researchers
R&D activity and leverage	• R&D expenditure • Private equity investment (cumulative) • Propensity for IPOs • Capital raised through IPOs • Current market capitalisation • Investor confidence in life sciences • Supply of private finance to life sciences sector	• Resources invested in translation research projects • Wider resource investment in translation research by HEIs (e.g. staff dedicated to identifying translation opportunities)
Early Employment & GVA	• Employment and GVA amongst grant recipients • Employment and GVA of CROs and CMOs	• Number of researchers working on translation research projects • Employment and GVA of CROs and CMOs
Collaboration	• Number of academic partners • Joint publications / patenting (proxy)	• Number of industrial partners • Joint publications / patenting (proxy)
Technical Progress	• Technology Readiness Levels • Regulatory approval • Propensity to progress to next stage • Propensity to submit follow-on application	• Technology Readiness Levels • Regulatory approval • Propensity to progress to next TRL stage • Propensity to submit follow-on application
Patenting	• Number of patents registered (by type)	• Number of patents registered (by type)
Publications	• Publication volumes • Nature of publications • Impact factor of journal publications	• Publication volumes • Nature of publications • Impact factor of journal publications
Exit Strategies	• Propensity to spin out • Number of licensing agreements • Sale of IP	• Propensity to spin out • Number of licensing agreements • Sale of IP
Economic impacts	For grant beneficiaries, CROs and CMOs: • Sales • Profits • Employment • GVA • Productivity (TFP / GVA per worker) • Displacement in product markets	For spin outs, CROs and CMOs: • Sales [not grant beneficiaries] • Profits [not grant beneficiaries] • Employment • GVA • Productivity (TFP / GVA per worker) • Displacement in product markets
Human Health effects	• QALYs gained	• QALYs gained
Spill-over / demonstration effects	• Patent citations • Publication citations	• Patent citations • Publication citations

A.6 Time Horizons

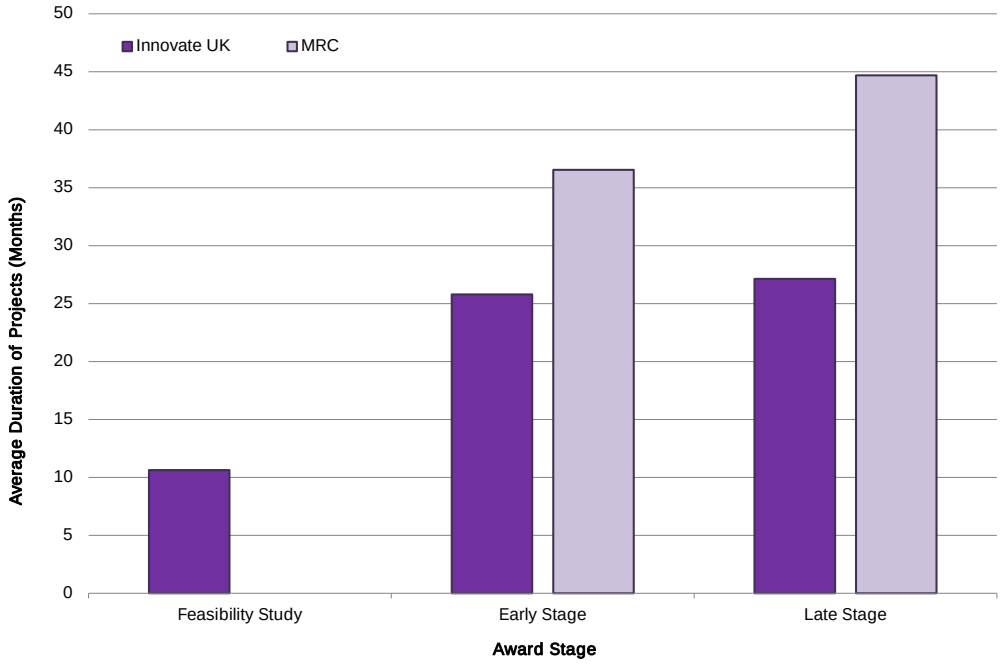
The time horizons involved with bringing biomedical research to market are long term in nature and this will influence the scope of outcomes it may be feasible to observe. A review of the literature[23] has suggested that, on average, around seventeen years elapse between the initial publication of a journal article and commercial application (though the review highlighted that there was also limited understanding of the factors driving these estimates and how these vary across different product areas). This estimate also covers the period of time during which basic scientific principles are developed into a potential idea for clinical application (development work that will have already taken place at the point of application for Biomedical Catalyst funding), so it is anticipated the effects involved will potentially be realised over periods shorter than this. Additionally, projects will be at varying stages of technical development and proximity to market depending on type of award.

To provide a firmer indication of the expected time horizons over which the effects involved might be realised (and therefore, which effects could be realistically observed over the three year time horizon for the evaluation), the figure overleaf sets out the average duration of projects that successfully passed through MRC and Innovate UK project selection processes (Confidence-In-Concept awards have been excluded from this analysis, as the awards fund packages of individual projects, the timings of which are not straightforwardly captured in application and appraisal data). While feasibility studies (at the earliest stages of technical development) tend to be short-term (an average of just over 10 months), Early Stage projects have an average duration of two to three years (which could take the project through pre-clinical work or early clinical stages) and late stage projects an average duration of two to four years (which would take a project through, at furthest, to Phase II clinical trials[24]).

With the first grants awarded in 2012/13 and the final grants awarded in 2014/15, it is anticipated that by 2018 (when this evaluation is due to complete), the majority of projects funded (and all Feasibility and Early Stage projects) will have completed. However, in order to commercialise, projects will still need to pass through Phase III clinical trials (or equivalent), as well as post-marketing testing. A number of studies summarised in the aforementioned review have estimated that the time elapsing between the start of clinical testing (i.e. the focus of late stage awards) and marketing approval is in the order of seven to eight years. This means that even for late stage projects funded through Round 1 of the programme, the economic impacts involved would not start to become visible until 2020 (and are unlikely to be fully realised until 2025 to 2030, given the sequential nature of commercial exploitation plans highlighted above). Such effects may be visible at an earlier stage for medical devices and other projects focusing on non-therapeutic technology areas (which in some cases can be brought to market relatively rapidly).

[23] The Answer is 17 Years, What is the Question: Understanding Time Lags in Translational Research, Zoe Morris, Steve Wooding, and Jonathan Grant, Journal of the Royal Society of Medicine, 2013.
[24] As noted previously, Innovate UK has funded one Phase III clinical trial.

Figure A.2 – Average Duration of Funded Projects



Source: Innovate UK and Medical Research Council Monitoring Data

As such, it is anticipated that over the lifetime of the evaluation, the focus will need to be on those outcomes that will realistically be visible over the course of the study. Consideration to these issues is provided in the table overleaf.

Table A.2 – Expectations on Anticipated Distribution of Effects over Time

	Baseline (2015)	Final Evaluation (2018)
R&D activity and leverage	In principle, effects on R&D expenditure and activity (as well as associated outcomes, such as project viability) will be visible even at the baseline study (though this would only likely represent a small share of the cumulative effect).	Impacts on annual R&D expenditure will continue to accumulate, though even at the final evaluation, the total effect of the Biomedical Catalyst on R&D spending will not be fully realised (with projects still needing to get projects through Phase III trials and marketing approval).
Early Employment & GVA	It is anticipated that the early employment and GVA effects associated with the Biomedical Catalyst will follow a similar distribution over time as R&D expenditure.	As with R&D expenditure, the employment associated with the delivery of Phase III trials and marketing approval will not be visible in the data.
Collaboration	Early evidence of the effects of the programme on collaboration is anticipated at this stage (particularly if the application process encourages collaboration between industry and academia).	It is anticipated that any effects on collaboration would also grow by the time of the final evaluation study.
Technical Progress	At the baseline stage, it is anticipated that an insufficient number of projects will have completed to make judgements on the effect of Biomedical Catalyst in accelerating technical development, though some effects are anticipated amongst those starting from the earliest stages of technical development, where progress can be made most rapidly.	It is anticipated that some projects will have progressed through TRL8 (completion of Phase III trials or equivalent), though with some remaining before marketing approval is obtained.
Patenting	Some projects may involve the creation of new intellectual property, though it is anticipated that patenting effects will be more strongly associated with the Feasibility / Confidence-in-Concept awards than other projects. These projects are relatively short term, and it is anticipated an effect may be visible in the short-term.	Again, it is anticipated that patenting effects may continue to accumulate though possibly begin to decay by 2018, as those projects most likely to deliver IP impacts will be completed by 2017. However, effects in terms of citations (a possible indicator of spill-over effects) may start to emerge at this stage.
Publications	No effects on publication output are anticipated at this stage.	A 1998 study estimated the lags between trial registration and publication at an average of 5.5 years. As such, it is feasible that effects on publication output may be visible at the final evaluation stage (though only for the projects funded through the first rounds of the projects). It may difficult to observe the *impact* of publications at this stage (using proxy indicators such as citations).
Exit Strategies	Very few projects will have completed (other than feasibility or Confidence-in-Concept awards) projects, and it is anticipated that exit strategies will not be clear at this stage.	Commercial plans should (by 2018) be substantially more clear, and it is anticipated that some evidence will be available/
Economic Impacts Human Health Spill-over Effects Demonstration Effects	It is not anticipated that economic impacts (and other effects contingent on the commercialisation of the products concerned) will be visible until at least 2020. Equally, given the lags involved in the publications associated with clinical trials, However, the validity of this assumption will need to be examined during the baseline phase of the evaluation.	

A.7 Contextual Issues

There are a set of contextual issues that will also require consideration in the evaluation. Firstly, there are a range of past and expected policy changes that have the potential to influence the likelihood that the Biomedical Catalyst achieves its stated aims and objectives. Secondly, there are also a number of potential alternative sources of funding that might be used by applicants to fund translation research or commercial R&D activity.

A.7.1 Broader Policy Context

The Biomedical Catalyst is operating within a changing environment for medical and translational research. The shifting industrial structure described in Section 2.2 above, has been matched by a recent and significant increase in public support (both financial and otherwise) for the life sciences sector. The industry has been identified by the government as one of 11 priority sectors for policy support. A number of initiatives has been packaged around this central policy objective:

- The 2011 Life sciences Strategy launched the Biomedical Catalyst, and introduced a broad range measures to promote the development of the sector including: a scheme to support early access to market approval processes for breakthrough therapies, plans for domestic and international regulatory reform, £130m investment in Stratified Medicine, a new platform for clinical trials, trade promotion events, skills investments and the appointment of independent Life sciences Champions[25].

- The establishment of Catapult Centres in the area of Cell Therapy and Diagnostics for Stratified Medicine is building new institutions focused on supporting collaboration between academics and industry as well as in bringing technologies forwards from academic concept to commercial reality.

- The Innovative Medicines Review was announced in November 2014 with the aim of considering 'how to speed up patient access to cost-effective and innovative medicines, devices and diagnostics'. This review represents the latest step in a series of initiatives to reform how the NHS operates as a purchaser of innovative life sciences products and services. The 2011 Life sciences Strategy identified an opportunity to better harness the NHS to support the adoption and diffusion of innovation. The strategy called on the NHS to play a more active role in realising innovations by 'pulling' through new therapies. Follow up actions to this have included reforms of how NHS data can be used, the expansion of NICE technology appraisals, and a doubling of the use of the Small Business Research Initiative (SBRI) to purchase new products and services.

In addition to these specific initiatives the government have sought to put in place a comprehensive system of support for the sector. The presence of a ten year strategy for life sciences and the fact that considerable civil service time has been dedicated to working in partnership with business and delivering two updates of this since 2011 demonstrates the central importance placed on this area.

At the same time as these life sciences-specific interventions, a number of more general policy initiatives have been introduced since the launch of the Biomedical Catalyst which have the potential to offer support to the types of translational research supported by the programme, potentially contributing to their success:

- Tax credits to support research and development have become increasingly generous. For SMEs the rate of enhanced deductions was increased from 175 per cent to 200 per cent in 2011, to 225 per cent in 2012 and

[25] Office for Life Sciences (2011) Strategy for UK Life Sciences, Department for Business Innovation and Skills,

will increase to 230 per cent in 2015. For large companies an 'above the line' credit of 10 per cent in 2013, increasing to 11 per cent in 2015.

- The central method for grading the quality of research within UK higher education institutions, the Research Excellence Framework (REF), was changed in 2014 to include an assessment of the impact of research on the economy and society more generally. The scores from this new approach were released in December 2014. It is too early to fully assess the impact of this change, but it seems likely that it will have acted to increase the incentives for academic institutions to pursue research which is of commercial value.

- The £500m Research Partnerships Investment Fund has been established to support joint capital programmes between universities and businesses. The Medical Research Council is also investing £170m in the Clinical Research Capabilities and Technologies Initiative to fund novel equipment to more effectively advance the UK's ability to explore new areas in clinical research. The increase in Innovate UK's budget of £185m to in excess of £400m for 2014/15 (of which £80m will be directed at health and care) will also offer support to translational research. A key fund, focused on supporting translational research and industry collaboration has also been sustained in the face of a tight fiscal environment. The £150m Higher Education Innovation Fund supports knowledge exchange between universities and business. The limited availability of other sources of public funding may also have acted to significantly increase the relative significance of these sources of public funds.

Given the breadth and scale of this activity it is clear that the life sciences area and translational research is a core government priority and that the Biomedical Catalyst is unlikely to be operating in isolation. This broader policy context is aiming to provide a positive environment for the life sciences sector, and for translational R&D activity in general. If successful, then together these policies may be creating necessary conditions within which the programme is able to succeed. Additionally, academics and companies who successfully attract Biomedical Catalyst funding may also be able to exploit these other new sources of public funding, improving their performance. Taken together these effects complicate the task of identifying the impact of the Biomedical Catalyst, and increase the importance of studying the programme within its broader context (and these areas may require qualitative, rather than quantitative, investigation).

A.8 Implications

- **Judging the success of the Biomedical Catalyst:** The time horizons associated with the launch of new biomedical products are long term in nature. While the programmes' objectives have an economic dimension, it will not be feasible to provide a rigorous assessment of how far these objectives have been achieved over the timescales for this evaluation. Instead, the focus will need to be on key intermediate outcomes, such as the acceleration of technological progress. Other intermediate outcomes include financial market or access to finance impacts, the overall level of resource invested in the R&D or translation process, and collaboration, patenting and publication effects.

- **Short term economic impacts:** However, there may be short term economic impacts as a consequence of any R&D expenditure levered by the Biomedical Catalyst in the form of employment and GVA effects. The evaluation will need to capture these effects, though they will need to be treated with caution as they represent a cost of the programme (rather than a benefit). Additional complexities are introduction by the vertically disintegrated structure of the market, and it is anticipated that the majority of these impacts will be experience outside of grant applicants (within CROs and CMOs). The evaluation will need to seek to obtain details of these CROs and CMOs to provide evidence those effects have been delivered.

- **Leakage:** The overall economic impacts of the Biomedical Catalyst programme will be likely to be linked to the international distribution of suppliers to grant applicants (and any firms licensing or acquiring IP). While a quantitative assessment of the net economic impacts of the Biomedical Catalyst may not be feasible within the timescale of the evaluation, it may be possible to form a reasonable expectation of the distribution of these suppliers and thereby make judgements as to the likelihood any benefits of the programme will accrue to the United Kingdom.

- **Value for money:** The direct benefits of the programme will be in part dependent on the successful commercial launch of new products and their net effects in terms of (1) improvements in the productive efficiency of the firms concerned, (2) benefits to patients in terms of enhanced health, and (3) benefits to the NHS in the form of reduced costs. The time horizons involved with bringing biomedical products to market may mean that there is no realistic way in which a cost-benefit analysis of the programme could potentially be delivered within the timescales of this study (and indirect effects, including any crowding-in of R&D spending through de-risking novel technologies, are likely to occur on an even longer timescale). Instead, the focus may need to be on cost-effectiveness measures such as leverage ratios (£s of additional R&D spending per £1 of public investment), cost per additional patent, or cost per additional publication. Some of these measures can potentially be benchmarked against comparator programmes (though there are few examples of rigorous quantitative evaluation of R&D programmes both in the UK and internationally).

Annex B: Process Evaluation Framework

The following section sets out in detail a framework for the process evaluation that will take place as part of the first stage of the study. The section sets out the range of processes employed by both Innovate UK and the Medical Research Council in the delivery of the Biomedical Catalyst programme and their anticipated contribution to the achievement of the policy objectives outlined in the preceding section. In addition, a framework of evaluation questions are specified with a view to examining the efficiency and effectiveness of the processes employed, building on those outlined within the invitation to tender (ITT). The process evaluation framework has been developed through an analysis of internal documentation describing the processes underpinning the delivery of the programme, and consultation with the range of individuals involved with the development implementation and delivery of the Biomedical Catalyst.

1.1 Scope of the Process Evaluation

The scope of the process evaluation is defined broadly within the Invitation to Tender as to *'assess the effectiveness of the joint Innovate UK and Medical Research Council Biomedical Catalyst process'.* The ITT also highlights three specific areas for consideration:

- The Innovate UK / Medical Research Council partnership and how it jointly delivers the Biomedical Catalyst
- The appropriateness and robustness of the current processes and funding mechanisms and,
- The current balance of the portfolio relative to the merit and scope

However, in early October 2014, the Medical Research Council commissioned the Audit and Assurance Services Group (AASG) to undertake a review of the relationship management between Innovate UK and itself. The overarching objectives of this audit were to ensure that - given the differing internal objectives, funding structures and stakeholders of these two organisations - the systems and processes used to maintain and manage relationships between these two organisations are adequate and effective. The audit focuses on four areas:

- The organisational relationships that set out the boundaries and apportion roles and responsibilities that facilitate the partnership
- The practical means of operation used to communicate, prioritise and coordinate activities when necessary
- How and where management information is shared between the two organisations, as well as how the information is used to inform decision making and
- What reporting and review structures exist to monitor and assess the projects funded by Biomedical Catalyst.

It was also agreed at the point of inception that, given their work, these topics would be out of scope of the data collection activities supporting this process evaluation, so as to avoid duplication of research activity. Therefore, the results of the audit were summarised within the process evaluation to highlight key aspects of the organisational relationship between Innovate UK and the MRC.

1.2 Process Overview

The Biomedical Catalyst programme is delivered jointly by the MRC and Innovate UK. The former administers grants for translation projects led by academic institutions, while the latter administers grants for research and development (R&D) projects originating from SMEs. Funding for the programmes originates from two separate directorates of the Department for Business, Innovation and Skills (the Science and Innovation directorates

respectively) and is not pooled for the purposes of the delivery of the programme (i.e. the MRC and Innovate UK are accountable for separate budgets).

In broad terms, the programme is delivered through the means of a funding competition (which will have involved eight rounds by the end of 2014/15) in which academics and SMEs submit applications for grant funding to the MRC or Innovate UK respectively. Processes to allocate resources are broadly similar across the two organisations. Applications are appraised by external experts, before being given detailed consideration by a project selection panel (the DPFS panel in the MRC arm of the programme or the Major Awards Committee (MAC) in the Innovate UK arm – and MRC applications close to commercialisation). Following the award of funding, there is more divergence across the processes employed by the two organisations in contracting and monitoring. Only one process is formally shared across the two organisations: the Major Awards Committee, which makes recommendations for funding decisions with respect to all strands of the Innovate UK programme and scores applications for 'Late Stage' awards to the Medical Research Council (i.e. those closest to commercialisation).

1.3 Processes in detail

This section provides a description of the various processes employed to deliver the Biomedical Catalyst and their associated role in contributing to the policy objectives of the programme (and highlights issues that may need to be explored through the process evaluation).

1.3.1 Programme Secretariat

Both the MRC and Innovate UK maintain a Programme Secretariat responsible for the design and co-ordination of funding competitions. They receive applications; organise appraisals, collect and compile appraisal results; and assist with the set-up of functions such as the DPFS and MAC panels which will be detailed later.

1.3.2 Competition Set-up

Innovate UK and the Medical Research Council run two to three funding competitions for the Biomedical Catalyst each year. To start the process, the organisations agree (internally) the funding for the round in question, where the amount of funding made available is based on projections for the necessary spend required as dictated by the over - or underspending in earlier rounds. This process is particularly significant for Innovate UK, which faces tighter constraints on the need to commit and spend the budget for the programme allocated by BIS (and little in the way of flexibility to vire budgets to or from other programmes). As noted, the Major Awards Committee, which is described in more detail below, is a shared process across Innovate UK and the MRC and as panel sessions last up to three days the dates for these sessions are agreed between the two organisations.

This initial investigation into collaborative processes merits further investigation through the process evaluation. Firstly, there is clearly a need for close working between Innovate UK and the MRC to align timetables for competition rounds owing to the shared process of the MAC (and it is anticipated that commentary on the effectiveness of these processes will be provided by the independent audit outlined above). Additionally, it will also be important to consider if and how far the budgetary constraints faced by Innovate UK have influenced approaches to resource allocation decisions (as if performance is judged on the basis of the ability to defray resources, there may be an incentive to favour lower risk projects with higher probability of defraying expenditure within the timescales allotted for the programme).

1.3.3 Marketing

Both Innovate UK and the Medical Research Council undertake a range of marketing activities both as part of the specific funding round and on an on-going basis, to promote the Biomedical Catalyst programme. The primary objective of these processes is to secure a pool of high quality applications from which to make funding decisions. However, as highlighted in the preceding section, there is a secondary goal to produce effects on the funding landscape (through raising awareness and confidence amongst the investment community).

The primary vehicles for promoting the programme include:

- **Knowledge Transfer Network:** Innovate UK's primary network to support business and thematic communities, KTN has provided a key role in promoting the Innovate UK element of the Biomedical Catalyst. Established to foster better collaboration between science, creativity and business, KTN has an outreach to 60,000+ SMEs, large business and academics. Communications are targeted through direct mail, monthly newsletters, events (including targeted BioMedical Catalyst meetings on digital health and medical devices) and one-to-one guidance to potential applicants.

- **MRC publicity activities:** The MRC primarily publicises calls for applications to the Biomedical Catalyst through university research offices (who then disseminate to individual academics). The MRC also undertakes outreach activities, visiting universities to raise awareness of the range of funding opportunities and offer guidance on priorities where appropriate.

- **Websites and webinars:** Both Innovate UK and the MRC have created websites (or more precisely, areas of their own websites) to promote the programme and offer guidance to applicants.

- **Leverage of industry bodies:** Additionally, Innovate UK and the MRC have also exploited the presence of industry bodies representing the life sciences sector to promote the programme on a broader basis (e.g. BioNow and MediLink).

- **Other events:** Innovate UK and the MRC have organised or participated in a small number of events for the investor community to raise awareness. This is the main process by which the Biomedical Catalyst is expected to produce its wider effects on the funding landscape, and will need to be examined in depth through the process evaluation to establish how far the programme is producing its desired effects.

Alongside considerations around the effectiveness of these activities in promoting awareness of the Biomedical Catalyst amongst the appropriate audiences, there are issues to explore regarding how far the dual nature of marketing activities works in support of, or against, the overall goals of the programme. One the one hand, Innovate UK and the MRC are targeting different audiences and specialised communication channels may be beneficial. On the other hand, possible hazards may include the risk of confusing potential applicants over the application process and programme goals, as well as inefficient duplication of activity. Finally, the consultations revealed that there were some concerns that the portfolio of supported projects was overly weighted towards drug discovery projects (with insufficient emphasis on medical devices or digital health projects): the evaluation will need to examine how far such concerns were justified (and if so, how far they can be attributed to the publicity activities undertaken or to factors outside of the control of the organisations concerned).

1.3.4 Applications

Each funding competition involves an application process in which the applicant describes (broadly speaking) the project proposal, and the scientific, commercial, and management cases for funding (in various levels of detail, depending on the type of funding being sought). The primary objective of the application process is to provide the MRC and Innovate UK (and other individuals involved in the project review and selection process) with sufficient information to assess alignment with programme goals and the strength of scientific and commercial cases for investment.

Potential applicants can submit an application to one of the 'sub-schemes' as outlined in the table below: Key features of the programme include:

- The MRC 'Confidence-in-Concept' award in which funding is provided at an institutional level to fund packages of translation research projects awarded on the basis of broad plans outlined by the institutions concerned (which ultimately have discretion on which projects to take forward). The rationale for these awards was not simply to minimise the MRCs transaction costs in the delivery of the programme, but also to allow the institutions some flexibility to maximise their ability to leverage other sources of funding into the translation research process (and the evaluation will need to explore both how far the scheme has been effective in achieving this goal, as well as examining how far allowing discretion has avoided any possible issues with funding being directed in areas less well aligned with the overall objectives of the Biomedical Catalyst).

- On the Innovate UK arm, there is a distinction between **Early** and **Late Stage Awards** which is not present under the MRC arm of the programme (at least from the perspective of prospective applicants). The rationale for this segmentation was to create a 'balanced portfolio' of projects at different stages of development and associated levels of risk. However, the evaluation will need to examine how far this distinction is helpful (for example, the division between stages will increase transaction costs for projects that successfully progress through pre-clinical work and in some cases may create confusion in boundary cases).

- The Biomedical Catalyst, MRC Early and Late Stage applications involve a **two stage process**: an initial outline bid or expression of interest (EOI), involving a reduced application form. The main rationale for the two step process is to ensure applicants receive early feedback on the quality of their bids to ensure they are able to build on advice of the expert reviewers involved. This also ensures that they receive an indication as to the likely probability of success at the full application stage (potentially minimising the transaction costs incurred by applicants). The process evaluation will need to consider how far these anticipated benefits have been realised.

Table B.1 – Application Types

Medical Research Council	Innovate UK
Confidence-in-Concept (CIC): These awards are a new development for the Medical Research Council in terms of their funding options. These applications are a form of delegated activity by Universities. Each bid must give a plan of how funding will be used but do not have to detail specific projects. The University has discretion as to which projects receive funding over the grant period. These are annual awards, offering between £250,000 and £1.2m.	**Feasibility Studies:** Focus of this category is the exploration and evaluation of commercial potential of a scientific idea. Projects can be but up to 12 months in duration, applying for a maximum grant of £200k. The grant may be up to a maximum of 70% of the total project costs. Applicants submit a full application for funding.
Early and Late Stage: Funding is available used for pre-clinical or early phase clinical trials. Applicants prepare an outline application and, if successful, they are invited to submit a full application for	**Early and Late Stage:** Evaluation of the technical feasibility or proof of concept or demonstration of the effectiveness of well-developed concepts. Projects can be up to 3 years in length and up to £2.4m is

funding (within 12 months of being notified of their success). The Medical Research Council determines which applications might be considered closest to market and most appropriate for a Late Stage award (i.e. review by the MAC).

available for projects. Applicants first submit an EOI, and if successful, are invited to submit a full application for funding. The funding and project durations are identical across Early and Late Stage grants, as is the application process.

1.3.5 Assessment and Peer Review

Most applications (including outline applications or EOIs) to the Biomedical Catalyst are assessed (or reviewed) by external experts with a view to providing an independent judgement on the scientific, commercial, and managerial merits of the applications received to the programme. However, there are differences in the way in which these experts are selected across the two organisations and bids scored across these two organisations:

- **Innovate UK:** Each bid is reviewed by up to five industry experts, academics, or consultants with expertise in the scientific area of the application. These assessors are selected from a database of external experts recruited via previous experience of their competitions and general recruitment activity. Applications are scored from 1 to 10 across 10 criteria (generating a score from 10 to 100) alongside a narrative response to support each judgement made. Written guidance is also provided to assessors to guide their assessment. Assessors also provide summary judgements on whether the project is in scope and whether it should be recommended for funding (or to proceed to the next stage). Scores are averaged across the five assessments to give an overall score for the application, resulting in a ranked list.
- **Medical Research Council:** Applications to the Early/Late Stage are assessed at outline stage by the Development Pathway Funding Scheme panel – formed of experts from across academic, industry and the investment community. At full stage the Medical Research Council identifies internationally renowned experts from across academia and industry with the specific scientific expertise needed to assess every element of the studies proposed in the applications received (with the aim of securing between three and five academics or industry experts to review each bid dependent on the duration of the grant). The peer review process leads primarily to narrative comments on the merits of the applications, though applications are also scored to provide a measure of quality.
- **Confidence-in-Concept Awards:** Applications to CiC are scored by an independent panel of experts (the CiC panel) with scores categorised in terms of those that are of high, medium and low priority.

1.3.6 Feasibility Studies and Confidence-in-Concept Awards

Awards for Feasibility Studies and CiC awards are awarded solely on the basis of the ranked scores given by the independent assessors or the CiC panel respectively:

- For **Innovate UK**, the minimum scoring threshold (the line draw) is set at 70 points in advance of the scoring process, and adjusted following scoring. The adjustment is made to account for the level of funding available and to ensure that there is at least a clear ‘one point’ difference between the lowest scoring successful applicant and the next highest scoring applicant. Adjustments to scores may also occur if the Lead Technologist decides assessments are likely to be unreliable due to misunderstanding of the science, and they will be deleted from the overall marks. The assessment scores are checked for anomalies and/or outliers; as are the comment judgements on whether the project is in scope, general viability if they would not recommend its funding of projects. If three assessors answer ’no’ on these two criteria the application must be fail this stage. Outlying scores can also be removed if the Lead Technologist believes judgement is that this is incorrectly distorting the average score. With these adjustments, there are examples of unsuccessful applications that have received higher scores than the minimum scoring threshold set for the round.

- For the **MRC,** funding for Confidence-in-Concept awards is given to all high priority applications, while all low priority applications are rejected. The CiC panel then reach a consensus view on which 'medium' priority applications should receive funding. Funding is rationed across successful applicants to align with funds available.

1.3.7 Outline Bids and EOIs

The decision on whether to progress an outline bid (Early, or Late Stage) to a full-stage application is close to identical to the process adopted to judge Feasibility Studies and Confidence-in-Concept awards. However, in the case of the Medical Research Council arm of the programme, the decision is taken by the DPFS panel (which has a larger membership than the CiC panel). Feedback is provided to applicants on their outline bids or applications following notification of success (or not).

1.3.8 Project Selection (Early, and Late Stage)

Full applications to the Biomedical Catalyst are also scored or reviewed using the general framework specified in Section 1.3.5 before being considered by a formal project selection panel (the DPFS panel or the Major Awards Committee). At this stage, the MRC determines whether a particular bid is sufficiently close to commercialisation to merit consideration by the MAC, with the underlying rationale being that the MAC provides a greater level of commercial expertise. Innovate UK, following the scoring of Early and Late Stage bids, undertakes a further 'line-draw' to limit the number of proposals considered by the MAC. The two panels operate in a similar manner:

- **Major Awards Committee:** The MAC was created so that a broad range of industry experts, covering the full range of knowledge required in scientific translation projects, are brought together to discuss and comment on projects at the same time. The purpose of the MAC is to fully assess the viability of projects on a wide range of criteria to make sure that those which have the best science and are most likely to succeed are funded. The MAC will generally have between eight to ten members at each sitting and will review applications over two or three days. At least three of its members will be selected by the MAC secretariat to lead the interview for each particular application, based on their knowledge of the technology or therapeutic area. Applicants have to present their bid to the panel and then take questions. After each presentation, MAC members discuss the application again, before each member gives an anonymous score of between 1 and 10 (with seven the approximate pass mark).

- **DPFS panel:** The DPFS panel serves the equivalent function to the MAC on the MRC arm of the programme, except that other than the applicant appearing in person, three or four designated panel members present the application to the overall panel when it sits to review all the applications. As with the MAC panel, applications are then ranked through anonymous scoring, using an electronic voting system. This rank is then used to make a selection for funding based on the available budget.

The MAC and the DPFS members are given similar scoring criteria to guide their judgements. The guidance provides a framework setting the anticipated features of projects that would receive different scores organised under the themes of quality (focused on scientific quality), impact (focused on the scale of potential health or commercial effects) and productivity (return on investment for the UK, leverage, probability of successful delivery, and additionality). Members of the panels give each a single score taking into account these factors.

1.3.9 Funder's Panel / Sign-off

The final application stage for Innovate UK is a meeting of the Funder's Panel. This process is to ratify the recommendation made by the MAC, as it is an independent expert selection process. In addition to the final confirmation of the award, subject to financial checks being made, the Funder's Panel assembles representatives of Innovate UK's operations team and allows them to review the new projects and provide formal sign-off against the relevant budget. This also allows other departments (e.g. monitoring or communications) to co-ordinate and plan future resource requirements, activity and marketing where relevant. For the Medical Research Council, sign-off on decisions is informed by discussions between the programme secretariat and panel chairs.

1.3.10 Contracting and Due Diligence

Innovate UK performs due diligence checks prior to a full grant offer letter being signed and this is completed by the internal project finance team (rather than at the cost of the applicant). As part of this process any issues relating to the financial plans or structure of projects are raised. Clarification will be sought but if action needs to be taken this will form part of the conditional offer letter sent to successful projects. The conditional offer letter sets out the terms of the project agreement with Innovate UK, and details any action points for the project team as part of due diligence. Under both strands of the programme, payment plans are agreed based on forecasted spending profiles for the projects, these will also be structured around the agreed deliverables and milestones set out in the project.

All successful applications to the MRC funding will have to finalise an award agreement. This is done using the milestones agreed within the application. The key information that is detailed within the agreement is the primary investigator receiving funding; the costs involved in the project; the timetable agreed; and the deliverables – in the form of outputs and/or exploitation plans. Administration of the awards is completed by UK Shared Business Services. As state aid restrictions do not apply to academic funding, institutions must show that they are eligible for funding from a research council (a RCUK approved research organisation). If an academic institution applies in collaboration with an industry partner an additional MRC Industry Collaboration Agreement (MICA) is needed. This summarises the contribution the industrial partner will be making to the project – either cash or in kind – and details the proposed arrangements for intellectual property assignment or licencing. MICA forms are used to check state aid requirements and MRC funding rules are adhered to.

1.3.11 Project Monitoring

Innovate UK and the Medical Research Council use different approaches to monitor the progress of projects:

- **Innovate UK:** Monitoring is organised around tracking financial progress (on a quarterly basis) alongside an on-going narrative assessment of progress to project delivery milestones organised around work packages (which are set out in the final grant offer letter). There is no formal quantitative monitoring of project outputs, though on project completion, applicants are requested to complete a survey to capture the project outcomes. There is no post-project monitoring (i.e. beyond the lifetime of the project). Projects are assigned to a monitoring officer, who reports to a monitoring liaison officer, who then reports to the Lead Technologist.

- **Medical Research Council:** The Medical Research Council adopts a similar approach to tracking project progress (though financial progress is monitored on an on-going rather than a quarterly basis). However, the project delivery milestones also incorporate validation of the scientific results (i.e. facilitating monitoring of how far projects are progressing in technical terms), and there is formal quantitative monitoring of the achievement of these milestones. Project outputs are monitored through ResearchFish, an on-line tool allowing grant applicants to detail project results (such as new collaborations, acquisition of further funding, publications,

patents, licensing, spin-outs, policy impacts, and a range of other measures). This monitoring extends for three years beyond the lifetime of the award (and is a mandatory requirement of the grant). Monitoring is led by monitoring officers within the Medical Research Council, who may take advice from the DPFS and MAC panel as appropriate.

Table B.2 – Monitoring Arrangements

	Innovate UK	Medical Research Council
Financial	Full financial plans are produced that profile the spend of each project. Deviation of no more than 10% in any one quarter is able to be agreed by monitoring officers.	Full financial plans are also set out within the agreement with the MRC.
Progress and outputs	Both progress and outputs are set out in the initial project plans and cannot be deviated from, without the authority of a lead technologist. These are checked quarterly.	Work plans are detailed as part of the application with gated progression criteria (milestones) agreed at key points in the project. Projects are reviewed quarterly and at milestones by the monitoring group.
Contract variation	Changes that deviate from the original contract must be referred back to MAC panel members and the lead technologist.	Issues must be discussed with the MRC programme manager and any deviations approved by the monitoring group with panel input as required.

Additionally, both the Innovate UK and MRC arms of the programme have processes in place to close down projects if it becomes clear that it will not be able to achieve the proposed goals. Innovate UK representatives stated that issues with projects generally occur very early in the process and so funding projects can be cancelled early to avoid wasted costs (though this will need validation through the evaluation). The MRC has specific termination plans that are enacted if it is decided that projects will not proceed. The termination plan is to make sure that staffing resources that may have been contracted can still be paid for, so universities are not impacted by unfunded costs.

Finally, across both arms of the programme, projects must produce final reports on completion of the project. These are in the form of narrative reports due to the diverse set of potential outcomes that have been agreed. However, in both instances there is a focus on exploitation plans being achieved in principal. Again, due to the variability in outcomes as well commercial and academic opportunities these are not rigidly set at application stage. For MRC, however there is always a need for funded projects to publish their results.

1.3.12 Aggregate reporting

There is aggregated data available on Innovate UK project progress by share of project resources used. We understand there is also a standardised RAG rating of projects but the study team has not had a benefit of receiving this information. Issues are raised with the Lead Technologist who has flexibility to re-phase projects, but extended completion dates were rare and the Lead Technologist cannot authorise any increases in awards. Final reports are saved but these are not scrutinised or analysed to follow impact from funding, or to inform funding activity in the future. The MRC requires IP reports to be submitted for three years after the award has finished. ResearchFish is the second mechanism by which MRC "follow[s] impact from funding, or to inform funding activity in the future". Across both programme strands there are ad-hoc analysis activities that occur at secretariat level, some monitoring liaison officers also compile aggregate reports for their allotted projects. The MRC has commissioned an external contractor to investigate impacts of Translation funding.

Innovate UK has recently conducted a survey amongst completed projects with questions on the impact of funding; receiving 37 responses. Financial data is collected via a payments system which details the actual spends, this data is collected and compared with the original and on-going financial plans for projects.

1.4 Process Evaluation Questions

This section sets out a range of process evaluation questions to be addressed in the study, building on the broad areas identified in the Invitation to Tender. Alongside these specific questions, there are a range wider issues that will need to be considered:

- **Cost:** It will be important to establish estimates of the overall cost of the processes employed in the delivery of the Biomedical Catalyst programme and relate them to the process benefits generated, to support a judgement as to how far the resources invested in the programme delivery represent value for money. This exercise should also highlight areas of inefficient duplication of activity (if any) to isolate any areas in which efficiency gains might be made.

- **Absence of processes:** The process evaluation will also need to consider how far the absence of processes may hinder the achievement of the Biomedical Catalyst's policy objectives. One example relates to the anticipated collaboration effects of the programme: there are no specific mechanisms built into the design and delivery of the programme to stimulate collaborative working between industry and academia (for example, this is not an area in which bids are explicitly scored, and the two programme secretariats do not undertake 'matching' activities in which academics and industrial applicants working in the same area are linked for the purposes of catalysing collaboration). Nevertheless, an academic working in collaboration with an SME on an Innovate UK project can receive funding (met by the MRC) which is viewed by the MRC as a considerable advantage. Collaboration is intrinsically rewarded by higher scores as an academic application that requires industrial input, and SME applications that requires academic input would score badly with regard to the deliverability aspect as they would not have the appropriate team in place.

- **Lessons learned:** The process evaluation will also seek to identify any broader lessons learned that may be helpful in supporting the design and delivery of future funding competitions targeting this sector and area of research.

The proposed process evaluation questions are defined in the table overleaf and mapped to various sources of evidence that will be gathered through the main-stage study. These are specified in more detail in Section 7, but it is anticipated that the process evaluation will synthesise the following forms of evidence:

- **Analysis of management information** including data gathered through application, appraisal, and monitoring processes (and secondary data where appropriate)

- **Consultations with key stakeholders** involved in all aspects of the programme delivery process

- **Quantitative and qualitative research** with successful and unsuccessful applicants.

Table B.3 – Process Evaluation Framework

Framework of Process Evaluation Questions	Analysis of MI	Stakeholder Consultations					Survey & Case Studies		Independent audit
		Programme Secretariat and Monitoring Officers	Assessors and peer reviewers	CiC, DPFS and MAC panel Members	Investors	Policy Stakeholders (BIS, OLS)	Successful applicants	Unsuccessful applicants	
Marketing and Communications									
How effective were marketing and communications in raising awareness of the Biomedical Catalyst amongst the target audiences (including across different technology areas)?	■	■			■	■	■	■	
Did marketing and communications make the objectives of the Biomedical Catalyst, eligibility criteria, and application process clear to applicants?							■	■	
Did marketing and communications materials make it clear how the bids would be appraised and assessed?							■	■	
How effectively has the Biomedical Catalyst engaged the investment community in terms of (1) raising awareness of the programme, (2) raising confidence in the processes employed to administer the programme, (3) raising the profile of life sciences more generally as potentially profitable sector for investment?	■				■	■			
Application Process									
Was the process of completing an application for Biomedical Catalyst funding straightforward?							■	■	
How helpful were the guidance materials and one-to-one support provided by the MRC and Innovate UK in aiding applicants to understand what was required?							■	■	
Was the scale of transaction costs incurred by applicants in the preparation of applications proportionate? What level of opportunity costs were incurred by unsuccessful applicants?							■	■	
Did the application process provide sufficient information to enable a high quality appraisal of bids?			■	■					
Did the process of completing an application lead to any benefits for the applicant (such as encouraging links with industrial partners?							■	■	

Framework of Process Evaluation Questions	Analysis of MI	Stakeholder Consultations					Survey & Case Studies		Independent audit
		Programme Secretariat and Monitoring Officers	Assessors and peer reviewers	CiC, DPFS and MAC panel Members	Investors	Policy Stakeholders (BIS, OLS)	Successful applicants	Unsuccessful applicants	
Assessment or Review Process									
To what extent are the criteria for making funding decisions sufficiently aligned with the overall policy objectives of the Biomedical Catalyst?	■	■	■	■	■	■			
How far do individuals involved in the appraisal process have sufficient scientific and commercial expertise to provide a rigorous assessment of applications received?		■	■	■		■			
To what extent does the guidance provided to appraisers provide a clear direction on the nature of the judgments to be made (and provide a consistent measure of project quality across applications)?	■		■	■					
How far do considerations of additionality through the assessment or review process (i.e. whether the project would be funded without the BMC) influence project selection outcomes in a way that optimises value for money?	■	■	■	■		■			
How far are the resources invested in assessment and review proportionate?	■	■				■			
How far did feedback given to applicants as a result of the assessment and review process lead to material improvements in project design and/or the avoidance of wasted resources invested in application preparation?							■	■	
Project Selection Process									
Are the terms of reference for project selection panels aligned with the overall policy goals of the Biomedical Catalyst? Do wider performance management regimes (including the need to defray resources) on resources influence project selection priorities in any way?	■			■					
Did project selection panels (CiC, DPFS and MAC) receive sufficient information from the assessment and review processes to make informed project selection recommendations?				■					
Are panel members given a sufficient amount of time to consider each application in sufficient depth?				■					
Contracting and Due Diligence									

Framework of Process Evaluation Questions	Analysis of MI	Stakeholder Consultations					Survey & Case Studies		Independent audit
		Programme Secretariat and Monitoring Officers	Assessors and peer reviewers	CiC, DPFS and MAC panel Members	Investors	Policy Stakeholders (BIS, OLS)	Successful applicants	Unsuccessful applicants	
Are the timescales between application and contract award appropriate and do they have any impacts on the commercial viability of projects?							■	■	
Did the specification of Conditional/Grant Offer/Award Letters make the deliverables and monitoring requirements of successful applicants clear (to both applicants and monitoring officers)?		■					■	■	
(Innovate UK only) Is the due diligence process sufficiently rigorous to avoid resources being lost through committing resources to businesses facing financial difficulties?		■					■	■	
Delivery and Monitoring									
Does project monitoring provide an adequate framework for understanding the progress of projects towards their objective and enable early identification of any possible issues?	■	■				■	■	■	
Are the costs incurred by grant recipients in complying with monitoring requirements proportionate?							■	■	
Are processes for agreeing variations in contracts proportionate and effective?		■					■	■	
How effectively does information on the performance of successful applicants feed directly back into the appraisal process for future rounds?		■							
Aggregate Performance Management									
Do monitoring systems support effective performance management, risk management, and decision making?		■				■			
How does aggregate performance management information feed back into the delivery of the programme (if at all)?		■							
Partnership Working									
Do Innovate UK and the Medical Research Council have sufficiently effective processes in place on an operational level to align the delivery of funding competitions and shared processes?									■

Framework of Process Evaluation Questions	Analysis of MI	Stakeholder Consultations					Survey & Case Studies		Independent audit
		Programme Secretariat and Monitoring Officers	Assessors and peer reviewers	CiC, DPFS and MAC panel Members	Investors	Policy Stakeholders (BIS, OLS)	Successful applicants	Unsuccessful applicants	
Does the level of partnership working between the two organisations serve to maximise the impact of the Biomedical Catalyst and the likelihood it will achieve its policy aims?									

Annex C: Technical Outline of Survey

This Annex sets out a technical description of the survey and how it was administered.

C.1 Sample

The target population comprised 590 lead applicants to Innovate UK's Feasibility Awards, and all applicants to the Early and Late Stage Awards which were not rejected at the outline bid or expression of interest stage in Rounds 1 to 6. Innovate UK and the MRC sent an advance letter to applicants explaining the purpose of the research and offering the chance to opt out. Innovate UK also contacted applicants who had previously selected an option not to be included on any marketing newsletters to give them the opportunity to participate. This process resulted in a skewed sample for the research with a higher proportion of academics, successful applicants and awards to Rounds 1 to 3 than in the population as a whole[26].

In total, Ipsos MORI received 427 possible leads to contact for the survey (72 per cent of the total population). Ipsos MORI removed a number of duplicates from the sample comprising applicants who had submitted two or more bids in different rounds. In these cases, the earliest application was selected for interview. This meant a total of 344 leads were usable for fieldwork.

Given the limited number of leads, a census survey was undertaken with the usable sample contacted during the fieldwork period. The sample comprised 194 firms and 150 academics, including a total of 129 successful applications and 215 unsuccessful applications. Around half the sample comprised applicants for Early Stage awards (175), 88 were applicants to Late Stage Awards and 81 were applicants to the Feasibility Studies programme. Out of the 344 leads, 160 had attended a MAC interview (28 academics and 132 firms).

Interviews were achieved with 207 lead applicants, comprising 91 academics and 116 firms. Overall 88 interviews were conducted with successful applicants and 119 with unsuccessful applicants. Reflecting the sample, around half were applicants to Early Stage awards (110), 57 were applicants to Late Stage Awards and 40 were applicants to the Feasibility Studies programme. Out of the 207 interviews, 106 had attended a MAC interview (18 academics and 88 firms).

[26] This was corrected by weighting the data as covered in section A5.

Table C.1 – Sample and interview profile

	Number of applicants				Proportion of applicants	
	Successful	Unsuccessful	Successful	Unsuccessful	Successful	Unsuccessful
	N	N	N	%	%	%
Sample						
Academic	48	102	150	37	47	44
Firm	81	113	194	63	53	56
Total	129	215	344	100	100	100
Interview						
Academic	32	59	91	36	50	44
Firm	56	60	116	64	50	56
Total	88	119	207	100	100	100

C.2 Fieldwork

Ipsos MORI interviewed 207 applicants by Computer Assisted Telephone Interviewing (CATI) between 13 February and 23 March 2015. The average interview length was 30 minutes. As part of the fieldwork, a live pilot was conducted with broad quotas on the type of respondent (e.g. outcome of application, applicant type) to test the flow and length of the questionnaire, and whether the contact procedure was working. Interviewers also received a full briefing as well as full written instructions about all aspects of the survey.

Advance notice of the survey was sent by email, including a datasheet providing information on the TRL scale for firms and researchers to assess the proximity of the project to the market. For all sample a named contact was provided. At the start of the interview, the interviewer verified this was the individual responsible for managing or co-ordinating the Biomedical Catalyst application. It was sometimes the case that the named contact was no longer in post. In these cases, we checked if there were any other individuals within the organisation involved in the preparation of the Biomedical Catalyst application who could participate in the interview.

C.3 Response rates

Ipsos MORI achieved 207 interviews from a total sample of 344 applicants. The unadjusted response rate is therefore 60 per cent, while the adjusted response rate, based on valid sample, is 69 per cent. Valid sample refers to sample that is contactable and excludes bad numbers. The response rate was higher among successful than unsuccessful applicants (e.g. 75 per cent and 67 per cent adjusted response rates respectively) and higher among academics and firms (71 per cent and 64 per cent adjusted response rates respectively).

Table C.2 – Unadjusted and adjusted response rates

	Total sample	Overall unadjusted	Overall adjusted
Valid Sample			
Achieved interviews	207	60%	69%
Refused	33	10%	11%
Abandoned	2	1%	1%
Soft appointments	12	3%	4%
No answer	32	9%	11%
Appointments outside fieldwork period	13	4%	4%
Total valid sample	299	87%	100%
Invalid sample			
Bad/wrong number	45	13%	
Total; sample used	**344**		
Total sample not used (reserve)	**110**		

Table C.3 – Response rates by group

	Overall adjusted	Successful adjusted	Unsuccessful adjusted	Academic adjusted	Firm adjusted
Valid sample					
Achieved interviews	69%	75%	67%	71%	64%
Refused	11%	6%	14%	12%	9%
Other (appointments outside fieldwork/soft appointments/no contact)	20%	19%	19%	17%	17%
Total	100%	100%	100%	100%	100%

C.4 Data coding and processing

Following the pilot, a number of pre-coded lists were developed for the 'other – specify' answer options. Coding staff checked verbatim answers entered by interviewers at the 'other – specify' answer options. Code frames were prepared by the coding team and checked and approved by the research team.

C.5 Weighting

As the sample provided by Innovate UK and the MRC was not all lead applicants to Early Stage, Late Stage or Feasibility Awards, it was necessary to correct for this and non-response bias and weight the data to reflect the

population. The data was weighted by type of applicant, outcome of application, stage and round, as shown in the table below.

Table C.4 – Unweighted and weighted profiles

	Unweighted profile	Weighted profile
Based: All respondents	(207) %	(148) %
Type		
Academic	44	29
Firm	56	71
Outcome		
Successful	45	37
Unsuccessful	55	63
Stage		
Early Stage	53	42
Late Stage	27	20
Feasibility	20	38
Round		
1 to 3 (including 3b)	66	57
4 to 6	34	43

Once the weights were applied, the profile of applicants did not completely reflect the population. This was particularly evident for the proportion of firms attending a MAC interview which was still significantly higher than the population as a whole. Different weighting schemes were applied in an attempt to correct this further. However, these significantly reduced the effective base size so it was decided this variable should not be included in the weighting scheme. Analysis was also conducted on a number of questions and the difference between those who had and had not attended a MAC interview was not sufficiently large to warrant further weighting.

The table below shows half the interviews were conducted with applicants who had attended a MAC interview, compared to a third of applicants in the population.

Table C.5 – Profile of applicants attending a MAC interview

	N	%
Population		
Total	194	33
Academic	30	17
Firm	164	39
Sample		
Total	160	47
Academic	28	19
Firm	132	68
Interview (unweighted)		
Total	106	51
Academic	18	20
Firm	88	76
Interview (weighted)		
Total	114	55
Academic	11	18
Firm	103	70

C.6 Statistical reliability

The respondents to the research are a sample of the total 'population' of Biomedical Catalyst Early Stage, Late Stage and Feasibility Study award applicants in Rounds 1 to 6, so we cannot be certain that the figures obtained are exactly those we would have if all applicants in our group of interest had been interviewed (the 'true' values).

However, the variation between the sample results and the 'true' values can be predicted from the knowledge of the size of the samples on which the results are based and the number of times that a particular answer is given. The confidence with which this prediction can be made is usually chosen to be 95 per cent - that is, the chances are 95 in 100 that the 'true' value will fall within a specified range. The table below illustrates the predicted ranges for different sample sizes and percentage results at the '95 per cent confidence interval'.

Table C.6 – Statistical reliability

Size of sample of which survey result is based	Approximate sampling tolerances applicable to per centage at or near these levels		
	10% or 90% ±	30% or 70% ±	50% ±
All applicants (effective base size: 148)	4	6	7
Firms (base size: 116)	5	7	8
Academics (base size: 91)	4	7	7
Successful applicants (base size: 88)	5	8	8
Unsuccessful applicants (base size:(base size: 119)	5	7	8
All applicants (effective base size: 148)	4	6	7

* With each group, sampling tolerances are corrected for small population sizes

For example, with an effective base size of 148 where 50 per cent give a particular answer, the chances are that the 'true' value (which would have been obtained if the whole population had been interviewed) will fall within the range of ±7 percentage points from the sample result (i.e. between 43 per cent and 57 per cent)

Annex D: Econometric Analysis

This annex sets out the results of the econometric analysis of the survey results gathered from successful and unsuccessful applicants to the Biomedical Catalyst. The econometric analysis has been conducted with a view to estimating the causal effects of the scheme on a range of key outcome variables of interest, including technical progress, R&D expenditure on the project forming the focus of the application to the scheme, as well as total annual R&D spending, R&D employment and total funding levels.

D.1 Selection Bias and Counterfactual Selection

A robust assessment of impact requires the selection of an appropriate counterfactual group of non-beneficiary firms or academic researchers (as a means of estimating what may have occurred in the absence of the funding provided through the Biomedical Catalyst). As funds have been allocated on a non-random basis (precluding the possibility of an RCT design), the selection of a counterfactual needs to address the potential issues of bias caused by selection into treatment. There are two core sources of selectivity:

- **Self-selection:** Applicants 'self-select' into treatment by submitting an application for Biomedical Catalyst funding. As such, applicants might be assumed to systematically differ from non-applicants in non-trivial ways. As an example, non-applicants may not be exposed to the same forms of financial constraints faced by applicants to the programme, which may be reflective of unobserved characteristics of the applicant (such as the level of risk associated with the technology, anticipated profit levels, or managerial qualities). If this scenario held in practice, then it might be anticipated that the use of a counterfactual sample of non-applicant firms or academic institutions would understate the impacts of the Biomedical Catalyst (as non-applicants would be expected to outperform applicants in the absence of funding). Additionally, non-applicants may not be involved in any innovation effort (this might arise if the firms concerned had completed their R&D activities and were focused on production), making them unsuitable as a comparison group (given the aim of the Biomedical Catalyst to accelerate the innovation process).

- **Appraisal process:** The appraisal process introduces the second major source of selectivity into the resource allocation process. Applications are judged primarily in terms of their scientific merits, technical feasibility, the quality of the team and the strength of the commercial opportunity. Provided that these judgements are made effectively by those involved in the appraisal process, it would be expected on an ex-ante basis that successful applicants would outperform unsuccessful applicants in the absence of Biomedical Catalyst (causing comparisons between the two to be biased upwards). However, if deadweight formed part of the deliberations of the assessors, DPFS panel, or Major Awards Committee, the bias could potentially run the other way (though the evidence gathered through this evaluation suggested that considerations of additionality were not always the primary focus of the selection panels).

In order to minimise these difficulties, a counterfactual sample of firms and academic bids were drawn from the pool of 397 unsuccessful full stage applications over Rounds 1 to 6 of the Biomedical Catalyst. It is assumed that this approach addresses issues of self-selection into treatment (as both successful and unsuccessful applicants can be assumed to share similar characteristics motivating their application for support). Additionally, systematic differences between successful and unsuccessful applicants are partially addressed by the exclusion of those applications that were deemed to be of insufficiently high quality to progress to a full-stage application (530 applications). While further refinements to this sampling strategy may have been feasible in principle (such as excluding consideration of applications that were not put forward for consideration by the Major Awards

Committee), they were not implemented in order to avoid further limiting the number of observations available for analysis. This sampling strategy alone does not address all issues associated with selection bias, and additional analytical steps are taken to minimise these issues as described below.

D.2 Data

The data driving the analysis described in this Annex was collected through a census survey of successful and unsuccessful applicants delivered using random probability survey techniques (technical details of this survey are provided in Annex C). This led to the collection of observations in relation to 207 applicants (88 successful applicants and 119 unsuccessful) to the Biomedical Catalyst. This survey was utilized to measure a range of pre-treatment characteristics (i.e. at the point of application) of applicants and the projects forming the focus of their proposals, including:

- **Project level characteristics:** Data was gathered on the cumulative total investment in the R&D project, levels of technical development (measured against the Technology Readiness Scale), the year in which project development work started, and the type of product forming the focus of R&D activity (therapeutics or biologics, medical devices, diagnostic tools).
- **Applicant characteristics:** Survey respondents were also asked to report a range of organisational characteristics, including overall R&D employment (research staff in the lead applicants' team in the case of academic led bids), annual R&D expenditure, and total levels of funding from private and public sources.

The survey was also used to establish how far the key outcome variables had changed since the application to the Biomedical Catalyst. For the purposes of this analysis, this included:

- Current state of technical development as measured against the TRL scale;
- R&D expenditure focused upon the project;
- Total annual R&D expenditure;
- Total employment of R&D workers; and,
- Total additional funding secured (from private and public sources).

Observations gathered through the survey were supplemented by a range of additional information gathered from monitoring, including the scores received by the application as part of independent assessments of firm led bids, the DPFS panel, or the Major Awards Committee (as appropriate), and the timing of the application.

D.2.1 Round 5 and 6

For applicants to Rounds 5 and 6 of the scheme, additional observations of the latter three measures were not taken as part of the survey on the assumption that insufficient time would have elapsed since the application to observe any material changes in these metrics (these rounds took place less than 12 months before the survey). Rather than exclude these observations from the analysis, an assumption has been applied that they remained unchanged at the point of the survey (this will likely lead to an understatement of the effects of the scheme at this stage). Where applicants reported that they had terminated the project early, an assumption was applied that no further development costs had been incurred, or technological progress made, since the application (this could lead to an understatement of the overall costs involved and progress made, and this may lead to some bias in results as unsuccessful applicants were more likely to report that they had terminated their projects early).

D.2.2 Profile of Survey Respondents Relative to Population

As set out in Annex C, the target population for the survey was all applicants for Feasibility Study Awards, and Early and Late Stage applicants that submitted full-stage applications (590 applicants). The sample made available for the survey was smaller than the population for two reasons:

- Firstly, both Innovate UK and the Medical Research Council offered applicants the opportunity to opt out of the survey research (applicants to Innovate UK that had opted out of marketing communications were not contacted as part of this process).
- Innovate UK also contacted those applicants that opted out of marketing communications to offer them an opportunity to opt-in to the survey.

The final sample for the survey comprised 427 lead applicants; of which 344 were unique (some organisations or individuals had submitted multiple applications to the programme). An overall response rate of 60 per cent was achieved through the survey (this response rate is not adjusted for invalid numbers), with higher response rates achieved amongst successful applicants (relative to unsuccessful applicants), and amongst academic applicants (relative to SME applicants). This creates some issues that need to be considered when interpreting the findings below:

- **Over-represented groups:** The process overall led to a sample of applicants in which a number of groups were over-represented relative to the population of applicants. Firstly, in part due to the additional mechanisms by which firms might have opted-out of the survey, academic applicants were over-represented in the sample. Secondly, those successful in their applications for Feasibility Study Awards were under-represented in the sample (primarily due to the high proportions that opted out). These biases in the sample may have influenced the overall treatment effects estimated in the following sections. Attempts have been made to examine the relative effectiveness by type of award, which will be less sensitive to this type of issue.
- **Successful and unsuccessful applicants:** While response rates were higher amongst successful applicants than amongst unsuccessful applicants, the analyses below are driven by comparisons between these two groups, and it is not anticipated that this will directly lead to biased estimates of the treatment effects involved.
- **Risk of attrition bias:** However, the presence of invalid numbers in the survey sample raises the possibility that some firms will have ceased trading following their application to the Biomedical Catalyst (this issue was less problematic for academic applicants). If a higher proportion of unsuccessful applicants have ceased trading, then this will lead to a form of attrition bias that will understate the overall impact of the Biomedical Catalyst (as those firms that have failed to progress their projects have been excluded from the sample). No attempt has been made to address this issue in the analysis that follows, but more detailed consideration will be given to this issue in the later phases of the evaluation.

D.2.3 Self-Reporting

Observations of the outcomes of interest were generated by asking respondents to report these outcomes through the survey. To maximise the reliability of the observations collected, respondents were sent a datasheet in advance of the interview describing the range of financial and non-financial data the survey was aiming to collect (including a table explaining the Technological Readiness Level scale adopted to measure the progress of projects through the development pathway). However, it is likely that the collection of data through such a process has led to a degree of measurement error. For example, survey respondents almost universally reported financial measures rounded to the nearest £100,000 (or in some cases, £1m). Additionally, while attempts were made to clarify the definition of key terms with applicants, there may have been differences in interpretation

The validity of the survey findings will be considered moving forwards through examining the correlation between the measures reported against secondary administrative and survey datasets (such as the Business Structure Database and the Business Expenditure on Research and Development survey held within the ONS Virtual Microdata Laboratory). However, at this stage, there was limited evidence available to validate the reliability of the data gathered. The extent to which this may bias the findings will be in part dependent on how far there is a differential tendency for successful and unsuccessful applicants to misreport against the measures of interest (for example, unsuccessful applicants may have thought they were further up the TRL scale than might have objectively been the case, particularly at the lower end of the TRL scale, possibly contributing to the rejection of their proposal).

D.2.4 Observations Available for Analysis

The number of observations on each outcome of interest was constrained by the following:

- **Missing observations:** Some respondents were unable to provide valid responses to the questions designed to capture the outcomes of interest (either baseline measures or measures at the time of the survey). Where respondents were unable to provide responses to either of these questions, they were excluded from the analysis.
- **Inconsistent responses:** The survey was designed to capture the cumulative expenditure on the project forming the focus of applications to the Biomedical Catalyst (i.e. lifetime expenditure on the project at the point of application, and at the point at which they were surveyed). In a small number of cases, inconsistent measures were collected from respondents whereby they reported that lifetime expenditure at the point of the application was higher than at the time of the survey[27]. These observations were also excluded from the analysis (7 successful applicants, and 17 unsuccessful applicants).

The table below sets out the number of valid observations available for analysis for each outcome (applicants to Rounds 5 and 6 are included in the table below, although as noted above, it was assumed that no change in the outcomes of interest would have been achieved at the point of the survey).

Table D.1 – Number of Valid Observations Available for Analysis, by Outcome

	Treatment Group	Comparison Group	Firm projects	Academic projects	Total
TRL levels	83	108	108	83	191
Cumulative project expenditure	63	86	86	63	149
Annual R&D expenditure	70	97	94	73	167
R&D employment	68	101	90	79	169
Overall funding levels	75	91	97	69	166

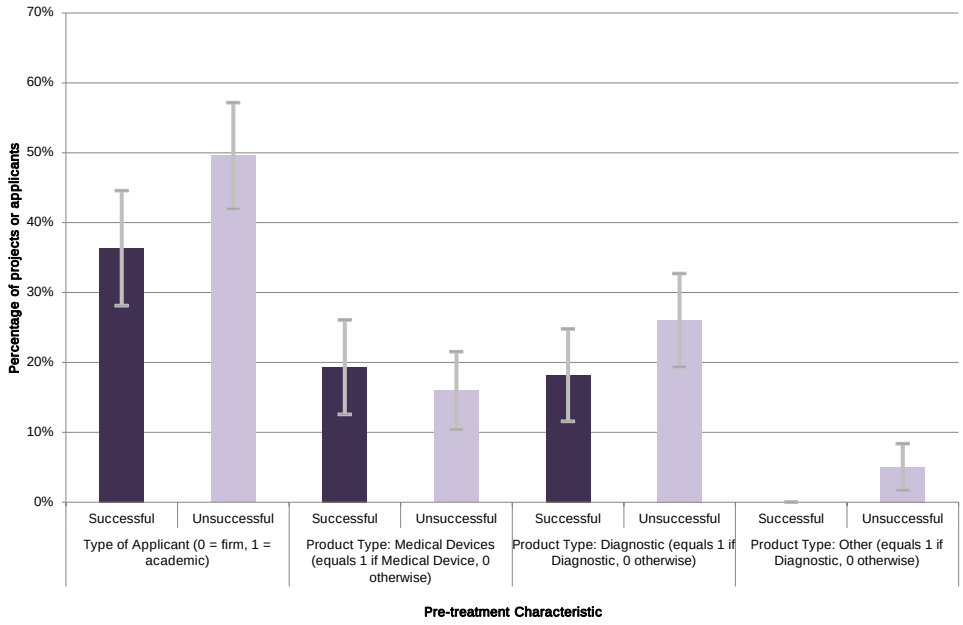
Source: Ipsos MORI (2015)

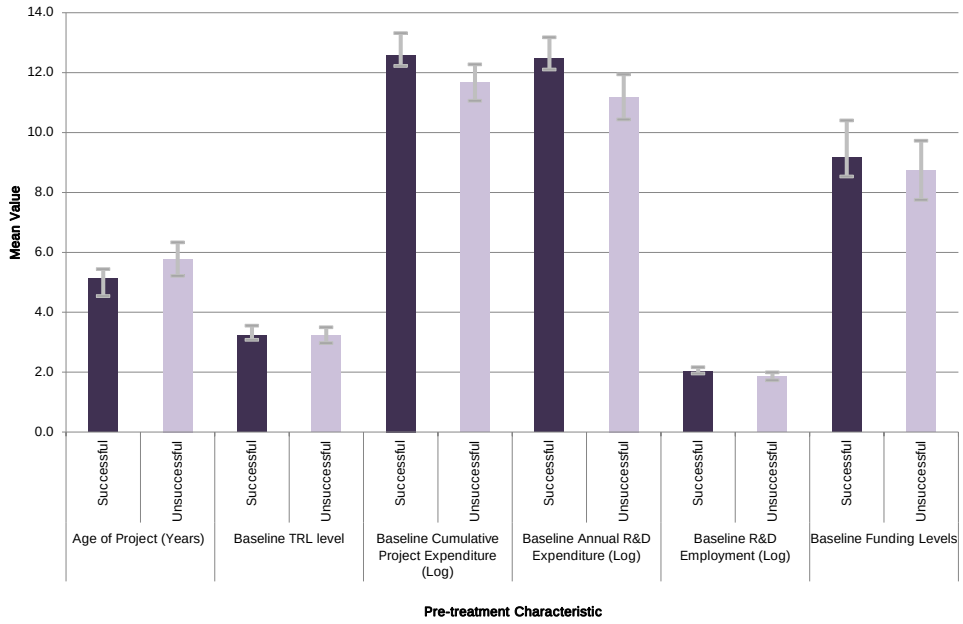
[27] Refinements to the next wave of the survey will be introduced to address this issue. Respondents will be reminded of their previous response to these questions, and constraints will be set accordingly.

D.3 Differences between Successful and Unsuccessful Applicants

Respondents to the survey were asked to provide information on a range of pre-treatment characteristics (i.e. at the point of application) of their project and their organisation. The figures below provide mean values and 95 per cent confidence intervals[28] for a range of these characteristics gathered through the survey research, and point to a number of observed differences between the samples of successful and unsuccessful applicants.

Figure D.1 – Pre-treatment Characteristics of the Sample of Successful and Unsuccessful Applicants





Source: Ipsos MORI (2015)

[28] Confidence intervals were calculated by applying a finite population adjustment.

As illustrated on the preceding page:

- **Applicant type:** Academic led projects accounted for a higher proportion of the comparison group (at 50 per cent) than the treatment group (36 per cent), with the reverse being the case for firm led projects.
- **Project type:** A higher proportion of the unsuccessful applicants had put forward proposals relating to the development of diagnostics, and a lower proportion had put forward proposals involving the development of medical devices. Project proposals involving the development of therapeutics (which acted as a baseline category, and is not shown in the chart) were more prevalent amongst successful applicants than unsuccessful applicants.
- **Age of project:** Unsuccessful project proposals tended to have been under development for a longer period of time (5.8 years) than successful proposals (5.1 years).
- **Baseline TRL levels:** There were no material differences in self-reported baseline levels of technical development (as measured through the TRL scale) across successful and unsuccessful applicants (at an average of 3.2 on the 9 point scale).
- **Baseline cumulative project expenditure[29]:** Reported cumulative expenditure on the project forming the focus of proposals was higher amongst successful applicants than unsuccessful applicants.
- **Annual R&D expenditure and employment:** Annual R&D spending at the point of application was also higher amongst successful than unsuccessful applicants.

A set of independent sample t-tests were undertaken to establish how far these observed differences between the two groups were statistically significant. The results of these tests are shown in the table overleaf, and suggest that while there are some marked differences between the two populations, there was also substantial variability in the observed data. The only statistically significant difference between the two groups observed was in terms of annual levels of R&D expenditure at the point of application (with unsuccessful applicants reporting an average of £800,000 per annum, while successful applicants reported £1.5m per annum).

D.4 Propensity Score Matching

Although the results set out in the table overleaf do not suggest that there were a large number of statistically significant differences between successful and unsuccessful applicants (beyond annual R&D expenditure) or in their project proposals, they do raise some concerns that observed differences between the two groups may bias findings. For example, differences in average total funding levels and cumulative project expenditure appear materially, if not statistically, significant. In order to minimise the observed differences between groups, a propensity score matching approach was adopted to match successful and unsuccessful applicants and projects where they shared similar characteristics.

A propensity score matching strategy would deliver unbiased estimates of the treatment effects involved, provided that there are no unobserved characteristics of the applicants or their proposed project that are influential in simultaneously determining the likelihood of selection into treatment and the outcomes of interest. As highlighted in the opening sections, it is not considered that this assumption will hold in this case, so this step of the analysis was used primarily to refine the matching of the two groups in terms of their observed characteristics (with other steps taken to address the issues associated with unobservables, as described below).

[29] Note that the figures on the preceding page report the natural logarithm of financial and employment variables, not the levels, for ease of presentation. The table on the following page reports the average of these values in terms of the levels.

Table D.2 – Independent Samples t-Tests for Equality of Means

	Group	Group Statistics			Equality of Variances			Independent Sample t-Test for Equality of Means					
	Success	N	Mean	Std. Dev.	Equal Variances	F	Sig.	t	Sig. (2-tailed)	Mean Difference	Std. Error Difference	Lower	Upper
Applicant Type: Academic Led Bids	Unsuccessful	119	0.50	0.50	Assumed	9.439	0.002	1.90	0.06	0.13	0.07	0.00	0.27
	Successful	88	0.36	0.48	Not assumed	-	-	1.91	0.06	0.13	0.07	0.00	0.27
Product Type: Medical Device	Unsuccessful	119	0.16	0.37	Assumed	1.554	0.214	-0.63	0.53	-0.03	0.05	-0.14	0.07
	Successful	88	0.19	0.40	Not assumed	-	-	-0.62	0.54	-0.03	0.05	-0.14	0.07
Product Type: Diagnostic	Unsuccessful	119	0.26	0.44	Assumed	7.564	0.006	1.34	0.18	0.08	0.06	-0.04	0.19
	Successful	88	0.18	0.39	Not assumed	-	-	1.36	0.18	0.08	0.06	-0.04	0.19
Product Type: Other	Unsuccessful	119	0.05	0.22	Assumed	20.644	0	2.15	0.03*	0.05	0.02	0.00	0.10
	Successful	88	0.00	0.00	Not assumed	-	-	2.50	0.01*	0.05	0.02	0.01	0.09
Year Project Started	Unsuccessful	116	2009.2	3.61	Assumed	0.304	0.582	-1.27	0.21	-0.64	0.50	-1.63	0.35
	Successful	87	2009.9	3.45	Not assumed	-	-	-1.28	0.20	-0.64	0.50	-1.62	0.35
TRL levels: Baseline	Unsuccessful	115	3.23	1.69	Assumed	1.431	0.233	-0.02	0.99	0.00	0.25	-0.50	0.49
	Successful	88	3.24	1.85	Not assumed	-	-	-0.02	0.99	0.00	0.25	-0.50	0.49
Baseline Project Expenditure	Unsuccessful	108	1462900	4941000	Assumed	3.227	0.074	-1.62	0.11	-1,371,430	845,931	-3040470	297,599
	Successful	77	2834400	6563810	Not assumed	-	-	-1.55	0.12	-1,371,430	886,328	-3124410	381,539
Baseline annual R&D expenditure	Unsuccessful	103	801408	1406710	Assumed	8.042	0.005	-2.33	0.02*	-707,592	303,728	-1307030	-108,150
	Successful	74	1509000	2599660	Not assumed	-	-	-2.13	0.04*	-707,592	332,475	-1366930	-48,257
R&D Employment: Baseline	Unsuccessful	118	8.0	7.76	Assumed	4.006	0.047	-1.48	0.14	-2.13	1.44	-4.98	0.71
	Successful	88	10.1	12.87	Not assumed	-	-	-1.38	0.17	-2.13	1.55	-5.19	0.93

Source: Ipsos MORI (2015) * indicates differences are significant at the 95 per cent confidence level

A kernel matching strategy was adopted, which involved the following steps:

- **Probit model:** The first step of the matching process was to implement a probit regression to predict the probability of assignment into treatment. The dependent variable in this regression was a dummy variable describing treatment status (i.e. 1 = successful, and 0 = unsuccessful), while the pre-treatment characteristics set out in table 2 overleaf were used as independent variables. It is important to note that an important predictor of assignment into treatment (the score given to the proposal through the project selection process) was excluded from these models. The main reason for this was that, as this score was used to determine assignment into treatment, there would be very little commonality between successful and unsuccessful applicants. The inclusion of these scores would therefore lead to the exclusion of the majority of the observations available for analysis, and to a very small matched sample. The results of these regressions are set out in the table overleaf.
- **Kernel matching:** A kernel matching procedure was implemented, in which each successful applicant in the sample was matched to a kernel weighted average of *all* unsuccessful applicants in the sample[30]. This has an advantage over other forms of matching (such as one-to-one matching), in that it uses more information from the comparison group[31]. The weights employed were determined by the differences between successful and unsuccessful applicants in their estimated likelihood of assignment into treatment (as predicted by the probit models described above). An Epachnikov kernel[32] was used with a bandwidth of 0.06 (the default parameters in STATA). This led to the exclusion of some observations from the treatment and comparison groups where they were insufficiently similar to any members of their complementary group (this is also illustrated in the table overleaf).

As the number of valid observations available varied across the different outcomes, this process was repeated five times (once for each outcome of interest). The table D.4 below illustrates the extent to which this process was effective in improving the balance between successful and unsuccessful applicants amongst those for which observations on TRL levels were available.

[30] The weight given to each comparison observation is given by: $\frac{K(\frac{p_i-p_j}{h})}{\sum_{j\in I_0} K(\frac{p_i-p_j}{h})}$, where K(·) is the kernel function with a bandwidth h, I_0 is the set of comparison observations, p_i and p_j are the estimated propensity scores for the treatment and comparison units respectively.

[31] See for example, 'Some Practical Guidance for the Implementation of Propensity Score Matching,' Caliendo and Kopeinig, Institute for the Study of Labour, 2005

[32] The Epachnikov kernel is given by $K(u) = \frac{3}{4}(1-u^2)\mathbf{1}_{\{|u|\leq 1\}}$, where $\mathbf{1}$ is the indicator function, and $u = \frac{p_i-p_j}{h}$

Table D.3 – Probit Regression Results (Dependent Variable: Success in Application Process (1 = Successful, 0 = Unsuccessful)

Outcome variable	Change in TRL levels		Change in Project Expenditure		Change in Annual R&D expenditure		Change in R&D employment		Change in overall funding levels	
	Co-eff.	St. Error	Co-eff.	St. Error	Co-eff.	St. Error	Co-eff.	St. Error	Co-eff.	St. Error
Constant										
Applicant Type: Academic Led Bids	45.670	-85.782	55.322	78.573	56.770	68.748	56.812	72.394	50.355	70.943
Product Type: Medical Device	-0.625	-1.118	-0.342	0.269	-0.561	0.251	-0.712	0.281	-3410691	0.262
Product Type: Diagnostic	0.109	-0.462	0.051	0.302	0.056	0.290	-0.260	0.341	436227	0.306
Product Type: Other	-0.251	-0.764	-0.138	0.280	-0.298	0.260	-0.195	0.295	4343004	0.270
Year Project Started	-0.023	-0.088	-0.028	0.039	-0.028	0.034	-0.028	0.036	-252017	0.035
TRL levels: Baseline	-0.029	-0.154	-0.051	0.069	-0.422	0.064	-0.052	0.069	-513249	0.678
Baseline Project Expenditure	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Baseline annual R&D expenditure	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
R&D Employment: Baseline	0.027	-0.004	0.027	0.016	0.278	0.016	0.027	0.017	295842.000	163812.000
Size of matched sample:										
- Treatment	86		73		84		77		75	
- Comparison	60		48		61		46		56	

Source: Ipsos MORI (2015) * indicates differences are significant at the 95 per cent confidence level

Table D.4 – Comparison of matched and unmatched samples

Pre-treatment Characteristic	Unmatched Sample			Matched Sample		
	Treatment	Comparison	% diff.	Treatment	Comparison	% diff.
Applicant Type: Academic Led Bids	0.32	0.51	-37.3	0.35	0.43	-16.2
Product Type: Medical Device	0.20	0.16	25.0	0.18	0.19	-0.5
Product Type: Diagnostic	0.21	0.26	-19.2	0.22	0.18	7.6
Product Type: Other	0.00	0.05	-100.0	0	0	0
Year Project Started	2010	2009	0.0	2010	2009	12.9
TRL levels: Baseline	3.15	3.30	-4.5	3.22	3.61	-22.4
Baseline Project Expenditure	3,124,848	1,457,033	114.5	2,200,000	2,400,000	-4.0
Baseline Annual R&D expenditure	1,593,015	818,901	94.5	1,100,000	1,000,000	3.9
R&D Employment: Baseline	10	7	44.9	7	8	-11.1
Number of observations	**66**	**91**		**60**	**86**	

Source: Ipsos MORI (2015), based on sample for which changes in TRL levels were observed

As shown in the table, the matching process was effective in reducing the pre-treatment differences observed between the two groups in terms of average levels of investment in the project, annual R&D expenditure, and R&D employment, as well as improving the balance of the sample by type of applicant and product type. The trade-off was an increase in the observed differences between the two groups in terms of self-reported TRL levels and the exclusion of six successful and five unsuccessful applicants from the sample. It should also be noted that the total sample sizes for all analyses was relatively small, restricting the power of the statistical analyses set out below.

D.5 Ordinary Least Squares and Negative Binomial Models

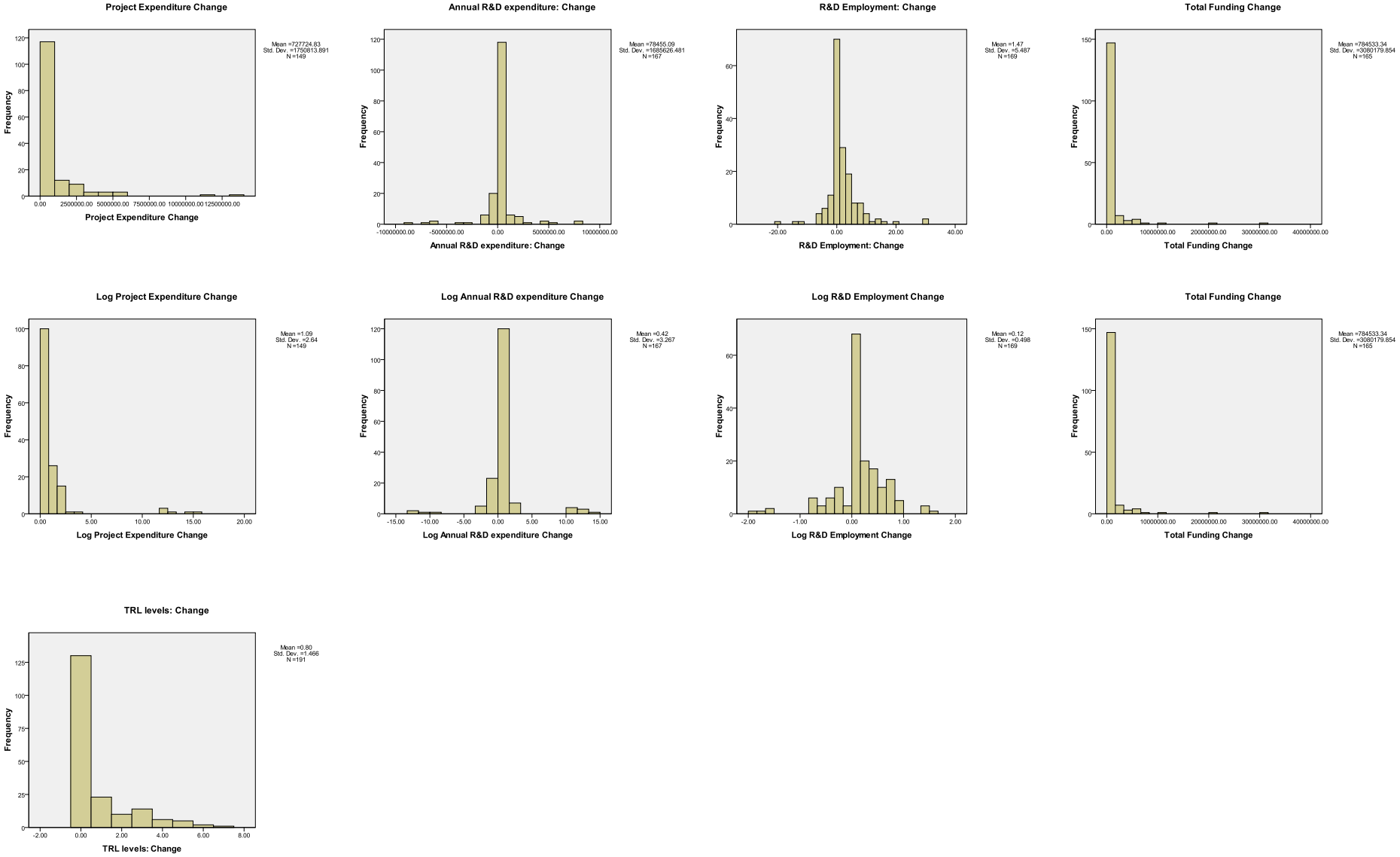
The matched samples described above were used to implement a set of regression analyses aimed at isolating the causal effect of the Biomedical Catalyst on the outcomes of interest.

D.5.1 Distribution of Outcome Variables

The distribution of the five outcome variables of interest is illustrated in the figures overleaf (with financial and employment variables presented both on an untransformed basis and in the form of natural logarithms). Three of the outcomes of interest were bounded at zero (change in TRL levels, change in project expenditure, and change in total funding levels), implying that Ordinary Least Squares (OLS) regression analyses would be inappropriate. The distributions also implied higher dispersion than would be predicted by a Poisson distribution, and a decision was made to model these outcomes on the basis of a Negative Binomial distribution[33]. In the case of changes in annual R&D expenditure and R&D employment, OLS was deemed appropriate, though the natural logarithms of these variables were a better approximation of the normal distribution than the untransformed values. As such, the OLS analyses presented below use the natural logarithm of changes in annual R&D expenditure and R&D employment, and the co-efficient presented can be interpreted as the percentage change in the outcome of interest predicted by a marginal change in the independent variable.

[33] See for Quasi-Poisson versus Negative Bionmial Regression: How should we model over-dispersed count data?' Hoef and Boveng, 2007

Figure D.2 – Distribution of Outcome Variables



D.5.2 Specification of OLS and Negative Binomial Models

The specification for the OLS and negative binomial regression models allowed for the following aspects that were thought to be influential:

- **Selection into treatment:** As noted above, there are likely to be systematic unobserved differences between successful and unsuccessful applicants and their proposed projects that will be correlated with both likelihood of assignment into treatment and the outcomes of interest. To allow for this, it has been assumed for the purposes of these analyses that these unobserved characteristics are to some degree reflected in the score received by applications through the independent assessment process (SME led bids only) and the MAC and DPFS panels (SME and academic led bids only). These scores[34] were included as control variables in these regression models to allow for such selection effects. In this case, positive coefficient estimates would suggest that higher scoring bids were more likely than lower scoring bids to deliver the observed outcomes (after controlling for the effects of the programme itself).
- **Time elapsed since application:** It was assumed that greater rates of progress would be observed amongst those applying to the programme in earlier rounds. The number of years elapsed since the application (taking the value of 2 for applicants to rounds 1 and 2, the value of 1 for applicants to rounds 3 and 4, and the value of 0 for applicants to round 5 and 6) was included as second control variable.
- **Increasing cost and time associated with project progression:** The cost of the R&D process tends to increase exponentially as the project approaches commercialisation. As such, it was assumed that projects with higher levels of baseline technical development would take longer (and incur greater costs) to progress to higher TRL levels. To allow for this, the square of baseline TRL levels was included as a third control variable.

In addition, the treatment itself was modelled in three ways. Firstly, an overall treatment effect was modelled by including a dummy variable taking the value of one for successful applicants, and the value of zero for unsuccessful applicants. Secondly, the treatment effect was allowed to vary over time (by replacing the treatment variable with two separate dummy variables indicating whether the applicant was successful two or one years ago[35]). Thirdly, the treatment effect was allowed to vary across different award types (by including separate dummy variables indicating whether the award was a Feasibility Study, an Early, or a Late Stage Award).

D.5.3 Results

The findings are set out in tables D.5 to D.7 below. These suggest:

- **Project progress:** The results indicate that the programme has had a significant and substantial impact in the acceleration of the projects forming the focus of Biomedical Catalyst applications. The estimates suggest that (on average) to date the Biomedical Catalyst has caused these projects to progress almost one TRL stage further than they would have done otherwise. These effects are strongest for Late Stage Awards and weaker for Early Stage Awards, with no significant impacts found for Feasibility Studies (though this may be due to the small number in the sample). Breaking down the effect by time, the bulk of the impact was achieved after one year, with no significant further progress visible in our results in the following year. However, this finding is considered to be a function of the discrete scale we are using (i.e. an applicant would move up a TRL level if they began a Phase II trial, but would not move up again until they started a Phase III trial).

[34] Only SME led bids received an independent assessment (scored from 10 to 100), and for academic bids, a value of zero was assumed for the independent assessment score. For feasibility awards and other applications that did not reach MAC or DPFS (which led to scores on a scale of 1 to 10), a value of zero was assumed for the MAC or DPFS score.

[35] As the impact on applicants to Rounds 5 and 6 was zero by assumption, the inclusion of a third treatment for those successful in these rounds would have exactly predicted the outcome of interest (and as a consequence, it would not have been feasible to estimate the model).

Table D.5 – OLS and Negative Binomial Results

	Change in TRL levels						Change in Project Expenditure (log)					
	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value
Estimation method	Negative Binomial						Negative Binomial					
Constant	*-1.567	0.005	*-1.605	0.010	-1.196	0.097	-1.047	0.057	-1.248	0.017	*-1.260	0.032
Independent Assessment Score	*0.010	0.032	*0.013	0.013	0.007	0.252	-0.008	0.090	0.009	0.066	-0.009	0.100
MAC or DPFS score	0.073	0.134	0.110	0.051	0.019	0.819	*-0.193	0.002	*-0.191	0.001	-0.117	0.100
Baseline TRL level (squared)	*-0.055	0.000	*-0.059	0.000	*-0.055	0.000	0.009	0.337	0.011	0.248	0.014	0.146
Years Elapsed Since Application	*0.454	0.039	0.381	0.289	0.430	0.053	*0.979	0.000	*1.080	0.000	*0.917	0.000
Success (dummy)	*0.769	0.016					*1.395	0.000				
Success: one year elapsed (dummy)			*0.800	0.013					*1.884	0.000		
Success: two year elapsed (dummy)			0.623	0.262					*1.192	0.002		
Success: feasibility (dummy)					0.639	0.209					*2.137	0.000
Success: early (dummy)					0.686	0.209					*0.803	0.008
Success: late (dummy)					1.198	0.025					*1.059	0.046
Alpha	1.251	0.473	1.267	0.477	1.197	0.459	0.886	0.244	0.805	0.207	0.710	0.255
Number of observations	146		146		146		121		121		121	
R-squared (OLS)												
Log-likelihood (NB)	-126.033		-126.214		-132.159		-115.948		-112.432		-113.019	

Source: Ipsos MORI (2015) * indicates differences are significant at the 95 per cent confidence level

Table D.6 – OLS and Negative Binomial Results

	Change in annual R&D expenditure (log)						Change in R&D employment (log)					
	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value
Estimation method	OLS						OLS					
Constant	-0.271	0.706	-0.309	0.637	-0.840	0.365	-0.116	0.364	-0.095	0.490	-0.013	0.947
Independent Assessment Score	*0.015	0.038	*0.014	0.031	0.019	0.067	0.001	0.438	0.001	0.426	0.000	0.922
MAC or DPFS score	-0.017	0.856	-0.029	0.731	0.095	0.448	0.020	0.384	0.021	0.350	0.002	0.948
Baseline TRL level (squared)	-0.008	0.540	-0.008	0.558	-0.009	0.525	-0.004	0.077	-0.004	0.088	-0.004	0.098
Years Elapsed Since Application	0.193	0.513	0.290	0.516	0.187	0.538	0.116	0.122	0.096	0.194	0.119	0.114
Success (dummy)	-0.484	0.396					0.070	0.562				
Success: one year elapsed (dummy)			-0.725	0.450					0.065	0.524		
Success: two year elapsed (dummy)			-0.495	0.508					0.098	0.642		
Success: feasibility (dummy)					0.366	0.724					0.011	0.965
Success: early (dummy)					-0.641	0.265					0.050	0.748
Success: late (dummy)					-1.349	0.249					0.235	0.278
Alpha												
Number of observations	145		145		145		123		123		123	
R-squared (OLS)	0.0463		0.0497		0.0580		0.0363		0.0374		0.0438	
Log-likelihood (NB)												

Source: Ipsos MORI (2015) * indicates differences are significant at the 95 per cent confidence level

Table D.7 – OLS and Negative Binomial Results

	Change in overall funding levels					
	Co-eff.	p-value	Co-eff.	p-value	Co-eff.	p-value
Estimation method	Negative Binomial					
Constant	*-1.765	0.037	-1.656	0.077	-1.439	0.133
Independent Assessment Score	0.003	0.773	0.000	0.981	-0.001	0.887
MAC or DPFS score	-0.008	0.933	-0.025	0.768	-0.088	0.456
Baseline TRL level (squared)	-0.008	0.693	-0.002	0.922	-0.003	0.885
Years Elapsed Since Application	*1.840	0.000	*1.687	0.004	*1.914	0.000
Success (dummy)	*-1.564	0.004				
Success: one year elapsed (dummy)			*-1.540	0.007		
Success: two year elapsed (dummy)			-1.002	0.293		
Success: feasibility (dummy)					-1.447	0.115
Success: early (dummy)					*-2.228	0.004
Success: late (dummy)					-0.855	0.265
Alpha	4.042	0.854	4.029	0.920	3.986	0.875
Number of observations	131		131		131	
R-squared (OLS)						
Log-likelihood (NB)	-114.369		-115.292		-113.517	

Source: Ipsos MORI (2015) * indicates differences are significant at the 95 per cent confidence level

- **Project spending:** The estimates suggest that the provision of funding has had a significant impact on investment in the projects forming the focus of the Biomedical Catalyst applications. The impact on spending grows in each year since the application, supporting our assumption that the lack of a 'treatment effect' in year two relates more strongly to the discrete nature of the TRL scale than a failure to progress further.
- **Applicant level impacts:** When looking at the findings at the level of the applicant, it was not possible to reject the hypotheses that the Biomedical Catalyst has had no impact on total R&D spending or R&D employment. The results also seem to indicate that the Biomedical Catalyst has had a negative impact (overall) on the levels of external funding raised following the notification of the award (this excludes any funding contingent on a Biomedical Catalyst award). This can be partly explained by the Medical Research Council funding rules preventing 'double-funding' of the project (i.e. academic applicants are prevented from seeking additional finance), and indeed this is confirmed by the results - the negative impacts are confined to the academic applicants, while no effect is observed amongst the firms.

D.6 Regression Discontinuity Design

The models set out above addressed selection issues driven by unobservables through the inclusion of project scores as control variables within a standard regression framework. If these controls did not fully capture the influence of unobserved differences, then the results set out above are likely to be subject to bias. A second set of analyses, based on exploiting the architecture of the project selection process, was employed to try and validate these findings.

The architecture of the fund creates formal discontinuity between the treated and the untreated at the minimum scoring threshold. Given this institutional feature of the programme, a plausible approach to the evaluation of the BMC would be a Regression Discontinuity Design (RDD). These methods are based on the assumption that, although successful and unsuccessful applicants will differ systematically on an overall basis, randomness in the scores in the immediate vicinity of the minimum scoring threshold will mean that the observed and unobserved characteristics of the two group will be close to identical at this point (i.e. comparisons between those that just made it, to those that just missed out). Provided that a set of key assumptions hold (discussed below), an RDD has an interpretation close to that of an RCT (and will be more robust than the OLS and negative binomial results set out above). However, these findings are considerably less generalizable, as they only capture the effect of the programme on the marginal applicant (i.e. those that 'just made it').

D.6.1 Distribution of Assignment Scores

In the Biomedical Catalyst, applications are assigned into treatment on the basis of the score given by the MAC or DPFS panels, or on the basis of the independent assessment score (SME led bids for Feasibility Studies, and Early Stage Awards in rounds 1 to 3, only). The minimum score required for selection into treatment varies from round to round. The MAC and DPFS panels score applications from 1 to 10, while the scores of the independent assessment are from 10 to 100. To normalise these scores over different rounds and scoring frameworks, a running variable was calculated which was defined as the percentage deviation of a bids score, from the lowest scoring successful application in the relevant round (i.e. the threshold score in that round)[36]:

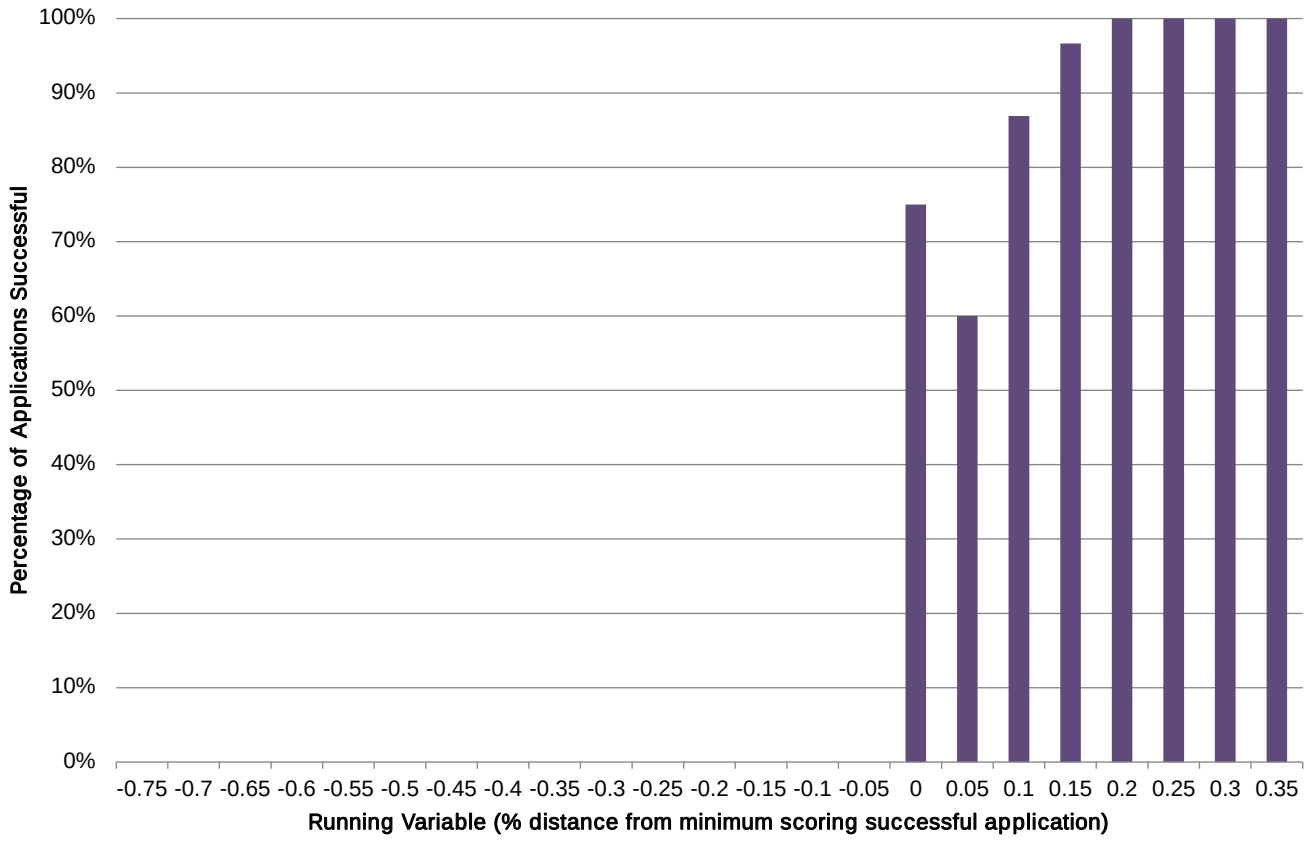
The figure below shows the probability of success by distance from the minimum scoring successful application over the first six rounds of the programme. As illustrated in the figure, there is a discontinuous jump in the

[36] $RV_i = \frac{S_{i,j} - LSB_j}{LSB_j}$, where S is the score received by bid i in round j, and LSB is the score of the lowest scoring bid in round j.

probability of assignment into the threshold score. However, 'borderline' SME led applications for Feasibility Studies and Early Stage applications in rounds 1, 2 and 3 entered a moderation process in which funding was allocated through a consensus process, meaning that on some occasions, applications with higher scores than the lowest scoring successful bid in the round were ultimately unsuccessful.

In these circumstances, application of RDD methods will yield the 'Intention to Treat' estimator (i.e. an estimate of the impact of the programme on those at the threshold score for assignment into treatment, regardless of whether they were ultimately approved for funding). Fuzzy RDD (FRD) methods are required to estimate the average treatment effect on the treated. These methods involve an additional step of estimating the discontinuous increase in the probability of assignment into treatment at the minimum scoring threshold, and introduce an additional source of uncertainty in the estimated treatment effects. In view of the small sample sizes available for analysis and the high variance in the outcomes observed, a decision was made to apply RDD rather than FRD methods.

Figure D.3 – Probability of Success by Distance from Threshold Score for Success



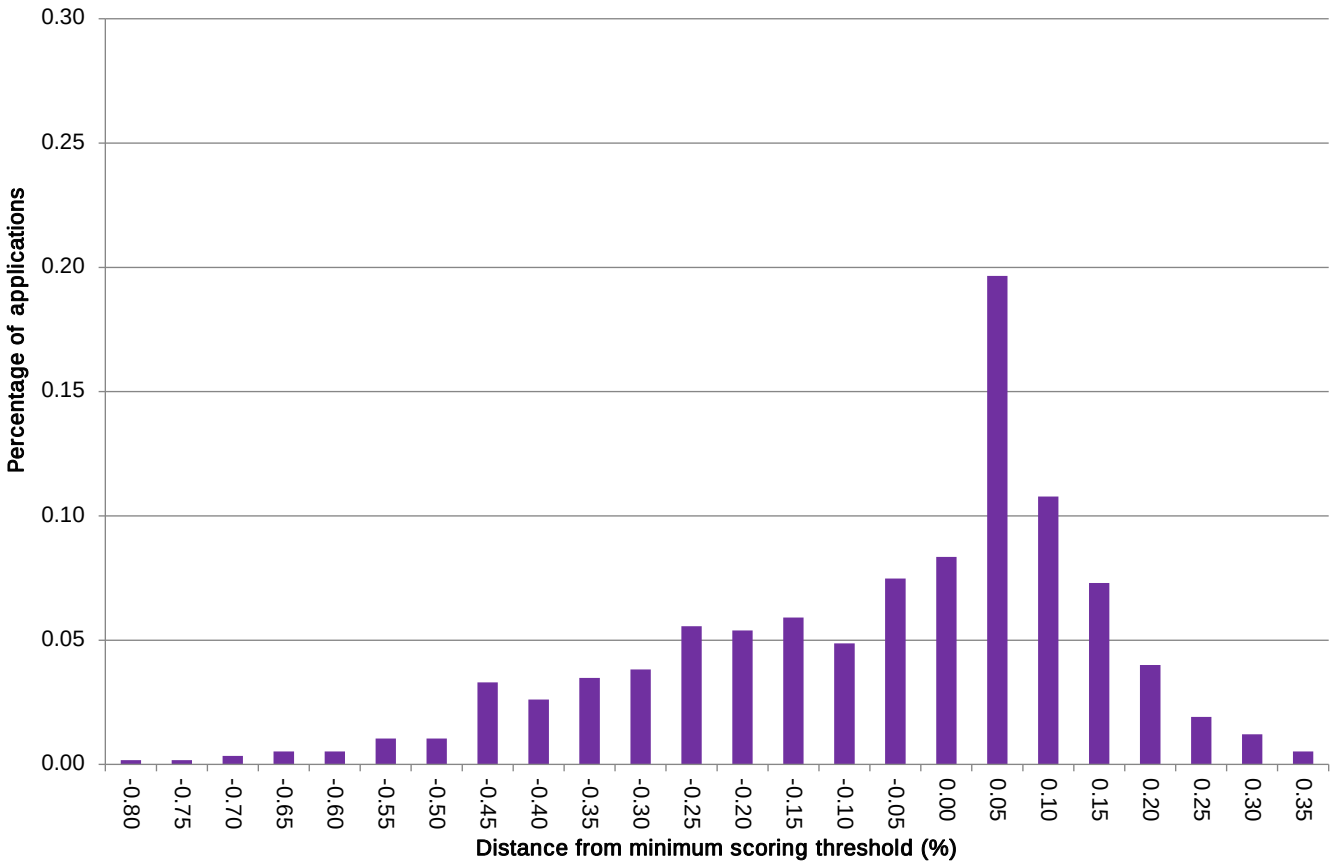
Source: Ipsos MORI (2015)

D.6.2 Manipulation of Treatment Status

A major threat to the validity of RDD methods is manipulation of treatment status at the threshold. If some marginal applicants are able to influence the likelihood that they are selected into treatment, then their characteristics will be unbalanced on either side of the threshold. At worst, this invalidates the interpretation of the RDD methods as an RCT (leading to biased results). Evidence of possible manipulation of treatment status would be seen in a drop-off in the distribution of assignment scores on either side of the thresholds.

The figure below shows the distribution of assignment scores and shows a major increase in the distribution on the higher side of the minimum scoring threshold. It is anticipated that this is primarily a function of the way in which the running variable has been calculated (i.e. as a percentage of the minimum scoring bid, leading to a clustering of observations close to the scoring threshold) rather than as any evidence of manipulation of treatment status.

Figure D.4 – Distribution of Assignment Scores (Rounds 1 to 6)

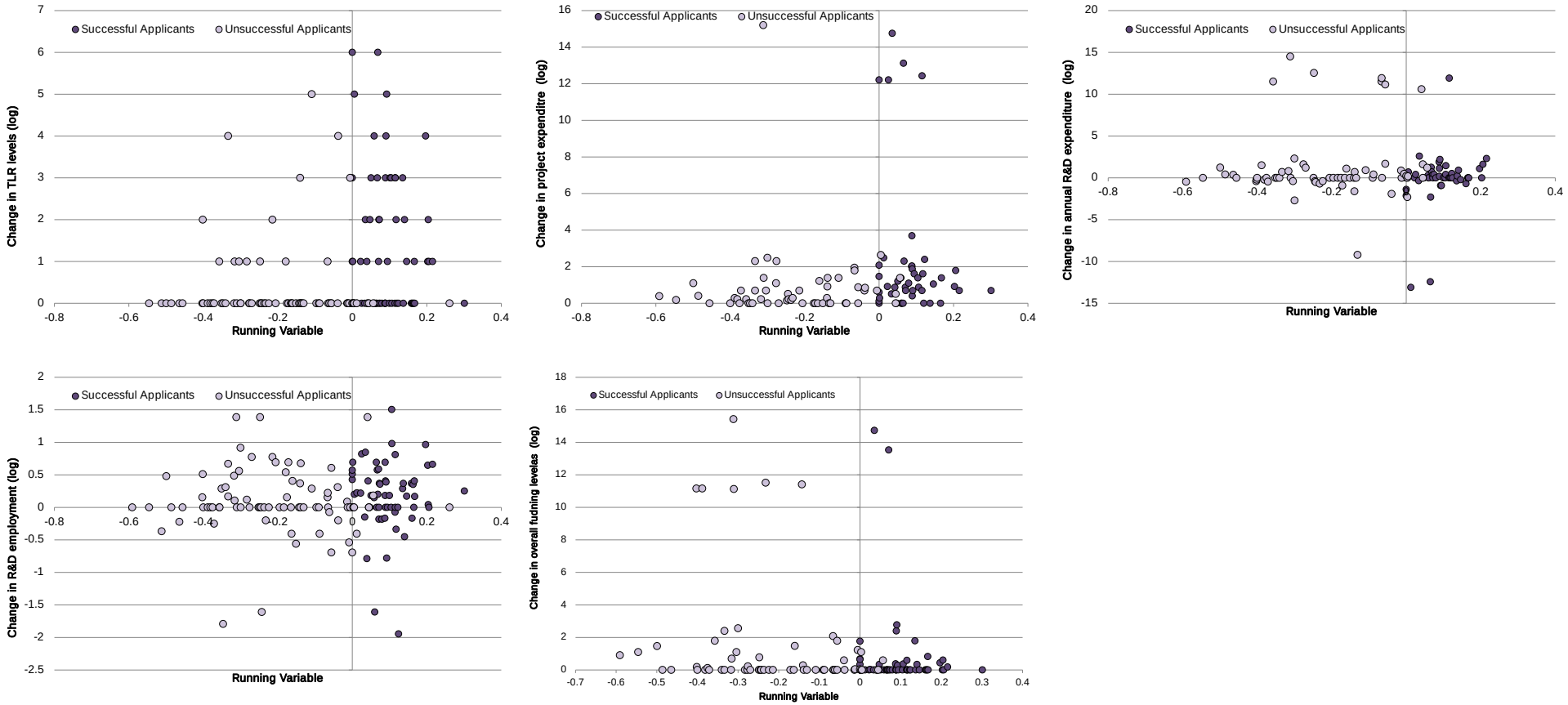


Source: Ipsos MORI (2015)

D.6.3 Outcomes by Running Variable

The distribution of the five outcome variables by the running variable are set out in the charts overleaf. These figures illustrate the high variability in the outcomes observed on both sides of the minimum scoring threshold.

Figure D.5 – Outcomes by Running Variable



D.6.4 RDD estimates

The RDD was implemented using a parametric form in which all observations were used to estimate the relationship between the running variable and outcome (and the discontinuous jump in the outcome variable at threshold). This approach can be less robust than non-parametric strategies focusing on a narrow bandwidth of observations in the vicinity of the scoring threshold. However, as the overall number of observations available was limited, a non-parametric strategy was not considered feasible.

In light of the high variance observed on both sides of the scoring threshold, the RDD was implemented using a flexible functional form, as follows:

$$\pi_i = \alpha + \beta T + (1 - T) \cdot (\gamma RV_i + \delta RV_i^2 + \theta RV_i^3) + T \cdot (\rho RV_i + \tau RV_i^2 + \varphi RV_i^3) + \varepsilon_i$$

In this model, T is a dummy variable taking the value of zero if the running variable (RV) is less than zero and unity otherwise. The co-efficient β captures the impact of treatment at the threshold. Iterations of this model were also performed excluding the squared and cubed terms of the running variable37. These estimates are displayed in the table overleaf and displayed graphically in the following charts.

The key findings from the analysis are as follows:

- **Project expenditure:** The findings supported the previous analyses in that under two of the three models, a statistically significant effect was found on the marginal project in terms of project expenditure. In addition, the estimated size of this effect was in the same order of magnitude as estimated through the negative binomial models set out above.

- **Other variables:** No other significant estimates of treatment effects were found on the marginal project or applicant. However, for most variables, the estimated co-efficient was of the expected direction (except in the case of annual R&D spending). In light of the limited sample sizes available for this analysis and the high variance associated with the outcomes, it is possible that the positive effects have been achieved, but were insufficiently large to be detected through this methodology.

[37] This formulation aligns with that taken in 'The Impact of R&D Subsidies of Firm Innovation,' Bronzini and Piselli, Bank of Italy (2009)

Table D.8 – RDD results

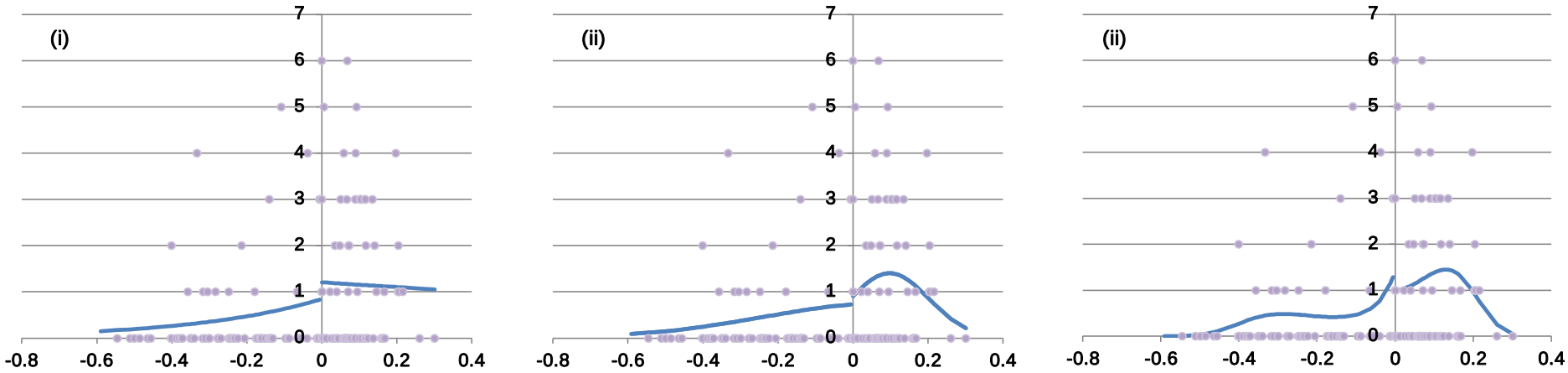
Variable	Change in TRL levels						Change in Cumulative Project Expenditure (log)						Change in Annual R&D spending (log)					
	Co-eff (i)	P-Stat	Co-eff (ii)	P-Stat	Co-eff (iii)	P-Stat	Co-eff (i)	P-Stat	Co-eff (ii)	P-Stat	Co-eff (iii)	P-Stat	Co-eff (i)	P-Stat	Co-eff (ii)	P-Stat	Co-eff (iii)	P-Stat
(1) Constant	-0.168	0.727	-0.315	0.632	0.359	0.684	-0.277	0.560	-0.858	0.215	-0.055	0.957	1.814	0.063	1.918	0.181	3.1682	0.099
(2) Threshold Dummy (= 0 if running variable < 0, 1 otherwise)	0.356	0.547	0.217	0.779	-0.368	0.709	1.444	0.010	1.9827	0.012	1.120	0.313	-2.360	0.061	-2.695	0.122	-4.0791	0.06
(3) Running Variable N (if running variable < 0, 0 otherwise)	2.914	0.137	0.825	0.779	19.217	0.248	-0.431	0.797	-6.513	0.283	9.151	0.571	2.455	0.061	3.586	0.761	29.192	0.065
(4) Running Variable (if running variable ≥ 0, 0 otherwise)	-0.449	0.891	8.920	0.306	0.814	0.963	-5.095	0.104	-3.779	0.624	0.160	0.992	8.937	0.263	17.913	0.453	32.849	0.543
(5) Square of (3)	-	-	-4.697	0.750	19.217	0.263	-	-	-11.92	0.250	55.241	0.406	-	-	2.138	0.920	114.33	0.320
(6) Square of (4)	-	-	-45.489	0.251	55.236	0.777	-	-	-6.16	0.853	-49.82	0.744	-	-	-49.053	0.689	-258.90	0.708
(7) Cube of (3)	-	-	-	-	142.56	0.252	-	-	-	-	78.210	0.313	-	-	-	-	131.48	0.320
(8) Cube of (4)	-	-	-	-	-299.4	0.607	-	-	-	-	113.04	0.769	-	-	-	-	709.38	0.757
R-Squared	0.286		0.0329		0.0386		0.0404		0.0446		0.0479		0.0098		-0.006		-0.0145	

Variable	Change in R&D employment (log)						Change in Total Funding Levels (log)					
	Co-eff (i)	P-Stat	Co-eff (ii)	P-Stat	Co-eff (iii)	P-Stat	Co-eff (i)	P-Stat	Co-eff (ii)	P-Stat	Co-eff (iii)	P-Stat
(1) Constant	-0.919	0.598	-0.092	0.598	-0.166	0.469	0.764	0.349	-0.288	0.438	0.323	0.833
(2) Threshold Dummy (= 0 if running variable < 0, 1 otherwise)	0.247	0.250	0.247	0.250	0.340	0.208	0.171	0.867	1.046	0.438	0.174	0.920
(3) Running Variable (if running variable < 0, 0 otherwise)	-1.947	0.182	-1.947	0.182	-3.544	0.313	-3.794	0.189	-15.93	0.095	-2.409	0.922
(4) Running Variable (if running variable ≥ 0, 0 otherwise)	-0.527	0.830	-0.5268	0.830	-1.780	0.721	-32.96	0.605	3.006	0.841	23.722	0.430
(5) Square of (3)	-	-	-3.559	0.184	-10.73	0.462	-	-	-23.59	0.181	36.145	0.723
(6) Square of (4)	-	-	3.991	0.693	17.327	0.713	-	-	-27.88	0.668	-252.2	0.383
(7) Cube of (3)	-	-	-	-	-8.552	0.617	-	-	-	-	69.672	0.553
(8) Cube of (4)	-	-	-	-	-34.16	0.772	-	-	-	-	577.36	0.426
R-Squared	-0.0168		-0.0168		-0.029		0.0170		0.0170		0.0082	

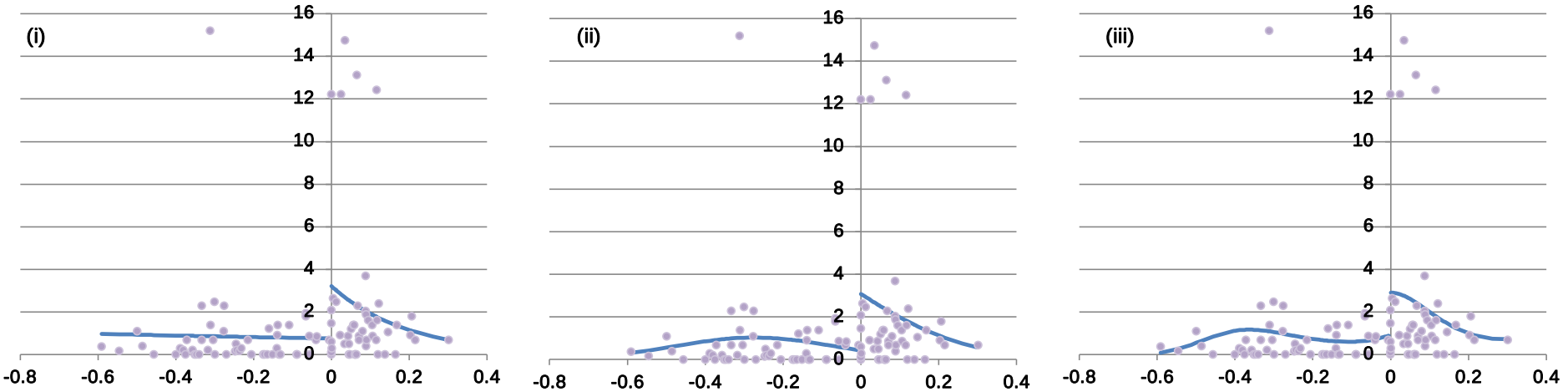
Source: Ipsos MORI (2015)

Figure D.6 – RDD results (continued on following pages)

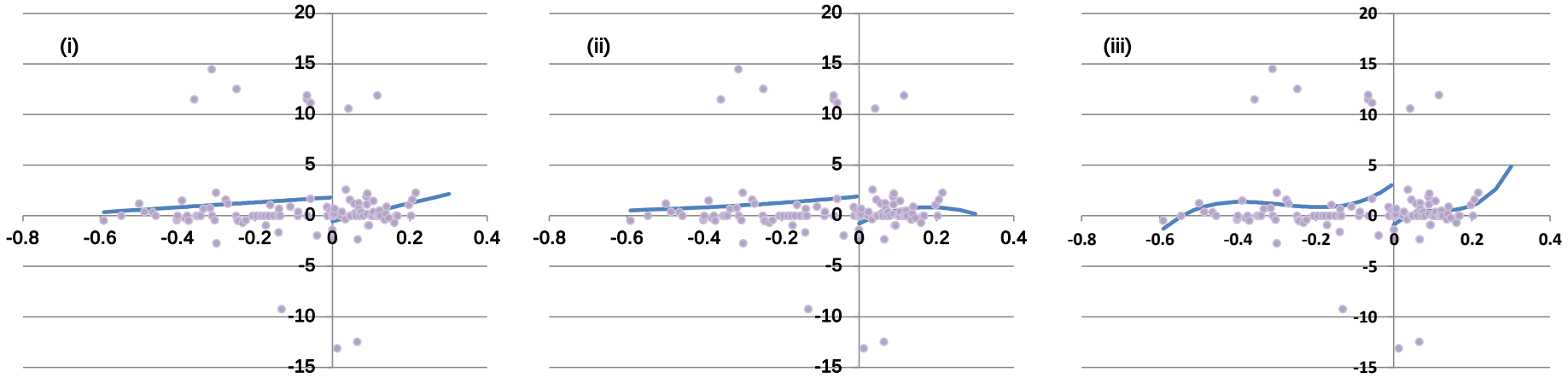
Negative binomial RD: change in TRL level



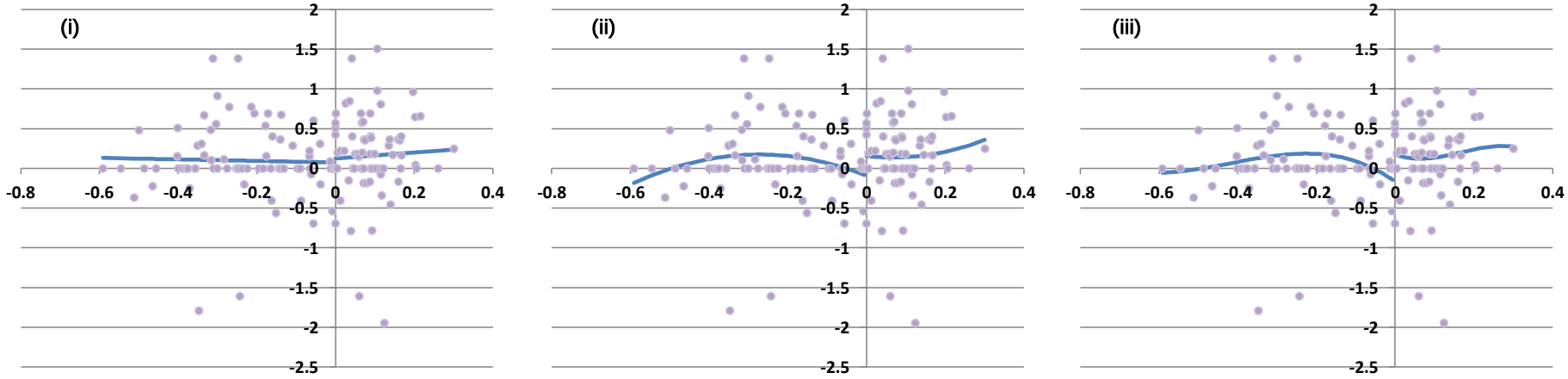
Negative binomial RD: Change in Cumulative Project Expenditure (log)



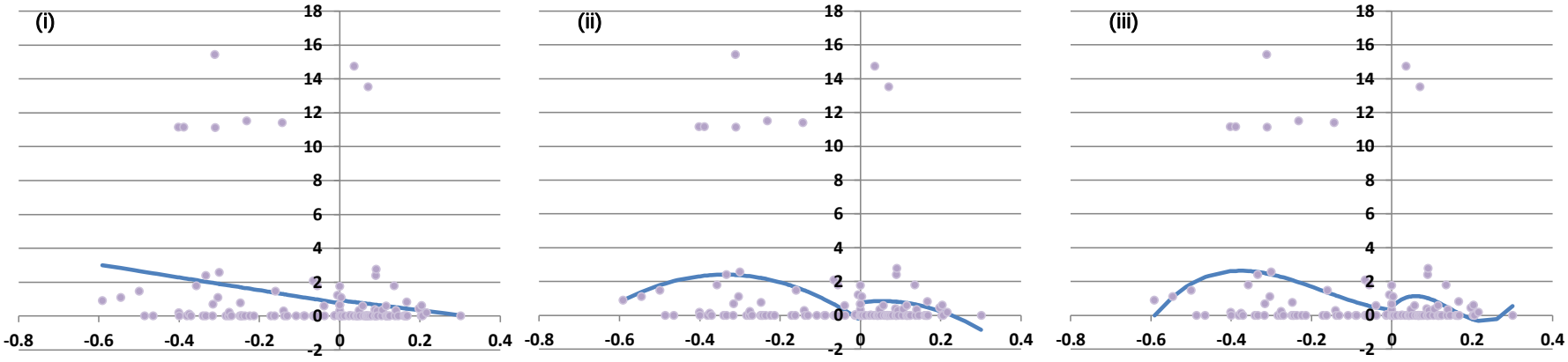
Ordinary least squared RD: Change in Annual R&D spending (log)



Ordinary least squared RD: Change in R&D employment (log)



Ordinary least squared RD: Change in Total Funding Levels (log)



Annex E: Case Studies

This Annex sets out an overarching framework for the evaluation of the Biomedical Catalyst programme. This framework specifies the policy objectives for the programme, the rationale for intervention, and defines a 'theory of change' outlining the causal process by which the Biomedical Catalyst is expected to deliver its outputs, outcomes and impacts. This understanding is formalised in the definition of a 'logic model' and a set of key outcomes that will need to be explored through the evaluation. Finally, this section sets out a range of contextual issues with the potential to influence the outcomes of the programme that will need to be considered.

Within this evaluation the study team undertook 20 case studies of applicants to the full range of Biomedical Catalyst schemes which included a mix of successful and unsuccessful applicants. These were prepared based on a review of application forms, management information, interviews with the lead applicants, and where possible, discussions with project collaborators. This annex presents 16 of these case studies as in four cases, interviewees requested not to have their case studies published (or to publish them at the later stage).

Case study 1: CiC grant recipient

Summary

This is a leading research university that received Confidence-in-Concept funding in 2012, 2013 and 2014. The department receiving and administering the funding forms around 10 per cent of the university's life sciences department and is focused on drug development and translational research.

The department's role is to (1) develop new projects which are of interest to Pharma companies but that are currently seen as insufficiently validated, and (2) de-risk them to the stage at which industry is willing to partner the project and develop it into a marketable product. The department operates similarly to a small biotech firm, with academics working together as a management team; they have close relationships with the rest of the department of life sciences, and also work with external clients from across the UK and worldwide seeking to translate their work. The department brings its drug discovery capabilities to collaborative project teams formed with academics working in particular disease areas, and others, such as clinical experts, if required.

Whilst operating like a biotech firm, the department commented that their not-for-profit focus was favourable to innovation, as it has allowed them to have a higher risk appetite, be more open-minded and flexible, and more willing to offer advice and guidance to academics. Moreover, the department has better access to equipment than a biotech firm of equivalent size.

Programme description and rationale

The university in which the department sits is particularly strong at drug discovery research and has therefore chosen to focus CiC funding on this area. Moreover, it has taken a unique approach to allocating the funding. Rather than giving grants to individual projects, the institution has used the funding to support a core team of biologists and chemists, with the funding manager and board deciding which projects can access this resource.

This approach was developed from 2009 as part of the MRC Devolved Portfolio pilot scheme, when the university received devolved funding and used this to support a portfolio of projects in combination with some individual grants. A portfolio approach was taken as it allows greater flexibility in how the money is used; if there are delays on one project, the team can work on another, which reduces downtime and is thereby more efficient. Moreover, a portfolio approach allows a core staff team to be retained and their expertise to be developed.

Principal investigators (PIs) and companies can apply to access the research resource. The drug discovery team supports applicants in completing a project proposal to ensure that the project is feasible, suitable and ready for translation. This proposal is then submitted to the Scientific Advisory Board; this board consists of senior staff from the life sciences department and external experts, and also oversees other funding applications, e.g. for Wellcome Trust funds. The make-up of the board has a focus on biology, to ensure the biological (as opposed to chemical) idea holds merit, and on industry, to ensure the projects are likely to lead to a viable product. One member is an external consultant from industry, and another external board member with industry expertise is being recruited.

The board looks for projects which take a novel approach, either in terms of a new target or a new approach to that target. The department sees a relatively greater risk appetite as one of their strengths and therefore avoids work on areas which are already well-explored, where there is little opportunity to add value. Projects must also be biologically validated and feasible within CiC timeframes. Those projects which are not approved are provided with feedback and given an opportunity to re-apply.

The funding manager explained that, despite having extensive experience working with the commercial sector, department managers were wary of being too prescriptive about requiring a clear commercial justification. Although the team will discuss potential projects with clinicians to establish medical need, past experience had demonstrated that the therapeutic application of a discovery might not be apparent at the beginning of a project, and that commercial interest in particular diseases is liable to change over time, so an open-minded approach is preferable. Demand may not necessarily be commercial; the department has also worked extensively with charities, foundations and other not-for-profit organisations on treatments for malaria and other developing-world diseases.

Funding issues and motivation for applying

The university had been seeking to do more translational work, but found that it was difficult to undertake early-stage activities at sufficient scale. In particular, allocating individual grants to projects was time-consuming and the university had already been advocating to Wellcome and the MRC that funding should move away from a project-by-project approach. The applicants therefore welcomed the flexibility of the CiC funding since it allowed them to apply their own approach, both in terms of being able to select more risky projects, and in terms of funding a core team rather than individual projects. This portfolio approach is similar to that taken by biotech firms, university departments conducting basic research, and in some developing world drug discovery projects. Had funding not been available for a core team, the department would have lost the ability to retain, train and develop staff, and instead had to start afresh for each project, with a detrimental effect on research.

In addition to the CiC funding, the department receives funding from university funds, an industry partner, the Wellcome Trust, and as part of the BMC:DPFS. Different funding streams are used to support projects at different stages, with CiC funding being used to support high-risk, early-stage ideas; if these are good enough to be developed then Wellcome Trust or BMC:DPFS funding will be used to progress them. This set-up ensures compliance with the requirement that the CiC grant must not be used as match funding.

The department undertakes a small amount of fee-for-service and commercial work, and recycles profits back into its research. The university also grants funds to the department, some of which goes towards paying salaries and some of which is unallocated.

Progress

The CiC funding has been used to support small, focused activities at a very early stage – for example, to investigate a protein that is believed to be of interest in drug development but for which a specific application has not yet been identified. The project will undertake high throughput screening and test for drug discovery starting points, from which to investigate in more detail and develop a more specific hypothesis. Another typical format for projects is developing a new cell-based assay of disease and then testing some molecules in that assay. The department explained that the team is able to learn from each project and adapt project plans accordingly, e.g. undertaking additional experiments to look at another aspect of the target's biology where the initial approach has proved unsuccessful.

In order to avoid disputes over intellectual property resulting from development of projects, the department agrees a royalty agreement up-front, which is usually that the academic will hold a 50 per cent stake in the project with the rest shared out.

A number of projects have been the subject of discussions with industry and charitable foundations, but as yet there have been no partnerships formed. One project received follow-on funding from the Wellcome Trust and is in the process of applying to the BMC:DPFS. Another project attracted additional funding from the university in the form of a PhD studentship.

Wider institutional impact

Prior to the CiC funding, the university had experienced a "translation bottleneck", whereby basic researchers lacked the resources and expertise to make their research robust and reproducible enough to support drug discovery projects. CiC has helped to fund assay development and develop it to industry standard, thereby removing this bottleneck. The industry-standard assay can then be provided back to academics to use for further investigation, providing a further benefit in addition to any drug discovery that may result from the assay development.

The department is putting together a business model for a ten-year fund that will take 10-14 projects from initial concept to commercial partnership. Although they have received interest from a number of Pharmaceutical companies in partnering this project, development requires further funding, and an improvement of the department's screening capability. Bespoke screening labs along with equipment have been purchased from internal institutional resources and grant funding and a PIF award plus a WT/Gates award is supporting re-purchase of the compounds library. CiC funding was used to support the screening activities for first world disease projects while other awards support disease specific activities, mainly developing world indications.

Moreover, potential Pharmaceutical partners would like to see the department undertaking more collaborative projects with other institutions; however, it has so far not been permitted to use CiC funding for such projects, and this is something the department would like to explore with the MRC.

The university works in close collaboration with one Pharmaceutical partner and is in discussions with a further two companies about undertaking joint projects. They have applied for an MRC "Proximity to Discovery" award in order to further their interactions with industry.

Process issues

The university appreciated the open format for applications as this allowed them to represent a divergent approach. However, this has not been the case for the reporting documents, which the department found to be too template-based and restrictive. In particular, it proved difficult to represent the progress of a rolling programme of projects, or attribute costs clearly to each project. Moreover, since activities roll over from one year to the next, the amount of money approved by the portfolio in one year might be different to the funding received, causing further difficulties in completing the reporting template.

The department appreciated the feedback from reviewers, but found it frustrating to receive feedback that they needed more resources for the size of their ambitions, while at the same time not being awarded the full amount requested. They had received a request that the university supplied more of an in-kind contribution, but felt that the university was already contributing substantially to the department's activities by way of expertise, resources and funding. The department noted that their desire for funding from CiC was greater than the funds available. They felt that they could have made use of a funding allocation which was 50 per cent larger.

Part of the rationale behind the portfolio approach was to support and maintain a core staff team, so the department rolls one fund into the next in order to avoid losing staff through gaps in funding. The department therefore reapplies each year and runs awards for 12 rather than 18 months. This means that the CiC cycle is very short in comparison to other programmatic cycles, which run for three or five years, and the administration required proportionally more demanding. Moreover, the department expressed concern that this instability would at some point lead to funding gaps and the consequent loss of the team and their expertise.

The reporting and application requirements were generally seen as reasonable, although it was noted that the requirement to report on all previous projects in each year's application would become unsustainable over time.

The guidance supplied had been useful to some extent, although managers still felt that they were unable to predict how the reviewing panel would respond. The department commented that the programme manager had a good understanding of their different approach and was helpful in trying to accommodate this.

Case study 2: CiC grant recipient

Summary

This is a leading research university that received Confidence-in-Concept funding in 2013 and 2014. The University is globally recognised for its research in health and life sciences, science and engineering, and humanities and social sciences. CiC funding forms a substantial part of the translationally focused overarching approach to funding early research ideas. The funding stream is of strategic importance.

The CiC scheme operated within one of the university's largest faculties (Health and Life Sciences) and included collaborative works with staff from the Faculty of Engineering.

Programme description and rationale

In the first year of CiC awards (2012) the university did not receive funding and as a result the subsequent applications were more focused and coordinated while demonstrating the assets that the university holds. The scheme in 2013 and 2014 operated within one of the university's largest faculties (Health and Life Sciences) and included collaborative works with staff from the Faculty of Science and Engineering. The underlying premise was to understand the fundamental mechanisms of disease to enable translation into better diagnosis and treatment of human disease through the development of new drugs, better ways of using existing drugs, and the development of mechanism-based biomarkers. The latest application sought support for up to ten projects where the funding was set out to accelerate the most promising projects by between 12-24 months. Projects had to demonstrate (i) excellence in science, (ii) a genuine prospect of translation, and (iii) that the funding will accelerate progress. In addition projects had to have 20 per cent of total project costs met by their school (in-kind) – a characteristic to ensure that the project has secured an internal buy-in. The scheme setup included selection panel comprising of members from the commercial sector recruited with the help of a relevant industry association. The themes that the CiC projects fit within are the universities research strengths, such as infectious diseases, clinical Pharmacology, and to some extent musculoskeletal disease. The initial decision was to have a relatively narrow focus was due to relatively small size of the university and the need to support its key strengths. Some of the funding was directed towards projects outside these themes to support projects that are at the right stages and fit under the remit of translational research.

An overarching characteristic of the project has been industry-academic collaboration. This engagement has grown out of the programme mainly due to high proportion of industry experts on the panel. The selection panel we set up specifically for the CiC programme and while most of them were already working with the university before this role spurred enthusiasm and further engaging with the university.

Typical size of the funded research projects is around £50k and typical length is between one and two years. Some of these were standalone projects and a proportion of them had previously secured funding and the CiC was used to match it. The fund selects only applications that are not too early or don't have enough commercial potential. "The project needs to be at the right stage and be going to lead somewhere – scientific merit is not enough".

Progress of the project is monitored by an internal 'Research Strategy Group' which regularly checks whether the project is meeting its milestones. If a project wasn't progressing it would be terminated early but so far there have been no issues. The internal programme management was described as "effective and running smoothly".

Motivation/rationale for applying

The institution's initial motivation for applying for a CiC award was to support the acceleration of specific ideas via project funding. In subsequent years the motivation – based on the success of projects supported by CiC awards – included greater engagement with industry which was identified as brining additional added value.

The university had not systematically considered other funding options for this work. The main reason for this was a lack of venture capital in the region and their belief that it is difficult to make the case for direct industry funding at this early stage of the development process; "There's not much funding for this space".

Progress

The university monitors the development of projects by looking at how the project progressed to the next stage. This progress might not necessarily constitute the BMC:DPFS award.

The faculty's first successful application to the CiC was in 2013 and resulted in seven projects being funded (three in therapeutics and four in biomarkers). To date, three of these have been completed, and six have been able to put in place follow-on plans to work with an industrial partner, in the following ways:

- Implementing a collaboration agreement via the university's business managers team, who are also progressing project data for patent filing;
- Submitting a Knowledge Transfer Partnership application;
- A confidential disclosure agreement is in place as well as an agreement on accessing data and samples for testing;
- An industrial partner has agreed to provide consumable support for a pilot study and funding for a research assistant;
- An industrial partner is supporting a BMC:DPFS application;
- Negotiations are underway around industrial partner producing materials for a follow-on study.

In summary, five projects have strengthened existing links with industry while one has resulted in a new collaboration with a Pharmaceutical company. The projects have fed into full scale applications for research projects (two BMC:DPFS applications and one MRC Technology) as well as securing additional follow on funding from industry. So far there were no spin-outs from the CiCs, however this may reflect the fact that only a small proportion of projects have finished.

Wider institutional impact

This funding is strategically important for the university. It has influenced their strategies and has been highly effective in changing the way they work with industry in practice – bringing them closer and building stronger links. Prior to the formation of this programme this interaction was less systematic. The programme manager described pre-CiC period as "functioning in a vacuum".

One of the main benefits of the work supported by the CiC award has been to raise awareness of the research expertise and to university researchers' exposure to working with industry. An example of this is that one of the panellists had been to the US in search of an academic partner and then through involvement on the panel discovered that someone at the university was a better fit for what they were looking for. This resulted in a specific

project. Also, some non-grant activities associated with the programme such as having an industry showcase day to encourage industry engagement – an event that required careful planning and work around the IP sensitive issues – have also helped to increase this exposure.

One additional wider benefit is that the industry engagement resulted in easier recruitment of collaborations for the university PhD programmes. The university strives to provide their PhD students to engage with industry but it's difficult to coordinate these efforts within the industry setup in which there is a large number of SMEs. An industry association that is represented at the CiC panel have formed links with the university to assist in matching students with industry (e.g. cancer research unit). Likewise other members of the panel can spot the kind of project they are looking for (working with drugs that haven't been progressing via industry and de-risking them, using charity funding).

The applicants view the CiC award as a relatively small and time-limited fund which is achieving "a huge change in industrial collaboration".

Process issues

In the first round of the CiC funding, the application process was not communicated as well as it could have been. This resulted in misunderstanding of the requirements and the university not securing funding.

Otherwise the programme was seen as running smoothly and no suggestions for improvement were made. It was described as "one of the most successful funding schemes that the university has had". Its features such as the delegation of decisions to the university while retaining clear metrics, was described as very successful. The programme manager stated that they were impressed by how it can positively influence internal strategies and that it was more effective than some larger longer term projects

Case study 3: CiC grant recipient

Summary

This is a case study of a leading research university that received Confidence–in-Concept (CiC) funding in 2012, 2013 and 2014. The CiC funding is one of a number of funding streams available to the university's life sciences researchers, including internal grant programmes, foundations, and a charity. The CiC forms a substantial proportion of this funding and provides opportunity for researchers in translational research. Most other initiatives at the university are broader and as a result more competitive; on the other spectrum is a narrowly focused charitable funding secured by the university.

Programme description and rationale

The CiC programme at this university invites applications from a broad array of translational research projects including applicants from chemistry and engineering departments, in contrast to charity-funded internally administered research programme which is limited to a few priority areas. The rationale for this is to ensure that the very best projects are supported regardless of scientific area; however, this decision is reviewed each year by an internal committee. The university is confident that there is good awareness of the programme across departments due to good working relationships between the grant administrator and department research support staff. They have not examined the balance of projects across scientific disciplines as this was not a relevant factor in assessing applications; however, they suggested that therapeutics and small molecule work was particularly well-represented.

It was centrally decided that the CiC funding would be used to provide in-depth support to a relatively small number of projects, to increase the impact of the funding by supporting these projects from basic science up to the point at which they can apply for the next stage of translational funding. Guided by the MRC's funding cycle, the university, in its first two iterations of CiC awards, funded projects up to one year but in the third year looks to fund shorter-term projects between six and nine months. Applicants must supply 50 per cent match funding for the costs of their project. This is most often from the applicant's department (internal funding sources), which is seen as representing a departmental endorsement.

The review process operates through two stages; half-page Expressions of Interest are looked at by small sub-groups, following which a panel looks at the final set of applications. The divisional administrator co-ordinates applications to the range of funds; however, applications to each fund are assessed by separate and tailored selection committees, as the large number of applications would result in an unmanageable workload for a single team. Moreover, assessors with a specific background in transitional research, technology transfer and business development were required for assessing individual CiC project applications. To secure funding projects need to demonstrate a medical and commercial need, as well as sound science. If the commercial need is not well-articulated then the university's business development or technology transfer subsidiary could be asked to help develop this. However, in practice the scheme is oversubscribed by applicants who are considered excellent on all three fronts.

Funding issues and motivation for applying

The university felt that, given their extensive research activity, there was significant untapped potential for translation of research findings. The nature of other funding sources (mainly responsive mode) made it more likely that, in the absence of an incentive to encourage translational work, researchers would apply for grants to do non-translational research instead. The grant programme also enables the university to improve their understanding of where translational research is taking place.

The institutional nature of the funding, with delegated decision-making and therefore considerable flexibility, was very appealing to the university. They appreciated being able to choose (or not bind themselves to) a scientific focus, and choose how to manage the programme (e.g. to require 50 per cent match funding). The match funding from the university highlights that it sees great value in this type of research funding. However, one disadvantage in comparison to other funding streams was the uncertainty as to whether and how much funding the university would receive in each round.

There are a number of other funding sources available to university researchers for early stage translational research, but these are either oversubscribed or have a much broader focus, so are unable to fund many translational research projects. There is a need for the grant administrator to manage researchers' expectations and the level of success rates from the number of applications submitted. The funds with broader focus tend to have as low success rates as 1:40. In the absence of CiC funding, some departments would still fund translational research, but some would choose not to and others might be unable to afford it. In particular, basic science departments, where some of the most successful projects have been based, would have lost out in the absence of the scheme. The CiC grant therefore creates a more level playing field across departments and enables funding of the best applicants in translational research regardless of which department they reside in.

Progress on projects

The first round of funding was disbursed with very little formal monitoring of projects once they have been awarded. In the second year of funding the project teams were asked to contribute to a progress report required for successive CiC applications. This provided a snapshot of funded projects for the portfolio report being written, including a description of each project, what additional funding it had attracted, project progress to date, any intellectual property resulting, and next steps for uptake and translation. The university also provided information on the spread of projects by department and the sources of match funding. The fund administrators would like to improve their monitoring of CiC projects in order to understand factors relating to success of the projects; it is hoped that the university's technology transfer subsidiary will be able to provide support around monitoring in future, helping projects to develop milestones and next steps once the projects conclude.

In terms of outcomes that the university aims to achieve, they are aligned to the MRC's view to become strong candidates for BMC:DPFS funding as a result of involvement with the programme. The number of proposals going to the full stage of BMC:DPFS is therefore the main indicator of success, and applicants are made aware of this, which helps them understand whether their project is at a suitable stage to apply. However, there are other possibilities for successful outcomes (e.g. forming a spin-out) and the university felt there could be a clearer framework of successful outcomes in place by the funder. One outcome of the process might be that unviable projects do not proceed to the BMC:DPFS stage, and so a reduced failure rate could be considered as an indicator.

The university made some attempt to monitor CiC awardees' rates of applications to other grant programmes and their success rates, but as this information is collected in departmental annual reports, there is no consolidated information available. However, while there are several potential sources of funding for translation work, information has not been collected on which grant applications requested translational funding, and with the total number of grants by university researchers in the thousands it has proved impossible to identify these.

Nevertheless the fund administrator could point at several projects supported by CiC that have attracted major funding to follow up the work; one project resulted in securing £5m in additional funding. Overall, projects had attracted over ten times the amount of MRC CiC award in match funding. This has not been assigned for translation work exclusively, but project teams have found it possible to use part of their match funding for this

purpose. CiC projects from the second round resulted in a successful DPFS application and several are in review stages, and another project has been funded by DCS.

As yet, there have been no direct spin-outs formed, but there is one in the pipeline. There have been several clinical trials as a result of the programme. A number of projects have resulted in publications, including front covers of *Nature* and *Anfewandte Chemie.* There are over 10 patents in draft, filed or progressing as a result of CiC work.

Wider institutional impact

The university is currently going through an in-depth review of how it can support innovation and create a culture of change around this, including the development of a translational science strategy. The CiC programme has helped to embed this innovation culture, providing case studies and showing the university's support for innovative projects.

The CiC administrative team hope to make more use of the university's technology transfer subsidiary in future, to provide hands-on technical support, guidance around monitoring, and more match funding; thus far, the subsidiary has provided funding to projects after their CiC funding period rather than simultaneously.

One challenge reported by the university is that they were approached by another university, also in receipt of CiC funding, to ask for a contribution for a collaborative project. However, providing funding support to such a project was felt to be prohibitively complicated, which had prevented valuable cross-institutional working.

Process issues

The 18-month timescale had caused a number of difficulties. (1) It was felt to create an unnecessarily large administrative burden through having to repeat the application process frequently and (2) the short timescales mean it is only possible to issue one call for proposals, in order to give potential applicants time to respond; however, this means that some projects are excluded as they are not developed enough to apply at the right time. The limited time applicants have to prepare also restricts their ability to secure external funding, so that the majority of match funding is found from within the University.

The university recommended a timescale of three years, which would halve the administrative workload. They stressed that this would also result in better scientific outcomes, since this timescale would allow two calls for applicants, meaning that more projects would be aware of CiC and able to apply at a suitable time, and allow the CiC funding to be aligned better with other funding streams. These extended timeframes could be accompanied by midterm or biannual reviews with reporting on progress in applications and projects.

So far, the university has not used any of the CiC funding for business development work or monitoring; however, if monitoring requirements increase, this will need to be considered. Currently, this means that the university is contributing its own resources to programme overheads in addition to the match funding of projects.

The timing of the application process was also seen as too short. It was felt that six weeks was not enough time to complete the application, particularly since this is required every 18 months, and in light of the submission deadline coinciding with that for another MRC programme; there were synergies from completing both applications together, but the time allocated for completing both at the same time was seen as inadequate. Moreover, a lack of direct communication with fund managers caused further delays while forwarding the message on.

The university also described a lack of clarity over what level and format of information they were expected to provide in the application, and felt that time had been spent ineffectively by collecting and supplying potentially

unnecessary information, e.g. vignettes. It was therefore suggested that the application form should be more structured or that more detailed guidance should be provided. In particular, they felt that it would have been helpful to clarify whether the judging panel make use of the progress report section of the application. It was further suggested that the requirement for submitting application forms could be scrapped altogether, following the example of other institutional funding streams where grants are allocated by an algorithm based on various measures.

In terms of monitoring, the university would welcome suggestions for specific KPIs or measures of success to use in the progress report and for on-going monitoring of projects. They felt that using ResearchFish in addition to writing progress reports represented a duplication of effort, and would prefer a single reporting process.

Case study 4: CiC grant recipient

Summary
This is a case study of a university with particular strengths in Pharmacy, biomedical sciences and chemistry which has a long track record of drug discovery. However, it has not previously benefitted from a large MRC portfolio compared to other HEIs. The institution received Confidence-in-Concept (CiC) funding for two years. The CiC funding was delivered along with a number of knowledge exchange activities that predated this programme. A distinctive characteristic of the university's application forms for CiC funding was the inclusion of a clear description of the types and number of activities that were proposed to be undertaken with the targets of how many projects would be funded and reports of progress to full BMC:DPFS or equivalent applications.

Programme description and rationale
The CiC programme's focus has changed slightly over the two years of operation. There is an internal working group led by the research and knowledge exchange manager who decided on the programme focus. In the first year, the funding was predominantly focused on drug discovery and encompassed only the institute of Pharmacy and biomedical sciences which has three research group areas:

- New Medicines
- Better Medicines
- Better Use of Medicines

In the second year of funding the programme extended its focus to diagnostics and involved the institution's department of pure and applied chemistry and in the third application reverted to a narrower focus to repurposing compounds for which translational potential had already been demonstrated, but for new disease indications.

The rationale for this move was based on internal discussions between the head of department and an external industry panel associated with the university. The focus for a third round was also discussed prior to submission with the MRC but did not receive high assessment from the CiC panel members. In the third year of the application the panel criticised the level of clinical expertise at the institution and the balance between the level of funding for scientific work and the institutional base supporting it.

CiC funding was also used to improve the institution's discovery projects by providing a framework for support and mentoring by senior industry decision-makers and venture capitalists. In practice this meant that a series of two-day residential workshops were organised, including one-on-one meetings between the academics and VC/industry and a two-stage selection process to encourage researchers to ask key translational questions of their projects before embarking on the drug discovery process. The main rationale behind this approach was to embed this question-asking behaviour at the institution and result in a culture change. The CiC funding was seen as a rare and invaluable support for this kind of activities and the feedback from participating academics was that they found it very worthwhile. The workshops were the university's main contribution along with the time from external participants.

Funding issues and motivation for applying
The applicant felt that the CiC is a rare kind of programme and is well aligned with the university's focus on drug discovery. They also felt that it addressed the specific need that the university's research team were facing. Full applications for the likes of BMC:DPFS require the team to come forward with existing pilot data which are not easy to produce. The CiC was therefore crucial for filling this gap.

The applicant felt that there are no alternative sources of funding for such initiatives. This is especially true for universities that do not have large internal research funding resources. The external company panel (detailed above) already contributes employee time and would not be willing to fund academic projects which might or might not result in a full BMC:DPFS application. Other research councils such as the BBSRC do not fund drug development. The scheme was seen as unique in its focus and was found to be of a very high importance.

Progress on projects

The programme manager saw the first two years of funding to be very successful in not only increasing collaboration and networking between academics and the industry but also in converting ideas into full BMC:DPFS and other applications. Typically after the workshop the programme would receive about 20 applications out of which it would choose to fund best four through the CiC programme.

The first year of funding resulted in four projects in drug discovery area and the second term resulted in two drug discovery and two projects in diagnostics. There were no medical device projects as they have their own source of funding at the university via an ERDF grant.

Of the eight projects, six have already had a successful outcome resulting in subsequent funding. One of the individual project holders was a professor of medicinal chemistry who used their CiC grants to produce physio-chemically advanced compounds as a progression from Cancer Research UK-funded work. The professor participated in a CiC project that allowed for discussions and feedback on research ideas from companies with interest in the end-product (such as Merck) and contributed to a steer towards future drug discovery projects. In this specific case, resulting in diversification of use in compounds from the treatment of prostate to haematological and pancreatic cancers. The first CiC generated interesting data and resulted in securing £250k and £200k grants from Prostate Cancer UK and Chronic Lymphocytic Leukemia (CLL Foundation). The second CiC grant resulted in further progress in the diversification of treatment of the new disease area. It was a collaborative research project with another University and produced additional pilot data which directly led to a strong full stage BMC:DPFS application which received £1.5m grant funding from the MRC. Without the CiC funding the study team would not have been able to produce such a strong application backed by the necessary data to evidence the case for a full grant. The BMC:DPFS applications are viewed as a substantial undertaking which cannot be successful without previous research effort into production of pilot / proof of concept data. The CiC funding was instrumental in production of this kind of data and other support such as hiring a new lab worker dedicated to this endeavour. The setup with support from downstream provided a clear thought and plan for how the final product would be marketed.

Each of the project grant holders met up with the programme administrator on monthly basis and presented on progress. Monitoring was based on previously defined milestones and did not limit themselves to technical milestones.

The driving force behind the projects was generally the crucial need for funding backed by a scientific rationale linked to a valid medical need (unmet market and patient benefit). In many cases it would be an ability to identify the need for a crucial experiment or pilot that would enable a strong application to a translational research programme.

The typical history of the projects varied but most of them were based either on an academic's idea that benefitted from discussion with an industrial partner or in the second round of funding from discussions between academics from a number of disciplines (biologists and chemists). These interdepartmental collaborations were new and resulted in sustained relationships.

Wider institutional impact

The institution benefited in establishing a working process for enhancing industry-academia and cross-disciplinary collaborations.

The key wider impact on the institution was that there is an increased focus on translation, not only in the areas of the six research groups of the onsite institute but new innovative medicines and therapies in general. In that sense there was a shift in strategy and a conscious decision towards innovation and knowledge exchange.

Impact of not receiving the award

The components surrounding the CiC were sustained but while the academics get the benefit from the university run workshops and meetings with private company advisors they are subsequently not able to take the new ideas forward.

Process issues

The opportunity to apply for CiC awards were – at least initially – not well promoted, especially amongst universities that were not the 'prime suspects' of the MRC. As MRC funding received by this university prior to 2012 was minimal it belonged to this group of institutions. This university only found out about the grant at the short notice through word of mouth and discussions with one of the universities that has a strong medical school on campus. The communication of new funding opportunities is always a challenge especially to institutions that are not in touch with the funder via active grants.

The main process flaw identified related to the level of feedback given by the CiC panel for the third round which was described as unhelpful and unjustified. There were no clear links with the progress highlighted in the application form with the project portfolio and the criticisms raised. It was the applicant's view that the panel members should refer to the whole application, especially the achievements to date.

Another point that was highlighted was that there are universities without medical schools and on-site clinicians which have a long tradition in drug discovery. These institutions draw on a number of partnering academic organisations on project by project bases in order to work with clinicians, who are integral to every drug discovery project. The perception that a university without a medical school cannot undertake drug discovery projects was by described by the representative of the HEI as "incorrect and disappointing".

The other shortcoming that was highlighted was the inconsistency in the message to the applicant by the MRC and CiC panel. If the MRC representative indicates that the new focus is in line with programme's objectives and then the panel provides negative feedback, the applicant is left confused. There were other inconsistencies in the received feedback. For example, a company which used the university's license was incorrectly described as a university spinout. In such instances applicants would welcome the opportunity to re-submit or respond to the feedback.

On the other hand, the application form was found to be of sufficient length and format, clear and self-explanatory.

Recommendations

The applicant stressed that outcomes and achievements from previous funding should form the basis for receiving subsequent awards. If the information received in support of an application is insufficient, then they felt that the format of the application needs to change to better provide this. They also felt that there was a risk that with the CiC funding allocations might be based on the reputation of institutions as well as performance. Finally, they suggested that there could be a better balance between clinician vs non-clinician positions on the CiC panel as well as representation from across all UK regions.

Case study 5: CiC grant recipient

Summary

This is a case study of a university with one of the largest BMC:DPFS portfolios and strong partnerships with the National Institute for Health Research (NIHR) and NHS. Having already established a department to support translational research and set up a fund for very early-stage projects, they have chosen to use Confidence-in-Concept (CiC) funding to, in effect, expand that fund and support the work of this department by helping projects progress their plans to apply for major funding or form an industrial partnership.

Programme description and rationale

In the first round, the department assigned CiC funding to support drug discovery projects, as the university felt it was "punching below its weight" in small molecule research[38] and wanted CiC to feed into its strategic plans to strengthen this area, alongside internal investment in infrastructure and support for drug discovery. Moreover, drug discovery projects in the major project portfolio were predominantly focused on repurposing existing medicines and other opportunities were considered to have been under-exploited. The department had wanted to put the grant funding directly into a drug discovery group, but had understood from the MRC that CiC funding had to be used in an explicitly project-focused way. While this was disappointing at the time, the flexibility that this gives in the use of the CiC award is recognised.

In the subsequent two rounds, the call for applications was broadened, although small molecule drug discovery projects were still particularly welcomed, as were projects where the funding would underpin the development of a formal industrial partnership. The majority of applications have fulfilled one of these two criteria, although some projects that fulfil neither have been funded.

The CiC funding opportunity is first promoted via the process of assembling vignettes for the application to the MRC; asking for these around the university raises interest and awareness in the programme. Following this, applications are solicited in a number of ways: on the intranet, in a variety of newsletters, on Twitter, and via a mass email, followed up by emails to department heads and Vice-deans of research and enterprise. The team working with BMC:DPFS applications also signposts projects to the CiC scheme if they are not yet ready for BMC:DPFS funding, and keeps a close oversight on the projects to grow them to the point at which they are able to make an application.

The department was clear that, for them, the purpose of CiC funding is to unlock specific, clearly articulated problems or hurdles preventing a promising project from progressing. It is essential that CiC projects demonstrate a clear path to the next funding step – for example, that they have drafted an application to Wellcome Trust or BMC:DPFS but need more data to resolve a particular question before this can be submitted. Other criteria by which applications are judged are novelty, feasibility, commercial potential and clinical need.

There is a two-stage application process. Expressions of Interest are scored on a number of criteria by members of the panel, ranked, and discussed at a panel review meeting. Around one third of projects are then invited to the full application stage, which requires more detail and financial costing – the department described this as a "cut-down BMC:DPFS application". These are reviewed again and around one-third are subsequently funded. While the application process is competitive, the department encouraged applicants to ask for advice and guidance in order to draw out the best bids.

[38] This was in comparison to relative institutional strengths in cell/gene therapy, biologics, and devices.

Funding issues and motivation for applying

The university had established a department to promote translational research in biomedicine in 2010, with the aim of moving early-stage research projects along the development pathway. The funding group within this department works with a range of translational funding schemes from early-stage funding to proof of concept and clinical trials.

Having identified a gap between research funding and the larger grants available through the BMC:DPFS scheme, the department established a fund to fill this gap, which is used to support five or six projects per year. The fund aims to progress projects to the stage at which they are ready to attract funds from major funders or form a partnership with industry, and is made up of contributions from nearby Biomedical Research Centres, the Wellcome Trust's ISSF and other sources. The experience of managing this fund allowed the department to demonstrate their ability to manage a devolved fund and develop a portfolio of BMC:DPFS projects. This helped the department make a strong case to the MRC for CiC funding.

The two funds now run in parallel and have some overlap, although the existing fund is focused on supporting project initiation while the CiC funding is used to support established projects; specifically, to overcome obstacles preventing them from progressing to the next stage. The department had considered merging the funds, but decided that each had a particular remit and that it was valuable to keep the CiC separate. Principal Investigators (PIs) are not allowed to apply to both funds simultaneously, and the department provides guidance as to which of the funds would be most likely to suit their project. There is also a separate Proof of Concept fund, which is focused on developing and protecting Intellectual Property (IP) for selected projects.

In the past the department had found it challenging to win funding for diagnostics projects. They commented that the MRC panel appeared to be more receptive to projects that answered a research question, and since diagnostic projects tend to be more focused on validation, optimisation and reproducibility they were less likely to be favourably received. The department had recently conducted an audit which had identified a backlog of diagnostic projects which was linked to this issue.

Progress and Wider institutional impact

Together with their existing fund, the CiC award has allowed the university to support 40 to 50 projects across a range of research areas, including devices and diagnostics as well as drug discovery. Many of these have gone on to secure BMC:DPFS, Wellcome Trust or industry funding; drug discovery projects supported by CiC funding have attracted external funding of over £600k, and six of the ten projects supported by the second round of funding have formed partnerships with industry. The department commented that injecting a small amount of money at this stage could create much larger effects later on – citing the example of a recent £30m spin-out which had received some early-stage translational funding in 2010.

The department monitors projects by requiring them to report half-way through the project on progress made against the plans in the original application. The department notes any new funds leveraged or new applications made, as well as assessing whether the original idea is still feasible. If so, feedback is given on how to develop the project beyond the CiC funding; if not, the department works with researchers to establish how they can get back on track or find an alternative means to get around the issue. This approach was seen as preferable to terminating projects, and no projects have been terminated for this reason. The department is considering having face-to-face meetings with successful awardees as well as a written report, but as yet this has not been instituted.

One project had failed to progress beyond the CiC stage, but this has been a decision made by the researchers based on the results obtained. The department commented that they worked with researchers to make them more comfortable with the nature of translational funding and understand that although some projects may not turn out

to be exploitable in a clinical setting, this does not in itself represent a failure of the project, nor of its underlying science.

The department remarked that this opportunity is highly valued by clinical and academic researchers, since there are few other opportunities for early-stage and proof-of-concept funding. They suggested that less than half of the projects would have received this seed funding in the absence of CiC, with a resulting knock-on effect on the department's BMC:DPFS portfolio.

Process issues

The application process was praised as straightforward, although the applicants objected somewhat to the requirement to write something distinctive each year, and welcomed a suggestion that future application forms would put more emphasis on past performance.

The feedback on applications was considered to be at around the right level of detail, although it was felt to contain some factual inaccuracies due to misinterpretation of the application. Attention is paid to the feedback and where relevant, adjustments have been made to the operation of the scheme – though due to previous experience with running a similar type of scheme, these changes were minor. Monitoring was seen as light-touch and largely consisting of the report submitted at the end of the funding process.

The department has absorbed the additional costs of triage and administration that accompanied the devolved nature of this award, and had appointed a research manager to administer the grant and support and supervise the awardees. Following this appointment, systems and resources have been created which are likely to streamline the grant administration process going forward. However, it had been difficult to persuade the university to invest in this role due to the uncertainty each year as to whether the CiC grant would be secured. The department suggested that a three-year rolling award, subject to annual reporting, would make it easier to create such support mechanisms, and reduce some of the administrative burden of applying.

The university commented that the 18-month timeline was also shorter than ideal from a project related perspective. While they had no desire to fund individual projects for longer than 12 months, the 18-month length of the grant restricted their ability to be imaginative about the application process. In particular, a two-year programme would allow for more collaboration with other CiC recipients (including those at other universities), which was currently precluded by the need to allocate the money in a short timescale.

Completing project data on ResearchFish was seen as burdensome, particularly as no guidance had been supplied on this. In future, the department will set up accounts for PIs to add in details of their own projects.

Example of a project supported by this CiC award

This was a 12-month research project focused on pancreatic cancer, which represents a large unmet clinical need; the current therapy treatments available have not changed the prognosis over the last 40 years. The project takes a novel approach to chemotherapy targeting cancerous genes, and is an outcome of a broader and continuing basic science programme funded by Cancer Research UK and the EU. The project team includes tumour biologists and Pharmacists, and is led by a PI who has been involved in two other therapeutic agents in humans – one of which is now in the clinic, and one in clinical trials.

A key challenge in developing any therapeutic is building a model system which closely relates to the human situation; typically, projects use laboratory animals, but often the results are not significant. The objective of the research funded by the CiC grant was to demonstrate that there was a model with a positive therapeutic outcome, as well as delivering chemistry development.

The PI heard an institution-wide call for applications for CiC funding, and spoke to an expert in the translational research department to confirm their eligibility. This source of funding was appealing since it was sufficient to move the project to the point at which it could progress to more major funding; moreover, the application process was seen as proportionate, with minimal bureaucracy. He had considered alternative options, including a start-up; however timescales would have been different, especially given the multi-national nature of the consortium. Although it is likely the project would have proceeded at some point in the absence of the CiC funding, the CiC grant allowed a more reasonable time-frame for securing funding.

Progress on the project was described as entirely satisfactory; all milestones were achieved and the project went smoothly, although care had to be taken in terms of timescales. All of the funding was spent. A key outcome is that the project has now been able to move on to industrial funding for proof of concept work, since there is now sufficient data to convince industry experts of the value of this approach. Two other collaborations have also been initiated; one patent has been granted, and another is being filed.

The project is now looking at and evaluating the compound in more relevant animal models. Results so far have been promising, and if this continues to be the case then the project will be around two years away from a human clinical trial. This is now a principal focus for the PI's team.

Case study 7: Successful academic applicant

Summary

This is a case study of an academic led project with the main objective of developing a novel human antibody (with cross-reactivity to rat for development purposes) that targets a protein found at increased levels within the diseased blood vessels of patients with a specific type of cardiovascular disease resulting in high blood pressure within the lungs i.e. pulmonary arterial hypertension (PAH). The project entails the team identifying a candidate antibody and then demonstrating therapeutic efficacy in pre-clinical rat models.

BMC:DPFS was seen by the applicant and the collaborator as a unique source of funding with a translational focus unlike any other Medical Research Council grants. There was a view that there is a sustained need for this funding source. The industrial partner complemented the breadth of support for development stages across the developmental pathway and welcomed the collaborative partnership with the academic body.

Project description and rationale

The project is organised under three main objectives/phases which feed into each other in a sequential manner:

Objective/Phase 1 - Identify candidate antibodies for pre-clinical models of the disease. This phase involves performing in vitro functional phenotype assays in primary human and rat vascular cells. Secondary screens were planned to assess their ability to inhibit protein induced migration in these cells. There was a target of five antibodies (balance of cost/time efficiency) that display an array of secondary effects on different types of protein binding. These targets were going to be fully humanised, re-assessed through the functional assays and then progressed to in vivo models described in Phase 2.

Objective/Phase 2 – In this stage the project was to determine whether the antibodies can prevent the progression of the disease in two pre-clinical rat models. An initial pharmacokinetics (PK) study was going to be performed by the industrial partner to determine the dosing regimen for each antibody in rats. The initial in vivo screen was to identify antibodies that can recapitulate the 'protected disease phenotype' in a specific type of rat model that the study team have previously observed with commercial rabbit polyclonal antibodies. Successful antibodies were then to be tested in the newer, a second rat model to identify a lead candidate antibody.

Objective/Phase 3 – This stage was to determine whether the lead candidate antibody can reverse severe disease in the newer rat model. A lead and backup antibody was set to be tested for its ability to reverse an established 'disease phenotype'. The problem that the project is addressing is a severe cardiovascular disease which has an urgent need for the development of new therapies. PAH occurs when specific arteries narrow due to constriction and cell growth causing an increase in pressure which over time causes heart failure. As a consequence the disease carries a high level of suffering and carries a median expected survival of five-six years from diagnosis. Current drug treatments carry an annual cost per patient of between £5,000 - £300,000, and target only the sustained constriction of the blood vessel constriction and do nothing to slow or halt the cell growth. Subsequently these current drugs do not cure this condition.

The proposed treatment would be suitable for all patients suffering from the PAH, addressing a $3bn global market. This includes idiopathic, heritable and associated forms of the disease (e.g. connective tissue disease, congenital heart disease, portal hypertension etc.). There is not one single figure on the numbers of these patients

in the literature and two forms of the disease are often interchanged. The estimated target population of patients (US, EU & Japan) in 2013 was between 10,052 to 25,443 patients. According to the 2012 NHS, there were 3,000 patients on targeted therapies in the UK. Currently there is no curative treatment available for these patients other than lung transplantation.

The project is setup to address this need by means of developing a therapeutic antibody. The TRL level at the time of application was at level 3 and initially was set up to pass the toxicology tests (TRL 4) but the industrial partner reduced it. This was driven by the reduced need of antibodies. Much of new drug discoveries are incremental innovation rather than blockbuster drugs such as statins (for lowering cholesterol)

Previous work undertaken by the project team has demonstrated that two related proteins are highly expressed in human disease. Data from multiple pre-clinical rodent models has demonstrated that both proteins are critical for the development of the disease in these models. Further preparatory work before the project indicated that targeting one of the proteins (the one subject of this application) was associated with the disease and normalised right heart pressures in rodent models.

The research department of the PI has a history of undertaking research studying the disease (e.g. British Heart Foundation and Medical Research Council grants). Through MRC Confidence-in-Concept (CiC) funding the study team initiated the development of these antibodies, and established the screening platform required for the project. The study team filed two application of patents, one each covering antibodies to the two proteins. These patents were owned by a university spin-out company and had a global reach. Success of the department is heavily driven by improving patient benefits and performing research resulting in saving lives. The group is a true translational research department with strong links to industry and the NHS (being based in a hospital). The department strives at becoming the global centre of excellence for treatment of this disease. The PI held an enterprise fellowship award from the Regional Development Agency which resulted in always being open to new opportunities. However, ownership of IP at the end and spinning out the company was not the main driver for application.

To progress towards the clinical translation, the PI has met with a number of potential industrial partners and MRCT (an independent life sciences medical research charity) and considered pursuing this stage of development by spinning out and purchasing antibodies from a contract research organisation however forming collaboration and pursuing public funding was considered the most optimal option.

As a result of a commercial decision during the application development the PI had to make a choice to target one of the two proteins, this resulted in pursuing the one which was more promising route (higher likelihood of success). This decision was mainly instigated by the need for a substantial amount of antibodies and increased risk of pursuing what are essentially two competing solutions. In addition, the collaborating industrial partner had this specific protein already on their radar.

The motivation of the industrial partner to take part in the project was to extend the portfolio of targets that are addressed with their antibodies and collaborating with an expert in the field and use of pre-clinical animal models. It was presented as an opportunity but the company would not be able to fund a project of this scale on their own. The industrial partner values the collaboration and MICA framework did not cause any barrier to collaboration or the ability to retain IP. There are options open still for funding clinical proof of concept, partnership model and setting up an entity or licensing out to a third party.

Project consortium

This is a collaborative project led by a PI who previously held an MRC Career Development Award and now holds a British Heart Foundation Senior Research Fellowship and has strong translational links through the affiliated hospital. The Fellowships held by the PI focuses on defining cellular and molecular interactions of the protein in the disease affected cells. The PI is predominantly engaged in research and has minimal teaching and administrative responsibilities due to holding these fellowships. The PI leads a team of nine researchers of whom the majority are based in the same location at the hospital.

The industrial partner collaborating through the MICA is a company which has developed a powerful technology to discover and develop therapeutic monoclonal antibodies. They are leaders in the field with a capability of rapidly generating an exceptionally broad diversity and quality of fully human antibodies against challenging disease targets. The precision engineering platform generates very high affinity, candidate-quality molecules without the need for further lead optimisation. The role of the industrial partner went beyond supply of high quality antibodies as it contributed with antibody-related expertise relevant for the screening processes. This industrial partner has a substantial funding from charitable sources such as the Wellcome Trust.

Prior to submitting application to the Biomedical Catalyst, the PI approached the industrial partner and pitched the project to their board of directors after becoming aware of them based on contact with Syncona Partners, an independent subsidiary of the Wellcome Trust.

Funding issues / Motivation for applying

On an individual level, the motivation was to remain in control of the development of the idea that originated in the research team.

It was the PI's perception that big Pharma would not provide investment unless there is a validated target with quality antibodies. The project team came to the conclusion that applying to the BMC:DPFS was the most appropriate route for funding as it provides non-diluted funding for translational research and provided good framework for collaboration with a leading provider for antibodies, necessary for the success of the project. The project team had a good understanding of market needs. MICA framework in combination with the university ownership of the two patents, one for each protein, provided a certain level of protection from the industrial partner and the ability to negotiate higher rights to the output IP, should the project succeed scientifically. One shortcoming of MICA is that it cannot be only setup for a part of the project.

The main motivation was to secure the finance for this stage of development and by that de-risk the project and make it attractive to progress down the development pathway, however even the industrial partner will most probably not be able to take the drug to the market. Scientific risk of this project is not as high as there is no novel development in methodology – the tests are repeating what has been done by the team previously but now with clinical grade antibodies. The risk is that the success will not be replicable.

Alternatives such as the MRCT and Wellcome Trust funding were considered however they are more suitable for pursuing the project fully via a spin-off company and using a specialised contract research organisation (CRO) for antibodies. Shortcomings of the MRCT were that they preferred the second choice target from historical reasons, and their aggressive IP strategy which would result in loss of equity. Also the industrial partner joined via the Biomedical Catalyst had a superior platform for the necessary tests (i.e. proprietary antibody technology). The subject of the project was initially prepared as a topic for the MRC senior fellowship scheme but due to high competition the application for this seven-year grant was unsuccessful. The motivation of the industrial partner to pursue this project is to broaden the range of targets addressed by their antibodies with additional in vivo modelling, however, the proposed project was too early on its development pathway to attract internal industrial

resourcing (financial and human resources). The industrial partner has own internal research funding programme but this is for more advanced development stage projects and will consider applying to the full Biomedical Catalyst programme of the Innovate UK for its core research work.

Another alternative to pursue the project would be via a spin-off company with Horizon 2020 funding but that would require searching for international partners and SMEs to fit the eligibility profile.

Progress (Interim outcomes)

The project is progressing on schedule and all milestones have been met as anticipated. Milestones two and three will now be pursued in parallel as there is no need to find another candidate antibody (there is one candidate and one backup). Therefore there was no need to wait three months to proceed and as a result the project might finish this stage three months early. The big experiment takes place in milestone four in the late summer. This will only be with the one candidate antibody but controlling for more factors and running regressions.

The final outcome efficacy will be as good as it gets and the relevant publication will be viewed greatly by the industry.

The final outcome of the project, if the experiments show what they are intending to (screening finished), will be to for the university team to license the IP to the industrial partner. This can be done either via the spin-off company owning the initial patents or via university owned patents. There is a possibility that the IP will be transferred back from the spin-off company to the University as part of the central decisions relating to the IP commercialisation company.

Following the project there will be need to undertake full safety and toxicology tests which could be pursued by another BMC:DPFS grant. Then phase one and two clinical trials will be undertaken.

Neither the industrial partner nor the university have the capability or facility to take a drug to the market without big Pharma. The industrial partner owns the IP on the platform and the university on the antibody.

The PI could have published the results from the pre-Biomedical Catalyst grant but it would mean that once this project is finished and the results will be based on much more robust gold standard methodology and antibodies, the research would not be considered novel. Therefore, the choice was made to refrain from early publishing and publishing in a high impact journal, with approved efficacy. The fact that the PI holds two fellowships keeps pressure off from having a need to publish papers every year.

Impacts on the organisation from the project (if project has been taken forwards at all)

The impact of this award rests in the increased ability to pursue translational research with 'high impact' potential, build up the capabilities and facilities to undertake large scale experiments with antibodies. The impact on forming collaborations and attending events is lower as the PI was involved in such activities already.

The collaboration with the industrial partner nevertheless resulted in knowledge sharing and the team learnt much about applying methods. In the long run it will result in high impact publication in a respected journal which would not be possible to achieve without the confirmed efficacy of the drug.

An additional MRC badge is good for boosting reputation and is welcome by both the PI and the collaborator. DPFS is also a good badge in these circles.

The project meant that the research team could retain staff and involve them in translational research project with state of the art equipment and methods contributing to building a centre of excellence in treatment of the disease. One new member of staff was hired. There will however exist a new challenge post award to keep the researchers busy and find grants to support them. The project allowed the whole team to get hands-on experience with antibodies.

Wider effects

The project will result in new IP owned by the university spin-off company. If the project fails to find the antibody with the necessary characteristics, it will disprove the hypothesis and will be a successful research project nevertheless. It will mean that the research team will have the ability to undertake high throughput studies with improved experimental processes and gold standard data production, equivalent to those of the leading Swiss research institutes. As a result the next experiment would become much more efficient to perform. The PI visited the Swiss colleagues prior to submitting the application to see the bespoke equipment that allows them to undertake these types of experiments in the required timeframes. They are still in a two-way dialogue with them and continue to share best practices.

The PI also learned to build in padding time into the experiments which means that the project is delivering on schedule and the monthly catch-ups contribute to it.

Impacts from being rejected as an applicant

If the project was rejected, the PI would pursue the MRCT/Wellcome trust route but it would have to sign up to the loss of equity.

Process issues – Communication

The MRC have communicated the BMC DPFS scheme broadly to universities and anyone in translational research knows of it. It is easy to find information about the DPFS rounds if someone is looking for it. The Innovate UK side and the connection within the two could be communicated better.

The industrial partner admitted that the awareness of opportunities within the BMC was low and that being involved as a collaborator was a win-win for the academic and them. The academic gains experience and an opportunity to work with best antibodies to validate their target and the industrial collaborator has an additional target validated using their antibodies.

Process issues – Application

The application form is less administratively extensive than other research council applications and similarity of preparing for the senior fellowship grant meant that much of the documents could be adapted.

The research team had support from their respective technology transfer office (TTO) and the application form benefited from a review by the industrial partner. The application form has gone through five to six pairs of eyes before submitting.

The PI saw value in going through the process of drafting the application as it identifies whether going ahead with the project is worthwhile. Some questions were seen as very valuable for this reason. The focus on market need is unique and beneficial. Some academics who are less close to industry or don't engage with it will struggle with the application.

Workshop for applicants after the outline stage can be beneficial for less experienced applicants but can be considered unnecessarily long and common sense for those who have been applying for similar grants in the past.

Process issues – Assessment and Review Process

The feedback from assessors was quite typical of this kind of competition and it was evident that the MRC attempted to find good fit assessments. Some of them were however too academic and focused on technical details of the application. This is especially true as the methods were well established (not novel). One of the assessors was from industry and did not understand the models applied. All comments were relatively easy to address.

The MAC interview was seen as a good test of the team and knowledge and there would be benefit for everyone to go through it. It is easier to hide a bad project behind the paper forms. People on the panel were viewed of high quality. Wellcome Trust has a similar process.

MICA framework did not cause any barrier to collaboration or the ability to retain IP.

Process issues – Recommendations

The project has a monthly reporting and quarterly reporting procedure which results in unnecessary administrative burdens despite having a dedicated project manager at university level (looking after a number of projects). Considering that this is a short two year project there is a need to have frequent monitoring meetings but they could be a compromise of every two months and not every one month and quarterly.

The quarterly meetings are face-to-face either in Cambridge or at the university and the programme manager from the MRC has the necessary level of understanding of science to be able to make the decisions.

The MRC was flexible in allowing the project team to progress with one of the stages earlier than anticipated which was seen as beneficial from the project team.

Case study 8: Successful academic applicant

Summary

This is a case study of a successful academic application in which the Principal Investigator (PI) is working with previously generated IP on a molecule that inhibits the effects of a hormone. The project had no external collaboration with firms or universities. The PI has had previous experience with translational research and has managed to patent a large number of their discoveries. One of these previous discoveries forms an integral part of the current project. Manufacturing of molecules for the project has been outsourced to a contracting manufacturing organisation (CMO) outside of the UK.

Project description and rationale

The project that is being funded as part of the Biomedical Catalyst aims to further the development of a hormone treatment for a rare growth condition. Presently the condition is poorly treated and is not effective. The condition leads to many other health issues and generally results in premature death. The PI is working on a hormone that combats excessive secretion of growth hormones in people suffering from this condition (Acromegaly). The initial discovery of the hormone resulted from the study of a family that had retarded growth. The PI identified and isolated the over-production of the hormone responsible for the problem for this family.

The IP on this hormone has been held by a University spinout owned by University commercial partner for a significant amount of time. The Biomedical Catalyst funding had allowed the PI to return to the discovery and progress the work further.

The work undertaken as part of the programme was set out in three work packages;

1. To evaluate the plausibility of four candidate versions of the molecule for future production; checking for toxicology, stability and efficacy of production. All candidates would need to be produced in volumes and purified for full testing.

2. Develop and improve on the manufacturing of the best candidate from the first stage of molecule testing. This stage includes the agreement on toxicology standards for regulators.

3. The final stage was to be phase I ready (ie. generation of full toxicology and chemistry information from tests on animal subjects - both rabbits and rats).

This final stage, once complete will allow for progress to phase I trials..

The therapy itself is there to address the 40 per cent of patients with the condition that do not respond to current methods of treatment, as well as reduce the cost of treatment, and reduce the side effects for those who receive the standard medications. Presently there are some 2,500 patients in the UK; it is believed that the condition is underdiagnosed. The secondary treatment for sufferers is not considered cost effective by NICE.

Funding issues / Motivation for applying

The PI advised that the Biomedical Catalyst was, in their view, the sole source of funding to progress the idea in the present climate. Of the other options that may have been plausible, such as the Wellcome Trust for example, they felt that their project idea would not have been well received by other funding opportunities based on the

type of risk that was involved in his work. It was their opinion would not have been funded. Without this funding his work in this area would not have gone ahead.

The PI had a great deal of experience in the field of translational research and approached Biomedical Catalyst without attempting to secure funding elsewhere. A further motivation for their application was that the project was perceived as too early phase for securing interest of a private investor.

Progress (Interim outcomes)

The feedback given to the applicant by the BMC:DPFS panel was that the science was of a high standard and that the panel believed there was a high chance of success. However due to the exploratory and early stage of the research it was plausible that none of the four candidate molecules would be acceptable to progress on to the second and third stage of his proposed plan.

Despite this real risk the project has been progressing well. The PI had completed the first stage of research and had selected a candidate molecule to evaluate in the second work package.

One of the important characteristics for the applicant was the support that they had received from the MRC for project management activities. As a result they were able to delegate most of the reporting activities and admin to the support and get on with the science.

Wider effects

Given the experience of the PI, it appeared that some of the benefits that might have been felt by a new entrant to translational research were not being accrued here. The PI was very happy with the process and positive about the work of the programme, more generally. They felt that the coverage of funding was important and had facilitated new activities in the field of life sciences to occur.

It is important to note that the manufacturing of the molecules for testing was however occurring outside of the UK. This was a necessary step taken by the PI to find the skills required to complete the work.

Process issues

Of most concern to the PI was the application process which was seen to have been unnecessarily complicated due to duplication of the application form in Joint Electronic Submissions (Je-S). Their view was that the forms could be easily integrated so that repeat work could be avoided. Aside from this issue, the applicant was satisfied with the experience, especially the pragmatic approach that allowed changes to the timetable.

Case study 9: Successful academic applicant

Summary

This is a case study of an academic led project with the objective of further developing a drug to support the treatment of heart attack patients. The project team intend to focus on the pilot-scale development of the compound before moving into increasingly sophisticated animal models.

The project is expected to commence in May 2015 and funding from the Biomedical Catalyst was seen by the applicant as key for bringing the project forward at scale. The applicants were highly positive about the application process overall, but suggested that offering clearer guidance about how much ambition a project should have or benchmarks for how much ground it should expect to cover would have helped them to improve their initial outline submission.

Project description and rationale

This project will focus on the further development of a drug which has the potential to reduce the negative effects associated with heart attacks. The drug may help to increase survival rates of heart attack patients. It also has scope to have an additional long-term beneficial effect. By reducing tissue damage caused during heart attacks the drug can reduce the likelihood of complications and other heart diseases emerging in subsequent years. This can have both a survival and a quality of life impact.

In commercial terms the project has the potential to support the introduction of a drug into a wholly new area of treatment associated with heart attacks and as such has no competing therapies. The scale of this market was identified in the application as including hundreds of thousands of suitable heart attack patients each year (61,000 in England and 250,000 in the USA). The costs of producing the drug are expected to be in the range of $1-4 per patient.

The project originates from the development of a suite of compounds on which the team have been collaborating for several years. The project had previously received support through a core MRC unit grant which supported the principal investigator, and a (£230k) grant from the British Heart Foundation held by a UK project partner. The collaborator from New Zealand has also sourced and secured external funding.

The delivery of the project will involve the pilot-scale synthesis of the drug followed by a series of tests of its efficacy on a series of increasingly sophisticated animal models; first mice and then pig studies. The primary risks identified by the team are the difficulty of scaling up the production of the compound behind the drug and the challenges inherent when scaling animal models from small to large animals.

Project consortium

The project is led by an experienced academic who has previously taken a drug through to Phase II trials in humans. The lead applicant is based within an MRC unit which is viewed by the applicant as a leading place for both basic research and translational research focusing on heart attacks. Project partners include:

- A biochemist
- A clinician who is also a clinical Pharmacologist

- A UK university research facility for animal models
- A contract research organisation (CRO) in New Zealand

The team came together previously to develop the project to this point and the CRO together with the principal investigators unit own the background IP for the work. This has created a strong incentive for collaboration amongst the team. During the application process the team identified the UK research facility for the animal models as they believed this was a good way to respond to the comments received on their application and would help to secure its approval.

Funding issues / Motivation for applying

The applicants felt that the current position of the project made it very difficult to secure funding through any other route because of what they see as a key strategic gap within the funding landscape for translational research commonly termed the 'valley of death'. The project was seen as too far from market and too risky to be able to secure private sector funding. It was seen as an expensive translational research project involving multiple levels of animal models, each of which could present new risks to the ongoing development of the drug.

Had the applicants not been successful in securing Biomedical Catalyst funding they believe their next approach would have been to bundle the IP behind this project together with a broader range of assets to form a spin-out company. One member of the consortia believed that this could have had the potential to bring in private funding. But, perhaps reflecting the uncertainty of this approach, another applicant felt that this project was at too early a stage for this to have been successful in securing any form of private funding. They agreed however, that despite the potential for rushing the scientific development, this approach would definitely have been slower to put in place. They also identified a risk that once funding was in place they would have faced much greater pressures to develop their drug more quickly if privately funded. They feared that this could have reduced the quality of their work and had negative implications for patient welfare.

At the same time as being too early to secure private funding, the applicants felt that it was not sufficiently novel from a scientific perspective to secure further public research funding. They suggested that toxicology, dosing and passing MHRA are very expensive but "tedious science". The DPFS was identified as unique in providing funding through the "valley of tedious work".

The applicants also identified particular features of the Biomedical Catalyst funding which made it of particular appeal:

- Non-diluting helped – The IP behind the project has already been filed, and is owned jointly. Requiring an ownership stake would have complicated this.
- The large size of the award was important – They believe that this will enable them to offer a yes or no answer about the potential of the drug. Securing a string of smaller grants (such as further funding from the British Heart Foundation) would have resulted in a stop-start project that could have taken much longer and they believe it would have been more difficult to reach a definitive conclusion.

Progress (Interim outcomes)

The project is due to commence in May 2015 so no progress had yet been made at the point at which the study team contacted the applicant. The lead applicant had also not developed the project during the application process, choosing instead to focus on other compounds.

Impacts on the beneficiary

Even at this early point there appear to be some benefits arising from the project to the applicant. Success in securing funding was perceived positively within the principal investigator's institution. Securing funding for this work helped to confirm that this area of investigation is important and worth the team investing their time here.

Wider effects

The project draws on existing IP which is protected with a patent. The novelty of the IP revolves around the specific mechanism used by the molecule used in the potential drug, as well as the new molecule itself. If successful the project would increase the value of this patent. The applicant anticipates that should the project be successful they would be in a position to exit from the work by selling the IP on to a large Pharmaceutical firm at the end of the funding period.

The ultimate market effects of any new drugs created from the project could be very significant. The drugs would generate new sales in an area where there are no existing therapeutic interventions. They would therefore not displace any existing activity at the point of use. However, by supporting improved recovery pathways from heart attacks, the drug will reduce the likelihood that patients develop long term heart conditions as a consequence of their initial heart attacks. In this sense this drug could therefore displace the use of other therapies.

The project is also expected to have a key capacity impact on one of the applicants. The project is expected to enhance their capacity to deliver a particular type of animal models in pigs. This is something which is only currently available in a very small number of sites across Europe. It will be the first project of its kind in the UK and therefore has scope to strengthen the UKs infrastructure for biomedical research.

Process issues – Communication

The applicants were unable to pinpoint who they had heard about the scheme from, but were sure it was through word of mouth. One of the applicants is based within an MRC unit where they knew it had been marketed. The applicants felt that there is a high level of awareness and colleagues generally saw it as a widely known route for advancing translational research.

They did however suggest that the specific requirements of the programme could have been better communicated prior to their outline application. They felt that they had misunderstood what a 'good' Biomedical Catalyst project would look like in terms of scope and ambition. They saw this as the main reason why their initial outline application was rejected.

Process issues – Application

The applicants were content with the application process. They had no particular issues with the application forms and were particularly positive about the briefing event (which was described as 'brilliant' at setting out exactly what was needed for a good full application). They also stressed the importance of an outline stage to the application process as this saved wasted effort preparing a full bid – something they would like to see replicated in other competitions such as Horizon 2020 funding.

Process issues – Assessment and Review Process

The applicant found the appraisal process to be slow. Having received feedback on their initial outline submission and resubmitting they will have experienced a significant break between application and the start of the project. The project has been largely on hold during this time. They felt that receiving some preliminary feedback on their submission earlier on in the process would have been very useful.

The peer review feedback was seen as highly constructive and useful for the ongoing development of the project. The feedback on their rejected initial outline application was felt to be exceptionally clear. This was described as stating that "we want you to reapply" (as well as waiving the 12 month resubmission rule). Often in the applicant's experience phrases such as 'could be improved by …' are used which offer far greater room for ambiguity and potential misinterpretation of what the panel thought of the submission.

Feedback received from the committee stage review of the bid was viewed less favourably. There was a sense that the panel had focused in on a few very detailed points of the application which were all the applicants view issues that could have been resolved either at contracting or during the delivery of the study.

Process issues – Monitoring

The project had not commenced at the point of interview. However, there was concern that there had been an extended period of discussions with the MRC to agree milestones. For example, work was required to justify the specific use of any future animal tests, even though these tests may not occur in this form, or at all. The results of initial project research will determine the scale and nature of future testing requirements, making it difficult to specify this in the level of detailed required by the MRC at the outset of the project. This was something which the applicant felt could have been better handled flexibly through the course of the research.

Process issues – Recommendations

The applicants did not identify any specific recommendations for the development of the programme.

Case study 10: Unsuccessful academic applicant

Summary

This is a case study of an academic led project application which did not receive funding as a result of concerns about the appropriateness and deliverability of the plan, the likely clinical impact, and the likely competition. The project's main objective was to progress a development path of a more effective coagulant without the risk of bleeding.

Project description and rationale

The proposed project was organised under three main objectives/phases which feed into each other in a sequential manner:

1) Successful conclusion of a manufacturing process to produce a batch of the drug for toxicology and stability studies.

2) Successful conclusion of single dose toxicology studies in rat and dog.

3) Successful conclusion of repeat dose toxicology studies in rat and dog and submission of a regulatory dossier for permission to conduct Phase I clinical trials.

The BMC:DPFS panel agreed with the description of a strong medical need in treating a blood clot in one of the deep veins in the body as a common cause of mortality. The proposal detailed how anticoagulants are employed to treat thrombosis and their deficiency in the high risk of bleeding. The referenced studies stated that there is a high incidence of 1-3% of major bleeding (of which 1 in 8 people will die) and a small bleeding risk of 15-18% which is of particular concern during and after surgery when the risk of bleeding has to be balanced against the need to stop the blood clotting. This therefore indicates that there is a considerable market for the drug. The project team have developed a novel medicine that is able to stop the blood clotting inappropriately with minimal risk of bleeding, unlike any other drug of this kind available. Their therapy was described as being far superior to the main drugs used to prevent blood from clotting. The proposed project was aimed at taking the drug through the development programme to the point at which approval to conduct a clinical trial would be sought. The described likely eventual clinical use would be in hip/knee replacement surgery, a common pathway taken for the clinical development of new anticoagulants.

The project was set to progress the therapeutic from TRL level 2 (Scientific review and generation of research ideas, hypotheses, and experimental designs) to TRL level 5 (Safety and toxicity established to GLP-standards (in animal models) and manufacturing process established at the required scale).

The history of the project was that a research project undertaken by the collaborator resulted in the lead applicant testing and coagulation expertise. The initial tests indicated exciting reductions in bleeding effects. The background IP was held by the zoology department at the partnering academic organisation but the PI secured IP for dosage and escalation of dosage in the data. The origin of the project relates to a similar project developing a small molecule for same application.

Project consortium

The project consortium was led by a professor of Cardiovascular and diabetes research at a research institution with a focus on basic and applied research. This institution focuses on helping to explain the aetiology and pathogenesis of common chronic diseases, thus contributing to alleviating morbidity and mortality. The specific research group focuses on researching discovery of novel therapeutics against thrombosis taken orally with safer bleeding profiles than other antibiotics.

The project consortium consisted of a zoology department at one HEI and a department for cardiovascular sciences at another academic institution. The second academic partner would only have taken a minimal role in the project and was involved mainly due to resourcing constraints.

There was an industrial partner for the application, a global company that holds custom-designed facilities, and focuses on development of clinical candidate into an optimum formulation, and manufacture drug product for all phases of clinical trial supply (Phase 0 – Phase IV). Their main role was provision of peptides and expertise in regulation and progressing the therapeutic downstream.

Funding issues / Motivation for applying

This project was seen by the applicant as well aligned with the programme objectives as it has strong translational focus. The characteristic of Biomedical Catalyst funding of allowing collaboration was seen as particularly positive. At the end of the project the applicant would be well positioned for collaboration with big Pharma.

The main motivation for the application, in addition to the above, was to deepen expertise in the subject area. Other characteristics that were highly attractive are that the programme provides a unique broad translational focus non-dilutive funding. Full economic costing was another beneficial feature of this instrument. An interesting point of view was that this funding allows for the academic not to rush and spin out prematurely and allow the academics to focus on translational research when the focus is required the most.

The proposal was a result of a close collaboration with the technology transfer office but the PI attends relevant conferences which allow for networking with large companies involved in drug development.

Alternative sources of funding such as Wellcome Trust funding and venture capital (VC) were thought to not fund a project of this kind unless the progress specified in this project was made. Internal funding was inappropriate due to the size of the undertaking and seed funding would require establishment of a spinout company. The team was on the verge of creating a spinout but the director of commercialisation decided that the university-wide policy gives preference to this kind of project resulting in a license agreement.

Impacts from being rejected as an applicant

The effect of being rejected was initial disappointment with the decision. The result is that this endeavour has not progressed in the UK. The South-East Asian part of the industrial partner was successful in receiving National Medical Research Council oversees funding for initial development but not on the full pre-clinical package. The project in South East Asia will only develop further the methodology and set up animal models.

The PI has submitted applications to the Health Innovation Challenge Fund and National Institute for Health Research and is awaiting the results of these. But without substantial funding the project will not go ahead.

The research group has BHF funding and funding from another BMC:DPFS project which resulted in filing a patent in small molecule and are in discussions with a large Pharma company. Therefore the rejection did not affect the research group's translational research. What was affected is the pursuit of a peptide with the same characteristics which would have a different application (intravenous after surgery).

There was a knock-on effect from the rejection of the grant on the Oxford based industrial partner whose patents are expiring.

Progress

The project's future progress is up in the air, and will depend on new funding opportunities being successfully pursued. The two academic applicants are in discussions about approaching the British Heart Foundation (BHF) for funding of up to 250k which would result in the project progressing but with a reduced size. The main barrier to reducing the cost of the project is the expense of producing peptides for testing.

Wider effects

The key effects that were expected from participation in this project were to have a post doctoral academic gain experience in vivo, working on an unmet clinical need with a direct patient benefit and MHRA assessment. The main exit route set out in the application would have been to license the IP from the research to a large Pharmaceutical company. The market for this type of drug is substantial.

Process issues – Communication

The academic side of the Biomedical Catalyst programme is easy to find if someone is looking for funding. The PI found out about this opportunity via a colleague involved in translation and from colleagues who work with the CiC programme at the university.

There are opportunities to better present the programme at the institution through channels such as visits organised by the BBSRC. These visits could be organised through the department, through the university based Pharmaceutical and BioPharmaceutical innovation hub or directly through the dean. The presentation could include stratified medicine and diagnostics.

Process issues – Application

The design of the application form was viewed by the applicant as inviting them to pitch the right level of detail. It was seen as having many components which are common to the Medical Research Council (MRC) standard grants but asks more specific questions about the route to market. These additional questions and other documents such as the annexes were viewed as lengthy but required to enable a rigorous assessment.

Process issues – Assessment and Review Process

The applicant felt that the application process would benefit from the inclusion of a panel interview. The interviewee felt that they should also have had the option to respond to panel comments. The PI would consider re-submitting their application if is it was possible to respond to the panel after the decision. The applicant noted that, for example, the BHF conducts a panel interview and gives the applicant a list of negative comments which can be remedied in response. The applicant felt that interviews were a more robust way to review an application as the paper form does not allow for explanation of some questions that the panel members might have when reading it.

Some of the appraisers were seen to provide constructive feedback. The response from the panel was not found to be useful and in some cases the panel were seen as not demonstrating a good understanding of the science presented. On the other hand the time taken from application to notification of a decision was seen as adequate and appropriate by the applicant.

When a relevant question is received in a panel discussion (such as for example to include a clinician in the team), the PI is willing to improve the bid. The BMC:DPFS process was not seen to give enough opportunity for this.

Case study 12: Successful SME applicant

Summary

This case study relates to a successful application to the Innovate UK Late Stage programme. The grant was awarded to part fund a Phase II clinical trial for a treatment for a common skin disorder in a specific subset of the population while targeting the 'itch' component. The trial was unsuccessful, with the key benefit to the applicant being the operational learning from conducting the study.

Project description and rationale

Biomedical Catalyst funding was sought to deliver a Phase IIb clinical trial for a new treatment for a chronic skin disorder. The treatment opportunity relates to the development of a new compound using the applicant's platform technology which underpins several other compounds also under development at the company.

The skin condition affects both children and adults. It can have a high impact on quality of life among children in particular due to its association with sleep disturbances and psycho-social issues. The prevalence of the disease is high; among children in the UK and Australia it is experienced by one in five, and by almost half in Japan.

Current treatments are available, but these have significant safety issues and are not suitable for long-term use, presenting particular issues among children. The proposed new treatment potentially had many advantages over existing options. If successful, it would be able to treat all the symptoms of the skin condition, including the 'itch' component which particularly impacts on quality of life. It was anticipated that it would be possible to use the treatment on a long-term basis because of its safety profile.

Because of the clear advantages of the new treatment over current treatments, it was anticipated that there would be high potential to rapidly gain market share. The estimate provided on application of peak sales of $500m globally was described as "conservative" by the applicant.

Prior to application, successful Phase II trials had already been run exploring the efficacy of the drug for treating the 'itch' component for a related disease state to the application. As part of the drug development process for that treatment, the applicant's scientific board deliberated upon the potential of using the treatment for different disease states and among a younger population. These exploratory discussions identified a chronic skin disorder as another candidate disease to be treated by this drug. The hope was that this would be particularly beneficial since this new application focused on a younger population where issues of 'itch' can be more significant. Because of the success of these previous trials for the closely related disease state, a high probability of success was expected.

Project consortium

The applicant is a small late-stage European biotech company which is funded mainly by venture capital. As a biotech company they are, in the applicant's words, "quite old", having been founded in 2003 and received their first round of funding in 2008. UK operations started in 2011 and the applicant's head office and development functions are now based in the UK.

As the applicant is a clinical stage biotech company with previous experience of conducting trials, there were no formal project partners.

Funding issues / Motivation for applying

The key driver for applying to the Biomedical Catalyst was financial. It provided the applicant with another funding stream, in addition to their investors, which could finance a large proportion of the cost of the study:

"To be blunt, the benefits of the Biomedical Catalyst for a company in the phase that it is in is allowing another funding stream to help us through what the ex-CEO of this company used to call 'the valley of death', to allow us to do the science to hopefully get us to the next inflection point with data that will allow us to have other discussions with investors or partners".

The applicant tried to persuade current investors to fund the project but they were not willing to provide the full amount required. The applicant did not want to go to new investors "because you end up diluting yourself".

The possibility of getting a large proportion of the study funded by the grant gave them the opportunity to go back to their current investors to request additional funds:

"The very fact that we could get 60 per cent of this study funded gave us great potential to go back to our current investors, who have been with us since 2008, and actually say we need to do this study, it has great potential, we can fund it 60 percent, you guys have only have to put in 40 per cent of the total cost. That was enough to sway them to fund us. If it had been 100 percent, they wouldn't have done it".

In terms of the delivery of the study, there was no particular benefit sought or derived from getting funding from the Biomedical Catalyst rather than anyone else. This is because the applicant is already very experienced in conducting late stage research which is their core business.

Progress

The project has been completed and the Phase IIb trial completed and data analysed. The treatment performed no better than a placebo in targeting the 'itch' component of the skin condition. It started at TRL 7 and stayed at that level. Had the trial been successful, it would have then had "accelerated" the applicant into Phase III trials. Given the size of the population suffering from the skin disorder, it would have been an attractive candidate for Phase 3 trials.

Impacts on the organisation from the project

The main positive impact from the project was operational learning. The study team successfully responded to challenges around recruiting a paediatric population and finding the right sites to conduct the research. This puts them "in very, very good stead should we want to rapidly run another study in [skin condition]".

There were no articles or papers produced because the trial had not been successful. It was stressed that Biotech companies do not tend to invest resources in publishing results of unsuccessful trials for reasons of disclosure of confidential information and reputational impact of having conducted a failed trial. The project was fairly late stage, and there was therefore less of a need for academic liaison and interest.

The main benefits for staff were that the project helped them develop contacts at the research sites. Given the applicant's previous experience of conducting clinical trials, they did not develop new skills.

There was a positive reputational impact to receiving the grant, although it was not seen to be unique to this particular funding.

"It's a good news story and the very fact that we announced that we were embarking on a large Phase IIb proof of concept study raises awareness of the company, gets other partners potentially interested. It creates that kind of vibrancy that we need being a biotech company to keep people's interest up. That's the positive but it's not unique".

Wider effects

The "vast majority" of the funding received was spent in the UK, both within the applicant and their sub-contractors. The only area where funding was spent outside the UK was to procure a small number of specialist procedures in relation to manufacturing the treatment. These are not available in the UK.

If the project had been successful, the applicant would have progressed to partnership discussions with Pharmaceutical companies to conduct Phase III trials and file the drug. Other options under consideration were another round of fundraising or a trade sale.

From a scientific perspective, the negative results from the trial have forced the applicant to go back to basics and consider why this was the case. It has helped them refine their thinking about the compound and the likely disease states that have an itch component that it can treat. They are going to file looking purely at the disease state treated in the successful clinical trials. They are also going to try to find other populations with the same underlying mechanisms.

The applicant reported that they will "almost certainly" be exploring the potential of treating the skin condition targeted in this project using another compound they have developed. This may offer opportunities to make use of the organisational learning detailed above.

Impacts from being rejected as an applicant

If the application had been rejected, the applicant would have considered running a smaller study just looking at adults.

Being able to run the study among a paediatric population was seen as a big advantage both because of the high unmet medical need among children suffering from the skin condition and because the applicant had not researched this population before. The funds also enabled the applicant to run a larger study in terms of patient numbers and dose.

Process issues – communication, application, assessment and review process

The for application form template was not particularly user friendly and did not facilitate what the applicant described as a "massive cycle of edits and corrections" because it was not possible to edit it in tracked changes. In the end they had to print the different drafts off and get people to edit it in red pen on a printed copy.

Other than the issues with the template, the applicant could not identify any other barriers or problems in relation to the application process. The guidance documents were seen as clear and provided expected level of detail. The level of rigour around the sections which had to be filled in in the application form was described as "useful in terms of helping the applicant explain its case".

The applicant thought there was certain level of repetitiveness around some of the sections and that some of the depth required was "a bit of an overkill". However the applicant also felt it was important that the application had to justify itself.

The assessment and review process was regarded as a very positive experience. The written feedback from the initial application was seen to be "pretty rapid" and "very helpful" as it identified which areas the applicant needed to work on in the next round. The face-to-face review was described as "highly professional" and the reviewers as "a very impressive body". The feedback received here was very useful in helping them apply for another grant.

Process issues – monitoring

The monitoring was seen to be a good experience and the applicant did not find it particularly burdensome and described it as "pretty light touch". The applicant thought that this was because the project ran smoothly and on time.

The presence of an external individual as a monitoring officer was seen to be helpful "to keep you on track and focused and conduct yourself in a way that you realise you have to present back to others".

One issue for the applicant was that the funding could only be claimed once work had been done, leading to a six week wait between the money being spent and paid back. This created cash flow problems which were mitigated by firm's private finance but resulted in careful monitoring of costs. If the grant had been for 100 percent, the applicant was not sure how they would have financed the start of the project – "we would have been in a Catch 22".

Two positives mentioned by the applicant were that the grant is paid on time and there is no issue once it has been agreed.

Case study 13: Successful SME applicant

Summary

This case study relates to a successful application to the Innovate UK Early Stage programme. Funding has been used to support the development of a diagnostic tool which it is expected will support the development of clinical trials in the area of dementia research.

Project description and rationale

The overall aim of the project is to develop an improved diagnostic tool to strengthen the way that patients, with memory problems and dementia are diagnosed. The product aims to bring together different types of information to provide a tool which can be used by a non-specialist. The project drew on the company's own IP developed from running Pharmaceutical trials. Project funding was allocated to develop an initial prototype and to test it in a healthcare setting. Through machine learning processes this testing will also help to support the ongoing development of the product.

The applicant believes that existing approaches are inadequate. Current techniques offer diagnosis too late for many therapies to be of use. The poor quality of diagnosis is also holding back medical research in the area as it complicated clinical trials. Existing diagnosis systems are also heavily stretched in the UK. Wait lists for NHS memory clinics (a primary current route to diagnosis) are typically in excess of six months.

They feel that this device can tap into a global dementia diagnosis market that they forecast will exceed £1bn. They estimate that 700,000 people in the UK and 36 million worldwide have dementia, a figure likely to double in 20 years. The early detection of dementia will allow for more appropriate interventions which have the scope to delay the onset of the disease. This was associated by the applicants with cost savings of £8,000 per patient. The increasing political priority given to dementia diagnosis from Cameron, Sarkozy and Obama has given them the confidence to focus here.

The company felt that they could not privately fund such a significant R&D investment. This activity represented a significant departure from the company's core business model (the delivery of clinical trials on a fee basis). The board had expressed reluctance to diversify their business in this way unless the grant could be secured. Other institutional investors approached also were not willing to invest without some de-risked business plan because this project represented a considerably leap from the markets where they were previously operating.

At the point of application one of the investors wanted to exit the company, without this diversification strategy the applicant feared that the whole business could have been sold to a US firm. The company also felt that since the product could deliver a significant cost saving to the NHS there was a strong case for public support.

Project consortium

The lead applicant was a contract research organisation predominantly focused on running clinical trials for large Pharmaceutical firms. They are an SME employing approximately 50 employees (growth from 35 at the point of the grant award). While the majority of these are focused on fee earning work, others are supported by a number of Innovation UK grants as well as a European grant.

When preparing the application, the lead applicant felt that they had the core technological component for the new device but did not have the technical capacity to convert this into a medical device, experience using it in a

hospital environment, or knowledge of how to sell such a product to the NHS. So to deliver the project they are working with a specialist provider of cognitive assessment software. They have also partnered with two academic organisations in order to gain access to clinical environments (something they find difficult as a private company). These academic collaborations had been maintained for a number of years, but the project has offered the opportunity for the company to work with these individuals in a new and more closely linked way. From their experience they felt that the Biomedical Catalyst worked well to support collaboration.

Progress

The applicant felt that progress on the project has been mixed. They feel they have been able to set up a strong team which is now gathering momentum. The product is developing and starting to generated interesting results. For example, they appear able to predict from cognitive data if a person is at a low or high risk of rapid progression in their condition.

However, the clinical trials component of the work has proved very difficult to set up. In particular they have found the NHS and individual GP surgeries very difficult to work with. The company spent nine months pursuing one route to clinical trials that proved unsuccessful and now believe that this component of the project is approximately 12 months behind.

The applicant felt that the TRL scale fitted well with the development of the diagnosis product and machine, but was not full applicable for the digital health development process. Against the TRL scale the applicant felt that their project had been characterised by elements of three, four, and five at the point of application. They feel it now demonstrates elements of TRL levels 6, 7 and 8.

Changes in the management of their partner company have also held back the project. The priorities of this organisation have changed, and they now have much less interest in advancing this project. This has resulted in the lead applicant taking on more of the work of the project than originally anticipated.

Finally the team felt that the market for their device had evolved differently to what was anticipated at the point of application. In their view, the diagnosis model is changing. Clinicians have less interest in abstract diagnosis than before, but are now looking for more integrated solutions which link the diagnosis to a treatment pathway. The applicant has found that offering details on diagnosis was not sufficient, but that they were required to offer insight into the pathway, “The diagnosis of the patient and the post diagnosis of the patient support should be linked, there should be a pathway”. This resulted in them adapting the project; they started looking into the diagnosis and the post- diagnosis, rather than focusing primarily on the diagnostic event; “The product that now needs to be commercialised is a pathway technology, rather than a diagnostic technology alone”. This has complicated the development of the product.

Impacts on the organisation from the project

The project was identified as having a major impact on the recipient company. They felt that the funding had given the company the confidence to be ambitious. The applicant felt that the Biomedical Catalyst project gave the company the ability to be ambitious, and looked impressive to investors, “Investors don’t want to be spending all their money on R&D, but strengthening the management and commercialisation”.

It supported a change in their business model from that of a contract research company towards a more diversified research and development company. Their board perceived the grant, and similar funding, as a “key validation step for their whole business strategy of diversifying into the clinical practise market, not just clinical trial market”.

The pursuit of this strategy has enabled them to sell their clinical trials business to a US company which raised funding to allow the exit of one investor, and helped to establish a full R&D department within their company. The Biomedical Catalyst project supported formation of new relationships and collaborations with partnering companies. It enabled them to have more strategic conversations with Pharmaceutical companies about these partnerships.

Furthermore, the Biomedical Catalyst funding allowed them to invest in longer term projects. "We couldn't previously invest in something that was six to 12 months away from revenue, let alone something that was three to four years away from revenue, which was the focus of this project".

Receipt of the Biomedical Catalyst award enabled them to become credible for other key funding sources. It allowed them to have a longer term view about how they could get the business to grow and develop into a broader brain health company powered by digital technologies.

Process issues – communication, application, assessment and review process

The applicant was generally content with the application process. The application form was seen as highly business centric and well designed for companies to use. The questions were seen as sensible. And they felt that the application followed a reasonable approach of requiring only limited details for the submission, to be supported by further information if the application is successful; "This means the work you have to do is appropriate for where you are in the stage".

Process issues – monitoring

The applicant was highly satisfied with monitoring arrangements. They described the monitoring officer as being one of the best they've worked with, detailing that they were: very pragmatic, engages well , understands the need - for companies like them - to collaborate with the NHS and academic centres. They felt that the monitoring officer understood SME's very well and their logic and that the officer had a very good understanding of their project and was able to engage with them and make recommendation on how they should be managing risk. This enabled the officer to engage with the company in a constructive way. When the project faced challenges, the officer had made recommendations and offered help based on what Innovate UK would have wanted to see, and helped to explain what was needed to reassure the funder that the company had any risks under control.

Recommendations

The applicant had no specific recommendations for the development of Biomedical Catalyst funding, but instead suggested an alternative route through which Innovate UK could support the impact of the initiative on the sector. They believed that setting up a networking group for mid-level staff would be beneficial. While they see many good networking opportunities for senior staff members, they felt that there needs to be something put in place for people below that level. Their fear is that when senior staff meet they may be too commercially focused, and avoid discussing the detail of what they are working on. Instead they would like to see something that is available for technologists and individuals who are actually involved with advancing research to meet to share ideas and learn from each other.

Case study 14: Successful SME applicant

Summary

This case study relates to a successful application to the Innovate UK Feasibility Study programme. The grant was required to explore the feasibility of a platform for developing new antigen products for use in vaccine research. The project has moved from pre-proof of concept to a prototype stage, and the applicant has just filed for a patent. The applicant hopes to reach TRL 8 within 6-8 months. Without grant funding, the project would have proceeded at a much slower pace, more as a hobby than a well-defined development programme.

Project description and rationale

The project focused on the feasibility of an alternative platform for developing new antigen products. The behaviour of antigens in vaccine research can cause delays in vaccine development, as well as failures at clinical trial. If the technology is demonstrated to be feasible, it would shorten the discovery phase to produce successful vaccines for viruses and reduce manufacturing costs.

The target for the feasibility study was a particular human antigen for an infection. This area represents one of the highest healthcare burdens because of a lack of a suitable vaccine (US healthcare costs associated with this infection have been estimated at around $4 billion).

The project relates to the company's core business (manufacturing antigens). It was the brainchild of the applicant's lead development scientist and chief scientific officer who wanted to find a way to present antigens in research which would enhance their performance.

"It was the germ of an idea that developed internally. They did a little bit of work to try and asses the viability of the project but then it needed to be driven much harder with additional resource which we weren't able to provide without the grant application".

Project consortium

The applicant manufactures infectious disease antigens and toxins for use by the in-vitro diagnostic and Pharmaceutical industries. The company has been trading since 2010, with the business financed by two successful investment funds (a seed fund, business angels and senior management). It started making profit in 2012.

Funding issues / Motivation for applying

The Biomedical Catalyst was the first port of call because of the scale of the funding involved. The applicant tried to match the stage of the project with the funding available. The main driver of applying to the Biomedical Catalyst was in particular financial:

"We wouldn't have been able to do this work in the timescale without the grant".

The grant enabled the applicant to explore the feasibility of the new platform at a much earlier stage than would have been possible and to analyse several approaches simultaneously to increase the chances of success.

Progress

Overall the project has helped to advance an idea for new antigen products towards a clinical treatment. Before the grant was awarded, the project was at TRL 2, a "pre-proof of concept idea". It is currently at TRL 5. The technology has been developed to a stage where the applicant knows that it works with one specific type of molecule and one specific type of antigen:

"We have gone slightly beyond proof of concept, in general terms we are probably at the prototype stage. We know it's doable but there may be limitations to how many types of molecule we can use this technology with".

The applicant hopes to reach TRL 8 within 6-12 months. The requirement is to demonstrate that the technology is working effectively and that will be done internally. The applicant is also trying to establish how wide the applicability of the technology is:

"What we're trying to understand now is what are the limitations of the platform that we have developed because that will impact significantly on how large a market opportunity there is for this potential project".

Work undertaken since the grant has been funded through shareholder investment. The plan is to continue to fund it within the business for now but this is a challenge and the applicant will be considering further grant funding.

The applicant has a very clear commercialisation path. Once they have been able to demonstrate that the technology is working effectively, they will start seeking partners for very specific applications as well as selling defined products which are an advance on what they are already selling. The aim is to create new product generations from the technology and to enter into collaborative licensing deals.

The applicant flagged that the project overcame significant obstacles. Scientifically, there were "enormous problems" in making the technology work and it has proved to be very difficult. However these challenges were anticipated: "if it was easy, everybody would have done it". However, the project was delivered on time and the end goal has remained the same.

Impacts on the organisation from the project

The applicant was very positive about the impact of the grant on the company:

> *"This grant has been incredibly beneficial to [company] and in terms of its award and then its implementation, it's been very successful".*

The applicant has not yet published anything relating to the project but hopes to do so once its IP has been protected.

The grant has enabled the applicant to support extra staff. Because it has been a very challenging and scientifically complex study, it has made individual roles more challenging and interesting than they would have been. This has enabled the applicant to "keep a certain level of resource on board – some of our more routine work wouldn't have been terribly appealing".

Wider effects

The project has generated new IP for the applicant and they filed for a patent a fortnight ago. The applicant is confident that this will be granted.

In terms of an exit strategy, the applicant is planning a trade sale. The timescale of this is yet to be determined as it depends on how long it will take "to get the broader business to a scale where it is of value to someone else". This will not be less than three years.

The applicant felt that there would be some displacement that will arise from the technology. However it is "quite ground breaking" and should meet some "well-defined needs" of life sciences research by helping to make antigens which are more immunogenic. It could have a significant impact on the ability to produce vaccines for emerging pathogens. For instance the technology could assist with a number of tropical diseases which are difficult to raise a vaccine against.

Impacts from being rejected as an applicant

If the grant had not been awarded, the project would have continued but at a much slower pace:

"We might have scrabbled around a little bit, it would have carried on but it would have been more of a hobby than a determined push and a well-defined development …it would have taken us a lot longer to get to a point where we would be thinking about commercialising it".

Process issues – communication, application, assessment and review process

The applicant did not specify any issues with relation to communication, application, assessment and review process.

Process issues – monitoring

The monitoring process has been straightforward. However a more consultative monitoring officer, who could ask more "searching questions", would have been more beneficial. This would require monitoring officers to have life sciences background, ideally in a relevant field.

Case study 15: Successful SME applicant

Summary

This case study relates to a successful application to the Innovate UK Early Stage programme. The grant was awarded to part fund a project developing a demonstrator of a new type of heart pump. At the time of the interview the project was coming to a successful end.

Project description and rationale

The project funding a demonstrator of a new type of heart pump that is not only better with respect to its unit cost and size, but also outperforms the current market leaders in terms of the impact on blood cells and proteins.

The work packages that have been conducted to achieve this were:

- Development of a whole suite of novel blood assays (investigative procedures/tests) to test the impact of pumps on blood tissue from various sources (in vivio)
- Develop and refine the initial pump design
- Build a working prototype that could be implanted in a human

The medical need for a lower cost pump is clear from the application and the high levels of usage of these sorts of pumps in modern medicine. Additionally, the company had identified that the impact of pumps of this sort had an adverse effect on blood chemistry and cellular structures.

The project first developed due to the academic relationship that the chief technical officer (CTO) of the company had with his colleagues who had pioneered the original pump. They believed they could develop a better idea and decided to form the company – the CTO described it as a 'spin in' rather than a 'spin out' of the university because these three colleagues were in a private company with weak links to the university but the project strengthened these working relationships The early stages of the development have been funded in part by other Innovate UK schemes to develop the idea with computational modelling of the pump. Additionally the company have received several different grants from the Welsh Government.

When preparing to move the project onto the next stage, the key risks identified were the scientific ones – that they were heading to new ground and so fundamentally the science not working (with respect to the new tests they were developing) would render their ideas worthless.

- It was necessary to perfect the antibodies, biomarker and machine effectiveness
- The pump design went through several iterations
- Perfecting the collection of data so that comparisons could be made with those pumps currently on the market.

Project consortium

The consortium was led by an SME. This firm was set up as a former academic (CTO) with two colleagues with links to a strong technical research university came together to develop their idea of creating a new and more effective heart pump for humans.

At the beginning, the CTO, realised that the current stock of pumps on the market was out of date and could be significantly improved upon. Initially with his background in engineering his plans were to simply improve on the size and cost of producing pumps, but as his ideas developed there was a realisation that the current pumps were also performing badly with respect to the damage they were causing to blood cells and proteins in the blood while working.

Currently the company is still in the 'micro' category, consisting of 5 staff. During the project the university have made available 1.5 FTE to assist with testing and other scientific/lab based activity.

The project was initially planned to have two other partners, receiving scientific support from university and an RTO. After the initial application it was decided instead that the RTO would instead be used as a commissioned subcontractor, performing the necessary assays to specification of the project consortia.

The firm is based at the university campus and as part of the partnership they are able to make use of the facilities and skills of their academic partners. As engineers there were some gaps in their own abilities to demonstrate the improvements in performance of their pumps in comparison to the current market so the university provided some of those skills.

The relationship with the academic partner has been a long one and the principal investigator (PI) at the unit had been identified previously to work on developing the assays. The PI had a personal desire to do much more work in translational research, and advised the SME that the university itself had a strong culture of working with industry to develop ideas with business. The university itself was founded on these industry and academic collaborations and as such have always maintained this desire for collaboration. PI noted that there has been a strong push for business-academia collaboration since the early 2000s.

Funding issues / Motivation for applying

The Biomedical Catalyst was an immense help to the firm in securing the necessary funding they required to progress their project into the valley of death. The project lead stated that they felt that they were making some headway with securing funding from the venture capital (VC) community but decided that initially there was not sufficient level of support available and that the larger VC players would hold back generally until a project had passed the riskiest stages before they would commit to funding ideas. This meant that the project team had a reduced pool of possible funders to make use of.

The academic partner stated that the main motivation was to do more work particularly in translational research and to gain further experience in working within TSB/Innovate UK funded projects (had previously worked on TSB grants). Furthermore the PI was personally motivated to see the impact of the work in practice first-hand rather than be isolated in the lab.

The ability to attract academic support to the project through offering 100% funding to academic partners make the Biomedical Catalyst immensely helpful for the SME.

Progress

The project began work a little under two years ago and as such is coming to the end of its period of funding. To date, apart from the expected difficulties in creating wholly new assays, the project has been 100% successful and is progressing to completion very well. The data that has been generated on the improvements realised by their pump has allowed them to begin raising funding for the next rounds of development, gaining agreement to begin full human trials. The consortium has been able to generate a lot of interest (including large VC) in their project due to the solid data.

While there have been some challenges with making the pump and assays work, the project has successfully resulted in a whole new store of knowledge. Project team has generated new IP with respect to the pump mechanism, and has also anchored a new understanding of blood chemistry and how it is impacted by medical devices. The CTO felt that this had resulted in a whole new field of expertise in the UK and could help bring further innovation to the region in the future.

It should be noted that the project has received additional funding for some bespoke work on the bearings that were used in the pump.

The academic partner felt that funding had been mindful of the specific challenges around work in this field of science and that it gave them space and time to sort out their challenges without excessive pressure.

There is an expectation that the company will produce the pumps in the UK once the project reaches full production stage.

Impacts on the organisation from the project

The Biomedical Catalyst resulted in the ability of the SME to attract highly specialised academic partner to the consortium through offering 100% funding to academic partners. This was seen as a particularly helpful in combination with benefiting from going through the application process. Going through the application process allows the applicant to have an extra level of scrutiny on the partnering academics. The process eliminates a risk when partnering with academics first time as they may not be as good as they suggest, or they may offer poor service when they are finally working on the project (slow to respond/complete tasks etc.).

Fundamentally, the money allowed the SME to secure their private funding more easily. They were also able increase the scope of their work with the larger amounts of money (giving them time to disseminate and publicise their work through publications and attendance of conferences – which has been of high importance).

The Biomedical Catalyst was well known in the biotech sector and so it was very helpful to be able to tell funders that they had been successful with the application – they used this as a selling point to raise their profile too.

The flexibility of funding has made a difference, too. The SME was able to make some adjustments to their financial plan throughout the project with minimal impact.

During the project the SME secured additional help from university staff. Now the project is coming to a successful end these academics were offered permanent contracts (in addition to 3 new staff).

The academic partner felt that funding had been more mindful of the specific challenges around work in this field of science. They felt that the programme overall gave them space and time to sort out their challenges without excessive pressure. Furthermore the academic partner cemented the relationship with the SME which resulted in

strong collaboration which benefits the SME, university staff and PhD students. Additionally the university has agreed to complete a Knowledge Transfer Partnership with the SME (supported by Innovate UK).

The PI felt that their own personal skills in dealing with the complexities of finance had improved – allowing to pre-empt issues with university level sign off.

"It had been a valuable learning process with regards to running translational projects"
Finally, the PI gained awareness of the differing focus of industry.

Impacts from being rejected as an applicant

The SME may have been able to secure enough funding to progress the project without the Biomedical Catalyst, but it would result in a reduced scope for the project – essentially making the task tougher and giving them less money to work with.

The CTO stated that the success of the Biomedical Catalyst application was critical to their progress.

Process issues – communication, application, assessment and review process

The SME representative advised that the communications about the programme were clear and the Biomedical Catalyst programme was well known in the biotech sector. The lead applicant receives regular bulletins from the KTN and Innovate UK

Process issues – application

The university partners provided a lot of input to the application itself but did not attend any selection panels. The consortium found the process relatively easy, although as usual there were time challenges toward the end. PI felt that the earlier collaborations between the SME and the university team made the joint application easier. They worked on the EOI and main stage applications together so this was helpful in both stages.

Process issues – assessment and review process

The applicant felt that success was a lot to do with working out what assessors wanted rather than having a good/detailed submission. In their words "the application feels like a game". EOI stage was to some degree more difficult due to very little space to set out the detail that was required to do the project justice.

The applicant also felt that there was not sufficient scrutiny of the assessors. Details provided on the market size referred to data from the lead firm in the market (so it was factually correct) but the assessors disregarded them as incorrect. Lead applicant challenged this comment with the lead technologist. The reason behind these shortcomings in the assessment appeared to stem from time constraints under which the assessors worked. "It was clear that the assessors didn't have enough time to make assessments of the projects correctly".

Process issues – assessment and review process

The rest of the process was seen as satisfactory despite slight delays at time when asking for adjustments to the project plan. Biomedical Catalyst's financial reporting was found to be straightforward and easy to use.

Case study 16: Successful SME applicant

Summary

This case study relates to a successful application to the Innovate UK Late Stage programme. The grant was awarded to part fund a three year project to develop an orthopaedic implant to treat osteoarthritis and damage in a particular joint of the body. The applicant is about a third of the way through the project, and an advanced prototype has been developed. The key benefits of obtaining grant funding to the applicant to date have been the capacity to attract equity finance, accelerate product development and hire more staff.

Project description and rationale

Biomedical Catalyst funding was sought for a project which is, in the applicant's words, "fairly ambitious" with eight different work packages encompassing design and development, manufacturing upscale, preclinical trials and a clinical stage. A health economic assessment will also be conducted. The project is due to last for three years in total.

This project involves the development of a novel, proprietary orthopaedic implant. It is designed to treat osteoarthritis and damage in a particular joint of the body. There are an estimated 46 million people in the US and EU who suffer from osteoarthritis in this joint. It is a leading cause of work disability, with an economic impact estimated in the billions.

The main treatment option currently available involves total replacement of the joint. The procedure is expensive, costing the NHS £1bn annually, partly because it involves physiotherapy and a long recovery period. There are also high complication rates. The replacements wear out within 5-15 years and surgeons are therefore usually reluctant to fit them in people under 60. As osteoarthritis can develop as early as the thirties, this results in a large patient population living with a disabling condition for many years.

Other forms of treatment are regenerative strategies, but these are historically expensive and are not appropriate for joints with osteoarthritis. Scaffold products are more cost effective but are not recommended in joints with osteoarthritis. The absence of effective treatments means that currently less than 20% of patients with a particular form of damage in this joint are being treated.

The implant is expected to be both mechanically functional and regenerative. It can be inserted with a minimally invasive surgical procedure. Clinical interviews conducted by the applicant have identified a clear clinical need for a device with these attributes.

"There's a huge clinical problem and surgeons really don't have many options. …..You've got a functional implant but also an implant which is supplemented by regenerated tissue over time. And that we hope will address [xxx] damage which others have so far failed to do".

The procedure will be suitable for patients of all ages and will involve shorter operating theatre time and patient rehabilitation periods compared to current replacement treatment.

The project has its roots in the work of two scientists at a university local to the applicant. Their research focused on a naturally occurring material and how to manipulate it to obtain the toughest materials possible. A spin off company was set up in 2002 to exploit this knowledge. The CEO of this company and co-invented and developed a material which emulates both the functional and molecular properties of specific human cells. This technology

was developed through a series of Innovate UK and Wellcome Trust awards. The applicant holds the patents for this process technology.

The applicant is in parallel developing another orthopaedic implant using the same material. This is further progressed and at the clinical stage. This uses the same material and concept, but from a surgical and engineering perspective "it's quite different".

Project consortium

The applicant is a pre-revenue med-tech SME which was founded in 2008. It has been granted exclusive licenses to exploit the technology developed at the predecessor company.

The applicant firm currently employs 10 staff, and expects to grow and develop into a manufacturing company over the next clinical period.

The applicant decided to apply for the award as a single entity and then subcontract:

"Fixing your partners at the beginning of the project is extremely difficult because relationships change over the course of the three year period and you aren't necessarily going to be able to identify your clinical partners before you've got a product to show them to interest them with"..

All the sub-contractors up until the pre-clinical stage are in place. In terms of the clinical stage, the applicant is now in the process of forming relationships as a prototype product is ready to demonstrate to surgeons its functionality.

Funding issues / Motivation for applying

There were two main drivers behind the decision to apply to the Biomedical Catalyst; the quantum of funding available and the "light-touch bureaucracy" associated with Innovate UK.

The quantum of the funding is an advantage because there is no need to stop the project to raise more funding:

"It does make a significant difference when you are mapping out the path of a product like ours which is a long-to-market ambitious development that having enough funding and not having to stop the project half way through and go out and fundraise again is a major attraction".

The applicant spoke positively about the lack of bureaucracy associated with Innovate UK awards compared to other funding available:

"The second thing is the light-touch bureaucracy associated with TSB, now Innovate UK, applications. You could go to the EU for funding of that quantum but the process, from having done it before myself, it is very much longer to get the project off the ground and much more bureaucratic and clunky, with a huge number of more rules regulations and reporting requirements than are set in place for Innovate UK projects"..

Equity finance was not seen to be an option because "is very hard to raise in our sector" despite the fact that there is "a huge clinical opportunity and therefore a huge market opportunity".

The applicant attributed this to two factors. Firstly, there have been "a huge number" of companies who have failed in their efforts to develop products, so many investors have had "their fingers burnt".. Secondly, it is difficult for pre-clinical companies to raise finance because products are long to market which can be a problem because

funds only have a limited lifetime. At the clinical stage, it becomes much easier to benchmark what the return on investment is.

The funding from the Biomedical Catalyst has been matched by a Wellcome award.

Progress

The applicant has developed an advanced prototype and they are now at TRL 3, having obtained "good preliminary data" from the animal trials. The project has been running for just over a year (of a proposed three year project period).

They are a little behind schedule – it has slipped by a quarter – because there have been technical challenges in making the implant:

"The technical challenges have been very significant but we've overcome the majority of them and we are well on the way to having a clinical stage product"..

There are likely to be some more humps ahead: "it is rare that a clinical trial takes place in the shortest time allowed".. Recruitment may take longer than planned, particularly as the regulatory environment for research is becoming more challenging.

The scope of the project has remained "exactly the same" as per application.

Impacts on the organisation from the project

The applicant identified three key benefits of being awarded the grant; the capacity to attract equity finance, to accelerate product development and to hire more staff.

The applicant is currently seeking equity funding for the next stage of the project. They have found that "Biomedical Catalyst has made the equity finance easier to access".

The award has enabled the applicant to hire more staff. It will eventually create 11 full time new posts in total. They have already increased staff levels by four employees.

The award has had a positive reputational impact:

"There is no doubt that the Biomedical Catalyst awards carry quite a lot of kudos. They are still comparatively young, but because of the quantum of the funding they don't go to a lot of people and having one is a big tick in the box certainly. Plus there is a recognition that the award has gone to the Major Awards Committee and here has been a panel presentation which also lends credibility"..

Both the quantum and the reputation of the award ("it carries an element of a stamp of approval") have allowed the applicant to engage with "a great deal more" collaborative partners than they would have done, at the academic, clinical and industry levels.

At this stage, they have not had the opportunity to publish or publicise findings. This will happen at the exploitation/dissemination stage of the project.

Wider effects

The applicant expects the project to result in new IP. The IP situation is being kept under review, and the applicant will file "when it becomes commercially sensible" to do so. The timing of this is impossible to predict and may or may not be within the lifetime of the project. It will depend upon whether it is sensible to wait to gather more data or to go ahead and file.

The implants will be manufactured in house, because the applicant believes this will safeguard IP and reduce production costs. Because the implants are made from a naturally occurring material, the production costs are low and it will be possible to sell them at a low price and/or a very attractive margin. The price undercuts most scaffold therapies and is significantly less than regenerative therapies and joint replacements.

The applicant estimates the market opportunity to be in the region of £660m-£1.75bn. The market is likely to grow "sharply" as obesity rates rise and the age of the population increases.

The strongest likelihood at this stage is that is that commercialisation will be with a major orthopaedic partner who will be able to give the applicant access to the global market. This will also enable the applicant's partners to develop the instrumentation required to support the product. They are currently in early stage discussions. The applicant's present thinking is that they will enter into a licensing deal in the latter part of this decade or the early part of next.

The applicant expects that the other orthopaedic implant being developed which is currently at the clinical stage will be on the market by the time this one is launched.

The applicant does not believe that the product will displace existing products on the market:

"We're an unmet need. We're not going to be blasting anything else out of the market…we are very much a product that is meeting a currently unmet clinical need".

Impacts from being rejected as an applicant

If the grant had not been awarded, the applicant would have had to focus on taking the other implant forward:

"This one would have been on the backburner or the shelf. We simply wouldn't have had the finance or resource to get it off the ground".

They may have been able to come back to it later "but it would have been a lot later". Also this would not be guaranteed, because equity finance may not have been happy with diverting money to R&D once they were on the market with the other product.

Process issues – communication, application, assessment and review process

The applicant was aware of the Biomedical Catalyst programme before it launched due to their links with their local Bioscience Network.

The applicant described the Biomedical Catalyst as a "very well publicised funding programme" known throughout the biomedical/life sciences community ("everybody's heard of it").

The applicant was happy with the application process and had not encountered any barriers:

"I think it's been well run, it's been well scoped. There aren't too many hoops to jump through. Broadly speaking, it's not a difficult thing to apply for".

The guidance documentation was described as good. The guidance notes were changed part way through one call, which led to some confusion, but there was flexibility about accepting proposals written to the old guidance. The situation was "handled well".

The applicant form was described as "very well structured", "straightforward" and a "swift" proposal to write. The applicant felt that the written feedback was "good" and "comprehensive".

The applicant especially liked the Major Awards Committee element which is not usually a feature of funding competitions:

"You've got the opportunity to clarify anything in person, so you're not left feeling they don't understand what you're proposing. If you've understood it and don't like it that's fine, at least you've had the opportunity to argue your corner properly".

The applicant also particularly valued the speed of the award:

"One of the strongest things of the Innovate UK awards in general is that they are swift to turn around, and that's the way it should be. The quicker the better".

There were no particular improvements that the applicant would like to be made to the application process: "I'm wary of offering improvements in case something gets taken away".

Process issues – monitoring

The applicant has been "very happy" with the monitoring. They have had several Innovate UK projects so understand how the process works. The applicant commented that every monitoring officer has their own style, but once you have learnt how each other works there are generally no issues.

The applicant mentioned some frustrations with _Connect not being as flexible as it could be, particularly from a financial/forecasting perspective. However this is a minor quibble. Everything is "generally ok" and the applicant appreciates that the wrapping up of each quarter is "turned around quickly".

Overall/other comments

The applicant was very positive about the Biomedical Catalyst programme overall:

"I think it's a very good programme. It's doing a good job of basically getting funding into UK life sciences companies and our experience of it is that it is one of the best programmes out there to date".

The applicant felt that no particular changes were required to the programme and stressed the importance of continuing to fund late stage projects:

"I don't think it is something which should be meddled with too much, it should just be supported…life sciences projects are long time to market and every opportunity should be taken both to continue the Biomedical Catalyst and also to allow it to support late stage near market developments as well as early stage feasibility stuff. You can get things started but it's the keeping them going that is the difficult thing".

The applicant also spoke positively about Innovate UK more generally:

"I am a big supporter of Innovate UK and what they do and I think that they do a good job and I think that the application process and the way in which they administer their projects is excellent".

Case study 17: Successful SME applicant

Summary

This project aimed to develop a diagnostic blood test for Alzheimer's disease. Following a self-funded pilot, Biomedical Catalyst funding has allowed the applicant to achieve this goal and also to extend the range of tests to discriminate between patients diagnosed with Alzheimer's disease, Parkinson's disease or Parkinson's with dementia. The final stage of the project undertook large-scale testing of clinical samples, in order to achieve statistically significant evidence on the effectiveness of the test. This will allow them to promote a testing service to Pharmaceutical companies undertaking clinical trials. Recent publications show that accurate characterisation of patients using biomarker levels can improve the quality and reduce the costs of clinical trials on drugs for these neurodegenerative diseases. The ultimate aim is to produce a diagnostic kit for clinical purchasers. The applicants also believe their findings will be applicable to related conditions and intend to market a research kit for researchers in similar areas.

This case study is an example of a successful collaboration between a small enterprise and a university partner. The applicant chose to collaborate with a specific academic partner on this project to access clinical samples in the form of whole blood (all other biobanked samples are processed into plasma, which is less suitable for the applicant's assays). They see the data from these samples as one of their most valuable asset and secured further funding from their existing investors as a direct consequence. Meanwhile, their academic collaborators stand to benefit from the development of the diagnostic tool since it will be of use to projects they are undertaking on treatments for the condition.

Project description and rationale

The aim of this project was to develop a blood test to improve the diagnosis of a neurological condition affecting more than 500,000 people in the UK (Alzheimer's disease). Current biomarker testing processes are not routinely applied as they require a sampling procedure that is painful and risky for the patient (cerebrospinal fluid collected by lumbar puncture). Samples need to be sent away to a lab for analysis, and the results are 'noisy', difficult to interpret and do not allow for repeat measurement. This research aims to bring together a number of existing technologies to produce a testing kit for ultimate sale to hospitals. The applicant also plans to produce a research kit to enable scientists in other fields to conduct similar research into other conditions, such as epilepsy, which have analogous indicators.

Project consortium

The project was initiated by the lead organisation, an SME initially formed in 2012 to undertake stem-cell isolation and harvesting. The applicants have backgrounds in start-ups, diagnostics and clinical research, and one of the partners has been working on the neurological condition in question for the last 15 years. Following a discussion of the diagnostic challenges relating to this disease, the applicants undertook a literature review which revealed potential for their existing technology to be applied to this challenge.

The applicants explored this potential with an initial, self-funded pilot project in collaboration with a university partner. This collaboration was needed in order to access whole blood clinical samples, which are required for testing the diagnostic tool and comparing its measurements against clinical diagnosis. An institution with access to relevant clinical samples was found by word-of-mouth recommendation.

Funding issues / Motivation for applying

The academic partner on this project explained that they were motivated to collaborate within this project since they had been undertaking work on detecting markers for this disease for some time themselves. They were therefore intrigued by the project's potential to develop a successful diagnostic tool. Moreover, such a diagnostic tool would benefit the academics' other projects; for example, it could be used in testing a drug they are currently developing to inhibit the progress of the condition.

The resulting initial collaboration produced one working assay. Funding was required to develop several more assays in order to increase the accuracy of the test, and to conduct testing on a larger number of samples to achieve statistical significance.

The applicants initially sought private funding from a venture capitalist fund that had previously invested in another of their projects. However, in this case the funding request was declined due to insufficient data. The applicant sought funding from the Biomedical Catalyst as the match funding of 75% was considered to be affordable.

Progress

At the time of the research (February 2015), the project is currently three-quarters complete and progress is on target; further assays have been developed and the substances in question can be detected easily using the methodology. Differences have been observed between those diagnosed with the condition and the control group in the small number of samples undertaken so far. Further evidence provided by the applicant suggested that at the project was complete at the end of June 2015. In total assays have been developed for the aggregated form of three different biomarkers and the substances in question can be detected easily using the methodology. Four sets of data have been generated. The first compared 17 patients diagnosed with Alzheimer's disease against age matched controls using a single biomarker. A significant statistical difference was shown between the two groups. Secondly, a small number of patients with Alzheimer's disease, Parkinson's disease and Dementia with Lewy Bodies (a form of Parkinson's with dementia) were screened for 2 biomarkers. The relative levels correlated to the predicted levels based on post mortem histological studies (i.e. the AD patients were high for the AD biomarker and low for the PD one, the PD patients were low for the AD marker and high for the PD one and the DLB patients were generally high for both). Thirdly, blood from a rat model was screened for all three. The rats have been genetically altered to develop human AD symptoms, but at a much faster rate. Significant levels and differences were measure against control rats at less than half the time point when plaques would be visible in the brain. This shows great promise in accelerating the screening of drug compounds allowing measurements in a single animal without having to kill it to measure the response. Finally 25 AD patients were screened against age match controls for all three biomarkers and significant differences shown to be present. More detailed statistical analysis will be conducted on this data over the coming weeks.

This is seen as a great achievement in a short space of time. At the time of the research, the project currently has passed to technology readiness level 2, and is still a number of years away from having a product that can reliably supply a yes/no diagnosis with an accompanying data set that can be presented to potential clinical purchasers. However, in the meantime the applicants plan to supply a testing service to Pharmaceutical companies undertaking clinical trials, who will be able to use the tool to assess the condition and progress of patients who have already been diagnosed and are undergoing treatment.

Impacts on the organisation from the project

The technology partially protected by a patent, covering the measurement of the aggregated form of a biomarker which is the toxic form of the proteins. The applicants had filed a patent application before the start of the project and were able to incorporate data from the study along with improving the drafting based on more experience from the experimental procedure, greatly improving the clarity and protection provided. Under the Innovate UK grant rules, the applicant was able to cover some of the costs of prosecution into the international PCT phase as patent maintenance costs under overheads.

In addition to patent protection, the applicants believe that a key asset they hold is the dataset of clinical samples which demonstrates the positive results of the work funded by the Biomedical Catalyst; it is this which is commercially valuable and which will allow them to strike a testing service deal with a Pharmaceutical company or CRO.

The academic collaborators are planning to publish their findings should the large-scale testing produce successful results. The applicants also believe that their findings will be applicable to improving testing for other conditions with analogous indicators, e.g. epilepsy. They were successful in another small Innovate UK competition that paid for the costs of a number of companies to present their findings at Biotrinity in May 2015, which generated a lot of interest, including introduction to statistical specialists to help with data mining, meeting CROs and grant specialists to help with Horizon 2020 applications, meeting antibody developers to help drive down the costs of their research reagents and finally investors and a crowdsource funding organisation interested in helping them with a Series A funding. The applicants plan to develop and sell a research kit, which will supply basic components and protocol to allow researchers to conduct similar tests for other conditions.

The project has supported the development of the company. The applicants' investors, who became aware of the grant award due to having a position on the board, have consequently supplied 2 additional rounds of seed funding during the project to improve the assays and speed up the testing process. The applicants commented that this was the first time that they had been approached by investors, rather than having to approach them. The funding has enabled the applicant to retain staff and strengthen the team with development expertise and a part time chairman to assist with fund-raising. Moreover, they commented that the funding had enabled them to engage with academics in a more robust and rigorous way. The academic collaborators themselves commented very positively about the project and the engagement it had allowed them with the private sector, which had previously been limited. This project has encouraged them to undertake more work in future with this business and with the private sector more widely.

Impacts from being rejected as an applicant

Had the bid to the Biomedical Catalyst been declined, the project consortium would have persevered in applying for other grant funding when further calls for bids were issued; but that the amounts they received could have been smaller and the project consequently more limited.

Application, review and monitoring processes

The applicants had received funding from Innovate UK in the past and heard about the Biomedical Catalyst as a result of a mailing list. They sought no guidance on their application other than that supplied with the form, which they found to be very clear. However, they commented that due to the very small size of their organisation there were difficulties in setting out a budget to include overheads.

The applicants did not recall the feedback from the review process. They had focused on the confirmation that their application has been successful. They felt it was extremely unlikely that any feedback received would have changed the course of the project.

Overall, the applicants felt that the monitoring process had gone smoothly and that they had regular and constructive discussions with their monitoring officers. The academic partners had attended one of these, but felt it would be unnecessary for them to attend subsequent meetings.

The applicants however criticised the amount of administration associated with the grant relative to the size of the funding. They commented that the paperwork required was comparable to that required for much larger grants, and that project management disciplines were imposed that were inappropriate for the size of the organisation and project. They also reported mistakes and confusion, such the repeated need to re-issue the grant letter, but felt that this was as a result of a new team administering the grant rather than underlying issues.

The applicants found particular issue with the way in which payments were made by Innovate UK. It is only possible to draw down the grant against expenditure. In a micro sized enterprise such as theirs which has very limited commercial revenues cash flow issues will arise which delay the payment of salaries. Innovate UK's policy of only paying out against expenditure means that if they don't have the funds to pay for the salaries they can't claim back the matched funding. The use of director loans had complicated the picture further still as Innovate UK funding can't be claimed against debts.

Case study 18: Unsuccessful SME applicant

Summary

This case study relates to an unsuccessful application to the Innovate UK Late Stage scheme, relating to a development of a diagnostic device to check the amount of coagulant in the blood. The device would be used for sufferers of heart conditions that needed to take long term medication to control blood coagulation. The resulting device, if cleared for home use, would represent a step forward in diagnostic terms and would save patients attending hospitals.

Project description and rationale

The project hopes to create a hand held device that works via a mechanical process to test the viscosity of blood for patients on anti-coagulation drugs. Presently there are a high number of people who depend on hospital based testing to monitor their blood chemistry (so as to avoid repeat heart problems). The CEO believes that a home use hand held device will represent a step change in the monitoring of this condition much like the introduction of home testing kits for diabetics; resulting in greatly reduced costs to the NHS. Globally there are 10m users of anti-coagulant drugs. There are significant numbers in the UK and US representing a large market to for a successful new device.

The SME progressing this idea has 35 employees, and has been working on this particular concept for 15 years. It is looking to develop a home blood coagulation test machine for patients with a long term need for anti-coagulants. The idea hoped to address the demand issues resulting around heavy usage of anti-coagulation medication in the population The applicants believe that a home test device would be able to revolutionise care provisions for these patients. It would also allow for the freeing up time for practitioners. The CEO used the usage of personal testing devices by diabetics – they believed these devices offered similar benefits to those felt by diabetes patients who previously had to make use of professionals to test their blood insulin levels.

The device would work via a completely mechanical process and was based on testing the resistance of blood as a paddle is passed through it.

The innovation within the project is the creation of a home use device. The focus of the funded project was it to be successful was to bring an early stage prototype to a stage of efficient production. Achieving this outcome would allow for clinical tests on the products accuracy; and importantly certification for home use to be obtained.

Project consortium

The SME that made the application are a single idea company, and have been working on the concept since 2004. They have no collaborators but included a use of a subcontractor in Scotland to produce parts of the device.

The latter stages of the project have been ongoing for some time and some of the earlier stage testing had already occurred; completed in Germany. The CEO suggested that early stage clinical trial work was easier to conduct in Germany. The company was moved to North Wales so that they could make use of some of the local

support but also because they are all originally from the UK. The applicant also advised that at the later stages of clinical trials the UK was as easy to operate in as Germany.

The manufacturing of the product itself would have been conducted in a variety of locations, producing pars for the device. Some electronics work would have been conducted in Europe, but relationships had been formed with UK academics to facilitate the testing of the devices.

Funding opportunities and challenges

When looking for additional funding for this idea the firm believed that the Biomedical Catalyst was clearly the right option for them. The firm had been funded from private finance from several years and had been successful in raising cash with business angels and other grant funding opportunities; however the firm believed that a large award would be beneficial to the progression of the device towards market. The CEO was well aware that other options were out there but they felt that the Biomedical Catalyst was most appropriate for the project, as it focused on the same outcomes as they were looking to achieve, rather than job creation, for example. They used the example of the SMART Cymru grants, which had a focus on job creation but were a possible option for the firm. While the firms have employed more staff to progress the project this was not the ultimate goal for them, and having this as a condition of the grant for Biomedical Catalyst, for example, would have been a negative.

The firm believe that there is limited opportunity for businesses to gain access to the necessary funding for R&D in the sector. The firm have been successful in gaining some additional funding from other sources since the application was rejected, however they felt that the Biomedical Catalyst funding allowed for greater depth of work to be conducted as part of the project. When funding opportunities were few and far between it was necessary to focus on the core competencies, rather than spend time on valuable, but less critical, tasks such as promotion and marketing activity.

Importantly the firm have been able to progress their concept further since the rejected application. The CEO felt that despite the work of the Biomedical Catalyst to promote the sector and develop the funding landscape, there was still a significant gap for life sciences and med-tech firms.

Impacts on the organisation from the project

The CEO suggested that the larger funding opportunity that Biomedical Catalyst represented allowed for more critical work to occur as part of the project, such as allowing for publications of articles and promotional activities such as attending conferences. It was felt that with private sources of finance, the demands on the R&D was towards reaching market as soon as possible and this may not always be the right path.

Progress

To date, despite the absence of public funding via the Biomedical Catalyst specifically, they have been able to complete part of the project and now have a device that has been certified for use by nurses. However, they have struggled to get the necessary money together to be able to obtain certification for home use by patients. Presently the device is only CE marked and cannot be used in the US.

The CEO felt that there was a significant additional cost involved in the sector to be able to complete the necessary work and gain certification. The costs can arise from the need for a certification professional to be involved, something that larger firms may have as part of their workforce, but is a significant cost to an SME. Overall the CEO felt that the project had been delayed by around a year as a result of the failed application to the Biomedical Catalyst, being unsuccessful.

The firm now intends to sell the product idea and finished products to an Asian firm that had shown interest in their concept. The SME had been in talks with the Asian firms and were fully expected to move production and eventually sell their device to a Chinese business. The firm believed that there were limited opportunities in the UK to progress ideas such as these and so other international markets offered a chance to products. The CEO felt that Asian markets were willing to invest more into new ideas and bring them to market sooner so as to capture intellectual property and production.

In the opinion of the PI, the funding landscape in the UK is still in very poor shape. The sector has not benefited from the Biomedical Catalyst grant funding; the CEO believes that often overall funding commitments have been too small per project and as a result too diffuse. They compared this to the attitude in the US where a strong VC sector offered substantial amounts of money to businesses with ideas so that they had time and resources to develop an idea. They believe that there is a greater tolerance for failures in sectors outside of the UK and there is less risk aversion.

Wider effects

It would be expected that the successful introduction of a home testing coagulant device would impact on the levels of associated health problems such as deep vein thrombosis, stroke and heart disease. The use of in house devices would reduce the need for patients to visit hospitals and GPS for testing from clinicians. Furthermore the effectiveness of the drugs being used should also increase as patients are more able to control their specific dosage needs.

Process issues – Communication, Application, and Assessment and Review Process

The application process was identified by the applicants as a very costly exercise. The firm had viewed the application as an investment and were disappointed that it had not paid off.

To assist with the application process the firm had employed the services of a former Innovate UK employee. He had advised them on the details of the application process. It was the firm's belief that the feedback that this consultant gave them would have made them very likely to secure the grant funding. The applicant felt that they had been led to believe that if the firm reached the award panel that it would be almost certain that the application would be successful in their application. They were therefore very surprised that their application failed at this hurdle.

The applicant felt that they had not received feedback from the panel. The CEO reported being told that feedback would not be provided but that they should re-apply. Due to the firms unhappiness with the result, and the substantial cost that they attached to a repeat application they had decided to reject the offer of a resubmission and to not submit another application.

The CEO noted that two members of the major awards committee (MAC) were part of firms with competing ideas to their product. They did not believe that there was necessarily a conflict of interests, or that these individuals had been unduly negative about their application. However they expressed concerns about being asked to present their project to representatives of a potential competitor.

Case study 19: Unsuccessful SME applicant

Summary

This case study relates to an unsuccessful application to the Innovate UK Feasibility Study programme.

Project description and rationale

The application was for a project to explore the feasibility of a technology platform for novel therapeutics development. It would have tested the predictive power of several molecules involved in diseases that impact upon a substantial part of the population, especially children and the elderly.

The project is currently at TRL levels 1 and 2 because it is testing what could develop into a therapeutic option but also includes some discovery science. If the technology works as anticipated, it is thought that it would enable the development of low toxicity drugs in a more streamlined way than is currently the case. Because development is quicker and cheaper, this in turn could facilitate much easier personalisation of treatment. The technology platform potentially could have a very wide application if validated, leading directly to the development of new drugs in markets worth billions of dollars.

Proof of the principle behind this project would allow the applicant to apply the technology to key targets that are of interest in their existing drug development programme, as well as targets chosen by a Pharma client. Due to a positive pilot test, the expectation is that the technology would work.

Project consortium

The applicant is a small bioinformatics company which was founded in 2013. The company reached break-even in the first six months of operation through sales of software packages and reagents[39]. The company founder is a published academic who specialises in early stage companies and has many years of experience in this area.

The applicant creates the technology but requires partnerships with universities to perform feasibility studies using their existing models. The company founder was previously based in Europe but moved most of his activities to the UK two years ago:

"The major reason why I decided two years ago to move most of my activities to the UK was that we require a lot of collaborative studies with universities and British universities are very approachable in that sense and it is very easy to find academic partners".

The grant would have been paid 50:50 to the applicant and two academic partners. Two universities were named on the application form, but only one was involved with the application (and interviewed for this case study). The applicant has been working with this university for over two years and is "highly satisfied" with their work.

The relationship originally came about because the applicant had contacts at the university and knew the business development director. It is one of several academic units which the applicant works with.

[39] compounds or mixtures, usually composed of inorganic or small organic molecules

The applicant has released another technology platform using bioinformatics approaches to streamline drug and vaccine development. This was at the pre-launch stage at the time of the grant application.

Funding issues / Motivation for applying

The applicant was unable to fully fund the project from their own cash flow.

"Otherwise I would just pay for it because it's not that huge money we are talking about".

It is the partnership with academics, in particular, which requires the financing. The applicant applied to the Biomedical Catalyst because "there are practically no other funding options". The only other option for this sort of project is Horizon 2020. Venture capital is not appropriate given the relatively small amounts of money required for this study.

Progress

The project has not progressed further since the grant application was made. The applicant was "extremely surprised" by the unsuccessful result of the application process and was of the opinion that the Biomedical Catalyst realised that it is a very, very important area".

"I'm really amazed, it's so straightforward. With proper financing by the end of the year, we could go to Stage I trials already".

Had the project secured funding, the next step would have been to develop one or two well characterised candidate drugs ready for preclinical trials in animal and ex vivo test models. The first round of investment for preclinical studies of the developmental drugs would have been sought towards the end of the project.

Once the technology platform has been validated, the applicant expected that they would sell software licenses on an annual renewable basis. Two separate markets were identified for this software – Pharma companies and academic researchers. The intention is to charge cheaper prices to academics in return for research data which will help update and refine the performance of the software.

Impacts from being rejected as an applicant

The applicant had not had time to fully consider how they might respond to the rejection of their application at the time of the interview. The applicant stated that they are considering moving the project to Korea:

"Very negative impact. It is not that the company is getting bankrupt, but at this moment I am not sure where I will go further on. I already started discussing the possibility of transferring the project altogether to Korea, where there is a lot of money for biotech now".

Another project which was turned down for funding in the UK has already moved been moved to the US:

"The first stage money but also later stage money when the industry comes on board will not be gotten by a British university but a university in Austin. That's the outcome".

The project partner stated it was "very hard" to see what the impact could be upon the academic unit in which he works. Next steps would be decided upon discussion with the lead applicant, although as a previous application for a related grant had been turned down, there was an indication that it is not worth pursuing further; "not terribly keen to keep banging my head against a brick wall". Both the applicant and the partner mentioned previous grant

applications to the Biomedical Catalyst but this is the application under consideration in this case study is the only one which has been made by this particular company.

Process issues – communication, application, assessment and review process

The applicant found out about Biomedical Catalyst by browsing the internet and clicking onto Innovate UK and signing up to its email newsletter.

The applicant felt that the application form was a "great improvement' on other forms previously submitted. The time investment required was adequate for the grant being sought. Companies should have the answers to most of the questions to hand "so it is just a question of formulating them properly".

Some of the questions were seen to be less relevant for a feasibility grant. Talking about market share at this stage in the process, for instance, was described as "a little bit early and a bit senseless". The applicant queried the business and ideas sections being given equal weight, commenting that feasibility grants are all about innovation. The applicant's partner, on the other hand, felt that making the financial and scientific models as important as each other helped facilitate translation. A lack of detail about the business potential of the project had been a factor in the application receiving a score below the threshold for success.

From the partner's perspective, there were a few glitches in the system, including a last minute requirement to submit something to determine their eligibility. They were only given 24 hours' notice for this which was quite stressful. Having to cross-sign the forms between the university and the applicant was a different system from what they were used to and was seen to be "quite a complicated process to get right".

The main criticism of the review process was a delay in providing the decision outcome and that no feedback from the applicant is accepted during the review process.

Overall/other comments

The applicant discussed his wider experience of applying for grant funding in the UK. He had been unable to obtain any funding for feasibility trials even though they are already discussing early human trials for one of the molecules developed. The applicant felt that the system was unfair:

"From all the similar technology funds I've been working in, or been the recipient of grants, or been the reviewer and followed the fate of the projects I reviewed, I would say the British system is the least cricket game, it doesn't give the impression of any fair or reasonable or equal opportunities review process".

They felt that if there are other criteria which influence the decision making process – "like we don't grant companies who have been on the market less than two years, or are not supported by a large company". They felt that these should be stated.

"What is required is a much more honest approach to stating who is eligible for grants not in principle but in reality".

The applicant was very critical about the "horrible" reviewing process he had encountered in the UK. He compared this to his previous experience over the past 25 years of both applying for and reviewing grant applications.

"All other foundations where I was involved in, or have had the chance to review, Technology Strategy Board is, so far, the lowest on the quality of review".

The applicant queried how the reviewers are chosen, as some did not appear to know the specifics of the technology or the particular diseases. Sometimes "quite illiterate statements" were made about applications. It could feel like reviewers were looking at any reason to reject an application.

The applicant felt there should be more transparency in the Biomedical Catalyst's application process. They felt that it would be useful to know the number of submitted and granted projects announced for each competition, as well as scores and cut off scores.

"At this moment there is no transparency whatsoever, except the titles of some granted proposals have been published".

The applicant argued there should be more clarity about gateways "otherwise you have some areas which are outside the financing all the time". The impression was that most of the time money is given for "safe secure projects which can be done anyway".

The applicant felt that there should be some acceptance by the Biomedical Catalyst and other grant funders that some money for feasibility studies would be "wasted" because even a 20% success rate would "help streamline technologies".

Annex F: Research Instruments

This is a compilation of all research instruments used within the evaluation of the Biomedical Catalyst. They consisted of the following:

- Stakeholder Topic Guide: Programme secretariat, monitoring officers, assessors and peer reviewers, panel members and policy stakeholders
- Stakeholder Topic Guide: Investment community – Industry associations and Investors
- Project Case Study Topic Guide – Successful applicants to full bids
- Project Case Study Topic Guide – Successful applicants to full bids
- Project Case Study Topic Guide – Confidence-in-Concept Awards
- Biomedical Catalyst Applicant Survey Questionnaire

Biomedical Catalyst Stakeholder Topic Guide: Programme secretariat, monitoring officers, assessors and peer reviewers, panel members and policy stakeholders

Purpose of stakeholder interviews: The objective of this strand of the evaluation is to offer in-depth insight about the operation of the programme to feed into the process evaluation, and to understand how the Biomedical Catalyst is perceived by stakeholders.

Pre-interview preparation: Prior to speaking to the stakeholder, the consultant will review relevant material collected during the familiarisation exercise and identify key points to explore during the interviews.

Introduction: Ipsos MORI have been commissioned by the Medical Research Council and Innovate UK to undertake an impact and process evaluation of the Biomedical Catalyst programme. The overall aim of our research is to identify the intermediate and final impacts of the projects funded through the Biomedical Catalyst as well as to learn what worked well and what could be improved about the delivery of the programme.

We wanted to speak with you as part of this work because we understand from [contact source] that you have a good understanding of [why we're talking with them].

All information that you provide will be treated in confidence by Ipsos MORI and presented in the report in an aggregated form. The report will be for internal use by Innovate UK (also known as the Technology Strategy Board), and the Medical Research Council.

Interviewee Tracking:

- Name
- Role
- Contacts
- Length of time in post
- Area of knowledge over the programme
- Date
- Venue / mode

Key to different stakeholders covered by the topic guide:

- Programme secretariat and monitoring officers – PSMO
- Assessors and peer reviews[40] - APR
- CiC, DPFS and MAC Panel Members - PM
- Policy Stakeholders - PS

Please answer from your experience of the programme… / to the best of your knowledge …

[40] As peer reviewers need to remain anonymous, we will cover the questions with stakeholders who have been involved in MRC peer review process: Jonathan Seckl and Herbie Newell

Marketing and Communications:

1. How effective was the marketing and communications effort? [prompt if needed around marketing literature, emails, events] How successful was it in raising awareness of the Biomedical Catalyst amongst the target audiences you work with? **[PSMO Innovate UK Only, PS]** How were academic departments made aware of the programme? How widespread would you estimate this awareness was? **[PSMO BMC]**

2. How effectively has the Biomedical Catalyst engaged with the investment community in terms of: **[PSMO, PM, PS]**
    - Raising awareness of the programme?
    - Raising confidence in the processes used to administer the programme? (test awareness of the MAC)
    - Using it as a tool to raise the profile of life sciences as a potentially profitable sector for investment?
    - Did this vary for different parts of the sector, or types of investors? Were certain groups more aware? For example how aware was the digital health sector?

3. How well did Innovate UK and the MRC work together to promote this programme? **[PSMO and PS]**
    - Capture examples of good working and areas where it could have been improved.

Application Process

4. Did the application process provide sufficient information to enable a high quality [assessment for Innovate UK and review for the MRC] of bids? **[APR]** / you to offer a high quality appraisal of bids? **[PM]**
    - What areas could be improved to raise the quality?

Assessment, Review and Project Selection Process

5. The overall policy objectives of the Biomedical Catalyst were to support the pull-through of academic research into the commercial sector and the growth of the life sciences sector by responding to market failures associated with the commercialisation of IP. Based on your experience of the programme, to what extent are the criteria for making funding decisions aligned with this? **[ALL]**
    - Examples of market failure terms to record against from the evaluation framework: moral hazard and finance, transaction costs, asymmetric information, spill-over effects and monopsonistic purchasing,

6. How far do individuals involved in the appraisal process have sufficient scientific and commercial expertise to provide a rigorous assessment of applications received? **[ALL]**
    - Prompt separately on scientific and commercial. Examples of commercial expertise include knowledge of health products, global markets or financing of investments

7. How clear have you found the guidance provided to [assessors for Innovate UK and reviewers for the MRC]? Does it provide a clear direction on the nature of the judgments to be made and does it provide a consistent indicator of project quality across applications? **[APR, PM]**
    - Did you feel that your project selection panels (CiC, DPFS and MAC) received sufficient information from the assessment and review processes to make informed project selection recommendations? **[PM]**
    - Were panel members given a sufficient amount of time to consider each application in sufficient depth? **[PM]**
    - How far was project selection influenced by considerations of whether the project would be funded without the BMC? To what extent was the assessment or review process focused on

additionality and displacement (i.e. how far the projects would have otherwise been taken forward without Biomedical Catalyst funding or extent to which they may displace existing products)? **[ALL]**

- Do you feel the resources (time and money) invested in the assessment and review of applications were too little / adequate / too much? **[PM, PS]**

- Do you feel that the process of moving from appraisals to decisions was handled effectively?

8. How would you rate the feedback that was given throughout the application process? **[PSMO, APR, PM]**
    - Was it too little, adequate, too much?

9. Did you feel the time taken to review the application and process the award was appropriate? [Note: if delays identified] Do you have any examples where this had negative impacts? [Note: If not sufficient] How much extra time is needed? **[AII]**

10. To what extent was project selection influenced by the need to defray resources? Did this influence project selection priorities and the likelihood of success? **[PM]**

Contracting and due diligence

11. Did the conditional/grant offer/award letters (award agreement for the MRC) make the deliverables and monitoring requirements on successful applicants clear to both applicants and monitoring officers? **[PSMO]**

12. Is the due diligence process specified at an appropriate level of rigour? Does it avoid waste through avoiding committing resources to businesses facing financial difficulties? **[PSMO** (IUK only)**]**

Delivery and Monitoring

13. How effectively do project monitoring systems capture project progress and identify emerging issues? And how could these be improved? **[PSMO, PS]**

14. How effective are the processes for agreeing variations in contracts? **[PSMO]** Note: Post Award Agreement Amendment for the MRC

15. What are the routes through which lessons learnt from the experience of previous rounds fed into future delivery or the appraisal process for future rounds? How effectively does this work? **[PSMO]**

Aggregate performance management

16. Do the current monitoring systems support effective performance management, risk management, and decision making? **[PSMO, PS]**

Partnership working (additional, not specified in the evaluation framework)

17. To what extent do you feel the programme has supported the formation of new collaborations in the industry? (academic/commercial/clinical) **[ALL]**
    - Please provide examples if possible

Close / round up

18. Any other comments on the Catalyst? Any areas where you would like to see it develop? Reflections on where it has worked well / could develop such as for large / small grants / firms
19. Anything which you feel we should have asked? Any questions for us about our work? **[ALL]**

Biomedical Catalyst Stakeholder Topic Guide: Investment community – Industry associations and Investors

Pre-interview preparation: Brief internet research to gauge scale of operation and focus of the organisation.

Project introduction: Ipsos MORI have been commissioned by the Medical Research Council and Innovate UK to undertake an impact and process evaluation of the Biomedical Catalyst programme. The overall aim of our research is to identify the intermediate and final impacts of the projects funded through the Biomedical Catalyst as well as to learn what worked well and what could be improved about the delivery of the programme.

We wanted to speak with you as part of this work because a core aim of the programme is to support the development of early stage life sciences projects until they are ready to receive investment. So we are keen get an industry perspective on how this is working.

All information that you provide will be treated in confidence by Ipsos MORI and presented in the report in an aggregated form. The report will be for internal use by Innovate UK (also known as the Technology Strategy Board), and the Medical Research Council.

Tracking (not necessary to start interview with these questions)**:**

- Name
- Role / area of expertise
- Contacts
- Length of time in post
- Date
- Venue

Context:

1. Interviewee's knowledge of the programme – query the extent to which they are:
    a. Aware of scheme? Knowledge of individual projects? Knowledge of the three routes through which funding is delivered (to academic led, company led and awards to university departments)?
    b. Extent to which they have a view of the general member (investor) experience of the scheme?

Climate for investment

2. How do you believe the willingness to invest in the UK life sciences sector has changed over the past five years?
    a. What do you think is driving this?
    b. What are the main barriers to further investment in the sector? And how have these changed?
3. How has the analyst and investor community developed over this time?

Marketing and Communication

4. How effectively has the Biomedical Catalyst programme engaged with the investment community in terms of:
    a. How effective was consultation with industry and investors both before the programme was established and over the course of its delivery?
    b. Raising awareness of the programme amongst the investment community?
    c. Ensuring confidence in the processes used to administer the programme?

d. Using it as a tool to raise the profile of life sciences as a potentially attractive sector for investment?
e. Did this vary for different parts of the sector, or types of investors? Were certain groups more aware?
[Note: prompt if not clear from response to select between highly effective through to highly ineffective]

5. How aware is the investment community of the Biomedical Catalyst? Is there any awareness amongst investors who do not already focus on life-sciences?
[Note: Prompt if not clear from response to select between fully aware/ partially aware / not aware at all]

6. How is it viewed? Any features of the BMC which make it stand out for your members from other public funding schemes?
   - From a financial perspective
   - From a de-risking perspective
   - From a collaboration perspective

Impacts

7. Has the scheme raised the profile of life sciences as a potentially profitable sector for investment?

8. Does a project's receipt of funds from the BMC change how it is viewed by investors? If so, how? [Note: if not clear from response prompt around willingness to invest in the phase of the project receiving BMC funding, follow on phases. Is the scheme taking projects to the point at which the private sector can take over?

9. Are there any particular types of organisation which appear to particularly benefit from engagement with the Biomedical Catalyst?

10. Do investors have trust in the Biomedical Catalyst processes? Does this cut down the costs of due diligence they face when engaging with a project?

11. Is funding from the Biomedical Catalyst seen as a rival source to equity funding or other sources of funding?

12. Are you aware of any university departments using Biomedical Catalyst funds to develop their internal support arrangements?

13. Finally, a central objective of the Biomedical Catalyst was to plug a perceived funding gap facing early stage commercialisation activity in the life sciences. Do you agree with this premise? and if so do you think it is working? If so can you offer any examples of how it is working in practice?

Close / round up

14. Any other comments on the Biomedical Catalyst? Any areas where you would like to see it develop? Reflections on where it has worked well or could develop such as for large / small grants / firms **[ALL]**
15. Anything which you feel we should have asked? **[ALL]**

Project Case Study Topic Guide – Confidence-in-Concept (CiC) Awards

Background information

Purpose of case study: The purpose of this research is to allow for more in-depth exploration of the interim outputs and outcomes achieved within the projects to date.

Pre-interview preparation: Prior to speaking to the project leader, the consultant will analyse relevant project documentary evidence. This will include:

- Application form;
- Appraisal documentation;
- Monitoring data and project file (including Researchfish – Medical Research Council's monitoring system and survey output received from the applicant/project lead)

After speaking with project leads, the consultants will schedule a telephone conversation with the monitoring officer to discuss the findings and elicit the perspective of the monitoring officer on any issues raised.

Case study interview

Introduction

Introduce the context of the case studies – that they are being undertaken as one of the components of the evaluation and that 20 projects are being case studied to explore both the interim outcomes and applicant's views on the process. Describe that the CiC awards to [XY] has been identified as a case study and that we have received the application and monitoring data about the project. From this information we know that funding to your institution was awarded in year [years award given in from ranking spreadsheet]. Instruct interviewee to respond in general about the programme across this period, across the mix of individual projects supported by the award, and to comment specifically where things changed between rounds.

All information that the interviewee provides will be treated in confidence by Ipsos MORI and the case studies will be anonymised prior to disclosure to Innovate UK (previously known as the Technology Strategy Board), and the Medical Research Council. The case studies will only be used by Innovate UK and the MRC for their internal purposes, and to publish an aggregated and anonymised summary of the outcomes of the evaluation. We will provide an opportunity for you to offer (any potentially critical) comments which will be taken into account but can be kept separate from the case study write ups.

To confirm, we would like to use your experience as a grant recipient under the programme as a case study and request your permission for the following:

i) To use your confidential information already provided to us together with any additional information you choose to disclose ("Information") for the evaluation study, which the MRC and Innovate UK will use for internal purposes;

ii) To share the Information and any analysis from the evaluation study with the MRC for its own internal purposes only; and

iii) To publish an anonymised form of the case study with all confidential information and personal data removed as part of a broader publication of the outcomes from the evaluation of the programme.

Institution / department

1. Please provide an overview of your organisation's scale and focus?
    a) Understanding of how significant a source of funding this is for the organisation?
    b) Balance between fundamental research and more translation oriented research objectives?
2. Please tell us about your role here?

Programme description and rationale

3. Focusing on your application, what were the key areas and types of activities that you proposed to support?
4. What formal process did you go through to decide how to allocate funding?

Funding issues / Motivation for applying

[Note on sources and prep: This section will rely on interviews]

5. What was your motivation to apply to the Biomedical Catalyst CiC award?
    - Which characteristics of the Biomedical Catalyst CiC award were the most significant in motivating your application?
6. What other options had you considered for raising the finance needed to fund this type of work?
    - To what extent did you actively pursue these options (e.g. applying for finance, applying to other government schemes or foundations)?
    - What sources proved successful?
    - Why were those other financing options unsuitable / not secured / not sufficient?
7. How does this source of funding compare to other sources in terms of scale and nature:
    a) For your Research Organisation or institution? (What proportion of total funding for the organisation comes from the Biomedical Catalyst?
    b) Compared to other available sources of funding for translational research within your organisation or department?

Progress (Interim outcomes)

[Note: We have requested monitoring data from the MRC but if we do not receive it, this section will rely on interviews]

8. How has the CiC funding been used? / What has been achieved to date? [Note: anticipate some delay between being awarded the funding and the projects moving forwards]

    a) Specific translational research projects supported - we'd like to look into these if possible and speak with those responsible for managing them [using successful project case study template]

    b) Broader activity including institutional support and capacity building

9. Are there any themes in terms of supported projects? How is it balanced between:

i. Therapeutic - e.g. small molecules (drugs), biologics, vaccines, gene therapy, cellular and regenerative medicine, surgical, radiotherapy, psychological / behavioural, physical (physiotherapy, occupational therapy, speech therapy etc.) and complementary therapy.

ii. Medical Device – e.g. implants, mobility aids, dressings, medical equipment (other than that used for diagnosis), and prostheses

iii. Diagnostic Tool – e.g. imaging (x-rays, MRI etc.), clinical tests, sensors etc.

iv. Other (specify) [pre-complete where possible]

10. What would you say is the balance of factors driving the development of the projects you support?

    i. Medical need (i.e. the impact of the disease area on human health and quality of life)

    ii. Commercial rationale (availability and/or effectiveness of existing treatments, and where relevant, development work being undertaken by competitors in developing products)

    iii. Scientific rationale for the project (i.e. the strength of the scientific evidence suggesting the solution being explored is a plausible candidate for providing a more effective solution to the underlying medical need. Which TRL level was the project at when you applied – referring to the table from questionnaire).

11. For the projects you support with CiC what are the any typical partnership models? Are funds typically used to leverage in other funding?

12. What are the typical histories of the projects that you support?

    i. Where have they emerged from?

    ii. Are they typically continuing previous projects and activities? (From within or outside of their departments)

    iii. What are the typical processes for forming partnerships to apply? [If applicable]

13. What has driven this progress to date? [Note: Link back to Q7 and any comments highlighting success across the CiC award prompt to take a systems view of progress and the role of the Biomedical Catalyst in context of other factors, funding etc.]

14. How do you manage this activity?

    c) Decisions of where to focus / which projects to support?

    d) Monitoring and assessment – how do you track performance? [Check against MRC requirements]

    e) Does this include tracking any of the following KPIs?

    i. Technological progress measured against TRLs

    ii. Academic outputs (publications, conference papers etc.)

    iii. Patents and other forms of IP

    iv. Commercial revenues and licencing deals?

15. How would you have responded to your application being declined? (If your more recent application was declined how did you respond to that?)

    - Would you or your colleagues have been able to take the translational activities supported by the Biomedical Catalyst CiC award forward internally, through other public programmes or private sources of support?

    - If so what would have been the impacts on scale, focus and timing of the work supported?

    - What would the researchers who are currently supported by the CiC award have been doing otherwise? [Note: prompt around basic vs. translational research and the extent to which BMC funding for the project has freed up resources for use in other ways]

16. Thinking ahead, do you expect to be able to achieve all your expected outputs in line with the application? If not, what are the reasons for this? [Try to differentiate whether anticipated scientific, medical and commercial benefits likely to be realised]

17. What were the main challenges faced to date?

    - How were they mitigated?

18. Was any research stopped early?

    - What was the reason for this discontinuation?

Impacts on the institution [note: cumulatively across all projects]

[Note on sources and prep: This section will rely on interviews]

19. How have you benefited from receiving the Confidence-in-Concept Biomedical Catalyst award?

- Forming collaborations
- Facilitating learning about other organisations and drivers (esp. academic-commercial skills exchange)
- Producing conference papers academic publications
- Attending events
- Securing finance from other sources
- Support offered to academics with an interest in seeing their projects move towards a commercial outcome
- Attracting and retaining staff
- Setting up a spin-out
- Securing follow-on funding (at a project level).

20. How has this fund impacted on your institution? Have you become more focused on translational research

Wider effects

[Note on sources and prep: This section will rely on interviews, but may draw from ResearchFish]

21. Has the package of funding resulted in any new IP, products or services?
    - Or are these expected to follow in the coming months?
22. Have any commercial exploitation plans or timescales estimated been for activities supported by the award? (Exit strategy)
23. Are there any other wider impacts that you can identify?
24. How much was the competitor landscape a factor in your approach and decision making process (i.e. in terms of your application and project selection process)? (link to possible displacement effects)

Note that now I'd like to conclude the interview by focusing on your relationship with the MRC.

Process issues – Communication

[Note on sources and prep: This section will rely on interviews]

25. How did you first hear about the CiC component of the Biomedical Catalyst fund?
26. Did you meet directly with anyone from the MRC or receive and materials from them before deciding to apply? Or speak to anyone or attend any events?

27. Are there any comparable sources of funding that you are aware of?

28. How effective were the BMC's marketing and communication activities in ensuring understanding of the scope and objectives of the competition, eligibility requirements and competition processes?

Process issues – Application

[Note on sources and prep: This section will rely on interviews]

29. How did you find using the application form to prepare your bid?

30. In broad terms, how much time and cost was involved for your organisation in the application process (including time spent engaging in marketing and communication activities, and collaboration building prior to starting your application)? Do you think this was reasonable and proportionate? Are there any ways that the process could be made more efficient? Did you gain any wider benefits from the process of preparing your application?

31. Did you find any feedback received during the process lead to improvements/ changes in your planned activities?

32. What, if any, barriers did you face in the application process and how did you overcome them?

Process issues – Review

[Note on sources and prep: This section will rely on interviews]

33. What was your experience of the review process?

34. Did you feel the time taken to review the application and process the award was appropriate? [Note: if delays identified] What impact did this have?

35. Were there any changes as a result of the review process/reviewer feedback?

Process issues – Monitoring

[Note on sources and prep: This section will rely on interviews]

36. How effective are the tools and systems for monitoring the Biomedical Catalyst CiC award?

37. Are you satisfied with the process and what features could be improved to reducing burdens or improving effectiveness?

Process issues – Recommendations

[Note on sources and prep: This section will rely on interviews]

38. Can you identify any improvements that could be made to the processes relating to the communication, application, appraisal and monitoring?

Close / round up

39. Any other comments on the Biomedical Catalyst? Any areas where you would like to see it develop? Anything which you feel we should have asked?

[Note: our evaluation runs to 2018 and that we would like to speak to you again in 2016 or 2017 to see how things have gone forward.]

Project Case Study Topic Guide – Successful applicants to full bids

Background information

Purpose of case study: Purpose of case study: The purpose of this case study is to allow for more in-depth exploration of interim outputs and outcomes achieved within the projects to date and explore any process issues identified by the applicants. The information we collect will be confidential and only will be shared with Innovate UK and Medical Research Council in anonymised form or synthesised in the report.

Pre-interview preparation: Prior to speaking to the project leader, the consultant will analyse relevant project documentary evidence. This will include:

- Application form;
- Appraisal documentation (including presentation to the MAC and [for MRC applications] DPFS minutes);
- Monitoring data and project file (including Researchfish – Medical Research Council's monitoring system and impact survey output received from the applicant/project lead)
- Details of any other successful or unsuccessful applications associated with the individual in order to maintain focus on this case.

After speaking with project leads, the consultants will schedule a telephone conversation with the monitoring officer to discuss the findings and elicit the perspective of the monitoring officer on any issues raised.

In general this topic guide is suitable for project leaders and project partners (collaborators). Interviews with collaborators will supplement information provided by the project leaders and confirm the findings on interim outputs / progress made. Therefore not all questions will be of relevance to collaborators. Note that collaboration was not a requirement and therefore some projects may not have formal partners in the project. The interview should be tailored accordingly.

Case study interview

Introduction

Introduce the context of the case studies - that they are being undertaken as one of the components of the evaluation and that 20 projects are being case studied to explore both the interim outcomes and applicant's views on the process. Describe that the project [XY] has been identified as a case study from round [XY] and that we have received the application and monitoring data about the project. From the information we know that the project has been funding under the [XY] round and is meant to run from Month Year for [Z] months.

All information that the interviewee provides will be treated in confidence by Ipsos MORI and the case studies will be anonymised prior to disclosure to Innovate UK (previously known as the Technology Strategy Board), and the Medical Research Council. The case studies will only be used by Innovate UK and the MRC for their internal

purposes, and to publish an aggregated and anonymised summary of the outcomes of the evaluation. We will provide an opportunity for you to offer (any potentially critical) comments which will be taken into account but can be kept separate from the case study write ups.

To confirm, we would like to use your experience as a grant recipient under the programme as a case study and request your permission for the following:

i) To use your confidential information you have already given us together with any additional information you choose to disclose ("Information") for the evaluation study, which Innovate UK will use for internal purposes;

ii) To share the Information and any analysis from the evaluation study with the MRC for its own internal purposes only; and

iii) To publish an anonymised form of the case study with all confidential information and personal data removed as part of a broader publication of the outcomes from the evaluation of the programme.

Project description and rationale

1. Can you briefly describe the project's objectives? [Note on sources and prep: find these in the application form and validate if they haven't changed]

2. What is the problem that the project was set up to address? Describe the scientific, commercial, and human health rationale of the project?

[Note: Rationale is described in the application but ask for any supporting evidence for the extent of the problem/any new evidence]

Can you point at evidence relating to the:

a) Medical need (i.e. the impact of the disease area on human health and quality of life)

b) Commercial rationale (availability and/or effectiveness of existing treatments, and where relevant, development work being undertaken by competitors in developing products)

c) Scientific rationale for the project (i.e. the strength of the scientific evidence suggesting the solution being explored is a plausible candidate for providing a more effective solution to the underlying medical need.

d) Which TRL level was the project at – referring to the table from questionnaire but also record a narrative to be more precise – e.g. half way through a Phase II clinical trial).

3. How was the project set up to address this need?

[Note on sources and prep: information in application form but might need to generalise and translate into less scientific terms]

a) Therapeutic - e.g. small molecules (drugs), biologics (including plasma treatment), vaccines, gene therapy, cellular, molecular and regenerative medicine, surgical, radiotherapy, psychological / behavioural, physical (physiotherapy, occupational therapy, speech therapy etc.) and complementary therapy.

b) Medical Device – e.g. implants, mobility aids, dressings, medical equipment (excluding those developed for use in diagnosis, including diagnostic in vitro tests), and prostheses

c) Diagnostic Tool – e.g. imaging (x-rays, MRI etc.), clinical/in vitro diagnostic tests, sensors etc.

d) Other

4. What is the history of the project?

[Note on sources and prep: This is an important question and we will not have information on this from any other means than the interview]

- How did the project get established?
- Who was involved?
- Is it a follow on project of another research project? (If yes, was it a project you were working on?) (If yes, can you point us towards any documentation of that project?)
- What key risks were identified?
- What was the process for forming your consortium?

Project consortium

5. Please provide an overview of your company / organisation (for academic participants, ask about the department or unit)

[Note on sources and prep: Have a look at the company/university website to know what they do].

Firms (Startups or SMEs) – name, sector, size in number of employees, how long it has been operating (gather this information from the company website prior to the interview)

Research Institutes or Higher Education Institutions - name and type of your organisation (e.g. university, research institute etc.), main academic field and subfield

6. What is your role within the company / organisation (for academic participants, ask about the department or unit)

7. The project has [XY] partners in the application form. Are these the partnering organisations in the project and what are their roles in achieving the project objectives? Has the setup changed since the application? … or are there any informal partners?

[Note on sources and prep: Review the application form].

Funding issues / Motivation for applying

[Note on sources and prep: This section will rely on interviews. Issues of funding are likely to be of more interest for firms than researchers. If clearly of limited interest/ limited ability to comment proceed over more quickly]

8. What was your motivation to apply to Biomedical catalyst?

- Prompt around: improve collaboration, secure finance, de-risk projects? (other possibilities: receive feedback on the design of the project, increase the scope or quality of the project, delay the need to seek private investment)

9. Which characteristics of the Biomedical catalyst were the most significant in motivating your application?

- Prioritise responses from high to low

10. What other options had you considered for raising the finance needed to fund the project?

To what extent did you actively pursue these options (e.g. applying for finance, applying to other government schemes)? How far were these successful?

Why were those other financing options unsuitable / not secured / not sufficient?

11. How would you have responded to your application being declined?

12. Would you have been able to take the project forward internally or through other programmes? Possible effects on focus, scale, timing, etc.

Progress (Interim outcomes)

[Note: We have requested monitoring data from the MRC and Innovate UK but if we will not receive it, this section will rely on interviews]

13. How far has the project progressed in terms of delivering your expected outputs?

- In relation to each of the projects targets, has the project progressed as expected? Are they on track / behind schedule / ahead of schedule? What were the challenges in meeting each of these targets? If the targets were not met, what were the reasons for this? How did you address this? What learnings did you take from this?

- What were the main risks and challenges faced to date? How were they dealt with or mitigated?

- Do you have any supplementary information or resources (such as REF case studies) that you can share with us to support our assessment of impact?

14. What technical progress have you made against TRLs? [note: refer back to grid if appropriate but also record a narrative to be more precise and to pick up other technical progress points – e.g. half way through a Phase II clinical trial]

15. Has the project progressed against the schedule and passed the expected milestones?

- If your project is behind schedule in any way, what impact, if any, will this have on the project (e.g. delays to grant payments, failure to achieve contracted outputs within expected timescales)?

16. What has driven this progress to date? [Note: prompt to take a systems view of progress and the role of the Biomedical Catalyst in context of other factors, funding etc.]

17. Thinking ahead, do you expect to be able to achieve all your expected outputs in line with the schedules agreed in the contract? If not, what are the reasons for this?

- Prompt between fulfilment of wider anticipated scientific, medical and commercial objectives

18. How do you plan to take your project forwards? [Note: discuss around the milestones on the technology roadmap (create commercial entity to develop the product further, sell the intellectual property to another organisation or business, enter into licensing agreements with another organisation or business, produce the product using contracted manufacturers, produce the product using own manufacturing facilities, make the product freely accessible (digital health application or behavioural health))]

19. Was any research aborted or focus changed?

- Why and what impact did this have?

20. What future challenges do you anticipate?

Impacts on the beneficiary

[Note on sources and prep: This section will rely on interviews]

21. How have you benefited from participating in the Biomedical Catalyst?

- Forming collaborations, [if so] how many? What was the result?
- Facilitating learning about other organisations and drivers (e.g. skills exchange)
- Producing conference papers academic publications (etc.) [if so] which ones?
- Attending events
- Securing finance from other sources
- Boosted reputation of the organisation from having received the award
- The process of how (best to) translate ideas into practice
- Support offered to academics with an interest in seeing their projects move towards a commercial outcome
- Attracting and retaining staff
- Wider benefits, effects on scale of research activity, research studentships (new research topics)

Wider effects

[Note on sources and prep: This section will rely on interviews]

22. Has the project resulted in any new IP, products or services or is it anticipated that it will?

23. What are commercial exploitation plans, and the anticipated timescales involved? (Exit strategy)

24. Are there any other wider impacts that you can identify? [e.g. effects within your organisation (e.g. hiring translational managers), community effects (e.g. great confidence), policy impacts etc] or are aware of?

25. [if commercial exploitation plans identified] What impact might this have on the market? For example will it displace existing products?

Note that now I'd like to **conclude the interview by focusing on your relationship with the MRC / Innovate UK.**

Process issues – Communication

[Note on sources and prep: This section will rely on interviews, and we can expect Innovate UK supported projects to cover this content in greater depth than the MRC (Questions 28-31)]

26. Where did you first hear about the Biomedical Catalyst?

27. To what extent were the Biomedical Catalyst marketing and communication activities effective in encouraging you to apply to the programme?

28. How effective were the communication activities and briefing events run by the MRC, Innovate UK and/ or KTNs in terms of building your consortium and developing your project?

29. How effective are marketing and communication activities in ensuring understanding of the scope and objectives of the competition, eligibility requirements and competition processes?

- Have you received any guidance in advance of the application?

Process issues – Application

[Note on sources and prep: This section will rely on interviews]

30. How did you find the application process, not specific to but including, the application form, guidance material, input and advice from the Funding organisation(s)?

31. What, if any, barriers did you face in the application process? And how did you overcome these?

Process issues – Assessment and Review Process

[Note on sources and prep: This section will rely on interviews]

32. What was your experience of the appraisal process?

- Prompt around both the pre-committee assessment and panel review

33. How valuable was the feedback at each and every stage of the assessment review process?

34. Did you feel the time taken to review the application and process the award was appropriate? [Note: if delays identified] What impact did this have?

35. What was the impact of any feedback received on the project?

Process issues – Monitoring

[Note on sources and prep: This section will rely on interviews]

36. How effective are the tools and systems for monitoring projects?

37. Are you satisfied with the process and what features could be improved to reducing burdens or improving effectiveness?

Process issues – Recommendations

[Note on sources and prep: This section will rely on interviews]

38. Can you identify any improvements that could be made to the processes relating to the communication, application, appraisal and monitoring?

Close / round up

39. Any other comments on the Catalyst? Any areas where you would like to see it develop? Anything which you feel we should have asked? Any questions for us about our work?

Note that we plan to come back and contact them in [when?], if this is acceptable.

Finally, it is sometimes possible to link the data we have collected with other government surveys or datasets to enable further statistical analysis. Would you be happy for this to be done?

Project Case Study Topic Guide – Successful applicants to full bids

Background information

Purpose of case study: Purpose of case study: The primary purpose of this case study is to allow for more in-depth exploration of whether and in what form projects which were the subject of unsuccessful applications went ahead. In case the project was taken forward, we plan to find out about progress and the interim outputs and outcomes achieved. The secondary purpose of the case studies is to explore any process issues identified by the applicants. The information we collect will be confidential and will be shared with Innovate UK and Medical Research Council only in anonymised form or synthesised in the report.

Pre-interview preparation: Prior to speaking to the project leader, the consultant will analyse relevant project documentary evidence. This will include:

- Application form;
- Appraisal documentation (including presentation to the MAC and [for MRC applications] DPFS minutes);
- Details of any other successful or unsuccessful applications associated with the individual in order to maintain focus on this case.

In general this topic guide is suitable for the project. Interviews with collaborators may supplement information provided by the project leaders and confirm the findings on interim outputs / progress made. Therefore not all questions will be of relevance to collaborators. Note that collaboration was not a requirement and therefore some projects may not have formal partners in the project. The interview should be tailored accordingly.

Case study interview

Introduction

Introduce the context of the case studies that - they are being undertaken as one of the components of the evaluation and that 20 projects are being case studied to explore both the interim outcomes and applicant's views on the process. Describe that the project [XY] has been identified as a case study from round [XY] and that we have received the application and data about the project. From the information we know that the project applied for funding under the [XY] round but was unsuccessful.

All information that the interviewee provides will be treated in confidence by Ipsos MORI and the case studies will be anonymised prior to disclosure to Innovate UK (previously known as the Technology Strategy Board), and the Medical Research Council. The case studies will only be used by Innovate UK and the MRC for their internal purposes, and to publish an aggregated and anonymised summary of the outcomes of the evaluation. We will provide an opportunity for you to offer (any potentially critical) comments which will be taken into account but can be kept separate from the case study write ups.

To confirm, we would like to use your experience as a grant applicant under the programme as a case study and request your permission for the following:

i) To use your confidential information you have already given us together with any additional information you choose to disclose ("Information") for the evaluation study, which Innovate UK will use for internal purposes;

ii) To share the Information and any analysis from the evaluation study with the MRC for its own internal purposes only; and

iii) To publish an anonymised form of the case study with all confidential information and personal data removed as part of a broader publication of the outcomes from the evaluation of the programme.

Programme description and rationale

40. Can you briefly describe the project's objectives? [Note on sources and prep: find these in the application form and validate if they hadn't changed]

41. What is the problem that the project was set up to address? Describe the scientific, commercial, and human health rationale of the project?

[Note: Rationale is described in the application but ask for any supporting evidence for the extent of the problem/any new evidence]

Can you point at evidence relating to the:

e) Medical need (i.e. the impact of the disease area on human health and quality of life)

f) Commercial rationale (availability and/or effectiveness of existing treatments, and where relevant, development work being undertaken by competitors in developing products)

g) Scientific rationale for the project (i.e. the strength of the scientific evidence suggesting the solution being explored is a plausible candidate for providing a more effective solution to the underlying medical need.

h) Which TRL level was the project at – referring to the table from questionnaire but also record a narrative to be more precise – e.g. half way through a Phase II clinical trial).

42. How was the project set up to address this need?

[Note on sources and prep: information in application form but might need to generalise and translate into less scientific terms]

e) Therapeutic - e.g. small molecules (drugs), biologics (inc plasma treatment), vaccines, gene therapy, cellular, molecular and regenerative medicine, surgical, radiotherapy, psychological / behavioural, physical (physiotherapy, occupational therapy, speech therapy etc.) and complementary therapy.

f) Medical Device – e.g. implants, mobility aids, dressings, medical equipment (excluding those developed for use in diagnosis, inc. diagnostic in vitro tests), and prostheses

g) Diagnostic Tool – e.g. imaging (x-rays, MRI etc.), clinical/in vitro diagnostic tests, sensors etc.

h) Other

43. What is the history of the project?

[Note on sources and prep: This is an important question and we will not have information on this from any other means than the interview]

- How did the project get established?
- Who was involved?
- Is it a follow on project of another research project? (If yes, was it a project you were working on?) (If yes, can you point us towards any documentation of that project?)
- What key risks were identified?
- What was the process for forming your consortium?

Project consortium

44. Please provide an overview of your company / organisation (for academic participants, ask about the department or unit)

[Note on sources and prep: Have a look at the company/university website to know what they do].

Firms (Startups or SMEs) – name, sector, size in number of employees, how long it has been operating (gather this information from the company website prior to the interview)

Research Institutes or Higher Education Institutions - name and type of your organisation (e.g. university, research institute etc.), main academic field and subfield

45. What is your role within the company / organisation (for academic participants, ask about the department or unit)

46. The project has [XY] partners in the application form. Are these the partnering organisations in the project and what are their roles in achieving the project objectives? Has the setup changed since the application? … or are there any informal partners?

[Note on sources and prep: Review the application form].

Funding issues / Motivation for applying

[Note on sources and prep: This section will rely on interviews. Issues of funding are likely to be of more interest for firms than researchers. If clearly of limited interest/ limited ability to comment proceed over more quickly]

47. What was your motivation to apply to Biomedical Catalyst?

- Prompt around: improve collaboration, secure finance, de-risk projects?

48. Which characteristics of the Biomedical Catalyst were the most significant in motivating your application?

- Prioritise responses from high to low

49. What other options had you considered for raising the finance needed to fund the project?

50. To what extent did you actively pursue these options (e.g. applying for finance, applying to other government schemes)? How far were these successful?

51. Why were those other financing options unsuitable / not secured / not sufficient?

Impacts from being rejected as an applicant

52. What effect has being declined for Biomedical Catalyst funding had on you or your organisation?

Prompts around: forced to dissolve / close the business, left academia, have lost research and development staff, increased focus on existing alternative research and development projects, increased focus on new alternative research and development projects

53. Did you increase your focus on alternative research and development projects? [if so] What types of alternative research and development projects?

Progress (Interim outcomes)

Please note that we are interested in progress you have made with this project in spite of not receiving funding from the Biomedical Catalyst.

54. Has the project described in the Biomedical Catalyst application gone ahead?

- If yes, how did your fund it?
- If yes, in what form (unchanged, a later stage, in a different country, at a reduced scale of investment, with reduced scope, n another organisation)?

55. Has the project progressed since your application to the Biomedical Catalyst was declined? [if so] How far has the project progressed in terms of delivering your expected outputs?

- In relation to each of the projects targets, has the project progressed as expected? Are they on track / behind schedule / ahead of schedule? What were the challenges in meeting each of these targets? If the targets were not met, what were the reasons for this? How did you address this? What learnings did you take from this?
- What were the main risks and challenges faced to date? How were they dealt with or mitigated?
- Do you have any supplementary information or resources (such as REF case studies) that you can share with us to support our assessment of impact?

56. What technical progress have you made against TRLs? [note: refer back to grid if appropriate but also record a narrative to be more precise and to pick up other technical progress points – e.g. half way through a Phase II clinical trial]

57. What has driven this progress to date? [Note: prompt to take a systems view of progress and the role of the Biomedical Catalyst in context of other factors, funding etc.]

58. Thinking ahead, do you expect to be able to achieve all your expected outputs in line with the plans you had when you applied? If not, what are the reasons for this?

- Prompt between fulfilment of wider anticipated scientific, medical and commercial objectives

59. How do you plan to take your project forwards now? [Note: discuss around the milestones on the technology roadmap (create commercial entity to develop the product further, sell the intellectual property to another organisation or business, enter into licensing agreements with another organisation or business, produce the product using contracted manufacturers, produce the product using own manufacturing facilities, make the product freely accessible (digital health application or behavioural health))]

60. Was any research aborted or focus changed?

- Why and what impact did this have?

61. What future challenges do you anticipate?

Impacts on the organisation from the project (if project has been taken forwards at all)

[Note on sources and prep: This section will rely on interviews]

62. How have you benefited from participating in the project?

- Forming collaborations, [if so] how many? What was the result?
- Facilitating learning about other organisations and drivers (e.g. skills exchange)
- Producing conference papers academic publications (etc) [if so] which ones?
- Attending events
- Securing finance from other sources
- Boosted reputation of the organisation from having received the award
- The process of how (best to) translate ideas into practice
- Support offered to academics with an interest in seeing their projects move towards a commercial outcome
- Attracting and retaining staff
- Wider heuristic type benefits, effects on scale of research activity, research studentships

Wider effects

[Note on sources and prep: This section will rely on interviews]

63. Has the project resulted in any new IP, products or services or is it anticipated that it will?

64. What are commercial exploitation plans, and the anticipated timescales involved? (Exit strategy)

65. Are there any other wider impacts that you can identify? [e.g. effects within your organisation (e.g. hiring translational managers), community effects (e.g. great confidence), policy impacts etc] or are aware of?

66. [if commercial exploitation plans identified] What impact might this have on the market? For example will it displace existing products?

Note that now I'd like to conclude the interview by focusing on your **opinion on the process that you went through.**

Process issues – Communication

[Note on sources and prep: This section will rely on interviews, and we can expect Innovate UK supported projects to cover this content in greater depth than the MRC (28-31)]

67. Where did you first hear about the Biomedical Catalyst?

68. To what extent were the Biomedical Catalyst marketing and communication activities effective in encouraging you to apply to the programme?

69. How effective were the communication activities and briefing events run by the MRC, Innovate UK and / or KTNs in terms of building your consortium and developing your project?

70. How effective are marketing and communication activities in ensuring understanding of the scope and objectives of the competition, eligibility requirements and competition processes?

- Prompt around both the pre-committee assessment and panel review

Process issues – Application

[Note on sources and prep: This section will rely on interviews]

71. How did you find the application process, not specific to but including, the application form, guidance material, input and advice from the Funding organisation(s)?

72. What, if any, barriers did you face in the application process? And how did you overcome these?

Process issues – Assessment and Review Process

[Note on sources and prep: This section will rely on interviews]

73. What was your experience of the appraisal process?

- Prompt around both the pre-committee assessment and panel review

74. How valuable was the feedback at each and every stage of the assessment review process?

75. Did you feel the time taken to review the application and process the award was appropriate? [Note: if delays identified] What impact did this have?

76. What was the impact of any feedback received on the project?

Process issues – Recommendations

[Note on sources and prep: This section will rely on interviews]

77. Can you identify any improvements that could be made to the processes relating to the communication, application, appraisal and monitoring?

Close / round up

78. Any other comments on the Catalyst? Any areas where you would like to see it develop? Anything which you feel we should have asked? Any questions for us about our work?

Note that we plan to come back and contact them in [when?], if this is acceptable

Biomedical Catalyst Applicant Survey Questionnaire

Introduction and confidentiality

ASK FOR NAMED RESPONDENT

Good <morning, afternoon, evening>. My name is …… from Ipsos MORI, the research organisation, and **we are carrying out a survey on behalf of Innovate UK and the Medical Research Council in relation to the application and appraisal process of the Biomedical Catalyst (which you may also know as the Development Pathway Funding Scheme). We hope that you received an email about the evaluation over the past few days.**

We would therefore like to talk to you or someone at your organisation who is responsible for the BIOMEDICAL CATALYST project [INSERT PROJECT FROM SAMPLE]].
[IF UNSUCCESSFUL READ OUT: We would like to speak to you even if your application was not successful].

S1 (V1) **Can I check that you are the** [IF SAMPLE TYPE = ACADEMIC **principal investigator or coordinator of the,** IF SAMPLE TYPE = FIRM **person responsible for managing or coordinating the] BIOMEDICAL CATALYST project on** [INSERT PROJECT FROM SAMPLE]? INTERVIEWER; IF NO, GET NAME & ASK TO BE TRANSFERRED TO CORRECT PERSON

Yes	1	GO TO SECTION A
No	2	TRANSFER TO CORRECT PERSON

READ OUT FOR UNSUCESSFUL APPLICANTS (THOSE WHO DID NOT HAVE ANY SUCCESSFUL APPLICATIONS)
We would like to talk to you or someone at your organisation who was responsible for your application for funding through the BIOMEDICAL CATALYST that was submitted in [INSERT YEAR FROM SAMPLE FILE]

S1 (V2) [IF SAMPLE TYPE **= Can I check that you are the person responsible for the application for BIOMEDICAL CATALYST funding IF** SAMPLE TYPE = FIRM **Can I check that you are the person responsible for the application for BIOMEDICAL CATALYST funding for** [INSERT COMPANY NAME FROM SAMPLE]? INTERVIEWER; IF NO, GET NAME & ASK TO BE TRANSFERRED TO CORRECT PERSON

Yes	1	GO TO SECTION A
No	2	TRANSFER TO CORRECT PERSON

REASSURANCES TO USE:

- **Your details were obtained from the Innovate UK or the Medical Research Council.**
- All information that you provide will be treated in confidence by Ipsos MORI and anonymised prior to disclosure to Innovate UK (also know as the Technology Strategy Board), and the Medical Research Council as part of an evaluation report into the Biomedical Catalyst programme. Innovate UK and the MRC will only use the evaluation report for their internal purposes, and to publish an aggregated and anonymised summary of the outcomes of the evaluation.
- Are you content to proceed on this basis?
- On average, the survey will take about –25-30 minutes to complete.
- IF ASK FOR FURTHER INFORMATION: You can contact sophie.amili@ipsos.com from Ipsos MORI.

SECTION A: Project Specifics (Baseline) and Motivation to apply

READ OUT. **I would like you to think about the following application to the Biomedical Catalyst, which was titled** [INSERT NAME OF BID FROM SAMPLE].

ASK ALL
QA1 What disease area did your Biomedical Catalyst application focus on?
DO NOT READ OUT. CODE ALL THAT APPLY

Blood	1
Cancer / oncology	2
Cardiovascular / coronary	3
Congenital Disorders	4
	5
Ear/Hearing	6
Eye	7
Infection/ HIV	8
Inflammatory and Immune / Transplants / transplantations	9
Injuries and Accidents / Reconstructive surgery	10
Mental Health / Developmental disabilities (inc. Autism)	11
Metabolic and Endocrine	12
Musculoskeletal	13
Oral and gastrointestinal/Dental	14
Renal and Urogenital	15
Reproductive	16
Respiratory	17
Skin	18
Stroke	19
	20
Other (specify)	21
Don't know/can't remember	22

ASK ALL
QA2 Which of the following <u>best</u> describes the product forming the focus of your application to the Biomedical Catalyst?
READ OUT A TO C. SINGLE CODE ONLY.

A. Therapeutic - e.g. small molecules (drugs), biologics (inc plasma treatment), vaccines, gene therapy, cellular, molecular and regenerative medicine, surgical, radiotherapy, psychological / behavioural, physical (physiotherapy, occupational therapy, speech therapy etc.) and complementary therapy.	1
B. Medical Device – e.g. implants, mobility aids, dressings, medical equipment (excluding those developed for use in diagnosis, inc. diagnostic in vitro tests), and prostheses	2
C. Diagnostic Tool – e.g. imaging (x-rays, MRI etc.), clinical/in vitro diagnostic tests, sensors etc.	3
Other (specify):	4

ASK ALL
QA3 Which of the following best describes the proximity of the project to the market at the point at which you made your application to the Biomedical Catalyst?

PLEASE READ OUT THE RELEVANT LIST OF DEVELOPMENT STAGES BELOW BASED ON CODED RESPONSE TO QA2.

TRL	IF CODE 1 AT QA2. Therapeutics	IF CODE 2 AT QA2. Medical Devices	IF CODE 3 AT QA2. Diagnostic Tools / Digital Health / Other	IF CODE 4 AT QA2 Other
1	**Discovery research**	**Discovery research**	**Discovery research**	**Discovery research**

	with potential application addressing a medical need.	**with potential application addressing a medical need.**	**with potential application addressing a medical need.**	**with potential application addressing a medical need.**
2	**Development of Hypotheses and Experimental Designs:** **Scientific review and generation of research ideas, hypotheses, and experimental designs**	**Development of Hypotheses and Experimental Designs:** **Scientific review and generation of research ideas, hypotheses, and experimental designs**	**Development of Hypotheses and Experimental Designs:** **Scientific review and generation of research ideas, hypotheses, and experimental designs**	**Development of Hypotheses and Experimental Designs:** **Scientific review and generation of research ideas, hypotheses, and experimental designs**
3	**Candidate Identification and Characterisation of Preliminary Candidate(s):** **Initial product development (e.g. compound screening) through to demonstration of proof-of-concept efficacy for candidate therapeutic in vivo.**	**Prototype Identification and Characterisation of Preliminary Prototype:** **Development of a functional prototype through to demonstration of proof-of-concept efficacy for device in vitro and in vivo.**	**Prototype Identification and Characterisation of Preliminary Diagnostic:** **Biomarker quantification studies through to establishing specificity of biomarkers using clinical samples**	**Prototype Identification and Characterisation of Preliminary Product:** **Development of a functional prototype through to demonstration of proof-of-concept in vitro and in vivo or in a test set.**
4	**Candidate Optimisation and Pre-regulatory In Vivo Demonstration of Safety & Efficacy:** **Safety and toxicity of candidate formulations demonstrated in defined laboratory or animal models (non-GLP)**	**Prototype Optimisation and Pre-regulatory In Vivo Demonstration of Safety & Efficacy:** **Efficacy and safety of candidate devices demonstrated in defined laboratory or animal models (non-GLP)**	**Prototype Optimisation and Pre-regulatory Demonstration of Efficacy:** **Retrospective and prospective biomarker qualification studies complete, or analytical parameters acquired and optimised.**	**Prototype Optimisation and pre-regulatory In Vivo Demonstration of Efficacy (& Safety if applicable) :** **Proof-of-concept demonstrated to pre-regulatory standard.**
5	**Advanced Characterisation Candidate & Initiation of GMP Process Development:** **Safety and toxicity established to GLP-standards (in animal models) and manufacturing process established at the required scale.**	**Advanced Characterisation of Prototype and Initiation of GMP Process Development:** **Safety and toxicity established to GLP-standards (in animal models) and manufacturing process established at the required scale.**	**Advanced Characterization of Prototype and Initiation of GMP Process Development:** **Assay suited to target clinical setting has been developed and manufacturing process established at the required scale.**	**Regulatory Characterization of Product and Initiation of Process Development or Manufacturing Process Prior to Clinical Trials**
6	**Phase I or equivalent studies in humans to assess drug safety [to completion]**	**Phase I or equivalent studies in humans to assess device safety [to completion].**	**Usability of tools has been established with end user groups in situ or assay parameters have been established with**	**Clinical Refinement:** **Phase I or equivalent studies in humans to assess device safety [to completion].**

			clinical samples [to completion].	
7	**Phase II or equivalent studies in humans to assess drug efficacy [to completion]**	**Phase II or equivalent studies to assess efficacy and performance [to completion]**	**Small-scale or single site evaluation of whether the application of the diagnostic improves clinical outcomes complete [to completion].**	**Early Clinical Assessment: Phase II or equivalent studies to assess efficacy and performance [to completion]**
8	**Phase III or equivalent studies and Market Authorisation [to completion]**	**Phase III or equivalent studies and Market Authorisation and CE marking complete.**	**Multi-site evaluation of whether the tool improves outcomes complete. Market Authorisation / CE marking achieved.**	**Late Clinical Evaluation/Market Authorisation**

ASK ALL
QA4 In what year did [IF SAMPLE TYPE = ACADEMIC **you or your research team,** IF SAMPLE TYPE = FIRM **your organisation**] **begin working on this project?**

RECORD YEAR

ASK ALL
QA5 Which of the following best describes the initial stimulus for the project?
READ OUT CODES A TO D. MULTICODE OK FOR CODES 1 TO 5

A. Medical needs were not being addressed effectively	1
B. Identification of a basic research discovery that had not been translated into clinical practice	2
C. Identification of potential areas for NHS/national health system efficiency gains	3
D. A response to the availability of funding for work in this area	4
Other (specify)	5
Don't know/can't remember	6

ASK ALL
QA6 At the point at which you applied for Biomedical Catalyst Funding, approximately what level of funding had been invested in the development of the <u>product</u> forming the focus of your application?
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE
ENTER £s.
CANNOT MAKE THE ASSESSMENT

ASK IF QA6 > £0
QA7 What percentage of this investment was funded from ….?
IF SAMPLE TYPE = FIRM SHOW CODES 1, 2, 3, 4, 5, 6 and 8. IF SAMPLE TYPE = ACADEMIC SHOW CODES 6 AND 7 ONLY. CODE ALL THAT APPLY AND CHECK TOTAL SUMS TO 100%
IF NONE IN ANY,WRITE IN ZERO (0).

A. Debt or loans	1 ENTER %
B. Equity finance – venture capitalists	2 ENTER %
C. Equity finance – business angels	3 ENTER %
D. Corporate Venture Funds	4 ENTER %
E. Profits / company's own funds	5 ENTER %
F. Grants from Research Councils, Public Sector or Third Sector (inc. EU, Regional Growth Fund (RGF), AMSCI)	6 ENTER %
G. Internal funding/money/grants from the University	7 ENTER %

H. Friends or Family	8 ENTER %
Other (specify):	9 ENTER %
Don't know/can't remember	

QA9 At the point at which you applied for Biomedical Catalyst funding, approximately how much funding had you raised in the form of private equity investment and/or research grants in total? Please exclude Biomedical Catalyst funding here, or any investment that was contingent on an award from the Biomedical Catalyst.

ENTER £s.
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE
CANNOT MAKE THE ASSESSMENT

ASK ALL
QA10 At the point of application had you collaborated with either of the following types of organisations to advance this project?
READ OUT CODE 1 AND 2. MULTICODE OK FOR CODES 1 AND 2

A. Academic partners	1
B. Industrial partners READ OUT – **please exclude any Contract Research Organisations or Contract Manufacturing Organisations you may have commissioned.**	2
No collaborators	4
Don't know/ Can't remember	5

ASK ALL
QA11 At the point of application had you registered any intellectual property relating to this project (also known as background IP)?
SINGLE CODE ONLY.

Yes	1
No	2
Don't know / Can't Remember	3

ASK IF CODE 1 AT QA11 AND NOT CODE 4 AT QA10
QA12 Was the ownership of this intellectual property shared with collaborators?
READ OUT SCALE. SINGLE CODE ONLY.

None	1
Some	2
Most	3
All	4
Don't know / Can't Remember	5

ASK IF CODE 1 AT QA11
QA13 At the point of application did you have the intellectual property for this project valued?
SINGLE CODE ONLY.

Yes	1
No	2
Don't know / Can't Remember	3

ASK IF CODE 1 AT QA13
QA14 What was the approximate value of this intellectual property at the point of application?

ENTER £s
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE

CANNOT MAKE THE ASSESSMENT

SECTION B : Broader activity of the firm / academic at the point of the application

READ OUT TO ALL: **We would like to ask a few questions about your activities more generally at the point you made your application for Biomedical Catalyst funding.**

ASK ALL
QB1 Prior to your application to the Biomedical Catalyst how many ongoing R&D projects [IF SAMPLE TYPE = ACADEMIC **were you,** IF SAMPLE TYPE = FIRM, **was your organisation] involved in, including the one that formed the focus of Biomedical Catalyst application?**

RECORD NUMBER

ASK IF SAMPLE TYPE = ACADEMIC AND QB1 > 1
QB2 How many of these projects could be considered to be translational research?
NOTE TO THE INTERVIEWER: **Translational research is where basic scientific concepts or knowledge is developed so that ideas can be practically applied or used.**

RECORD NUMBER

ASK IF QB1 > 1
QB3 How many of these projects involved an external academic partner, by this I mean a partner outside your institution?
RECORD NUMBER

ASK IF QB1 > 1
QB4 How many of these projects involved an external commercial or industrial partner?
READ OUT – **Please exclude any Contract Research Organisations or Contract Manufacturing Organisations you may have commissioned.**
RECORD NUMBER

ASK ALL
QB5a In the year before your application how much money did [IF SAMPLE TYPE = ACADEMIC **your team raise and deliver in research income?** IF SAMPLE = FIRM **your company spend on research and development activities] in the life sciences area?**]
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE

RECORD NUMBER £
CANNOT MAKE THE ASSESSMENT

ASK IF AMOUNT PROVIDED AT QB5A INCLUDING ZERO BUT NOT INCLUDING DK
QB5b… And to which year does that figure relate? Is that a UK tax year, calendar year or academic year?

DO NOT READ OUT. SINGLE CODE ONLY.

2010 Calendar Year	1
2011 Calendar Year	2
2012 Calendar Year	3
2013 Calendar Year	4
2014 Calendar Year	5
2010/11 UK Tax or Academic Year	6
2011/12 UK Tax or Academic Year	7
2012/13 UK Tax or Academic Year	8
2013/14 UK Tax or Academic Year	9
2014/15 UK Tax or Academic Year	10

ASK ALL
QB6 Prior to the point of application, [IF SAMPLE = ACADEMIC, **what was the size of your research group,** IF SAMPLE = FIRM, **how many of your colleagues working in your company were involved in R&D activities?]**
INTERVIEWER NOTE: IF THIS HAS FLUCTUATED, THEN PLEASE PROVIDE YOUR BEST ESTIMATE OF THE AVERAGE.
- INCLUDE TEMPORARIES/CASUALS, BUT NOT AGENCY STAFF
- EXCLUDE SELF-EMPLOYED
- EXCLUDE OWNERS/PARTNERS, BUT OTHER DIRECTORS COUNT AS EMPLOYEES

RECORD NUMBER

ASK IF SAMPLE TYPE = FIRMS
QB6b Prior to the point of application how many of workers did your company employ in total?
INTERVIEWER NOTE: IF THIS HAS FLUCTUATED, THEN PLEASE PROVIDE YOUR BEST ESTIMATE OF THE AVERAGE.
- INCLUDE TEMPORARIES/CASUALS, BUT NOT AGENCY STAFF
- EXCLUDE SELF-EMPLOYED
- EXCLUDE OWNERS/PARTNERS, BUT OTHER DIRECTORS COUNT AS EMPLOYEES

RECORD NUMBER

ASK IF SAMPLE TYPE = FIRMS
QB7A Prior to the point of application, what were your annual sales?
RECORD NUMBER £s

ASK IF AMOUNT PROVIDED AT QB7A INCLUDING ZERO BUT NOT INCLUDING DK
QB7B… And to which year does that figure relate? Is that a UK tax year, calendar year or academic year?

DO NOT READ OUT. SINGLE CODE ONLY.

2010 Calendar Year	1
2011 Calendar Year	2
2012 Calendar Year	3
2013 Calendar Year	4
2014 Calendar Year	5
2010/11 UK Tax or Academic Year	6
2011/12 UK Tax or Academic Year	7
2012/13 UK Tax or Academic Year	8
2013/14 UK Tax or Academic Year	9
2014/15 UK Tax or Academic Year	10

ASK IF SAMPLE TYPE = FIRMS
QB8 When was your company established?
RECORD YEAR

SECTION C : Motivations for applying to the Biomedical Catalyst

ASK ALL
QC1 How did you / your organisation first hear about the Biomedical Catalyst?
DO NOT READ OUT. SINGLE CODE ONLY

Knowledge Transfer Network (KTN)	1
University Research Office	2
Innovate UK website	3
MRC Website	4
Industry Body / Trade association	5
Innovate UK Event	6
MRC event or visit	7
Innovate UK/ MRC Website	8
Accountant or Consultant specialising in Biomedical Catalyst bids	9
Bank Account Manager	10
Business Support Helpline / Business Link Helpline	11
Contact with BIS Local	12
Conference / Exhibition / Trade Event / Workshops	13
Local Business Groups (e.g. Local Enterprise Partnerships, Chambers of Commerce)	14
Social Media (e.g. Twitter)	15
Local council / government	16
Was approached by a member of the supply chain	17
Colleague or Collaborator	18
Academic Partners/ Consultants	19
Word of mouth	20
Internal advertising in organisation	21
Email flyers / alerts	22
Other (Specify)	23
Don't know/can't remember	24

ASK ALL
QC2 Why did you need to apply to Biomedical Catalyst funding in order to take this project forward? ? PROBE FULLY.
Why else? DO NOT READ OUT. CODE ALL THAT APPLY.

To receive feedback on the design of the project	1
To increase the scope or quality of the project	2
To reduce level of risk associated with the project	3
Could not obtain sufficient finance from other sources / only funding available	4
Could not lever in private funding without Biomedical Catalyst funds / leverage for fundraising	5
Could not secure the involvement of key partners without subsidies	6
Project would not deliver sufficiently high rate of return	7
To delay the need to seek private investment	8
Most suitable source of funding - substantial levels of funding and non-dilutive funding as opposed to equity funding	9
Best fit of funding	10
Other (specify)	11
Don't know/can't remember	12

ASK ALL
QC3 Had you sought any alternative sources of funding for the project? SINGLE CODE ONLY

Yes	1
No	2
Don't know/Can't remember	3

ASK IF CODE 1 AT QC3
QC4a Which other sources had you sought?
DO NOT READ OUT. MULTICODE OK CODES 1 TO 17

Internal funding from Board or Parent Company / other internal funding (i.e. non-external)	1
Equity finance – Venture Capitalists	2

Equity finance – Business Angels	3
Biotechnology and Biological Sciences Research Council (BBSRC)	4
Engineering and Physical Sciences Research Council (EPSRC)	5
Economic and Social Research Council (ESCR)	6
Other Medical Research Council programmes (i.e. not Biomedical Catalyst or DPFS) **INTERVIEWER NOTE:** Do not record 'DPFS' or the 'Development Pathway Funding Scheme' here if mentioned by respondent as it is part of Biomedical Catalyst funding.	7
Chief Scientist Office, Scottish Government Health and Social Care Directorates (Scotland)	8
HSC R&D Division of the Public Health Agency (Northern Ireland)	9
Department of Health (DoH)	10
National Institute for Social Care and Health Research (NIHR)	11
Arthritis Research UK	12
British Heart Foundation	13
Cancer Research UK	14
Welcome Trust (Welcome)	15
NHS Trusts	16
EU funding	17
Other (specify)	18
Don't know / Can't Remember	19

ASK IF NOT CODE 1, 2 OR 3 AT QC4a

QC4b Can I check have you sought … READ OUT CODES 1 TO 3 FOR FIRMS; READ OUT CODES 2 OR 3 FOR ACADEMICS IF NOT MENTIONED AT QC4a**?** CODE ALL THAT APPLY

Internal funding from Board or Parent Company	1
Equity finance from Venture Capitalists	2
Equity finance from Business Angels	3
None of these	4
Don't know/can't remember	5

ASK IF CODES 1 TO 3 SELECTED AT QC4a OR CODES 1 TO 3 SELECTED AT QC4b

QC5 Why were private sector finance options insufficient or inappropriate to fund the project? DO NOT READ OUT. CODE ALL THAT APPLY. PROBE FULLY

Finance rejected due to too much risk for creditors or investors	1
Finance rejected due to insufficient assets to act as security on lending	2
Terms of finance (e.g. interest rates, security required or covenants built in) were unattractive	3
Monitoring requirements of investors were too intensive	4
Finance offered would not cover the full cost of the project / difficult to raise required amount	5
Funding not available for early stage conceptual research	6
Grant funding is preferable along with private sector funding	7
Other (specify)	8
Don't know/Can't remember	9

SECTION D: Application Process

READ OUT TO ALL: These next questions focus on the process of applying for Biomedical Catalyst funding, covering your experiences of preparing the application.
In answering these questions, I would like you to think about the following application to the Biomedical Catalyst, which is [INSERT NAME OF APPLICATION FROM SAMPLE].

ASK ALL

QD1 **Can you tell me if you were personally involved in preparing the Biomedical Catalyst application?** SINGLE CODE ONLY.

Yes	1
No	2
Don't know	3

ASK IF CODE1 AT QD1

QD2 **Before submitting an application to Biomedical Catalyst, did you and your colleagues?**
READ OUT a) TO f). SINGLE CODE ONLY FOR EACH

	Yes	No	Don't know
a) Access on-line information and guidance describing the Biomedical Catalyst application process	1	2	3
b) Contact Innovate UK or MRC for guidance	1	2	3
c) Attend an application briefing event for Biomedical Catalyst	1	2	3
d) Receive one to one assistance from the Knowledge Transfer Network	1	2	3
e) Receive university support, e.g. Research Office or Technology Transfer Office	1	2	3
f) Collaborate with an industrial or academic partner in the preparation of the application	1	2	3

ASK IF ONE OR MORE RESPONSE CODED YES AT QD2

QD3 Thinking about this information you used before making your application, to what extent do you agree or disagree that it clearly explained:
READ OUT a) to f). RANDOMISE ORDER OF STATEMENTS. READ OUT SCALE. SINGLE CODE ONLY FOR EACH.

	Strongly agree	**Tend to agree**	**Neither agree nor disagree**	**Tend to disagree**	**Strongly disagree**	Don't know/ can't remember
a) The objectives of Biomedical Catalyst	1	2	3	4	5	6
b) Overall application process	1	2	3	4	5	6
c) Criteria against which applications would be assessed	1	2	3	4	5	6
FIRMS ONLY **d) Time required for due diligence before authorisation for a project to kick off**	1	2	3	4	5	6
e) Monitoring requirements for successful applications	1	2	3	4	5	6
f) Payment terms of the grants	1	2	3	4	5	6

ASK ALL INVOLVED IN APPLICATION PROCESS (CODE 1) AT QD1

The following questions relate to the time spent on the Biomedical Catalyst application. We will first ask about the amount of time you spent personally on the bid, followed by the time spent by colleagues in your organisation, and then if external organisations were consulted.

QD4 How much time did you <u>personally</u> spend on your application to the Biomedical Catalyst [IF APPLICATION TYPE NOT = FEASIBILITY**, separating the [**IF SAMPLE TYPE = ACADEMIC**, outline bid stage,** IF SAMPLE TYPE = FIRMS**, EOI stage] from the full application]? I would like you to include the time that you spent at the briefing events, discussing the application internally and with partners, completing the application form itself and any time spent on research relating to the Biomedical Catalyst bid.**

Please just think about the time spent up until you submitted your bid to the Biomedical Catalyst; Firstly for READ OUT a)

And now for READ OUT b)

	ASK IF APPLICATION TYPE NOT FEASIBILITY **a) your EOI/ Outline application**	ASK ALL **b) your full stage application**
ENTER NUMBER (HOURS)	1	1
OR	2	2
ENTER NUMBER (DAYS)	3	3
Don't know	4	4
Refused	5	5

ASK ALL INVOLVED IN APPLICATION PROCESS (CODE 1) AT QD1
QD5 How much time did your colleagues from your organisation spend on your bid for the Biomedical Catalyst [IF APPLICATION TYPE NOT = FEASIBILITY, **separating the** [IF SAMPLE TYPE = ACADEMIC, **outline bid stage**, IF SAMPLE TYPE = FIRMS, **EOI stage**] **from the full application**]**? Again, I would like you to include the time your internal colleagues spent at the briefing events, discussing the application, completing the application form itself and any time spent on research relating to the Biomedical Catalyst bid. Do not include the time of third parties, your partners in the project, or other external organisations.**

Please just think about the time spent by colleagues in your organisation up until you submitted your application to the Biomedical Catalyst; firstly for READ OUT a)
And now for READ OUT b)

	ASK IF APPLICATION TYPE NOT FEASIBILITY **a) your EOI/ Outline application**	ASK ALL **b) your full stage application**
ENTER NUMBER (HOURS)	1	1
OR	2	2
ENTER NUMBER (DAYS)	3	3
Don't know	4	4
Refused	5	5

ASK ALL
QD6 PROBE FULLY. **Which third parties or external organisations did you or your colleagues consult to assist you with the preparation of your Biomedical Catalyst bid?** PROBE FULY. **What other types of organisations did you or your colleagues consult?** DO NOT READ OUT. MULTICODE OK CODES 1 TO 14

A Bank	1
Regulatory bodies	2
Consultants	3
Enterprise agency/business support services	4
Legal Advisors	5
Local Enterprise Partnership	6

Trade association	7
Chamber of Commerce	8
Academics external to your Organisation	9
Industrial partners	10
Contract Research Organization / Contract Manufacturing Organisation	11
The Knowledge Transfer Network	12
Innovate UK Business Support Group	13
Another organisation (Specify)	14
No – did not consult any third parties or external organisations	15
Don't know/Can't Remember	16

ASK IF CODE 1 AT QD1

QD7 **Thinking about completing the application, how far do you agree or disagree that the process of applying led you to …** READ OUT a) TO c). RANDOMISE ORDER OF STATEMENTS. READ OUT SCALE. REVERSE SCALE. SINGLE CODE ONLY FOR EACH.

	Strongly agree	**Tend to agree**	**Neither agree nor disagree**	**Tend to disagree**	**Strongly disagree**	Don't know/can't remember
a) Give additional scrutiny to the strength of the scientific rationale for the project	1	2	3	4	5	6
b) Improve understanding of regulatory requirements	1	2	3	4	5	6
c) Improve project or development planning – e.g. in clinical trials	1	2	3	4	5	6
d) Strengthen plans for future exploitation (INTERVIEWER NOTE: THIS MIGHT BE COMMERCIAL EXPLOITATION)	1	2	3	4	5	6

ASK IF CODE 1 AT QD2F

QD8 **Thinking about applying in collaboration with academic and/or industrial partners, how far do you agree or disagree that the process of applying in collaboration encouraged you to …?** READ OUT a) TO d). RANDOMISE ORDER OF STATEMENTS. READ OUT SCALE. REVERSE SCALE. SINGLE CODE ONLY FOR EACH.

	Strongly agree	**Tend to agree**	**Neither agree nor disagree**	**Tend to disagree**	**Strongly disagree**	Don't know/can't remember
a) Give additional scrutiny to the strength of the scientific rationale for the project	1	2	3	4	5	6
b) Improve understanding of regulatory requirements	1	2	3	4	5	6
c) Improve project or	1	2	3	4	5	6

development planning – e.g. in clinical trials						
d) Strengthen plans for future exploitation	1	2	3	4	5	6

ASK IF APPLICATION TYPE NOT = FEASIBILITY AND IF CODE 1 AT QD1

QD9 Thinking about the formal feedback you received after the <u>EOI/ outline application</u>, how far do you agree or disagree this led to any changes in the design of your project in terms of … READ OUT a) TO d). RANDOMISE ORDER OF STATEMENTS. READ OUT SCALE. REVERSE SCALE. SINGLE CODE ONLY FOR EACH.

	Strongly agree	**Tend to agree**	**Neither agree nor disagree**	**Tend to disagree**	**Strongly disagree**	Don't know/ can't remember	Not applicable: did not receive feedback
a) Adjustments to the objectives of the research project	1	2	3	4	5	6	7
b) Design or planning of project- e.g. of clinical trials	1	2	3	4	5	6	7
c) Adjustments to the costs associated with the project	1	2	3	4	5	6	7
d) Improvements to the exploitation plan	1	2	3	4	5	6	7

ASK IF ATTENDED A MAC PANEL INTERVIEW IN THE SAMPLE

QD10 How much time did you personally spend preparing for the MAC interview panel? I would like you to include the time that you spent discussing and planning the presentation internally and with partners, writing the presentation itself and any time spent on research relating specifically to the MAC interview. Please just think about the time spent on preparing for the MAC interview.

IF NOT INVOLVED FOR PREPARING FOR THE MAC INTERVIEW CODE APPROPRIATELY

ENTER NUMBER (HOURS)	1
OR	2
ENTER NUMBER (DAYS)	3
Don't know/can't remember	4
I was not involved in preparing for the MAC interview	5

ASK IF ATTENDED A MAC PANEL INTERVIEW IN THE SAMPLE AND INVOLVED IN PREPARING THE INTERVIEW AT QD10

QD11 Thinking about while you were preparing for the MAC interview, to what extent do you agree or disagree, that …? READ OUT a) TO c)? READ OUT SCALE. SINGLE CODE ONLY FOR EACH

	Strongly agree	**Tend to agree**	**Neither agree nor disagree**	**Tend to disagree**	**Strongly disagree**	Don't know/can't remember
a) We received clear instructions on how to prepare for the panel	1	2	3	4	5	6
b) We received sufficient notification so that we had time to prepare	1	2	3	4	5	6
c) The questions we	1	2	3	4	5	6

received from the MAC panel were relevant	

ASK ALL
QD12 Thinking about your overall experience of the Biomedical Catalyst application process, how satisfied or dissatisfied were you with… READ OUT a) AND b)? READ OUT SCALE. SINGLE CODE ONLY FOR EACH

	Very Satisfied	Fairly Satisfied	Neither satisfied nor dissatisfied	Fairly Dissatisfied	Very dissatisfied	Don't know /can't remember
a) The time taken from initial application to decision	1	2	3	4	5	6
b) The clarity with which the reasons for the funding decision were communicated	1	2	3	4	5	6

ASK ALL
QD13 Which of the following issues, if any, did you encounter as a result of the time it took between your initial application and the outcome of your application?
READ OUT a) TO d). CODE ALL THAT APPLY.

	Yes	No	Don't know/can't remember
a) Delaying activity on the project	1	1	1
b) Securing private sources of matched funding for the project	2	2	2
c) Retaining any private matched funding already secured for the project	3	3	3
d) Loss of staff working on the project	4	4	5

SECTION E: Effects on project viability (Successful and Unsuccessful Applicants)

ASK UNSUCCESSFUL APPLICANTS ONLY
QE1a What effect has being declined for Biomedical Catalyst funding had on you or your organisation? DO NOT READ OUT. MULTICODE OK FOR CODES 1 TO 6

Forced to dissolve / close the business	1
Left academia	2
Have lost research and development staff	3
Increased focus on existing alternative research and development projects	4
Increased focus on new alternative research and development projects	5
Other (specify):	6
No impact	7
Don't know/can't remember	8

ASK IF NOT MENTIONED CODES 4 OR 5 AT QE1a
QE1b Did you increase your focus on alternative research and development projects? SINGLE CODE ONLY

Yes	1
No	2
Don't know/can't remember	3

ASK IF MENTION ALTERNATIVE R&D (CODES 4 OR 5) AT QE1a OR INCREASED FOCUS (CODE 1) AT QE1b
QE1c What types of alternative research and development projects?

DO NOT READ OUT. PROBE FULLY. CODE ALL THAT APPLY

Basic health or disease research (as opposed to translation research)	1
Therapeutics	2
Medical devices	3
Diagnostic tools	4
R&D projects outside of the biomedical sector (inc. non UK-based collaboration)	5
Other (specify):	6
Don't know/can't remember	7

ASK ALL

QE2 [IF SUCCESSFUL **Would the,** IF UNSUCCESSFUL **Has the] project** [IF SUCCESSFUL **have] proceeded in any form** [IF SUCCESSFUL**, had your application to the Biomedical Catalyst been unsuccessful?,** IF UNSUCCESSFUL**, since your application to the Biomedical Catalyst was rejected?]**SINGLE CODE ONLY.

Yes	1
No	2
Don't know/can't remember	3

ASK IF CODE 1 AT QE2

QE3 [IF SUCCESSFUL **If your project would have gone ahead in some form had you been unsuccessful, would it have** IF UNSUCCESSFUL **Has the project] gone ahead…**
READ OUT a) TO f). MULTICODE OK FOR b) TO f)

a) Unchanged	1
b) At a later stage	2
c) In a different country	3
d) At a reduced scale of investment	4
e) With reduced scope (e.g. met less objectives)	5
f) In another organisation	6
Don't know/Can't remember	7

ASK IF CODE 2 AT QE3

QE4 **What** [IF SUCCESSFUL, **would have been the anticipated changes in timescale,** IF UNSUCCESSFUL **what were the changes in project timescales?**
PROMPT WITH BANDS. SINGLE CODE ONLY

Delay of up to 1 year	1
Delay of about 1-2 years	2
Delay of about 3-5 years	3
Delay of more than 5 years	4
Don't know/Can't remember	

SECTION F: Project Delivery

ASK ALL

QF1 **What is the current status of the project as defined in your application for Biomedical Catalyst funding, regardless of whether the project was funded through the programme or not?**
READ OUT OPTIONS. SINGLE CODE.

A. The project has been postponed	1
B. The project is in its initial phases (DO NOT READ OUT IF UNSUCCESSFUL AND CODE 2 AT QE2)	2
C. The project is approximately mid-way through delivery (DO NOT READ OUT IF UNSUCCESSFUL AND CODE 2 AT QE2)	3
D. The project is in its later phases but not yet completed (DO NOT READ OUT IF UNSUCCESSFUL AND CODE 2 AT QE2)	4
E. The project is complete (DO NOT READ OUT IF UNSUCCESSFUL AND CODE 2 AT QE2)	5
F. The project has been terminated early	6
Don't know/can't remember	7

ASK IF CODE 6 AT QF1

QF2 **Why has the project been terminated early?**
DO NOT READ OUT. CODE ALL THAT APPLY

Difficulties securing finance	1
Failure to meet key pre-clinical milestones	2
Failure to meet key clinical milestones	3
Competitor has launched a comparable/better product	4
Concerns over costs of further research and development	5
Concerns over potential returns/revenue (including likely adoption by NHS/CCGs and other national health systems)	6
Other (specify)	7
Don't know/can't remember	8

ASK IF CODE 2 TO 5 AT QF1

QF3a **Thinking about the results of the project to date, do they support, or not support the initial scientific hypotheses, or is it too early to say?**

Support the initial scientific hypotheses	1
Not support the initial scientific hypotheses	2
Too early to say	3
Don't know/can't remember	4

ASK IF CODE 2 TO 5 AT QF1

QF3b **And do the results of the project to date …** READ OUT A TO E**. READ OUT ANSWER OPTIONS.** SINGLE CODE ONLY FOR EACH

	Yes	No	Or is it too early to say?
A. Raise concerns relating to the safety of the product under development	1	2	3
B. Raise concerns relating to the efficacy of the product under development	1	2	3
C. Raise concerns about future development costs	1	2	3
D. Raise concerns about likely future revenues or impact	1	2	3
E. Raise concerns about the feasibility of manufacturing the product under development	1	2	3

ASK IF CODE 2 TO 5 AT QF1

QF4 **Which of the following statements describes the current proximity of the product under development to market?**

DO NOT READ OUT THE UNDERLINED TEXT UNLESS NEEDING TO PROMPT.

DO NOT DISPLAY CODES AT EARLY STAGES DEVELOPMENT BASED ON RESPONSE TO QA3. I.E. IF CODE 3 AT QA3, DISPLAY CODES 3 TO 8

TRL	IF CODE 1 AT QA2. Therapeutics	IF CODE 2 AT QA2. Medical Devices	IF CODE 3 AT QA2. Diagnostic Tools / Digital Health / Other	IF CODE 4 AT QA2 Other
1	**Discovery research with potential application addressing a medical need.**	**Discovery research with potential application addressing a medical need.**	**Discovery research with potential application addressing a medical need.**	**Discovery research with potential application addressing a medical need.**
2	**Development of Hypotheses and Experimental Designs: Scientific review and generation of research ideas, hypotheses, and experimental designs**	**Development of Hypotheses and Experimental Designs: Scientific review and generation of research ideas, hypotheses, and experimental designs**	**Development of Hypotheses and Experimental Designs: Scientific review and generation of research ideas, hypotheses, and experimental designs**	**Development of Hypotheses and Experimental Designs: Scientific review and generation of research ideas, hypotheses, and experimental designs**
3	**Candidate Identification and Characterisation of Preliminary Candidate(s): Initial product development (e.g. compound screening) through to demonstration of proof-of-concept efficacy for candidate therapeutic in vivo.**	**Prototype Identification and Characterisation of Preliminary Prototype: Development of a functional prototype through to demonstration of proof-of-concept efficacy for device in vitro and in vivo.**	**Prototype Identification and Characterisation of Preliminary Diagnostic: Biomarker quantification studies through to establishing specificity of biomarkers using clinical samples**	**Prototype Identification and Characterisation of Preliminary Product: Development of a functional prototype through to demonstration of proof-of-concept in vitro and in vivo or in a test set.**

4	**Candidate Optimisation and Pre-regulatory In Vivo Demonstration of Safety & Efficacy:** Safety and toxicity of candidate formulations demonstrated in defined laboratory or animal models (non-GLP)	**Prototype Optimisation and Pre-regulatory In Vivo Demonstration of Safety & Efficacy:** Efficacy and safety of candidate devices demonstrated in defined laboratory or animal models (non-GLP)	**Prototype Optimisation and Pre-regulatory Demonstration of Efficacy:** Retrospective and prospective biomarker qualification studies complete, or analytical parameters acquired and optimised.	**Prototype Optimisation and pre-regulatory In Vivo Demonstration of Efficacy (& Safety if applicable) :** Proof-of-concept demonstrated to pre-regulatory standard.
5	**Advanced Characterisation Candidate & Initiation of GMP Process Development:** Safety and toxicity established to GLP-standards (in animal models) and manufacturing process established at the required scale.	**Advanced Characterisation of Prototype and Initiation of GMP Process Development:** Safety and toxicity established to GLP-standards (in animal models) and manufacturing process established at the required scale.	**Advanced Characterization of Prototype and Initiation of GMP Process Development:** Assay suited to target clinical setting has been developed and manufacturing process established at the required scale.	**Regulatory Characterization of Product and Initiation of Process Development or Manufacturing Process Prior to Clinical Trials**
6	Phase I or equivalent studies in humans to assess drug safety [to completion]	Phase I or equivalent studies in humans to assess device safety [to completion].	Usability of tools has been established with end user groups in situ or assay parameters have been established with clinical samples [to completion].	Clinical Refinement: Phase I or equivalent studies in humans to assess device safety [to completion].
7	Phase II or equivalent studies in humans to assess drug efficacy [to completion]	Phase II or equivalent studies to assess efficacy and performance [to completion]	Small-scale or single site evaluation of whether the application of the diagnostic improves clinical outcomes complete [to completion].	Early Clinical Assessment: Phase II or equivalent studies to assess efficacy and performance [to completion]
8	Phase III or equivalent studies and Market Authorisation [to completion]	Phase III or equivalent studies and Market Authorisation and CE marking complete.	Multi-site evaluation of whether the tool improves outcomes complete. Market Authorisation / CE marking achieved.	Late Clinical Evaluation/Market Authorisation

ASK IF CODE 2 TO 5 AT QF1

QF5 Have you used Contract Manufacturing Organisations or Contract Research Organisations in the delivery of this project? SINGLE CODE ONLY

Yes	1
No	2
Don't know/can't remember	3

ASK IF CODE 1 AT QF5

QF6 What percentage of project development costs are being spent with Contract Manufacturing Organisation or Contract Research Organisations located in:

READ OUT A TO C. CODE ALL THAT APPLY AND CHECK TOTALS 100%

A. The UK	1 ENTER %
B. The rest of the EU	2 ENTER %
C. The rest of the world	3 ENTER %
Don't know/can't remember	4 ENTER %

SECTION G: Broader Impact (Successful and Unsuccessful Applicants in Rounds 1 to 4 only)

READ OUT IF ROUNDS 1-4 ONLY: **The following questions relate to the broader impacts of the project <**INSERT PROJECT NAME> **which you applied for the BIOMEDICAL CATALYST support.**

ASK IF SAMPLE TYPE = ACADEMIC AND CODE 1 TO 5 AT QF1 AND ROUNDS 1 TO 4 ONLY

QG1 Have you or your academic institution created a commercial entity to exploit the product under development? SINGLE CODE ONLY

Yes	1
No	2
Don't know/can't remember	3

ASK IF CODE 1 TO 5 AT QF1 AND ROUNDS 1 TO 4 ONLY

QG2 What level of funding has been invested in total in the development of the product forming the focus of your application to date?

INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE

ENTER £s.

CANNOT MAKE THE ASSESSMENT

ASK IF CODE 1 TO 5 AT QF1AND ROUNDS 1 TO 4 ONLY

QG3a Have you been able to raise any additional funding for this project since you applied to the Biomedical Catalyst [FOR SUCCESSFUL = i**ncluding any other funding contingent on that award, but excluding the Biomedical Catalyst grant]?** SINGLE CODE ONLY

Yes	1
No	2
Don't know/can't remember	3

ASK IF CODE 1 AT QG3a

QG3b What effect do you believe being a Biomedical Catalyst award recipient has had on your ability to obtain the additional finance? READ OUT SCALE. SINGLE CODE ONLY

Made it much easier	1
Made it a little easier	2

Made no difference	3
Made it a little more difficult	4
Made it much more difficult	5
Don't know/can't remember	

ASK IF CODE 1 QG3a
QG4 How much funding has been raised?
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE

RECORD NUMBER £s

CANNOT MAKE THE ASSESSMENT

ASK IF CODE 1 QG3a
QG5 What percentage of this new investment was funded from ….?
CODE ALL THAT APPLY AND CHECK TOTAL SUMS TO 100%
IF NONE IN ANY, WRITE IN ZERO (0).

A. Debt or loans	1 ENTER %
B. Equity finance – venture capitalists	2 ENTER %
C. Equity finance – business angels	3 ENTER %
D. Corportate Venture Funds	4 ENTER %
E. Equity finance – IPO or forms of spin-out	5 ENTER %
F. Profits / company's own funds	6 ENTER %
G. Grants from Research Councils, Public Sector or Third Sector (inc. EU, Regional Growth Fund (RGF), AMSCI)	7 ENTER %
H. Internal funding / money/ grants from the University	8 ENTER %
I. Friends or Family	9 ENTER %
Other (specify):	10 ENTER %

ASK IF CODE 1 TO 5 AT QF1 AND ROUNDS 1 TO 4 ONLY
QG7 Has the project resulted in any new collaboration with external organisations?
SINGLE CODE ONLY

Yes	1
No	2
Don't know/can't remember	3

ASK IF CODE 1 AT QG7
QG8 How many of these new collaborations are with…?
READ OUT A AND B. WRITE IN NUMBER

A. Academic partners	ENTER NUMBER
B. Commercial partners	ENTER NUMBER
Don't know/can't remember	

ASK IF CODE 1 AT QG7
QG9 Have these collaborations had a positive impact on [IF SAMPLE TYPE = ACADEMIC, **you or your team's,** IF SAMPLE TYPE = FIRM, **your organisation's] …** READ OUT A TO E**?**
SINGLE CODE ONLY FOR EACH

	Yes	No	Don't know/can't remember
A. Understanding of the basic scientific principles underlying the project	1	2	3
B. Understanding of patient needs	1	2	3
C. Skills in planning and developing projects, e.g. clinical trials	1	2	3
D. Understanding of regulatory requirements	1	2	3
E. Commercial planning skills	1	2	3

ASK IF CODE 2 TO 5 AT QF1 AND ROUNDS 1 TO 4 ONLY
QG10 Has the project resulted in the registration of new intellectual property (also known as foreground IP)?
SINGLE CODE ONLY

Yes	1
No	2
Don't know/can't remember	3

ASK IF CODE 1 AT QG10
QG11 Is ownership of intellectual property relating to this project shared with collaborators?
SINGLE CODE ONLY.

Yes	1
No	2
Don't know / Can't Remember	5

ASK IF CODE 1 AT QG10 OR CODE 1 AT QA11
QG12 Have you now had the intellectual property for this project valued?
SINGLE CODE ONLY.

Yes	1
No	2
Don't know / Can't Remember	3

ASK IF CODE 1 AT QG12
QG13 What is the approximate value of the intellectual property?
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE

ENTER £s

ASK IF CODE 1 AT QG10 OR CODE 1 AT QA11 AND ROUNDS 1 TO 4 ONLY
QG14 Have any intangible assets or intellectual property associated with the project been sold (excluding licensing)?
READ OUT. MULTICODE 1) AND 2) ONLY

Yes – the intellectual property / patent	1
Yes – the business or spin-out	2
No	3
Don't know/can't remember	4

ASK IF CODE 1 OR 2 AT QG14
QG15 Was the buyer based in the UK, EU or elsewhere in the Rest of the World?
SINGLE CODE ONLY

UK	1
EU	2
Rest of World	3
Don't know/can't remember	4

ASK IF CODE 2 TO 5 AT QF1AND ROUNDS 1 TO 4 ONLY
QG16 Has the project resulted in any of the following?
READ OUT A TO D. SINGLE CODE ONLY FOR EACH

	Yes	No	Don't know
A. Conference papers	1	2	3
B. Results presented at conference or events	1	2	3
C. Article submissions to academic journals	1	2	3
D. Articles published in academic journals	1	2	3
Don't know/can't remember	1	2	3

ASK IF CODE 2 TO 5 AT QF1 AND ROUNDS 1 TO 4 ONLY
QG17 Have you entered any licensing agreements relating to the Biomedical Catalyst project?
DO NOT READ OUT. SINGLE CODE ONLY

Yes	1
No	2
Don't know/can't remember	3

ASK IF CODE 1 AT QG17
QG18 What is the approximate value of the licensing agreements?
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE

ENTER £s

SECTION H: Wider Measures (Rounds 1 to 4 only)

ASK ALL IF ROUNDS 1 TO 4 ONLY
QH1a How many ongoing research and development projects [IF SAMPLE TYPE = ACADEMIC **are you,** IF SAMPLE TYPE = FIRM **is your organisation] currently involved with, including any projects supported by the BIOMEDICAL CATALYST?**

RECORD NUMBER

ASK IF SAMPLE TYPE = ACADEMIC AND ROUNDS 1 TO 4 AND IF NOT 0 AT QH1a
QH1b How many of these projects could be considered to be translational research?

RECORD NUMBER

ASK ALL IF NOT QH1a = 0
QH2 How many of these projects involve an external academic partner?

RECORD NUMBER

ASK ALL IF NOT ANSWER QH1a WITH 0
QH3 How many of these projects involved an external commercial partner excluding contracted research organisations and contracted manufacturing organisations?

RECORD NUMBER

ASK ALL IF ROUNDS 1 TO 4 ONLY
QH4a In the last year how much money did [IF SAMPLE TYPE = ACADEMIC **your team raise and deliver in research income,** IF SAMPLE = FIRM **your company spend on research and development activities] in the life sciences area?**
INTERVIEWER NOTE: IF RESPONDENT IS UNSURE PROBE TO GIVE A ROUGH ESTIMATE

RECORD NUMBER £

CANNOT MAKE THE ASSESSMENT

ASK IF AMOUNT PROVIDED AT QH4A INCLUDING ZERO B BUT NOT INCLUDING DK
QH4b… And to which financial year does that figure relate? Is that a UK tax year, calendar year or academic year?

DO NOT READ OUT. SINGLE CODE ONLY.

2010 Calendar Year	1
2011 Calendar Year	2
2012 Calendar Year	3
2013 Calendar Year	4
2014 Calendar Year	5
2010/11 UK Tax or Academic Year	6
2011/12 UK Tax or Academic Year	7
2012/13 UK Tax or Academic Year	8
2013/14 UK Tax or Academic Year	9
2014/15 UK Tax or Academic Year	10

ASK IF ROUNDS 1 TO 4 ONLY
QH4c [IF SAMPLE = ACADEMIC],
What is the size of your research group IF SAMPLE = FIRM, **how many of your colleagues working in your company are involved in R&D activities?]**
NOTE: IF THIS HAS FLUCTUATED, THEN PLEASE PROVIDE YOUR BEST ESTIMATE OF THE AVERAGE.
- INCLUDE TEMPORARIES/CASUALS, BUT NOT AGENCY STAFF
- EXCLUDE SELF-EMPLOYED
- EXCLUDE OWNERS/PARTNERS, BUT OTHER DIRECTORS COUNT AS EMPLOYEES

RECORD NUMBER

ASK IF SAMPLE TYPE = FIRMS
QH4d And how many of workers does your company currently employ in total?
INTERVIEWER NOTE: IF THIS HAS FLUCTUATED, THEN PLEASE PROVIDE YOUR BEST ESTIMATE OF THE AVERAGE.
- INCLUDE TEMPORARIES/CASUALS, BUT NOT AGENCY STAFF
- EXCLUDE SELF-EMPLOYED
- EXCLUDE OWNERS/PARTNERS, BUT OTHER DIRECTORS COUNT AS EMPLOYEES

RECORD NUMBER

ASK ALL FIRMS IF ROUNDS 1 TO 4 ONLY
QH5a What are your annual sales in total now?

RECORD NUMBER £s

ASK IF AMOUNT PROVIDED AT QH5A INCLUDING ZERO BUT NOT INCLUDING DK
QH5b… And to which financial year does that figure relate? Is that a UK tax year, calendar year or academic year?

DO NOT READ OUT. SINGLE CODE ONLY.

2010 Calendar Year	1
2011 Calendar Year	2
2012 Calendar Year	3
2013 Calendar Year	4
2014 Calendar Year	5
2010/11 UK Tax or Academic Year	6
2011/12 UK Tax or Academic Year	7
2012/13 UK Tax or Academic Year	8
2013/14 UK Tax or Academic Year	9
2014/15 UK Tax or Academic Year	10

SECTION I: Future Plans

READ OUT: **Now thinking about your future plans for the product forming the focus of your Biomedical Catalyst application.**

ASK IF NOT CODE 6 AT QF1
QI1 At this stage, do you plan to progress research and development work relating to project [IF SUCCESSFUL, **beyond the lifetime of Biomedical Catalyst funding]?**
SINGLE CODE ONLY

Yes	1

No	2
Too early to stay	3
Don't know/can't remember	4

ASK IF CODE 2 TO QI1

QI2 **Why do you not intend to continue research and development work?** DO NOT READ OUT. CODE ALL THAT APPLY

Difficulties securing finance	1
Failure to meet key pre-clinical milestones	2
Failure to meet key clinical milestones	3
Competitor has launched a comparable/better product	4
Concerns over costs of further research and development	5
Concerns over potential returns/revenue (including likely adoption by NHS/CCGs and other national health systems)	6
Hypothesis or rationale no longer valid	
Other (specify)	7
Don't know/can't remember	8

ASK IF CODE 1 AT QI1

QI3 **How do you plan to exploit the product being developed?** PROBE FULLY. **How else?** CODE ALL THAT APPLY.

Create commercial entity to develop the product further	1
Sell the intellectual property to another organisation or business	2
Enter into licensing agreements with another organisation or business / collaboration with other organisations	3
Produce the product using contracted manufacturers	4
Produce the product using own manufacturing facilities	5
Make the product freely accessible (digital health application or behavioural health)	
Further sales/ marketing	6
Applying for further grants / venture investments	7
Other (specify)	7
Don't know/can't remember	8

ASK IF CODE 1 AT QI1

QI4 At this stage, do you anticipate that that the product will be mainly manufactured in…READ OUT A TO C**?** SINGLE CODE ONLY

A. The UK	1
B. The rest of the EU	2
C. The rest of the world	3
Too early to say	4
Don't know/can't remember	5

ASK IF CODE 1 TO QI1

QI5 At this stage, do you anticipate that that the product will be marketed in… READ OUT A TO C CODE ALL THAT APPLY

A. The UK	1
B. The rest of the EU	2

C. The rest of the world	3
Too early to say	4
Don't know/can't remember	5

SECTION J: Re-contact

ASK ALL SUCCESSFUL AND UNSUCCESSFUL APPLICANTS

QI6 We are now at the end of the survey. Do you have any other comments on the application and appraisal process of the Biomedical Catalyst fund? WRITE IN PROBE FULLY.

ASK ALL SUCCESSFUL AND UNSUCCESSFUL APPLICANTS

QJ1 **This survey forms part of a study that Innovate UK and the Medical Research Council is conducting on the Biomedical Catalyst. Would you be happy to be re-contacted by Innovate UK and the Medical Research Council, or Ipsos MORI for some follow up questions concerning this survey in the next 2 to 3 years?** SINGLE CODE ONLY.

Yes – Innovate UK/MRC or Ipsos MORI may re-contact	1
Yes – only Innovate UK/MRC may re-contact	2
Yes – only Ipsos MORI may re-contact	3
No	4

ASK ALL SUCCESSFUL AND UNSUCCESSFUL APPLICANTS

QJ2 **Finally, it is sometimes possible to link the data we have collected with other government surveys or datasets to enable further statistical analysis. Would you be happy for this to be done?** SINGLE CODE ONLY

Yes	1
No	2

Annex G: Datalinking

This Annex provides an overview of a wider data-linking exercise being undertaken as part of the evaluation of the Biomedical Catalyst. These activities involve linking records of successful and unsuccessful applicants to a variety of sources of longitudinal secondary data to provide supplementary insights into the effectiveness of the Biomedical Catalyst:

- Business Structure Database (via the Office for National Statistics Virtual Microdata Laboratory) to examine impacts of grants on the turnover and employment on firms applying or associated with applications to the programmes (including industrial partners, CROs, and CMOs).

- Business Enterprise Research and Development Survey (also via the ONS Virtual Microdata Laboratory) to examine the impact of grants on R&D activity (including expenditure).

- Computerised patent records to examine how far Biomedical Catalyst has led to an effect on overall patenting activity, the importance of those patents (measured through citation volumes), collaboration outcomes (measured through co-registration of patents and the list of inventors set out on the front page of a patent), and knowledge spill-overs (approximated through patent citations).

Data Lags

At this stage of the evaluation, these sources of secondary data will not provide evidence of the impacts of the Biomedical Catalyst owing to lags. The employment and turnover records within the Business Structure Database (BSD) are subject to a one to three year lag (so at the time of writing, the BSD only provides information on the employment and turnover of applicant firms for 2011 or 2012 - before the majority of Biomedical Catalyst funding was committed). Equally, the European Patent Office only publishes patent records 18 months after receipt from the applicant (to offer a period of secrecy). At the time of writing only patents registered before October 2013 were available.

As a consequence, these sources of data only describe the historical performance of the applicants involved, and are presented here for methodological interest. However, the data-linking exercise will be revisited as part of the final evaluation (scheduled to take place in 2017) to provide a long term assessment of the causal effects of the programme. In addition, applicant records will also be linked to sources of bibliometric data to provide an analysis of the effects of the programme on research output.

Data Cleaning

The evaluation team compiled a list of all organisations and individual academics associated with applications to the Biomedical Catalyst (including lead applicants, collaborators, and subcontractors). This led to the creation of a dataset containing details of 1,982 organisations across 421 applications, including 53 collaborators, and 1,445 subcontractors. Many organisations appeared in multiple applications and after de-duplication this resulted in a sample of 1,081 unique firms. It was possible to identify the Companies House Reference Number for 93 percent of these firms.

Linking to Business Structure Database and BERD

The sample of firms was provided to the ONS Virtual Microdata Laboratory to be linked to the Inter-Departmental Business Register (individual academics, universities and other organisations were excluded as they are not captured within the datasets held within the VML). Of the 1,081 firms provided to ONS, the VML team were able to obtain an IDBR reference for 901 (a matching rate of 83 percent). Anonymised details of these firms were transferred to the VML (i.e. the IDBR reference numbers – or 'EntRef') where they could be linked to the BSD and BERD datasets.

Business Structure Database: Employment and Turnover

The Business Structure Database is an annual snapshot of the IDBR taken in April each year. The IDBR is a live database of all firms registered for PAYE and VAT (covering 99 percent of economic activity in the UK). The IDBR includes records of turnover and employment drawn from a number of sources (including PAYE records, VAT returns, and responses to the Annual Business Survey and the Business Register and Employment Survey). Measures of employment and turnover are not currently 'time-stamped' by ONS and may in some cases be several years out of date, so some caution is required when using these datasets for evaluation purposes.

The table below provides the percentage of firms in the sample - for which an IDBR reference number was available – that could be identified in the Business Structure Database in each year between 2005 and 2014. The proportion of firms that could be matched rose over time. This was due to the high prevalence of firms that were created over the period of interest (who could not be identified in earlier years because they did not exist). Some firms also exited the dataset, likely either because the firm had closed or due to consolidation in the sector (e.g. mergers and acquisitions of CROs and CMOs). The high rates of matching achieved will create substantial scope for econometric analysis in 2017 as part of the final study.

Table G.1 – Matching Rates to BSD by BSD year (BMC applicants with IDBR reference number)

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
% matched to BSD	48%	51%	56%	61%	67%	71%	74%	79%	83%	89%

Source: Business Structure Database, Ipsos MORI analysis

Average turnover across the sample of BMC applicants by BSD year is set out in the table below. The figures below are not a longitudinally stable sample (due to firm entry and exit), and the declining pattern of average turnover over time is largely driven by the entry of new firms with low turnover. Outliers have not been excluded.

Table G.2 – Average turnover of all firms identified in the BSD (£ thousands)

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
All	90,158	70,721	68,237	67,720	66,636	66,221	66,305	63,903	53,939	48,112
Lead Apps.	18,375	12,759	10,378	10,144	8,088	7,509	9,991	7,588	8,239	7,942
Collabs.	475,515	370,913	390,408	378,784	386,899	382,323	378,378	380,108	303,569	266,038
Subs.	15581	16078	14,913	16,101	16,154	17,594	17,601	16,594	18,296	19,009

Source: Business Structure Database, Ipsos MORI analysis

The table below shows the average employment of all firms identified within the BSD. Again, the figures are not based on a longitudinally stable sample, and the declining pattern of average employment is largely due to the entry of new firms with low numbers of workers. Outliers have not been excluded.

Table G.3 – Average employment of all firms identified in the BSD

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
All	440	413	388	363	325	295	281	272	258	257
Lead Applicants	157	120	95	77	69	72	65	67	58	51
Collaborators	1,031	1,021	1,060	984	894	677	642	569	516	512
Subcontractors	261	249	240	235	213	205	196	202	201	215

Source: Business Structure Database, Ipsos MORI analysis

Business Expenditure on Research and Development

The BERD receives responses from 40,000 to 50,000 thousand businesses. It is a census survey of known 'R&D performers' and a sample survey of other firms. The table below shows the proportion of Biomedical Catalyst applicants that were identified in the BERD dataset in each year. Some issues were encountered with linking to the 2008 BERD survey that could not be resolved within the timescales for this initial analysis. It is less clear that a detailed econometric analysis of BERD findings will yield meaningful results as matching rates were generally low across years.

Table G.4 – Matching Rates to BERD by year (BMC applicants with IDBR reference number)

	2005	2006	2007	2008	2009	2010	2011	2012	2013
% matched to BERD	16	18	19	*	22	29	32	33	40

Source: Business Expenditure on Research and Development, Ipsos MORI analysis

Average R&D spending by category of expenditure is reported in the table below. There is an unexplained and substantial reduction in average R&D spending between 2012 and 2013, though this is likely due to the higher identification rate between the two years (i.e. composition bias) rather than actual changes in R&D spending.

Table G.5 – Average R&D spending across BMC applicants identified in BERD (m)

	2005	2006	2007	2008	2009	2010	2011	2012	2013
Salaries	10,566	11,022	10,474		8,043	6,132	5,160	5,082	1,201
Other expenditure	13,826	10,892	9,462		7,878	7,760	4,837	4,532	1,269
Capital expenditure	1,512	1,245	768		551	243	400	519	164

Source: Business Expenditure on Research and Development, Ipsos MORI analysis

Patenting

Applicant records were linked to computerised patent records held by the European Patent Office using the PATSTAT Worldwide Patent Statistical Database. Patent applications were identified by searching for patents where the patent applicant was similar to the name of the firm associated with an application for Biomedical Catalyst funding, or where the named inventor was similar to the name of the academic associated with application for Biomedical Catalyst funding. The sample of patents identified was cleaned to remove firms and individuals whose names were similar but not the same as those of interest. Duplicates of the same patent applications were also removed to avoid double counting.

As noted in the introduction to this section, only patents registered before October 2013 are included in the data and it is not of use in assessing the effects of the programme. However, after de-duplication, only a limited number of relevant patents were identified (51 across successful and unsuccessful applicants). These results are set out in the table overleaf. This may limit the value of this data in a later analysis to be completed in 2017 (an issue that will be revisited at that point). The search algorithm may also have failed to identify relevant patents and this will also be subject to robustness checks in 2017.

Table G.6 – PATSTAT analysis summary[41]

	Successful				Unsuccessful				
	Lead	Collaborator	Sub-contractor	Total Successful	Lead	Collaborator	Sub-contractor	Total Unsuccessful	Total
Total potentially relevant PATSTAT entries identified for BMC applicants	1,500[42]		3,043	4,543	710		318	1,028	5,571
Unique patent applications (after removal of irrelevant companies, duplicate IPC codes, foreign entities)	18	3	45	66	13	5	6	24	90
Unique applications to total entries (%)	1	0	2	15	2	1	2	2	2
Unique applications to total companies (%)	13	4	17	14	9	11	2	5	9
Total companies and individuals with at least 1 app	11	3	16	30	11	5	5	21	51
Companies and individuals with patent applications (%)	8	4	6	6	7	11	2	4	5

[41] Figures are given to the nearest whole integer.
[42] Total PATSTAT entries are grouped for lead and collaborator because they were searched for jointly in PATSTAT.

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