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Technology transfer in the biomedical sciences: The Medical Research Council approach

Date received (in revised form): 1st November, 2000

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Abstract This paper describes why the UK Medical Research Council participates in exploitation (an integral part of its mission), the objectives for exploitation (primarily to serve public food through contributions to the health and wealth of the UK) and how the organisation of exploitation is structured. Finally, an indication of some achievements is presented.

Keywords: MRC, technology transfer, licensing, conflicts of interest

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Background

The Medical Research Council (MRC) is the principal UK government agency for the support of biomedical research. The forerunner, the Medical Research Committee, was created in 1913 (renamed the Medical Research Council in 1920) with a specific mission, to fund research targeted at the management of ill-health, e.g. TB was then killing about 75,000 people in the UK each year.

The MRC approach was established many years ago: (i) to support research that might be applied to meet health needs, (ii) to extend medical knowledge to prevent or combat disease and (iii) to include all research bearing on health and disease. To move to modern times, the Science Engineering and Technology White Paper, in May 1993, reconfirmed the MRC incorporation under Royal Charter, and described the MRC's objectives in terms of a Mission Statement linking the support of scientific excellence and training for research to both the health and wealth of the nation.

While some of the MRC objectives can be met directly, eg the training of future generations of scientists for a broad range of activities, informing government policy, and making research findings directly applicable to the health of the public, a significant part of the research the MRC supports can meet its objectives only by further development through the application of the intellectual and financial resources of industry. Consequently, it follows that the MRC requires active participation in technology transfer in order to fulfil its mission.

Participation in technology transfer

UK government policy, since the mid-1980s, has been that ownership and management of intellectual property/intellectual

property rights (IP/IPR) resides with the employer of the researchers. Thus, MRC owns and manages IP/IPR arising in its own institutes/units; higher education institutions (HEIs) own and manage IP/IPR when their employees are successful in their grant applications to the MRC (except in limited and defined programmes, eg the AIDS Directed Programme, the planned DNA collections research).

The balance of the present paper focuses on the approach the MRC takes to managing the IP/IPR arising in its own institutes and units. MRC staff participate in Office of Science and Technology (OST) discussions/initiatives intended to foster exploitation of technology by HEIs, but the ownership and management of technology arising from Research Council grant funding to HEIs remains the responsibility of HEIs.

Objectives for technology transfer

The objectives for technology transfer, which reflect the overall MRC mission are (in order of priority):

- to work through the mechanisms, and with the partner(s) judged most likely to develop MRC technology into products and services useful to society;
- to maximise the contribution to national wealth creation, UK industrial competitiveness;
- to maximise income to the MRC in the medium to long term.

Delivery of exploitation in order to meet these objectives requires judgment, on a case-by-case basis by the MRC exploitation staff, working in partnership with the participating research scientist(s). The objectives provide an anchor, or a reference point, to aid what are ultimately often opportunistic and/or pragmatic judgments.

In the ideal world, a series of non-exclusive licences might best fulfil these objectives. If practical, as it has been on a limited number of occasions, this approach maximises the intellectual and financial resources available to further develop the technology into products and/or services useful to society. In practice, of course, rarely are companies or equity investors prepared to participate, and commit their own resources, on the basis of non-exclusive rights.

The question of whether to license technology, or to pursue the 'spin-out' company route is consistently an interesting challenge. Existing companies, especially large multinational pharmaceutical companies with their sophisticated R&D resources, should be ideal licensees. In practice, these companies often conclude that technology from the MRC, although potentially bearing high potential, is too 'early' to attract their interest and sustained commitment. In contrast, 'spin-out' companies are usually founded on a high-potential, limited scope, specific technologies; the motivation to make sustained commitment to that technology in each company is huge. While the 'spin-out' company will never match the financial resources of the multinationals, nor the breadth of their intellectual competence, 'spin-out' companies can recruit to match scientific intellectual excellence in their field of interest and good investors will sustain the company's financial resources, while it makes progress.

The manner in which technology transfer decisions impact on UK wealth creation is probably far more complex than the author understands, but clearly job creation/job retention is an important feature of national wealth, and jobs in the pharmaceutical and biosciences industries are deemed to be high-value jobs. Although retention of jobs in multinational company R&D requires continuing competitiveness in the company R&D, a licensing agreement with an academic body rarely, probably never, impacts directly on the R&D budget or establishment. In contrast, technology used to create a 'spin-out' company or expand an existing small company can both create new jobs and provide the basis of new or further investment.

It is too soon for the MRC to determine whether the financial returns to the MRC are greater through licensing or through equity in 'spin-out' companies. The MRC has specific examples where the value of

equity in 'spin-outs' is substantial. In addition, MRC 'know-how' also generates significant royalty income from licensing to existing companies. The ideal solution might be to negotiate a mix of equity and royalty rights, if possible.

Policy support structures

Incentive scheme

For scientists

The MRC has a long-standing incentive scheme to encourage its scientists and their MRC institute or unit to participate in successful exploitation; the 'Awards to Inventors' scheme; recently amended to be more generous to inventors and their institute/unit. The purpose is to reward participation in exploitation, while minimising the risk that the rewards are so great as to distort the scientific programmes of the MRC. In addition, the rigour of the peer review process offers a major protection against the risk of distortion.

The MRC scheme is unusual in that it distributes gross exploitation income, in contrast to many other bodies that distribute income after deduction of the costs directly associated with exploitation (eg patent and legal fees, exploitation staff salaries/overheads). Exploitation costs are inevitably front-loaded whereas the large income is often very delayed. There is minimal incentive in schemes that distribute exploitation income after deduction of costs when the immediate direct costs of exploitation can readily exceed the 'up-front' fees. The detailed distribution is illustrated in Table 1.

The MRC policies also allow MRC scientists to hold shares in 'spin-out' companies in their own name. These might be for their additional contribution at the foundation stage (this invariably requires much more of the scientist than does licensing) and also options for their sustained contributions to the 'spin-out' company (see the comments on conflict of interest below). The sustained commitment can be at a variety of levels, providing the basis is agreed in advance and transparent.

Table 1 MRC 'Awards to Inventors' scheme[a]

	Distributed to		
Income	**Inventor(s)[b]**	**Institute/unit[c]**	**Commercial fund**
1st £1.4k	100%	0%	0%
Up to £80k	33.3%	33.3%	33.3%
Next £520k (to £600k)	25%	25%	50%
Next £900k (to £1,500k)	20%	20%	60%
Over £1.5m (to £15m)	15%	15%	70%
Over £15m	10%	10%	80%

[a]Distribution of *gross* exploitation income. Sums are based on cumulative income per invention.
[b]Personal payments are normally made annually with the July salary, and are subject to income tax and National Insurance deductions. Staff may waive their entitlement in favour of the unit, provided the waiver is notified before payment. The identity of the individual inventors, which may be interpreted more loosely than the interpretation made by the Patent Office to reflect teamwork, is made by the director. Payments are made to individuals whether they remain on the MRC staff or leave, and may be paid to the estate of inventors.
[c]The payment to the institute/unit supplements the budget and maybe used at the discretion of the director.

Continuing participation by MRC scientists has ranged from membership of the company Scientific Advisory Committee through to part-time employment contracts with both the MRC and with the 'spin-out' company, for defined periods.

For technology transfer personnel

The MRC is examining ways to provide suitable incentives for its technology transfer personnel – but at the time of writing has no mechanisms in place. The MRC objectives for exploitation place 'public good' considerations as higher objectives than revenue raising. These 'public good' objectives are difficult to measure in the short term, and incentives linked to income might, indeed probably would, encourage a distortion of the exploitation objectives.

Conflicts of interest

The participation of publicly funded researchers in effective exploitation

provides potential for conflicts of interest. The MRC has a range of procedures intended to manage these potential risks; it believes these risks can be managed, but can be eliminated only by withdrawal from exploitation.

The key issues are:

- to ensure transparency of decision making, and the identity of potential conflicts, so that all decision-making parties know where conflicts could impact on decisions;
- to ensure that there is clear separation between decision makers and those who might benefit from the decisions;
- to ensure that the recipients of benefits are those whose work has earned the benefits.

Structures to support exploitation

Prior to the mid-1980s, exploitation of MRC technology was conducted through NRDC/British Technology Group/BTG. From the mid-1980s, MRC has increasingly invested to build its own competence to manage exploitation and, indeed, to lead creative thinking in the conduct of exploitation, eg the formation of an active Industrial Liaison Group (later expanded to form MRC Technology Transfer Group) within MRC Head Office administration. Under the leadership of Sir Dai Rees, then Director at the National Institute of Medical Research, the MRC pioneered the concept of laboratory-based technology transfer, a concept currently termed 'incubator/incubation' through the creation of the MRC Collaborative Centre, Mill Hill. The Collaborative Centre first provided 'start-up' company incubation facilities more than a decade ago. A second MRC Collaborative Centre was created in Edinburgh in 1997. Both Collaborative Centres were companies limited by guarantee and registered as charities.

In order to continue to build an effective and efficient exploitation function, MRC decided that its interests would be best served by combining the two Collaborative Centre activities and the Head Office-based Technology Transfer Group into a single entity, Medical Research Council Technology, MRCT (effective from 1st January, 2000) while retaining the benefits of the company and charity status of the Collaborative Centres. MRCT is a company limited by guarantee and a charity. Council appoints the Board of Directors, and the members have close affiliation to the MRC. The company comprises four divisions: Intellectual Property Management, Licensing & Agreements, Applied Research and Corporate Relations. Prolifix Ltd was first 'incubated' at Mill Hill, and there are currently three further companies 'incubating' within the Applied Research Division (Gendaq, Aeres Biomedical and Virogen). Management of MRC participation in the UK's LINK Programme (a defined programme to foster collaborative research jointly funded by companies and public bodies such as the MRC) is managed within the Corporate Relations Division.

The divisions of MRCT include a number of technology transfer managers with proven records as scientific researchers, prior to choosing a career change to contribute to exploitation activities. With the increasing successes in exploitation (see below), it has been possible to expand this key group of staff.

Key decisions are made by a management committee comprising the CEO plus each of the four directors of divisions, usually informed by input from the involved technology transfer managers. Oversight is provided through quarterly meetings of the Board of Directors and MRCT will make an annual report to the MRC Council.

In the second half of the 1990s, the MRC led an initiative to expand access to 'seed investment' capital for 'start-up' companies through the creation of UK Medical Ventures Fund. This fund, a ten-year limited partnership, is managed by MVM Ltd, a wholly owned subsidiary of the MRC, and subject to regulation by the Investment Managment Regulatory Organization (IMRO). UK Medical Ventures Fund successfully raised £40m of private funds. The sources of this private funding include 'city institutions', eg financial houses,

pension funds and also multinational corporations with a strong interest in the biosciences. There are legally binding rights and obligations between the MRC and the UK Medical Ventures Fund. These require the MRC to pursue its 'spin-out' activities through the UK Medical Ventures Fund, and that the UK Medical Ventures Fund is obliged to invest not less than an agreed proportion of its funds in companies exploiting technology that originated with the MRC laboratories.

Scale of MRC exploitation

The rate of new patent applications has shown a steady increasing trend to currently about 40 new applications each year; more than 300 in the decade of the 1990s. The number of annual licensing agreements has varied in both number and complexity, ranging from the sale of cell lines through to multiple non-exclusive licences for a single patent to the licensing or assignment of a series of patents as part of the process of building 'spin-out' companies. More than 250 agreements were completed in the 1990s.

The MRC has participated actively in the creation of 'spin-out' companies. The first MRC 'spin-out' company was Celltech, almost two decades ago, with a recent gathering of momentum. These companies have consistently grown, raised further investment in later financing rounds, with additional job creation. Using a rigorous definition based on meeting the criteria of:

- independent financing,
- independent management, and
- *exclusive licence* or *assignment* from the MRC,

there are now 16 'spin-out' companies. Others are expected to be created shortly. An additional large group of companies have built significant parts of their business upon non-exclusive access to MRC technology.

A list of MRC 'spin-out' companies is given Table 2.

Achievements of MRC technology transfer

Consideration of achievements should be set against MRC objectives for exploitation. A number of licences have now led to the successful introduction of products by MRC licensees. The more rapid product introductions followed from access to instrument technology, eg confocal microscopy. The time lines of pharmaceutical industry R&D are longer, but the past three years have seen the introduction of therapeutic products based on technology from the MRC. These include

Table 2 MRC 'spin-out' companies

1. Celltech Group plc: monoclonal antibody technology
2. Amylin Pharmaceuticals Inc.:[a] diabetes/metabolic diseases technology
3. Somatogen Inc. (subsequently sold to Baxter International):[a] recombinant human haemoglobin
4. Cambridge Antibody Technology plc:[a,b] human monoclonal antibody technology
5. Therexsys Ltd (partnership with Cancer Research Campaign; renamed Cobra Therapeutics; sold to ML Laboratories):[a,b] gene regulation technology
6. Prolifix Ltd:[a,b] drug discovery based on cell cycle technology
7. RiboTargets plc:[a,b] anti-infective drug discovery based on RNA target technology
8. Cambridge Genetics Ltd (with University of Cambridge, merged with Cambridge Drug Discovery):[a,b,] drug discovery through novel assay technology
9. Gendaq Ltd:[a,b] drug discovery through zinc finger technology
10. MVM Ltd.:[a,b] investment fund General Partner
11. Oxxon Pharmaccines (primarily Oxford University/Wellcome Trust):[a] vaccine technology
12. Aeres Biomedical:[a,b] monoclonal antibody technology
13. Virogen Ltd:[a,b] anti-viral technology
14. D-Gen (partnership with Imperial College, London and Wellcome Trust):[a,b] prion disease technology
15. Diversys Ltd:[a,b] monoclonal antibody technology
16. Ardana Bioscience Ltd:[a,b] female health technology

[a]MRC holds, or held, shares.
[b]MRC has the right to appoint a non-executive director.

'humanised' monoclonal antibodies, now marketed for serious conditions as diverse as transplantation, prevention of respiratory viral infection in premature babies, and treatment of a range of cancers (eg breast, leukaemias), with the introduction of further therapies for additional indications including major inflammatory conditions including arthritis, asthma and Crohn's disease believed to be imminent. The successful transfer of MRC technology to a range of companies is now leading to important healthcare benefits.

While it is difficult, perhaps impossible, to determine the impact of MRC exploitation on job maintainence and/or creation in large pharmaceutical companies, MRC 'spin-out' companies have grown and raised further income, leading to further job creation and recruitment; and it is timely to acknowledge the excellent management of these companies). The bulk of the jobs are in Celltech and Cambridge Antibody Technology, but most of the companies are growing rapidly, whether organically or through merger and acquisition; the total jobs in these companies is now measured in thousands.

Income to the MRC has grown significantly through the 1990s; increasing from about £500k in 1990/91 to about £7.5m 1999/2000, and expected to exceed £10m in 2000/01. These figures include income when MRC shares in 'spin-out' companies have been sold, but do not include the value of shares still held.