BiGGAR Economics

Evaluation of the Scottish Centre for Regenerative Medicine

A report to

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1 EXECUTIVE SUMMARY

This report presents the findings of an evaluation of the Scottish Centre for Regenerative Medicine (SCRM) undertaken by BiGGAR Economics in summer 2016. The main finding of the study is that the performance of the SCRM to date in relation to the original performance measures established in 2007 has been mixed. Although the translation of scientific outputs into clinical practice has been somewhat slower than anticipated, research related employment within the building has exceeded expectations and researchers working in the SCRM have delivered several important scientific outputs.

The main recommendation of this report is therefore that, in order to realise the full potential of these scientific outputs, it will be necessary to move the research currently underway at the SCRM beyond the pre-clinical phase by developing deeper relationships with industry. In order to develop these relationships a dedicated business development support function will be required, with the capacity to engage directly with industry and development agencies such as Scottish Enterprise and Scottish Development International.

1.1 Actual and Anticipated Performance

The cost benefit analysis prepared for the SCRM in 2007 considered five main types of benefit.

- temporary construction benefits associated with the initial capital investment;
- research funding that would be secured by researchers in the SCRM;
- research related employment supported on-site;
- additional turnover within organisations that licenced technologies developed at the SCRM; and
- turnover and employment of spin-out companies established based on research undertaken at the SCRM.

Taking each of these in turn.

The cost of constructing the SCRM was as expected in 2007 and although the employment benefits associated with this expenditure were lower than anticipated, this was due to changes within the Scottish construction sector rather than anything to do with the SCRM.

To date the SCRM has secured a total of £55.0 million research funding, approximately 35% less than the £85.2 million that was anticipated in 2007. Despite this, research related employment at the SCRM has exceeded expectations by some margin. In 2007 it was anticipated that by 2015/16 the SCRM might employ around 210 people but it now employs more than 250.

The SCRM has also performed reasonably well in relation to technology licencing. In 2007 it was anticipated that licensees might be able to generate £11.3 million additional turnover as a result of implementing SCRM technologies. In reality it was estimated that this figure could be around £10.7 million, 5% lower than anticipated.

The performance of the SCRM in relation to spin-outs has however been much slower than anticipated. To date there has been one significant spin-out from the

SCRM (which has recently split into two separate companies). Together these companies employ around 70 people and have a turnover of around £4.5 milion. In 2007 however it was expected that around 11 spin-out companies might have emerged from the SCRM and that these companies would employ almost 100 staff and have turnover of around £8.5 million.

The development of the SCRM has also enabled the University of Edinburgh to leverage in a substantial amount of new funding to support important areas of research. Of particular note has been the:

- Significant donation secured from JK Rowling to support the creation of the new Anne Rowling Centre;
- £10.0 million secured from the Medical Research Council to support the creation of the Centre for Computational and Chemical Biology of the Stem Cell Niche; and
- £10.7 million secured from the UK Research Partnership Investment Fund to support the new Institute for Regeneration and Repair (see section 7.2).

1.2 Non-Quantifiable Benefits

The quantifiable benefits described above do not however provide a full reflection of the potential contribution that the SCRM could make in the future. To help evaluate this potential it is also necessary to consider the scientific outputs that have emerged from the SCRM to date, many of which could have the potential to deliver real benefits in the future. This approach is consistent with latest thinking in EU institutions on assessing the economic impacts of medicine programmes (for example the Innovative Medicines Initiative).

To do this the scientific outputs from the SCRM to date were considered against a checklist of 12 clearly defined scientific outputs that other evaluation studies have shown have the potential to generate future benefits. Based on a series of consultations with key members of staff from the SCRM evidence of at least nine of the 12 outputs included in the framework were identified.

To date several important scientific outputs have emerged from the SCRM that have the potential to improve the understanding and treatment of life threatening diseases and conditions such as liver failure, multiple sclerosis and motor neurone disease. Although these outputs are all still in the early stages of development, if they can be successfully translated into the clinic then they could bring about significant benefits for both the patients and the industrial partners responsible for bringing new treatments to market.

In addition to the direct scientific outputs of the SCRM, there have also been several wider developments that have either happened as a direct result of the existence of the SCRM or which would otherwise have been significantly less advanced. Taken together these developments have helped to create the foundation for the Scottish regenerative medicine cluster that is emerging around Edinburgh's BioQuarter.

1.3 The Future

Despite this encouraging evidence it should not be overlooked that, as yet, none of the scientific advances identified in this report have resulted in improved clinical outcomes or new treatments.

While the long-term nature of the research undertaken at the SCRM means that this is not entirely unexpected, key stakeholders consulted during the course of the evaluation suggested that progress on the translation of research has been slower than expected. The main reason for this appears to be a lack of engagement between the SCRM and industry, which can in turn be traced back to an earlier decision to designate the SCRM building as a research facility for taxation (VAT) purposes. Another important factor has been that, to date, researchers at the SCRM have had very little the business development support.

At the time of writing much of the research undertaken at the SCRM was at the early pre-clinical phase of development. To take the next step toward translating the scientific outputs generated to date into clinical outcomes it will be necessary to move this research beyond the pre-clinical phase and into clinical trials.

To help achieve this the University of Edinburgh is currently progressing plans to develop a new building next to the SCRM. Taken together the new building and the SCRM will become the Institute for Regeneration and Repair (IRR). The fact that the University has already succeeded in securing significant funding contributions to support the new venture provides further evidence of the high regard with which the research undertaken at the SCRM is held.

The success of the new venture will however depend to a large extent on the extent to which the SCRM/IRR is now able to successfully translate the scientific outputs realised to date into clinical practice and achieving this will require significant industrial funding.

In order to secure the large-scale commercial support required, it will be necessary to significantly increase the level of engagement between the SCRM/IRR and industry. Achieving this will require dedicated professional business development support to identify opportunities to engage with industry and help realise them.

This should not only should this help maximise the economic impact of the IRR by enabling it to engage with industry around the world but, by raising the profile of developments in Scotland, should also support the development of the wider Scottish regenerative medicine sector.

1.3.1 Future Benefits

In order to demonstrate the importance of developing closer relationships with industry to the next stage of the SCRM/IRR's development this evaluation considers two future development scenarios. One in which the SCRM maintains similar level of collaboration with industry as it has at present and one in which collaboration with industry increases significantly.

This exercise shows that by 2020/21, which was the end of the period considered in the original cost benefit analysis, most the outputs of the SCRM are likely to be lower than what was originally expected under both scenarios. The reason for this is likely to be, at least in part, attributable to external factors outwith the control of the SCRM not least of which would be the global financial crash that started in 2008.

The more important point however is that the outputs of the SCRM are likely to be significantly higher under the second scenario, which assumes an increased level of industrial engagement, than under the first scenario, which assumes a similar level of engagement as exists in 2015/16.

If it were possible to significantly increase the extent to which the SCRM engages with industry it would be reasonable to expect all of the expectations set out in the original cost benefit analysis to be achieved by around 2023/24, just two to three years later than anticipated. The one exception to this could be employment in spin-out companies which has so far grown much slower than anticipated; however this could change quickly should a particularly successful company emerge over the next few years.

2 INTRODUCTION

This report presents the findings of an evaluation of the Scottish Centre for Regenerative Medicine (SCRM), undertaken by BiGGAR Economics in Summer 2016 on behalf of the University of Edinburgh.

2.1 Scottish Centre for Regenerative Medicine

The Scottish Centre for Regenerative Medicine (SCRM) building at the Edinburgh BioQuarter officially opened in 2012 and is home to the Medical Research Council (MRC) Centre for Regenerative Medicine (CRM).

The CRM is a University of Edinburgh research institute where scientists and clinicians study stem cells, disease and tissue repair to advance human health. Research at the CRM is aimed at developing new treatments for major diseases including cancer, heart disease, liver failure, diabetes and degenerative diseases such as multiple sclerosis and Parkinson's.

The building itself covers 9,000 sqm and contains state-of-the-art research facilities to pursue stem cell research and regenerative medicine as well as a 'Good Manufacturing Practice' (GMP) cell therapy facility operated jointly by Roslin Cells Ltd and the Scottish National Blood Transfusion Service.

The development of the SCRM was first announced by the First Minister in 2007. At that time it was anticipated that the new building would cost £59.0 million and it was agreed that £23.75 million of this funding would be provided by the Scottish Government, £16.0 million would be provided by Scottish Enterprise and the remaining £19.0 million would be provided by the University of Edinburgh. In order to address its £19.0 million funding requirement the University of Edinburgh made an application to the European Regional Development Fund (ERDF) and an associated major project application (which was required because the total value of the investment exceed €50.0 million).

2.1.1 Original Objectives

In 2007 the vision for the SCRM was to create a multi-disciplinary “flagship” centre that would become a magnet for academic, clinical and commercial development of stem cell applications and regenerative medicine. At that time the proposals for the SCRM were made up of three main elements:

- consolidation and expansion of the University of Edinburgh’s existing research groups, by providing academic facilities for 210 researchers;
- a 1,000 sqm centre for “scale-up” development and manufacturing of cells to a GMP standard for clinical trials and therapeutic applications; and
- approximately 675 sqm of multi occupancy space to accommodate and assist embryonic-stage spin-outs and other commercial stem cell research organisations.

2.2 Consultations

BiGGAR Economics would like to thank the following individuals for contributing to this evaluation:

Name	Role/Organisation
Aiden Courtney	CEO of Roslin Cells
Andrew Henderson	Scottish Enterprise
Anna Stamp	Head of Capital Projects at University of Edinburgh
Charles Ffrench-Constant	Former director of MRC CRM
Dave Hay	Researcher at MRC CRM
Ed Hutchison	Scottish Enterprise
John Casey	Scottish National Islet Transplantation Programme
Marc Turner	Head of SNBTS at SCRM
Marieke Hoeve	UKRMP Niche Hub Manager
Scott Johnstone	CEO of the Scottish Life Sciences Association
Stuart Forbes	Director of MRC CRM
Angus Stewart Liddon	Edinburgh Research and Innovation

2.3 List of Abbreviations

For ease of reference a list of common abbreviations used in this report is provided below:

- **GMP –** good manufacturing practice (a quality control system for ensuring consistent standards for pharmaceutical products);
- **iPSCs -** induced pluripotent stem cells (a type of cell generated directly from adult cells (i.e. from the skin or hair) that can be used to create other types of body tissue (such as liver or pancreatic cells);
- **IRR –** Institute for Regeneration and Repair (the collective name for the SCRM building and a new research building that the University of Edinburgh proposes to build nearby);
- **MRC CRM –** the Medical Research Council Centre for Regenerative Medicine (which is based in the SCRM); and
- **SCRM** – Scottish Centre for Regenerative Medicine.

2.4 Report Structure

The remainder of this report is structured as follows:

- section three places the SCRM in the context of the wider Scottish Life Sciences sector as well as the Edinburgh BioQuarter development;
- section four outlines the approach taken to evaluating the socio-economic impacts of the SCRM;
- section five describes the benefits that were anticipated when a cost-benefit analysis of the Centre was undertaken in 2007;

- section six outlines the current activities of the SCRM and evaluates these against the anticipated benefits of the Centre;
- section seven considers further sources of impact and intermediate outputs that could provide evidence of potential benefits and evaluates the SCRM against these;
- section eight discusses the potential future impacts that could arise from the SCRM; and
- section nine draws together the main conclusions of the evaluation.

3 BACKGROUND AND CONTEXT

This section places the SCRM against the backdrop of the Scottish Life Sciences Sector and in the wider context of the Edinburgh BioQuarter where it is situated.

3.1 Scottish Life Sciences Sector

Life sciences is one of the six growth sectors identified in Scotland's Economic Strategy[1]. The growth sectors have been identified based on the particular opportunities that they offer to build on existing comparative advantages and increase productivity and economic growth.

The Scottish Life Sciences strategy[2] sets short and medium term goals to fully realise the Scottish Government's vision to double the economic contribution made by the life sciences industry to £6.2 billion turnover and £3.0 billion GVA by 2020.

Based on the Scottish Government's SIC code classifications[3], the life sciences sector generated £1.9 billion in turnover and £1.0 billion GVA in 2013 (latest available figures) and accounted for 16,000 jobs in Scotland. This represents a 14% increase in GVA since 2008 and a 15% increase in employment since 2009.

The strategy identifies six priority actions to achieve its target, of which three are directly relevant to the SCRM:

- **success through collaboration** – encourage intensified business and research partnerships in order to accelerate the process of getting products and services to market;
- **a strong shared marketing proposition** – a well articulated business proposition to promote Scotland's global standing as a location of choice and a deeper public appreciation of major healthcare benefits arising from the life sciences industry; and
- **a vibrant innovative culture** – creation of an environment which stimulates the rapid commercial exploitation of leading-edge innovations through a culture of shared endeavour between business, research and the NHS.

Regenerative medicine and stem cells is identified as a key area of focus for growth as it offers the opportunity to capitalise on Scotland's world-ranking research strengths in this field. The MRC Scottish Centre for Regenerative Medicine, a rapidly expanding cluster of companies forming a comprehensive supply chain and a pipeline of potential stem sell therapies being progressed towards clinical use are all highlighted as assets.

3.2 Edinburgh BioQuarter

Extending to more than 100 acres, Edinburgh BioQuarter is a joint venture between Scottish Enterprise, the University of Edinburgh and NHS Lothian to bring together academic scientists, clinicians, nurses, patients and industry in

[1] Scottish Government (2015), Scotland's Economic Strategy
[2] Life Sciences Scotland (2011), Scottish Life Sciences Strategy 2011: Creating Wealth, Promoting Health
[3] Scottish Government (2015), Growth Sector Statistics

world-class facilities on one site. Initially the project involved a private sector real estate partner who following the global recession has since withdrawn.

Over the last decade, £428 million of investment has taken place delivering 100,000 sq m of medical, commercial, teaching and research facilities. £800 million of further investment is proposed over the period to 2025 to deliver an additional 150,000 sq m.

The Edinburgh BioQuarter was established to create a world leading, fully integrated centre of excellence in life sciences and health care supporting the complete lifecycle of patient care. It brings together two hospitals, a medical school, three leading medical research institutes and commercial office and laboratory space:

- **Royal Infirmary of Edinburgh –** a 900-bed hospital providing a full range of acute medical and surgical services. It is also the principal acute hospital for medical teaching and includes a clinical trials suite. Clinical trials suite. The University has 90 'embedded' academic offices in the Hospital, supporting integration of clinical and academic staff;

- **Royal Hospital for Sick Children –** the Royal Sick Children's Hospital, Department of Clinical Neurosciences and Child and Adolescent Mental Health Service will be brought together in a new purpose-built building adjoining the Royal Infirmary of Edinburgh by 2017. The building will include 233 beds, 10 theatres and have adjoining child and adult emergency departments;

- **University of Edinburgh Medical School –** established in 1726, the University of Edinburgh Medical School is one of the oldest medical schools in the English-speaking world. The School has a very strong research reputation, with Medicine, the University's largest REF submission, ranked in the top 5 in the UK. The School is located adjacent to the Royal Infirmary of Edinburgh in the Chancellor's Building which is the main undergraduate teaching and leaning centre. It also houses 250 researchers and clinical teaching staff working across the full range of medical conditions;

- **Queen's Medical Research Institute –** opened in 2005, QMRI houses over 600 researchers and aims to tackle a wide range of diseases at the most fundamental cellular level following a bench-to-bedside approach. It provides facilities for high quality interdisciplinary research in three centres in the key areas of Cardiovascular Science (in association with the British Heart Foundation), Inflammation Research and Reproductive Biology;

- **Scottish Centre for Regenerative Medicine –** opened in 2011, the Centre's research spans basic mechanisms of stem cell regulation to translational research and providing proof of principle for stem cell therapies. The building also has a GMP cellular therapy facility operated by Roslin Cells Ltdand the Scottish National Blood Transfusion Service.;

- **Anne Rowling Regenerative Neurology Clinic –** a purpose-built facility established in 2010 following a donation from the author J.K. Rowling. Work at the Clinic targets the discovery of treatments that will slow progress of conditions such as multiple sclerosis, motor neurone disease and related neurodegenerative conditions with the ultimate ambition of repairing damage. All clinical activity is undertaken in partnership with the NHS and

patients of the Clinic have first-hand access to research projects and clinical trials; and

- **Nine –** opened in 2012, Nine offers 10,000 sq m of commercial office and laboratory space for new and established life science companies. The ground floor bioincubator incorporates fully fitted laboratories and offices from 150 sq ft for immediate occupation and is 80% occupied[4]. The upper floors are available for bespoke fit-out so that they can be configured to suit individual company requirements. The building also houses the Farr Institute Scotland, which is a collaboration between six Scottish universities and NHS National Services Scotland. The Institute is developing procedures to securely curate electronic health records in order to use 'Big Data' sets for healthcare research.

In total, there will be around 1,500 hospital beds, 2,000 researchers and 6,000 clinical and support staff at the BioQuarter site by 2017, making it one of the most significant concentrations of medical assets and scientific talent in Europe. This co-location of academic research, clinical research facilities and business accommodation space provides opportunities for researchers and clinicians to collaborate and increase innovation in the Scottish life sciences sector.

[4] http://www.edinburgh.gov.uk/downloads/file/3777/edf_presentation_-_bioquarter_infrastructrure

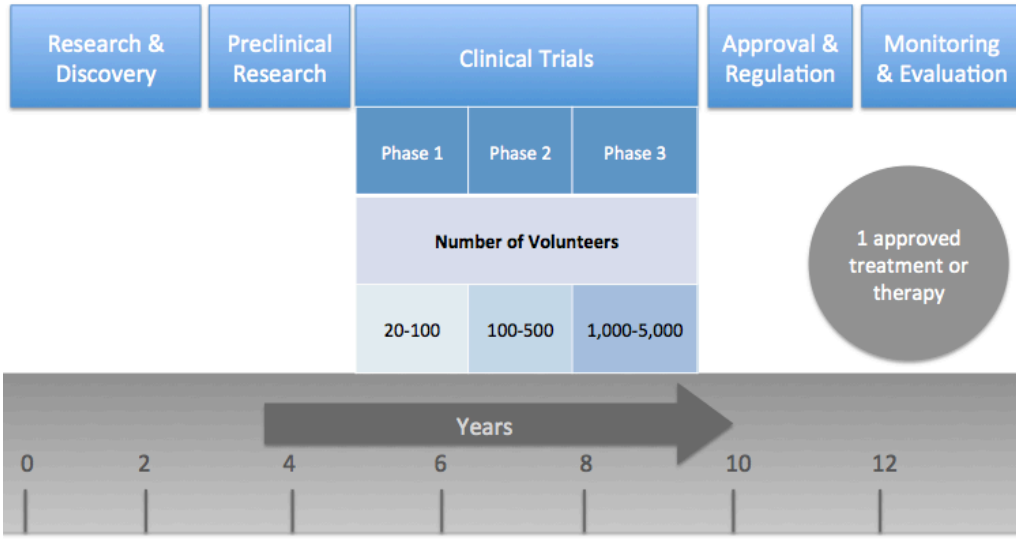
4 APPROACH

This section outlines the approach taken to evaluating the SCRM.

4.1 Pathways to Socio-economic Impacts

The ultimate objective of the research undertaken at the SCRM is to advance human health by developing of new treatments and therapies for major diseases. The economic benefits of this type of activity can be quantified by considering both the value of the health gains associated with new treatments or their market value. These benefits can however only be fully realised once a new treatment has entered widespread clinical use. As illustrated in Figure 4-1, this process is generally very time-consuming, typically requiring at least 12 years from fundamental research to regulatory approval.

Figure 4-1 – Typical Treatment Development Pathway



Source: Based on PhRMA profile pharmaceutical industry (2010)

The long-term impacts associated with the development of new treatment include commercialisation impacts such as the benefits to businesses from licencing new technologies from the SCRM as well as the additional turnover and employment generated through the creation of new spin-out companies. The starting point for this analysis was to consider the extent to which these impacts have been realised.

Given the long-term nature of the research undertaken by SCRM it is however likely that the benefits of the activity undertaken to date have not yet been fully realised. In addition, in most cases something else would also need to happen in order for quantifiable benefits to be realised (e.g. regulatory approval or adoption by the pharmaceutical industry).

To overcome this it was also appropriate to consider intermediate scientific outcomes, which can provide an indication of future impact potential. To do this a 'system of innovation' approach was adopted that describes the steps in the process of developing final product and process innovations and therefore can be seen as pathways to socio-economic impact.

This system of innovation typically includes ten activities (Figure 4-2) that are the main determinants of innovation processes. This encompasses activities not only on the supply side, but also the demand side. It also includes provision of the constituents for systems of innovation and support services for innovating firms as factors that influence innovation processes.

Figure 4-2 – Determinants of Innovation Processes

I. Provision of knowledge inputs to the innovation process
Provision of R&D and, thus, creation or recombination of new knowledge, primarily in engineering, computer sciences, medicine, life sciences and natural sciences.
Competence building, e.g. through individual learning (educating and training the labour force for innovation and R&D activities) and organisational learning.
II. Demand-side activities
Formation of new product markets.
Articulation of quality requirements emanating from the demand side with regard to new products.
III. Provision of constituents for Systems of Innovation (SIs)
Creating and changing organisations needed for developing new fields of innovation. Examples include enhancing entrepreneurship to create new firms and intrapreneurship to diversify existing firms; and creating new research organisations, policy agencies, etc.
Networking through markets and other mechanisms, including interactive learning among different organisations (potentially) involved in the innovation processes. This implies integrating new knowledge elements developed in different spheres of the SI and coming from outside with elements already available in the innovating firms.
Creating and changing institutions – e.g., patent laws, tax laws, environment and safety regulations, R&D investment routines, cultural norms, etc. – that influence innovating organisations and innovation processes by providing incentives for and removing obstacles to innovation.
IV. Support services for innovating firms
Incubation activities such as providing access to facilities and administrative support for innovating efforts.
Financing of innovation processes and other activities that may facilitate commercialisation of knowledge and its adoption.
Provision of consultancy services relevant for innovation processes, e.g., technology transfer, commercial information, and legal advice.

Source: Edquist (2011), Innovation Policy Design: Identification of Systemic Problems

These ten activities can also be intermediate outcomes in innovation processes as they can provide the basis for future innovations and can therefore provide useful indicators of future impact potential. Examples of intermediate outputs that could be measured to provide evidence of potential benefits of the SCRM include:

- new human cell lines;
- new tools that can be used to better understand diseases and identify targets for new medicines;
- biobanks of human tissue samples;
- validated or potential biomarkers of diseases;

- methods for predicting the toxicology of potential treatments;
- new animal models and humanised models;
- new approaches to identifying non-genotoxic carcinogens, which could reduce the need for animal trials in some circumstances;
- new knowledge from which new potential targets for medicines development could be identified;
- databases of findings and of data collected but not yet fully analysed;
- novel imaging techniques and tools;
- new guidance and best practice recommendations; and
- new collaborations.

Together, the ten activities described in Figure 4-2 define an innovation system characterised by a diversity of knowledge creation and utilisation processes with many interactions, pathways and feedback loops. These determinants cannot be expected to be independent of one another; they support and reinforce one another to form a dynamic, multi-causal system.

In recognition of the long-term nature of SCRM activity this evaluation therefore took a two stage approach that involved:

- quantifying the impact of activity to date in terms of;
    - the short-term construction benefits associated with developing the SCRM;
    - the value of research and other income secured;
    - the number of research staff employed;
    - employment and turnover of spin-out companies; and
    - income from technology licencing.
- identifying examples of the intermediate outputs listed above that could provide evidence of the future potential benefits associated with the SCRM.

This approach is consistent with latest thinking in EU institutions on assessing the economic impacts of medicine programmes (for example the Innovative Medicines Initiative[5]).

[5] Innovative Medicines Initiative (May 2016), IMI Socio-economic Impact Assessment Expert Group

5 ACTUAL AND ANTICIPATED BENEFITS

A cost benefit analysis was undertaken of the SCRM in 2007. This appraisal identified several potential sources of impact associated with the academic activity that was expected to happen within the SCRM, including benefits associated with:

- the construction of the SCRM building;
- the attraction of new research funding;
- the employment of the researchers expected to work in the new building;
- the licencing of technologies developed within the SCRM to third parties; and
- the creation of spin-out companies.

The original cost benefit analysis also considered the benefits associated with the multi-occupancy space that was part of the original proposals. As this element of the project did not proceed these benefits are not presented here.

This chapter describes the anticipated value of these benefits, the time-scale over which they were expected to occur and the assumptions made to estimate this.

5.1 Construction

The construction of the SCRM building would have generated wealth and supported employment within the Scottish construction sector. The value of this benefit would depend directly on the total cost of construction.

5.1.1 Anticipated Benefit

In 2007 it was expected that the construction of the SCRM would cost £39 million and that the necessary design work, legal fees, infrastructure, equipment, IT and contingencies would bring the total cost of the project to £59 million[6]. It was anticipated that work would start on-site in October 2008 and be completed by the end of the academic year 2010/11.

The economic impact of the construction of the SCRM was estimated using data for the Scottish construction sector published by the (then) Scottish executive. Using this data it was estimated that the construction of the SCRM could support 396 years of construction related employment. To meet European funding requirements this benefit related only to the construction costs of the new building, not the entire project cost.

5.1.2 Benefit Realised

The construction of the SCRM building was completed within the anticipated time-frame and on budget so the total construction cost was £39 million as anticipated in the original cost benefit analysis. The total cost of the project was somewhat lower than anticipated in 2007 due to VAT mitigation.

Using the same approach used in 2007 it can be estimated that the construction of the SCRM building supported 207 years of construction related employment.

[6] NB. In accordance with relevant guidance the original appraisal only considered the benefits associated with the construction of the SCRM, i.e. the £39 million construction costs and did not consider the benefits associated with the design and fit out of the new building

This estimate is lower than that estimated in 2007 because of changes to the turnover/employee in the Scottish construction sector. A variety of factors are likely to have been responsible for this change, not least of which would have been the financial crisis of 2008/9.

As highlighted above, the original cost benefit analysis only considered the direct benefits associated with the construction of the SCRM building; however this would not reflect the full benefit that the project generated for the Scottish economy. By taking into account the full cost of the project it can be estimated that the SCRM project as a whole directly supported 290 years of employment in the Scottish economy. A comparison of the actual and anticipated benefits during the construction phase is provided in Table 5-1.

Table 5-1 – Expected and Realised Benefits: Construction

Measure	Expected	Realised (£m)
Total project cost (£million)	59	54
Construction cost (£million)	39	39
Construction period	Oct '08 – Aug '11	Oct '08 – Aug '11
Construction job years supported	396	207

Source: BiGGAR Economics (2007), Cost Benefit Analysis of the SCRM

5.2 Research Funding

One of the main quantifiable benefits associated with the SCRM is the amount of research funding that researchers working in the building manage to secure.

5.2.1 Anticipated Benefit

The original cost benefit analysis considered a 15 year period from 2006/7 to 2020/21. It was anticipated that the SCRM would generate a total of £3.75 million 2009/10 and that this income would then grow by:

- 50% per year in years two and three;
- 35% per year in years four and five;
- 20% per year in years six to nine; and
- 10% per year in years ten to twelve.

Based on these assumptions it was estimated that by 2020/21 the total amount of research income generated would be £259.7 million. By the 2015/16 it was expected that researchers at the SCRM would be generating around £22.1 million research income/year and a total to date of have £85.2.0 million. These benefits and the assumptions used to estimate them benefits are set out in Table 5-2.

5.2.2 Benefit Realised

The SCRM building was occupied by researchers in 2011/12. During that year researchers at the SCRM secured £6.1 million of research funding. Between 2009/10 and 2011/12, before relocating to the new SCRM building, researchers at the MRC CRM also secured research funding that can be attributed to the new research infrastructure. Based on information provided at the time of the original

cost benefit analysis, it was assumed that this income amounted to around £9.4 million.

By 2015/16 the amount of research funding secured by researchers at the SCRM had increased to £11.1 million/year. This implies that the total amount of research funding secured between 2007/8 and 2015/16 was £55.0 million. The total amount of research funding actually secured by the SCRM since 2007 has therefore been around 35% below the level anticipated in 2007.

Considering the origin of SCRM income may help to provide some insight as to why this may have occurred. At the time of writing around three quarters of SCRM income was derived from UK research councils and charities and around a fifth came from EU government bodies. In contrast, income received from industry or earned through consultancy projects only represented around 1% of total income. The original cost benefit analysis did not estimate how much income the SCRM might secure from different sources; however, it is likely that if it had, the expectation would have been for industrial funding to have grown by more than it has.

A comparison of the actual and anticipated benefits is provided in Table 5-2.

Table 5-2 – Expected and Realised Benefits: Research Funding

Measure	Expected (£000)	Realised (£000)
Total secured 2007/8 - 2020/11	259,734	n/a
Total secured by 2015/16	85,176	54,975
Total secured in 2015/16	22,143	11,100

Source: BiGGAR Economics (2007), Cost Benefit Analysis of the SCRM and data provided by SCRM in 2016

5.3 Employment of Researchers

Another key measure of the performance of the SCRM is the number of researchers employed on-site.

5.3.1 Anticipated Benefit

Prior to the completion of the SCRM building around 120 researchers worked at the MRC CRM. It was expected that the development of the new building would enable the University to attract new researchers and that this number would increase to around 210 by 2010/11.

5.3.2 Benefit Realised

When the SCRM building first opened in 2011/12 a total of 159 researchers moved into the new building. Since then this figure has increased to 255 researchers, which is 21% higher than the level anticipated in 2007.

Table 5-3 – Expected and Realised Benefits: Researcher Employment

Measure	Expected	Realised
Number of researchers employed on occupation (2011/12)	210	159
Number of researchers employed by 2015/16	210	255

Source: BiGGAR Economics (2007), Cost Benefit Analysis of the SCRM and data provided by SCRM in 2016

5.4 Licencing

One of the important ways in which technologies developed at the SCRM can be translated into clinical practice is through the use of licence agreements with industry.

5.4.1 Anticipated Benefit

In 2007 it was estimated that 12 technologies would be licenced by the SCRM between 2009/10 and 2020/21 at a rate of approximately one per year. This implies that by 2014/15 it was expected that six licence agreements would have been negotiated. It was expected that each licence would enable the industry partner involved to generate an average of around £1.6 million turnover. This implies that in 2007 it was expected that licence agreements associated with the SCRM would enable industrial partners to generate a total of £11.3 million by 2015/16 and that this could increase to £19.3 million by 2020/21.

5.4.2 Benefit Realised

Since the SCRM was established licence agreements that are at least partially attributable to SCRM researchers have generated a total of £187,290 in royalty income. In addition to this, licence agreements that were made before 2011/12 that involved SCRM researchers have generated a further £293,742 income.

Although these licence agreements pre-date the SCRM building it is likely that many of them would not have been possible if plans to develop the SCRM had not been in the pipeline at the time. This is because, according to consultations with key partners involved in the development of the project, the SCRM proposals were key to enabling the University of Edinburgh/Roslin Institute to retain leading researchers. For this reason it is appropriate to attribute this income to the SCRM.

The royalty income that the University of Edinburgh receives from licence agreements only represents a proportion of the total turnover that licence holders might expect to generate from the associated technology. Research suggests that, on average, the royalty income generated by technologies licenced to the pharmaceutical and life sciences sector represents around 4.5% of the total turnover generated.

Using this assumption it was estimated that to date licences associated with the SCRM have generated around £10.7 million. This represents 95% of the total benefit anticipated by 2015/16. These benefits are set out in Table 5-4.

Table 5-4 –Expected and Realised Benefits: Research Funding

Measure	Expected	Realised
Total value of licence agreements by 2020/21	19.3	n/a
Total value of licence agreements by 2015/16	11.3	10.7

Source: BiGGAR Economics (2007), Cost Benefit Analysis of the SCRM and data provided by UoE in 2016

5.5 Spin-Outs

In 2007 it was also anticipated that the research undertaken at the SCRM would result in the creation of new spin-out companies, which would generate wealth and support employment in the local economy.

5.5.1 Anticipated Benefit

It was anticipated that a total of 11 spin-outs would be created by 2020/21 and that five of these would have been created by 2014/15. It was anticipated that at the outset each spin-out company would employ an average of three employees but that this would increase to around 30 employees over the space of about seven years. Based on these assumptions it was estimated that by 2015/16 spin-outs from the SCRM might employ a total of 98 staff. It was expected that by 2020/21 this could have increased to 289 staff. It was estimated that the turnover of spin-outs associated with the SCRM could be generating around £8.5 million turnover/year by 2015/16 and that this could increase to £25.2 million/year by 2020/21. These anticipated benefits are set out in Table 5-5.

5.5.2 Benefit Realised

To date the spin-out activity associated with the MRC CRM and the SCRM has all been linked to the activities of Roslin Cells Ltd, which was founded in 2006 with the aim of producing embryonic stem cells to GMP standards. Staff from the company were involved in designing the clean rooms in the SCRM and when the new building opened in 2012 the company became its first tenant and has been operating three of the cleanrooms within the building ever since.

Since 2012 the structure of Roslin Cells Ltd. has undergone a number of changes, the most significant of which was a decision to separate the cell manufacturing aspects of the business (i.e. activity associated with the operation of the clean rooms) from the drug discovery elements of the business. To facilitate this the capabilities of the company are now being delivered by two separate subsidiaries: Roslin Cell Therapies and Censo Biotechnologies.

When Roslin Cells Ltd. first moved into the SCRM it had around 15 staff and a turnover of around £1 million. At the time of writing Roslin Cell Therapies employed around 40 staff and was generating a turnover of around £2.5 million/year while Censo Biotechnologies had around 30 staff and was generating around £2 million/year.

Although Roslin Cells Ltd. predates the construction of the SCRM consultation with those involved in establishing the company confirm that the facilities within the building have been “transformational” for the company. Without the cleanroom facilities located within the SCRM it is almost certain that what has become Roslin Cell Therapies would have been unable to grow to any scale and possible that the company may not have survived at all.

Although the link between Censo Biotechnologies and the SCRM is slightly less direct, consultation with those involved in setting up the company confirm that the facilities at the SCRM were instrumental in enabling initial funding for the venture to be secured. If this funding had not been secured then Censo Biotechnologies probably would not exist. It is therefore reasonable to attribute the impact of both companies to the SCRM.

Taken together this means that in 2015/16 spin-outs associated with the SCRM employed around 70 people and were generating turnover of around £4.5 million/year. Although this means that the overall value of benefits to date is somewhat lower than was anticipated in 2007, this is because the total number of companies created has been lower than expected and not because the companies themselves have not performed as well as expected. These benefits are set out in Table 5-5.

Table 5-5 –Expected and Realised Benefits: Spin-outs

Measure	Expected	Realised
Number of spinouts by 2015/16	6	2
Number of spinouts by 2020/21	11	n/a
Employment in spin-outs by 2015/16	98	70
Employment in spin-outs by 2020/21	289	n/a
Turnover of spin-outs by 2015/16 (£m)	8.5	4.5
Turnover of spin-outs by 2020/21 (£m)	25.2	n/a

Source: BiGGAR Economics (2007), Cost Benefit Analysis of the SCRM and consultation with SCRM tenants

5.6 Summary

The cost benefit analysis prepared for the SCRM in 2007 considered five main types of benefit. Table 5-6 provides a summary of the extent to which each of these benefits has been realised to date. The key points to note are:

- The total cost of constructing the SCRM was as expected in 2007 and although the employment benefits associated with this expenditure were lower than expected, this was due to changes within the Scottish construction sector rather than anything to do with the SCRM.
- The amount of research funding secured by the SCRM has been lower than originally anticipated. It is likely that this is due, at least to some extent, to industrial funding being lower than anticipated.
- In terms of research related employment the SCRM has exceeded expectations and new employs more than 255 researchers, compared to the 210 anticipated in 2007.
- The total value of licence agreements associated with the SCRM to date 95% of the value anticipated in 2007, only slightly below expectations.
- The number of spin-out companies associated with the SCRM is below the number expected in 2007 and as a result the amount of employment supported in spin-out companies is 71% of the level anticipated in 2007.

Table 5-6 – Summary Expected and Realised Benefits

Measure	Expected	Realised
Construction benefits		
Construction cost (£ million)	39	39
Construction employment (job years)	207	396
Research funding		
Total secured by 2015/16 (£ million)	85.2	55.0
Total secured in 2015/16 (£ million)	22.1	11.1
Research employment		
Number of researchers employed by 2015/16	210	255
Licence agreements		
Value of licence agreements by 2015/16 (£ million)	11.3	10.7
Spin-outs		
Number of spinouts by 2015/16	6	2
Employment in spin-outs by 2015/16	98	70
Turnover of spin-outs by 2015/16 (£ million)	8.5	4.5

Source: BiGGAR Economics (2007), Cost Benefit Analysis of the SCRM and consultation with SCRM tenants

6 WIDER OUTPUTS

As discussed in section 4.1 the long-term nature of the research that scientists at the SCRM are engaged in means that the full benefits of much of the activity to date are unlikely to have been realised yet. In order to present a complete picture of the SCRM it is therefore important to consider whether there is any evidence to suggest that the activity undertaken to date is likely to generate benefits in the future. This section considers:

- identifies some of the important scientific outputs to have emerged from the SCRM to date and considers the future potential impacts associated with these discoveries; and
- considers how the SCRM has contributed to the development of a cluster of regenerative medicine expertise by facilitating and supporting the success of other, related, developments.

6.1 SCRM Scientific Outputs

One approach to evaluating the potential future benefits of the SCRM is to consider the scientific outputs that have been realised to date. Intermediate scientific outputs that can provide evidence of future benefit potential include:

- new human cell lines
- new tools that could be used to better understand diseases and identify targets for new medicines;
- biobanks of human tissue samples;
- validated or potential biomarkers of diseases;
- methods for predicting the toxicology of potential treatments;
- new animal models and humanised models;
- new approaches to identifying non-genotoxic carcinogens, which could reduce the need for animal trials in some circumstances;
- new knowledge from which new potential targets for medicines development could be identified;
- databases of findings and of data that have been collected but not yet fully analysed;
- novel imaging techniques and tools;
- new guidance and best practice recommendations; and
- new collaborations.

Consultation with SCRM staff have identified examples of at least nine of the 12 scientific outputs described above since 2012. This section describes these outputs.

6.1.1 New Human Cell Lines

One of the defining capabilities of the SCRM is the capability to manufacture induced pluripotent stem (iPS) cells, which have the potential to be differentiated into any other cell type in the body. These cells are of huge importance in regenerative medicine because they could be used to replace those lost due to damage or disease.

Consultations undertaken to inform this evaluation confirm that scientists at the SCRM have developed new cell lines relevant to a number of different diseases including:

- Parkinsons Disease;
- retinitis pigmentosa;
- motor neurone disease; and
- frontotemporal dementia.

Of particular note has been work undertaken to develop human liver tissue. This is expected to be of particular value both to patients with end-stage liver disease for whom a transplant is not a viable option and to the pharmaceutical industry.

Liver models are used by the pharmaceutical industry to "fast fail" candidate compounds in the drug discovery process. That is, to help identify those compounds that are unlikely to lead to satisfactory results before proceeding to costly pre-clinical testing. Identifying such compounds early not only helps to reduce the cost of drug development process but, by enabling industry to refocus its resources on alternative compounds that are more likely to be successful, can also help to streamline it. It is estimated that this "fast fail" approach has the potential to reduce the average R&D cost associated with developing a new drug by around $30 million.

To date scientists at the SCRM have successfully developed three prototype models, which have been evaluated by major industrial partners and shown to be comparable with existing "gold standard" models. A new company called Stemnovate has been established in Cambridge to bring these models to market. If successful Stemnovate therefore not only has the potential to significantly reduce the costs associated with drug development but could also help to increase the speed with which potentially life saving treatments can be brought to market.

6.1.2 Tools for Understanding Diseases

In addition to the work to develop cell lines, scientists at the SCRM have also been successful in developing a several other new tools for understanding diseases in areas including:

- the use of induced pluripotent stem cells (IPS) to model aspects of Multiple Sclerosis;
- the generation of high-purity stem cell derived liver cultures to enable scientists to model human drug toxicity and disease; and
- the generation of dopaminergic cells from clinical-grade human embryonic stem cells (hESCs) as part of an international consortium to bring cell therapy for Parkinson's to the clinic.

Understanding a disease is usually the first step toward developing an effective treatment so these tools are a good indication of the future impact potential of the SCRM.

6.1.3 Biobanks of Human Tissue Samples

One of the important challenges facing regenerative medicine is finding suitable, safe and ethical sources of stem cells. One source of adult stem cells is adipose tissue, which is responsible for storing fat in the human body.

Adipose tissue is readily available even in individuals with a healthy body weight and is routinely removed by plastic surgeons undertaking reconstructive and cosmetic procedures. The application of stem cells obtained from adipose tissue also raises fewer ethical issues than the use of embryonic stem cells and is less heavily regulated. Adipose tissue therefore provides an excellent potential source of stem cells for research and therapy.

Since 2010 scientists at the SCRM have been responsible for establishing a research tissue bank to collect, store and distribute human adipose tissue derived cells. Importantly the tissue stored at the Edinburgh Adipose Tissue Bank has all the appropriate ethical approval for subsequent downstream research, making it a potentially valuable resource for researchers engaged in this area of activity.

Since receiving ethical approval in November 2010 samples from 58 patients[7] had been collected. This tissue has since been made available to researchers outside the SCRM and led to the formation of around 10 research collaborations.

6.1.4 Validated or Potential Biomarkers of Diseases

Scientists from the SCRM have identified five biomarkers that have the ability to predict the severity of disease and likelihood of death from liver and kidney disease induced by paracetamol poisoning. At the time of writing pre-clinical testing was being undertaken on one of these biomarkers in advance of clinical trials. Ultimately it is hoped that these biomarkers could lead to new treatments for liver disease that would help to improve quality of life for patients.

Scientists at the SCRM have also successfully identified a number of biomarkers thought to be relevant to multiple-sclerosis and motor neurone disease. By working with patients at the regenerative neurology clinic based at the Anne Rowling Centre scientists from the SCRM are now using these biomarkers to measure disease progression.

It is hoped that the biomarkers could be used to measure the efficacy of candidate drugs in patients. The fact that the biomarkers have the capability to measure very small changes in patients cells is means that they could also make it less likely that an effective drug might be inadvertently overlooked.

6.1.5 Methods for Predicting the Toxicology of Potential Treatments

Bringing a new drug to market can take more than 12 years and cost anywhere between $800 million and $2 billion but very often after all this investment potential new drugs do not make it through the process. The second most common cause of human drug failure is liver toxicity and as a result a reliable

[7] West et. al. (2014), Ethical, legal and practical issues of establishing an adipose stem cell bank for research, Journal of Plastic, Reconstructive and Aesthetic Surgery

supply of good quality human liver cells to test new drugs is a major bottleneck in safety testing new drugs.

At present most drugs are tested using liver tissue from deceased donors but the supply of such tissue – particularly if particular genetic characteristics are required - is inherently unreliable. As a result of the work described in section 6.1.1, scientists at the SCRM are now able to use stem cells to produce human liver tissue, which can be used to evaluate the toxicity of potential new drugs. Importantly, because the cell models can be designed with different genetic parameters, they can also be used to help scientists to understand why some drugs can be effective on some people while being toxic to others.

The scalable nature of the cell models could provide a much less erratic alternative supply of liver tissue for drug testing. Ultimately this could help generate significant cost savings for the pharmaceutical industry and help to bring new treatments to market faster than would otherwise be possible.

6.1.6 New Animal and Humanised Models

A number of scientists at the SCRM have been involved in developing new animal models to help improve understanding of different diseases. One group for example is undertaking pre-clinical testing of a potential therapy for liver disease by investigating whether it is possible to replace the liver of imuno-deficient mice while another has developed a new way of analysing multiple sclerosis using an animal model.

A third group of scientists at the SCRM have successfully developed a lab-grown thymus gland after successfully transplanting reprogrammed stem cells into a mouse. The thymus gland plays a vital role in the human immune system and is one of the first organs to begin to degenerate with age. At the time of writing the approach developed by the SCRM scientists was still in the early pre-clinical phase of development but ultimately it is hoped that it could provide the basis for a therapy that could boost thymus function in patients with reduced immune function.

6.1.7 Identification of New Potential Targets for Medicines

The identification of new potential targets for medicines is the focus of much of the activity undertaken by the SCRM. Since 2012 scientists at the SCRM have published three papers that describe a molecule or signalling pathway that could provide a target for a new medicine. One example of this is potential new treatments for liver cancer, which at the time of writing was moving toward clinical trial. Another example is work being undertaken on Childhood lukemia.

Leukaemia is a blood cancer that involves large numbers of faulty white blood cells being manufactured by the body. Leukaemia stem cells are responsible for producing these cancer cells and fuelling the disease. Current therapies focus on destroying the faulty white blood cells but they do not destroy the leukaemia stem cells.

The research being undertaken by scientists at the SCRM aims to understand the biology of leukaemia stem cells and identify how they escape treatments. At the time of writing the group involved in this research had identified two potential treatments that it is hoped could eventually be used to successfully target leukaemia stem cells.

6.1.8 Novel Imaging Techniques and Tools

Being able to monitor what happens to cells after they have been implanted into an animal model or human patient is of vital importance to the experimental work undertaken at the SCRM. This has resulted in the development of several new microscopy techniques and 2D and 3D modelling methods. Scientists within the Centre have also been responsible for developing a number of innovations that should help move existing imaging technology. These innovations include new software and contrast agents for use with existing MRI technology and a new type of glass fibre rod that can be used to take images of damaged cells.

Scientists at the SCRM have also been particularly active in developing new analysis techniques for measuring myelin, a substance that provides an insulating sheath around many nerve fibres and increases the speed at which impulses are conducted. It is hoped that this work could support the understanding of and (ultimately) development of new treatments for multiple sclerosis.

6.1.9 New Collaborations

Collaboration with industry and academics from elsewhere is an important focus for the SCRM. Consultations with researchers based at the SCRM suggest that individual labs are engaged in multiple academic and industrial partnerships. The number of collaborations varies from lab to lab but it was estimated that each individual lab might be engaged in an average of around three academic partnerships. At the time of writing there were 20 labs within the SCRM, which implies that the total number of academic partnerships across the whole Centre could be around 60.

In addition to academic collaborations various groups within the SCRM are also engaged in collaborative projects with industry. At the time of writing it was estimated that scientists at the SCRM were engaged in 10-15 collaborative projects with industrial partners around the world. These projects, which were at various stages of the drug development process, included:

- **A new method of assessing patients with acute liver injury**. Currently it can be very difficult for clinicians to assess what treatment, if any, is appropriate for patients with acute liver injury. This project is based on a patented method of looking at markers in blood that could provide clinicians with an additional tool to help them assess patients.

- **A new compound that could be used to help patients with liver failure**. It is believed that the new compound could help to harness the immune system of patients in order to combat infections linked to the condition. At the time of writing the compound had been patented and scientists were working on early pre-clinical testing.

- **Development of protocols that yield enhanced differentiation of hepatocyte like cells**, which could be used as a replacement for donor organs for patients requiring a liver transplant and to undertake toxicity tests for new drugs. At the time of writing the new protocols had been patented and verified by industry.

- **Development of a non-destructive cell-imaging platform with direct applications in bone and cartilage regeneration research.** It is hoped that this platform could provide a diagnostic tool for patients and for monitoring

cells transplanted into patients. At the time of writing patenting of this platform was underway.

- **Development of screening assay tools based on stem cell derived hepatocytes.** It is anticipated that this assay could be used to produce liver cells of a sufficiently high quality and volume that it could provide a new and lower cost method of testing the toxicity of drugs. At the time of writing there was a patent pending for this assay.

- **Development of an in vitro model for remyelination research.** It is anticipated that this model could be useful for researchers undertaking research into Multiple Sclerosis by providing a tool for validating potential drug targets.

- **Identification of small inhibitors capable of promoting remyelination in patients with Multiple Sclerosis.** At the time of writing this project was part of an R&D project with the pharmaceutical industry that was aiming to identify a target for phase one clinical trials that could eventually lead to a new treatment for Multiple Sclerosis.

- **Definition of transplantable liver stem cell and new targets to boost liver regeneration.** At the time of writing this project was in the pre-clinical phase, close to phase one clinical trials.

- **Proof of concept of a new stem cell model for the treatment of drug overdose.** At the time of writing this project was at an early stage of development but it is hoped that it could ultimately be used to develop a novel approach to treating drug overdoses.

6.2 Contribution to Innovation Network

An important part of the original rationale behind the creation of the SCRM was to provide a catalyst for the development of a successful regenerative medicine cluster in Scotland. As a central component of the Edinburgh Bioquarter initiative, the project was expected to provide a vital bridge between academia, industry and clinical practice. This section considers the extent to which the SCRM has fulfilled this objective by exploring how the existence of the SCRM has supported a number of other related developments.

6.2.1 Scottish National Blood Transfusion Service

In addition to the MRC CRM, the SCRM building is also home to the Scottish National Blood Transfusion Service (SNBTS) Cellular Therapy Development Centre. The aim of the SNBTS Centre is to support the development of cellular therapies by translating research protocols into GMP to enable the production of clinical grade cellular therapies for clinical trial and, eventually, clinical practice.

The SNBTS Centre occupies three of the six cleanrooms located within the SCRM and employs around 10 people on-site. The activities of the Centre also support employment for between 30 and 35 people in other parts of the SNBTS.

The SNBTS Centre supports the development of a number of different cellular therapies including:

- corneal epithelial stem cells for ocular surface disorders;

- anti-EBC cytotoxic T lymphocytes for the treatment of post-transplant lymphoproliferative disease; and
- mesenchymal stromal cells in pancreatic islet transplantation.

At the time of writing the Centre was about to take two studies to clinical trial and was progressing a further two studies that were ready or nearly ready to go to clinical trial.

Consultation with the SNBTS suggests that the SCRM has played a key role in this by providing a unique trio of complementary elements:

- high quality manufacturing facilities that enable researchers to manufacture cells to GMP standards;
- world-leading research expertise from the MRC CRM; and
- access to clinical expertise, and patients, as a result of being collocated with the Royal Infirmary of Edinburgh.

Taken together this combination has made it possible for researchers at the SNBTS to take potential therapies from the development process and through to clinical trial. Something that may not have been possible if the SCRM did not exist.

6.2.2 Scottish National Islet Transplant Programme

Another important development that has been facilitated by the SCRM is the Scottish National Islet Transplant Programme.

The Scottish National Islet Transplant Programme is a national service commissioned by the NHS for some patients with Type I diabetes. These patients have problems managing their blood sugar levels and can suffer from hypoglycaemic unawareness, which means they can collapse without warning.

Treatment involves isolating islet cells, which make and release insulin, from a donor pancreas and transfusing them into the patient's liver. The aim of this treatment is to restore glycaemic awareness (the ability to detect life-threatening hypoglycaemia) and help patients to become insulin independent.

The bid developed to obtain the funding necessary to establish the Scottish National Islet Transplant Programme was put together when the SCRM was being built. Those responsible for the service were keen to establish a relationship with the SCRM from the outset and have confirmed that this was very important to the success of the initial funding bid.

The first Scottish transplants took place at the Royal Infirmary of Edinburgh in 2011. Since then the clinical programme has become the best of its type in the UK and the 2nd biggest in the world, delivering life changing improvements for patients with Type I diabetes.

In addition to the clinical programme, the researchers involved in the Scottish National Islet Transplant Programme are also engaged in a research programme. The focus of this programme is developing a protocol that would enable clinicians to develop an unlimited supply of islet cells from donor organs. At the time of writing, this protocol had been shown to be very successful at the experimental level and the research programme was considered the most advanced of its kind anywhere in the world.

From the outset there has been a close relationship between the research programme and the SCRM. Key members of staff from the SCRM have acted as co-Principle Investigators on several funding applications and the manufacturing facilities within the SCRM have made it possible to progress from scientific research to translatable technology relatively quickly.

Consultation with staff involved in the programmes confirm that if the SCRM did not exist then the research programme would be at least two to three years behind where it currently is and may not have happened at all. There are a number of reasons for this but perhaps most importantly has been the role that the SCRM has played in enabling collaboration to occur across academic disciplines and between academic researchers and clinicians.

At the time of writing the lab protocol developed as a result of the research programme was in the process of being turned into a clinical protocol that could be used to manufacture cells for human trials. The intention is that these cells would be manufactured using the clean room facilities within the SCRM. Without the facilities and co-location of relevant expertise available at the SCRM it is highly unlikely that this could have been achieved.

Ultimately it is hoped that the new protocol developed as a result of this programme could enable clinicians to extract enough cells from each donated pancreas to treat between five and ten patients. Currently two pancreas' from two separate donors are required to treat each patient. Clearly this would be a huge step forward in this area of medicine and the patients affected by it.

6.2.3 Research Funding and Collaborations

Researchers at the SCRM have also succeeded in attracting a significant amount of new research funding in recent years, which has supported the growth of a large cluster of regenerative medicine research expertise at the Bioquarter. Some key achievements include:

- The Centre for Regenerative Medicine in the SCRM was awarded MRC (Medical Research Centre) status in 2008, attracting initially £2.0 million funding which was successfully renewed in 2013 and granted a further £2.2 million.

- The MRC Centre for Regenerative Medicine successfully secured £4.5 million in 2013 to lead a collaborative research network to study how stem cells are controlled in the body. Understanding 'the niche' would help devise ways to stimulate the body's own repair processes with drugs or improve the function of transplanted cells. The United Kingdom Regenerative Medicine Platform is a £25 million initiative co-funded by the UK's Medical Research Council (MRC), Biotechnology and Biological Sciences Research Council (BBSRC), and Engineering and Physical Sciences Research Council (EPSRC). The Platform consists of five collaborative research hubs across the UK, each formed by an identified lead higher education institution and collaborating university groups. Each hub is focused on a different area of translational research that will advance regenerative medicine towards clinical applications, addressing unmet medical needs.

- In 2013 the MRC CRM received £10 million from the Medical Research Council[8] to build an extension to the SCRM building. The funding was awarded through the second stage of the UKRMP. The new laboratory space, the UKRMP Centre for the Computational and Chemical Biology of the Stem Cell Niche, was intended to function as a 'research hotel' available to all UK regenerative medicine researchers at minimal cost to support the rapid development of innovative new regenerative therapies for patients. Within the new laboratory facility scientists are seeking to develop an artificial system to simulate the environment that surrounds stem cells in organs in the body, called the 'niche'. The artificial niches would allow researchers to grow stem cells in a more controlled way and turn them into functioning cells that could be used to repair damaged tissue.

- In 2013, the Massachusetts-based biotechnology company Biogen Idec signed a deal to fund a three-year collaboration with the MRC CRM to explore the cell processes behind multiple sclerosis and motor neurone disease[9]. The collaboration also involves identifying drug compounds that could potentially be used as treatments for the neurodegenerative conditions. The partnership combines the expertise of the MRC CRM and the University of Edinburgh's strengths in translational medicine with Biogen Idec's strengths in drug discovery and development, particularly its portfolio of treatments for patients with multiple sclerosis.

- The MRC Centre for Regenerative Medicine has a 2-year collaborative partnership with GlaxoSmithKline (GSK) to conduct drug discovery research that could be used to develop new treatments for brain diseases[10]. The collaboration focuses on regenerating the protective myelin sheath around nerve cells that can be damaged during brain injury or demyelination (e.g. multiple sclerosis) and lead to brain complications.

- Part of the ground floor of the SCRM building houses the £2.5 million British Heart Foundation (BHF) Centre for Vascular Regeneration. The focus of work at the Centre is developing new treatments to repair the damage caused by a heart attack.

6.2.4 Anne Rowling Regenerative Neurology Clinic

The Anne Rowling Regenerative Neurology Clinic is a purpose-built clinical research facility funded by a philanthropic donation and designed to enable the assessment and treatment (within the framework of clinical trials) of patients with MS, motor neuron disease and other neurodegenerative diseases. The establishment of the Clinic in 2013 and the research funding it has since attracted can be attributed to the critical mass of research in regenerative medicine that the SCRM has created.

6.2.5 European Bank for Induced Pluripotent Stem Cells

Induced pluripotent stem (iPS) cells have the potential to significantly advance drug development and health research but collections of stem cells are scattered across the world, their quality cannot always be guaranteed and accessing them

[8] http://www.crm.ed.ac.uk/news/%C2%A310m-capital-funding-build-new-%E2%80%98stem-cell-niche%E2%80%99-facility
[9] http://www.crm.ed.ac.uk/news/transatlantic-partnership-tackle-neurodegenerative-disease
[10] http://www.edinburghbioquarter.com/news/item/university-of-edinburgh-gsk-collaboration-aims-to-tackle-myelin-regeneration/

is often difficult. In March 2016 the European Bank for Induced Pluripotent Stem Cells (EBiSC) was launched to address these issues.

The aim of the EBiSC is to establish a European wide iPS cell bank that will become the 'go-to' resource for the characterisation, storage and distribution of high quality iPS cells. Ultimately, it is intended that EBiSC will become an independent organisation, distributing high quality iPS cells on a not-for-profit basis to scientists worldwide.

The EBiSC Consortium is led by Pfizer Ltd and managed by Roslin Cells Sciences Ltd., which operates the main processing and storage facility at the Babraham Research Campus in Cambridge.

6.3 Conclusion

The evidence presented in this chapter suggests that several important scientific outputs have emerged from the SCRM that have the potential to improve the understanding and treatment of life threatening diseases and conditions such as liver failure, multiple sclerosis and motor neurone disease. Although these outputs are all still in the early stages of development, if they can be successfully translated into the clinic then they could bring about significant benefits for both the patients and the industrial partners responsible for bringing new treatments to market.

This chapter has also identified several wider developments that have either happened as a direct result of the existence of the SCRM or which would otherwise have been significantly less advanced. Taken together these developments have created the foundation for an emerging regenerative medicine cluster that is concentrated around Edinburgh's BioQuarter.

The development of the SCRM has also enabled the University of Edinburgh to leverage in a substantial amount of new funding to support important areas of research. Of particular note has been the:

- Significant donation secured from JK Rowling to support the creation of the new Anne Rowling Centre;
- £10.0 million secured from the Medical Research Council to support the creation of the Centre for Computational and Chemical Biology of the Stem Cell Niche; and
- £10.7 million secured from the UK Research Partnership Investment Fund to support the new Institute for Regeneration and Repair (see section 7.2).

7 NEXT STEPS AND FUTURE IMPACTS

This chapter considers the benefits that the SCRM could deliver for the Scottish economy in the future and what will be required to realise these benefits.

7.1 Translation of Research

As the previous chapter has demonstrated the SCRM has already made significant scientific progress in advancing understanding of several life threatening conditions and diseases. It has also developed improved approaches for developing treatments for a number of these diseases. While these scientific outputs represent a vital first step, as yet none of the advances have resulted in improved clinical outcomes or new treatments.

7.1.1 Engagement with Industry

Consultation with stakeholders undertaken to support this evaluation suggests that the main reason for this has been a lack of engagement between the SCRM and industry.

These consultees felt that the primary focus for the SCRM is on academic research and believed that this focus tends to override the need to translate research outputs into commercial/clinical outcomes. In particular, consultees suggested that, while the SCRM has been very adept at securing research funding it has not been as strong at developing fundable investment propositions. Given the amount of investment required to translate medical technologies into clinical practice this will be of critical importance to the SCRM going forward.

One consultee expressed the view that, at present, much of the research activity undertaken at the SCRM appears to be aimed at initiating first stage clinical trials and that not enough consideration is given to whether the NHS is likely to purchase the technology being tested. This consultee suggested that, as companies will only be interested in investing in technologies that have a demonstrable "route to market", securing investment for second and third phase clinical trials for such projects is unlikely. This consultee believed that to rectify this issue there was an urgent need for the SCRM to work with partners in industry, potential investors and the procurement section of the NHS to identify and then focus on those projects with the greatest commercial potential.

Importantly, the leadership of the SCRM are well aware of this issue and acknowledge that increasing the level of engagement with industry will be critical to the success of the next phase of the initiative.

By way of explanation it is necessary to highlight a decision that was taken during the early years of the SCRM to claim VAT relief on the building on the basis that it would be a medical research facility (and therefore exempt). In order to qualify for this relief the commercial space that was originally part of the plans for the building and would have provided accommodation for new spin-outs and collaborative research was not included in the final design. This decision has also placed limits on the SCRM's ability to engage with industry because it has meant that neither consultancy nor contract research can be undertaken in the building.

In addition to this since opening the SCRM has, for the most part, had no dedicated business development support function. (Although some resource was available at the outset this was only available for the first two years.)

Importantly, both the leadership of the SCRM and all of the consultees who voiced concern about the current lack of engagement with industry saw the proposals for the new Institute for Regeneration and Renewal (IRR) as an important opportunity to address these concerns.

7.2 Institute for Regeneration and Repair

To help translate regenerative medicine research into treatments the University of Edinburgh is currently progressing plans to develop a new building next to the SCRM. Taken together the new building and the SCRM will become the Institute for Regeneration and Repair (IRR).

The total cost of the project is expected to amount to £53 million. It is expected that the Medical Research Council will provide £5.0 million of the funding required and the UK Government Research Partnership Investment Fund will provide a further £10.7 million. The balance of the funding will be met by the University of Edinburgh using a mixture of its own funds and funds from donors and philanthropic sources.

The new building will house 270 scientists and will aim to address three bottlenecks in particular. Despite significant advances in understanding the role of stem cells in regeneration, there is still an incomplete understanding of the mechanisms that coordinate cell behaviour at the level of the tissue – a critical step for translation and effective clinical application. As well as this, there is a lack of drugs or small molecules that can directly promote regeneration. Thirdly, in many tissues even if drugs or cells able to enhance regeneration were available, it is currently not possible to detect critical functional and structural changes and track these over time.

The focus of the IRR will be to establish an interdisciplinary research platform focused on tissue structure and function during repair, drug discovery and the development of tools and technologies to quantify regeneration in clinical trials.

7.2.1 Clinical Trials

To date scientists at the SCRM have undertaken four stage one clinical trials. At the time of writing a further two trials were about to start and another one was ready to start. All of the trials undertaken so far have been phase one clinical trials, which are undertaken at the start of the clinical evaluation phase in the development of a new treatment (see Figure 4-1). Although these trials are all relatively small scale and early stage, each of them has the potential to lead to future commercial and health benefits if successful.

On average progressing a new treatment through from the lab to large-scale human trials and into clinical use can take 12-15 years and cost over $2 billion[11], with each successive stage in the process becoming increasingly more expensive. The scale of funding required means that progressing a technology beyond stage one clinical trials is almost certainly beyond the capability of any individual university or research council. The implication of this for the SCRM is that large-scale commercial support will be required to progress any of scientific outputs achieved to date into clinical outcomes.

[11] Scientific American (November 2014), Pharmaceutical drug now exceeds $2.5b

7.2.2 Realising the Potential of the IRR

In order to secure large-scale commercial support in the future it will be necessary to significantly increase the level of engagement between the IRR and industry. Achieving this will require dedicated professional business development support.

To date the business development capacity at the SCRM has been very limited. Although some resource was provided during the initial two years of the project, there has been no dedicated capacity to undertake this type of activity since then. In order to realise the future potential of the IRR it will be vital to address this.

The development of a dedicated business support function within the IRR would also enable the SCRM to re-engage with development agencies such as Scottish Enterprise (SE) and Scottish Development International (SDI). Although efforts were made to engage with these agencies at the outset of the project, at this time the SCRM had not yet developed a track record.

Now that significant scientific progress has been made, there is a strong case for reengagement between the IRR and SE/SDI. Not only should this help maximise the economic impact of the IRR by enabling it to engage with industry around the world but, by raising the profile of developments in Scotland, should also support the development of the wider Scottish regenerative medicine sector.

7.3 Future Benefits

The new building that the University of Edinburgh proposes to develop next to the SCRM should have the capacity to accommodate 270 researchers, which would bring the total number of researchers at the IRR to over 500. Within ten years it is expected that these researchers could be generating £43.4 million funding/year.

It is however worth highlighting that future income projections have been prepared on the expectation that in ten years time around 12% of all research income will come from EU government institutions. Given the current uncertainty surrounding the UK's exit from the EU the future of this funding is far from secure.

Another key assumption underpinning the future income projections for the SCRM is that in future 5% of research funding will be secured from UK industry or from consultancy. Although this would be a significant increase (currently these sources of income represent around 1% of the total) in absolute terms it would mean that income from industry would still be a relatively minor source of income.

Both of these factors are likely to have a significant impact on the future performance of the IRR. The next sections use two scenarios to illustrate this.

7.3.1 Scenario 1: Loss of EU Funding and Competitive Position

The UK's exit from the EU casts doubt on the future of an important component of of the IRR's research income. The worst-case scenario would be that over the next two years, as the UK negotiates to leave the EU this income falls significantly and that on exit EU government organisations completely withdraw future funding. If this were to occur and the shortfall in income were not made up from some other source then the income of the IRR would be 18% lower than anticipated.

As research income is crucial for attracting and retaining the best researchers and funding from one source is often used to leverage funding from other sources, a loss of this magnitude would inevitably have implications for the international

competitiveness of the IRR. This was modelled by assuming that other sources of funding would also fall by 5%.

Applying these assumptions suggests that by 2020/21 the IRR could be securing a total of £26.4 million research funding/year with a cumulative total of £161.4 million by 2020/21. Assuming that the ratio of research income to researchers remains constant then this would imply that by 2020/21 the IRR might employ around 434 researchers.

It would also be reasonable to expect that this reduction in competitiveness would have a detrimental impact on the IRR's ability to negotiate licence deals. To model this it was therefore assumed that the ratio between research income and licence income might also fall by 5% under this scenario. Applying this assumption would mean that by 2020/21 the IRR could be generating around £0.2 million/year in licence income. This would equate to approximately £6.0 million in additional turnover for licence holding businesses by 2020/21 and a cumulative total of £20.1 million since the SCRM was established.

It is also likely that any loss of competitiveness would damage the prospects for existing and future spin-out companies emerging from the IRR. This was modelled by assuming that employment in existing spin-outs would remain at the current level but that the ratio of research income to turnover and employment in new spin-out companies would decline by 5%.

In this way it was estimated that by 2020/21 spin-outs from the SCRM/IRR could be employing around 110 people and generating around £7.0 million turnover/year. This would equate to a cumulative total of around £42.3 million turnover between the time of the SCRM being established and 2020/21.

7.3.2 Scenario 2: Developing Closer Ties with Industry

Alternatively the IRR could set out to aggressively target commercial funding to help replace the funding currently provided by EU government institutions. If this strategy were to be adopted and the IRR were to succeed in replacing EU funding with industrial funding then it may be possible to maintain the competitiveness of the Institute. One consequence of this would be that the IRR would find it easier to attract and retain the top research talent and leverage funding from other sources, which should make it possible to achieve the target of employing over 500 researchers.

As discussed above, securing substantial industrial funding will also be necessary in order to realise the full potential of the many scientific outputs delivered to date. It is likely that this would have knock on benefits for the sector by creating new opportunities for start-up and spin-out companies and businesses servicing the sector's supply chain and, potentially, helping to attract inward investment.

This effect was modelled by assuming that in future the ratio between research income and licence income might be 5% higher than at present. In this way it was estimated that by 2020/21 the IRR could be generating around £0.3 million/year in licence income, which would equate to approximately £6.3 million turnover for licence holding businesses. Over the entire period from when the SCRM was established to 2020/21 this would represent a cumulative total of around £25.7 million additional turnover for licensees.

It is also reasonable to expect that closer relationships with industry would create new opportunities for spin-out companies. This effect was modelled by assuming that in future the relationship between research income and the turnover and

employment of spin-outs might also improve by around 5%. Using this assumption it was estimated that by 2020/21 spin-outs from the SCRM/IRR might employ around 220 people and generate around £21.7 million turnover/year. The cumulative value of this turnover between the time the SCRM was established and 2020/21 could be around £63.6 million.

7.3.3 Summary

A summary of the future potential impacts of the IRR under each scenario is provided in Table 7-1.

Table 7-1 – Summary Potential Benefits by 2020/21

Impact by 2020/21	Scenario 1	Scenario 2	Original Expectation
Cumulative value of research funding (£m)	161.4	178.3	259.7
Researcher employment by 2025/16	436	505	210
Turnover supported by licences (£m)	20.1	25.7	19.3
Employment in spin-outs by 2025/16	109	220	289
Turnover of spin-outs (£m)	42.3	63.6	114.3

Source: BiGGAR Economics

This demonstrates that by 2020/21, which was the end of the period considered in the original cost benefit analysis, most the outputs of the SCRM are likely to be lower than what was originally expected under both scenarios. The reason for this is likely to be, at least in part, attributable to external factors outwith the control of the SCRM not least of which would be the global financial crash that started in 2008.

The more important point to take from Table 7-1 is that the outputs of the SCRM are likely to be significantly higher under scenario two, which assumes an increased level of engagement with industry, than under scenario one. Indeed under this scenario it would be reasonable to expect the SCRM to have met or exceeded all of the expectations set out in the original cost benefit analysis before 2023/24, two to three years later than anticipated. The one exception to this could be employment in spin-out companies which has so far grown much slower than anticipated; however this could change quickly should a particularly successful company emerge over the next few years.

8 CONCLUSIONS

The cost benefit analysis undertaken to support the funding application for the SCRM in 2007 identified five potential benefits associated with the project:

- temporary construction benefits associated with the initial capital investment;
- research funding that would be secured by researchers in the SCRM;
- research related employment supported on-site;
- additional turnover within organisations that licenced technologies developed at the SCRM; and
- turnover and employment of spin-out companies established based on research undertaken at the SCRM.

The performance of the SCRM to date in relation to these original objectives has been mixed. The cost of constructing the SCRM was as expected in 2007 and although the employment benefits associated with this expenditure were lower than anticipated, this was due to changes within the Scottish construction sector rather than anything to do with the SCRM.

Although the amount of research funding secured by the SCRM to date has been lower than originally anticipated, expectations in relation to research related employment have been comfortably exceeded and there are now more than 250 researchers working in the building. This evaluation has also identified several wider developments that have either happened as a direct result of the existence of the SCRM or which would otherwise have been significantly less advanced. Taken together these developments have created the foundation for an emerging regenerative medicine cluster concentrated around Edinburgh's BioQuarter.

There is however room for improvement, particularly in relation to the commercialisation performance of the SCRM. Although the licence income generated from technologies developed, at least in part, by researchers working at the SCRM has almost achieved expectations, outputs relating to the performance of spin-outs have been much lower than anticipated. To some extent this is likely to reflect the fact that the nature of the research undertaken at the SCRM is very long-term in nature but it also highlights the importance of focusing on the translation of research going forward.

Given the long-term nature of the research undertaken at the SCRM this evaluation has also considered the extent to which activity undertaken to date is likely to generate benefits in the future. Evidence from consultations undertaken with staff at the SCRM and within partner agencies suggest that several important scientific outputs have emerged from the SCRM to date relating to various serious diseases and conditions. If these outputs can be successfully translated into clinical practice then they have the potential to bring about significant benefits both for patients and the Scottish regenerative medicine sector.

In order to realise these benefits it will be necessary to move the research currently underway at the SCRM beyond the pre-clinical phase and into clinical trials. Developing deeper relationships with industry will to be essential to achieving this. In order to develop these relationships the IRR will require a dedicated business development support function with the capacity to engage directly with industry and development agencies such as SE and SDI.