

# **Review of Microbial Science Research**

**A report for BBSRC Strategy Board**

**September 2006**

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## Foreword

Practising microbiologists and laypeople alike are acutely aware of the many threats and opportunities being presented worldwide due to the actions of microbes. The UK needs a robust microbial science research community if it is to capitalise on the opportunities and meet the threats effectively. BBSRC plays a pivotal role in supporting that community and its decision to review microbial science is indeed timely and has been warmly welcomed across the discipline.

The work of the review panel has been helped enormously by the willingness of the community to share opinions frankly and to speak candidly about the state of the field. Indeed the need to digest the vast amount of information provided by the many respondents to the consultation document posed a major challenge for the panel. One was struck by the large areas of agreement about the nature of the strengths, weaknesses, opportunities, threats and challenges facing UK microbial science. Naturally, there were also areas where opinions differed. These areas of agreement and disagreement were also reflected in the discussions of the panel, a large group that was representative of the main constituencies within microbiology. This document is the product of the panel's deliberations. It attempts to capture and distil the key issues and it makes specific recommendations so that BBSRC Strategy Board may help to ensure that microbial science in the UK has the brightest possible future. As chairman I wish to thank all of the panel members for their hard work, wisdom and good humour throughout this process and to thank BBSRC's Dr Jef Grainger, Dr Paul Burrows and Mr Peter Hurrell for their professionalism and unstinting support.

Charles J Dorman  
September 2006.

## Structure of the Report

We have divided this report into two broad sections. In Section 1 we set out the central importance of basic microbial science across the entire spectrum of bioscience research. We go on to outline the current state of the art and the major opportunities ahead for microbial science. By way of contextual information for the area, Section 1 also provides a summary of the current investments in basic and strategic microbial science funding in the UK and outlines the main players. Finally we address some important perceived challenges for the field that must be addressed to keep microbial sciences healthy and to grasp the opportunities ahead.

In Section 2, we develop the opportunities for microbial research further and through a set of key recommendations propose routes by which potential barriers to success might be addressed. In particular these address a number of issues around the funding and training of researchers, provision of relevant tools and resources, and the effective uptake of basic microbial science knowledge by UK industry and policy makers.

## **Acknowledgements**

The Review Panel would like to thank sincerely all of those who have contributed to this review, either by submitting responses to the consultation or by providing portfolio information. Both of these sources of information have been invaluable in informing our discussions. Much time has been invested by a wide range of people, and we gratefully acknowledge these contributions.

BBSRC is very grateful to Professor Dorman and the membership of the Microbial Science Review Panel for their considerable investments of time, effort and expertise in producing this report. The Council also wishes to echo the Panel's thanks to the numerous contributors and respondents to the consultation.

## Executive Summary

Microorganisms are the most diverse biological systems on Earth. Accordingly, they span the full spectrum of bioscience research, from the basic ‘blue-skies’ research to the very applied, from the most reductionist to the most holistic high-throughput approaches. Fundamental research into basic cell biology, physiology, biochemistry and genetics of microbial systems is a powerful catalyst for change, driving understanding and innovation throughout the full range of bioscience. Many strategically important research areas are underpinned by core microbial science, and microbial systems are pervasive throughout bioscience research and biotechnological innovation.

Fundamental microbial science therefore has a vital underpinning role at the centre of the biosciences, and accordingly it lies at the very heart of BBSRC’s remit. It also represents an area of historical UK strength, which is supported by influential Learned Societies such as the Society for General Microbiology (SGM) and is fostered through a core of high-quality research groups at Universities and Institutes.

### **Future opportunities and priorities: Basic research**

Something of the enormous scale of microbial genetic diversity is now beginning to be realised. Microbial science will lead the way in comparative genomics, allowing researchers to gain unprecedented understanding of the diversity of gene inventories and evolutionary relationships between the major life groups on the planet, including the radiation and proliferation of prokaryotes and the evolution of eukaryotes. At the same time, state of the art ‘omics approaches, harnessed appropriately with strong reductionist methodologies, provide new opportunities to work towards predictable models of a set of exemplar microorganisms. This work will provide a powerful biotechnological toolkit and set the ground rules for undertaking the computational description of more complex biological systems.

**Recommendation 1: BBSRC should consider the leading scientific priorities for fundamental/basic microbial science to be:**

- 1. understanding microbial diversity from genomics to physiology, encompassing the challenges arising from metagenomics and overcoming the current experimental intractability of ‘unculturable’ microbes;**
- 2. using a balance of reductionist and systems approaches to achieve a complete systemic description of the minimal microbial cell and its fundamental environmental interactions.**

### **Future opportunities and priorities: Strategic research**

Building on the opportunities for basic microbial science, there are currently extremely strong strategic drivers for research into emerging and re-emerging diseases of humans, animals and plants, and a critical need to engineer new therapeutic and resistance strategies. There are now unprecedented opportunities to improve our understanding and manipulation of microbial pathogenicity and translate this understanding into benefits for

UK, and Global, health and wealth. In addition, microbial science has an integral role in facilitating bioenergy and biocommodities options, and this represents a critical emerging area of strategic priority. The study of microbial systems has and continues to provide society with the most detailed insight into the function of cells, communities and the ecosystems that are critical to life on this planet.

**Recommendation 2: In seeking to extend and reinforce the fundamental microbial science pipeline, BBSRC should consider leading strategic priorities for microbial research to be:**

- 1. effective exploitation of basic science opportunities to gain new insights into the complex cellular-molecular-genetic webs determining microbial pathogenesis;**
- 2. to provide leadership in driving forward research in emerging and re-emerging infectious disease of animals, plants and humans, and exposing and developing the synergies between these research areas;**
- 3. new antimicrobial therapeutics and immunological strategies;**
- 4. the generation of high-quality critical mass in microbial research underpinning bioenergy and biocommodities applications.**

#### **Improving critical mass, coherence and focus of microbial research in the UK**

Microbial science is funded through a diversity of routes, both external and internal to BBSRC. This diversity is positive, and reflects the pervasive nature of microbial systems in bioscience research. However, there is also concern that core, fundamental microbial studies are experiencing erosion under current BBSRC funding structures. A wide sweep of UK bioscience researchers are dependent on strong basic microbial science, and strategic and Scientific Committee-level focus in this area must be improved.

**Recommendation 3: Noting that BBSRC is currently reviewing its funding committee structures, there is an opportunity to develop mechanisms that will improve coherence of fundamental microbial science funding, and promote the necessary culture change and coordination of research effort that will be needed to meet existing and emerging opportunities and challenges for the field.**

There are clear examples of where improved co-ordination of BBSRC research areas would be of benefit. Of particular note, BBSRC has made substantial recent investments in systems biology. However, outside of these focused investments, there is a community-wide need for co-ordinated effort directed at bridging the gap between well-advanced molecular genetic studies, high resolution cell biology and initial mathematical modelling of discrete cellular signalling events, and this represents an obvious area for improved focus.

**Recommendation 4: Acknowledging BBSRC's recent, focused investments in systems microbiology, there is a clear methods gap to be bridged between data acquisition (through biochemical investigations, molecular genetic studies cell physiology, and high resolution cell biology) and initial mathematical modelling of discrete cellular events. This represents a broad-scale challenge for UK microbiologists, and BBSRC should seek to further stimulate innovation in this area, which has the potential to drive forward the state of the art for systems microbiology and set the ground rules for systems analysis of more complex biological systems.**

#### **Co-ordination of funding interfaces**

There is a widely perceived need for improved cross-Council co-ordination to better serve strategically important areas of microbial science. In particular, strong synergies exist between studies of pathogens that infect humans, animals and plants, which need to be better understood, and there is an imperative strategic need to ensure a strong, unbroken pipeline from basic to applied infectious disease research.

**Recommendation 5: BBSRC must engage with other key funders of UK microbial science (including MRC/NERC/Defra/Wellcome Trust/EBI/ERC) to develop research synergies, to remove artificial barriers where they persist and, in particular, to ensure that an unbroken R&D pipeline exists from basic microbial science to medical and environmental microbial science applications. BBSRC should consider *microbial diversity* and *emerging and re-emerging disease* to represent, respectively, basic and strategic areas of high priority for which effective multilateral synergy will be critical to meet research challenges.**

#### **Increasing the supply of skilled people – repairing the skills pipeline**

It is widely perceived that there has been an erosion in core microbial science skills in the student and research community, representing an important potential hurdle to be surmounted if microbial scientists are to tackle effectively the research challenges. Greater critical mass is required in core areas, and in an era of integrated HEI bioscience departments, imaginative solutions will be necessary to link up and develop geographically dispersed research groups and expertise. Greater cohesion of UK microbial science will improve its appeal to high-quality career entrants.

**Recommendation 6: Strategy Board should seek to reinvigorate core microbial science capability in the UK, and foster the necessary critical mass of core microbial skills to meet identified strategic priorities. BBSRC should carefully consider targeting mechanisms such as dynamic networks and cross-funder capacity awards to achieve this aim, and seek imaginative ways of working with stakeholders to improve the attractiveness of graduate training opportunities in core microbial science areas.**

Those BBSRC-sponsored Institutes that have microbial science interests play critical roles in building skills and national research capacity in areas of high strategic importance, particularly relating to the interactions of microbes with other organisms and

with the environment. There is an urgent need to develop UK critical mass in microbial bioenergy and biocommodities research skills, and the BBSRC Institutes with a focus in plant and microbial research are well placed to drive forward this agenda.

**Recommendation 7: BBSRC should strongly support the strategic positioning of appropriate BBSRC-sponsored Institutes as centres of underpinning critical mass for core microbial research at the animal:microbe, plant:microbe and environment:microbe interfaces, with commensurate leadership and training roles. The Institutes are the ideal environments in which to develop the skills to meet the long-term challenges associated with strategic demands for bioenergy and biocommodities research in the 21<sup>st</sup> Century. The relevant Institutes should develop clear strategies and appropriate critical mass to meet the microbial research challenges therein.**

#### **Providing the tools and resources for world class microbial science**

There are important tools and resources challenges which also must be met if UK microbial scientists are to grasp the opportunities ahead. There is a need to generate critical mass in resource provision for microbial genomics and informatics, possibly in a geographically dispersed way, and a particular urgency with respect to mitigating a bottleneck in genome annotation/functional genomics. There is also a need to foster cross-disciplinary toolkit innovation to improve the tractability of microbial systems.

**Recommendation 8: BBSRC should seek to facilitate, unilaterally and multilaterally as appropriate, the provision of appropriate tools and resources in the following areas, which will be of critical importance in realising the leading scientific challenges as set out in Recommendation 1:**

- **appropriate infrastructure investment for functional genomics of non-pathogenic microbes;**
- **tools that facilitate accurate and reliable annotation of genomic sequence data and that protect the integrity of such data;**
- **new tools to improve the tractability of genes with functions in the quiescent cell and to provide access to the enormous variety of microbes that currently are ‘unculturable’;**
- **reinvigorated innovation in optical imaging and electron microscope tomography of microbial cells, working at the interface of EPSRC and BBSRC;**
- **sustainable, high quality curation of important UK microbial culture collections.**

#### **Translating microbial science into national enterprise and policy**

Microbial science is a deep source of opportunity for industrial innovation, but currently under-exploited on almost all fronts. There a clear need for UK academic and industrial researchers to find new ways to exchange ideas, expertise and personnel, and work together to remove barriers to the application of the UK’s excellent fundamental microbial science outputs. Working with others, BBSRC has a central role to play in fostering such linkages.

Microbial science also needs to be more embedded and prominent in Government policy, particularly given high profile of current infectious global disease challenges, the impact of microbes and microbial activities on this planet, the serious threat of bio-terrorism, needs for new biotechnology (e.g. renewable energy sources, use of synthetic biology to produce other products in microbial biorefineries) and the undeveloped synergies across these challenges.

In particular, BBSRC should take a lead in working with Government, other funders (e.g. MRC, Wellcome, Defra) and supported researchers to address how best to meet, at a high multilateral level, the needs of global infectious disease challenges and markets and provide focus on key issues (e.g. surveillance). There is also a need for BBSRC to maximise its influence in ensuring that policy, regulatory and media activity of relevance to microbial research and training is scientifically balanced and informed.

**Recommendation 9: BBSRC should strive to use the full range of mechanisms at its disposal to ensure that the world-class knowledge and innovation generated by basic and strategic microbial science is fed forward strongly into increased industrial innovation, appropriate public services, national security and strong policy making.**

# Section 1: The central importance of microbial science

## Context

1. Microbes represent *by far* the largest and most diverse group of organisms on the planet, on any scale, fundamentally shaping all aspects of biosphere function and the interactions of all higher organisms. The fact that microbial science covers such a diverse range of research areas and organisms (scientifically grouped only by the requirement in most cases for a microscope to see the subject matter) posed a significant challenge for this Review Group.
2. Microbial systems span the full spectrum of bioscience, from fundamental cell physiology to highly applied processing, food, biotechnological and pharmaceutical applications, from reductionist molecular studies to metagenomic analyses, and from the first steps towards understanding a 'minimal cell' to a diverse range of complex microbial interactions with higher organisms and the environment. Given the scale of 'microbial science' we start by noting the enormous scope of this review and that its outputs are potentially far reaching.
3. The review emphasises matters at a high strategic level, encompassing the exciting opportunities and challenges currently facing microbial research. It addresses problems posed by real and perceived barriers to success that must be overcome if researchers based in the UK (and elsewhere) are to grasp these opportunities, and if their research outputs are to be utilised effectively by society and industry.

## A catalyst for change

4. Whilst microbial science<sup>1</sup> is a broad and rather imprecise term, in a strict sense it describes a core of fundamental research into basic cell biology, physiology, biochemistry and genetics of microbial systems. For the purposes of this review, it is with this microbial research core that we are first and foremost concerned. The scope of the review encompasses research on archaea, bacteria, unicellular and filamentous fungi, protozoa and viruses.
5. The importance of a strong research base focussed upon advancing our understanding of microbial systems cannot be easily overstated. Fundamental microbial science is a powerful catalyst for change in the biosciences. Once a test-bed for molecular genetics, and now a proving ground for post-genomics, systems and synthetic biology, basic microbial science drives understanding and innovation throughout bioscience (see box 1. "UK Microbial Sciences Successes – Some Case Histories"). Furthermore, the sheer number of microbial genomes sequences that are available now or will become available in the near future provides an excellent perspective

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<sup>1</sup> We use the term synonymously with *microbiology*.

from which to consider evolutionary and gene transfer questions that are not approachable in other biological systems.

6. Stemming directly from this core activity is a diverse range of microbe-utilising research including: control and manipulation of pathogenic and commensal interactions of microbes and animal and plant hosts; antimicrobial strategies, therapeutics, vaccines and other pharmaceutical applications; microbial process/production technology; food production, standards and safety; rhizology and managed landscape ecology. Potentially radical opportunities are emerging in new areas of technological application, prominently including bioenergy, bioremediation and probiotics. Microbial systems notably also provide valuable research tools and resources for other areas of bioscience research; e.g. host/vector systems and enzymes for genetic engineering, the use of viral vectors for vaccinology and gene therapy and in support of numerous sectors of the biotechnology industry (fermentations, natural products, biocommodities, etc.).
7. Spokes from the core microbial science research 'hub' therefore span much of BBSRC's remit and have important interfaces with other Research Councils, notably NERC (environmental research), MRC (medical) and increasingly EPSRC (physical sciences and engineering). There are also important interfaces with medical research funders such as the Wellcome Trust and the cancer charities, with Government Departments (particularly Defra, FSA and SEERAD, increasingly in the future, DoH) and with International funding streams (e.g. the EU). Given the diversity of funding streams for microbial research, it is important to ensure that there are no gaps in coverage, and that BBSRC is positioned appropriately to take a leadership role.
8. Innovation stemming from a strong foundation of basic microbial science has been of great significance, both in UK and in global society. It has brought, and will continue to bring highly significant health and wealth outputs; for example, advances in medicine, food safety, agriculture, domestic animal health and welfare, advances in microbial production, fermentation, spoiling, bioremediation, and energy production technologies.
9. Emerging and re-emerging disease (e.g. HIV, SARS and avian influenza; TB, FMD and Bluetongue; respectively) and antibiotic resistance (e.g. MRSA, *Clostridium difficile*) represent major challenges for UK health and wealth, causing deep and widespread concern for sustainable human and animal health<sup>2</sup>. Given the economic, political and public significance of these issues, and given the synergies of the challenges for human, animal and plant health, it is perhaps surprising that microbial science does not currently occupy an even more prominent and coordinated position in national and international science and human, animal and plant health strategies. However, large-scale funding and international focus in HIV and TB research (for

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<sup>2</sup> *Bad Bugs, No Drugs* (2004). Infectious Diseases Society of America white paper. [http://www.idsociety.org/pa/IDSA\\_Paper4\\_final\\_web.pdf](http://www.idsociety.org/pa/IDSA_Paper4_final_web.pdf)

example) supported by numerous NGOs<sup>3</sup>, underline the importance of emerging disease: the UK needs to be positioned to play an effective and leading global role.

## UK strength in microbial science

10. The examples set out in Box 1 provide a flavour of the UK's solid and distinguished history and our current strength, in microbial research. They illustrate how basic microbial research has driven significant advances in bioscience knowledge and provided biotechnological innovation.
11. This UK's strength is maintained through a core of high quality university-based research groups and institutes. In areas of bioscience relevant to BBSRC, there is notable critical mass at many leading national universities and also at:
  - Norwich research campus (John Innes Centre (JIC), Institute of Food Research (IFR), University of East Anglia/Sainsbury lab), having one of the highest concentrations of microbial scientists in Europe (*Streptomyces*, *Rhizobium*, filamentous fungi/ microbial genomics, computational microbiology, molecular biology of foodborne pathogens, food safety, microflora and commensals<sup>4</sup>);
  - Institute for Animal Health (IAH; bacterial, viral, protozoan and TSE pathogens of animals);
  - Rothamsted Research (RRes; rhizosphere microbiology and crop pathogenesis) and Institute of Grassland and Environmental Research (IGER; rhizosphere and rumen ecology);
  - The SEERAD-sponsored Scottish Institutes; Macaulay Land Use Research Institute (rhizosphere and biodiversity); Moredun Research Institute (infectious disease of ruminants), Rowett Research Institute (gut health), Scottish Agricultural College (crops and soils; animal health; animal product safety), Scottish Crop Research Institute (crop pathogenesis).
12. The leading HEI and institute-based groups form a reasonably-integrated network, exchanging students and research staff at a reasonably high frequency. Learned Societies provide additional infrastructure and leadership; it is not an accident that the Society for General Microbiology (SGM), the world's second largest microbial learned society<sup>5</sup>, was established and is based in the UK. Alongside other notable UK-based group<sup>6</sup> and several important microbial science journals<sup>7</sup> this reflects the past and present strength of UK microbial science providing potentially invaluable communication infrastructure for researchers, nationally and internationally.

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<sup>3</sup> For example, IAVA; Gates Foundation.

<sup>4</sup> Although we note that previous capacity and capability in nitrogen fixation research has been lost from JIC, detrimental to the UK's ability to respond to timely research challenges, in particular related to microbial hydrogen production for bioenergy (a nitrogenase being a key component of such systems).

<sup>5</sup> After the American Society for Microbiology.

<sup>6</sup> E.g. Society for Applied Microbiology, Scottish Microbiology Society, Association of Applied Biologists (incorporating *Virology* and *Applied Mycology and Bacteriology* Groups), British Mycological Society.

<sup>7</sup> Including, for example, *Molecular Microbiology*, *J. General Virology*, *J. Medical Microbiology*, *Microbiology UK* and *J. Applied Microbiology*.

## **Box 1**

### **UK Microbial Science Successes – Some Case Histories**

The following represent a small selection of historical and more recent examples of UK-based, basic microbial research that has underpinned key advancements in bioscience research, and/or important strategic (economic/health/societal) outputs<sup>8</sup>.

#### **20<sup>th</sup> Century**

- Discovery of the antibiotic action of *Penicillium* mould on Gram-positive bacteria (Fleming, 1928) and the subsequent isolation, production and testing of penicillin (Florey/Chain/Heatley, 1938-1940). Fleming/Florey/Chain shared the 1945 Nobel Prize in Physiology or Medicine;
- *Pneumococcus* transformation work of Avery, MacLeod and McCarthy built on earlier transformation work of Griffiths, demonstrating that DNA, not protein, is the genetic material (1944);
- Discovery of Type 1 interferon through work on *Influenza* (Issacs and Lindenmann, 1957)
- The elucidation of the genetic code (system of three-base DNA/RNA codons corresponding to defined amino acids) based on work using T4 phage (Crick, Brenner *et al.*, 1961);
- Isolation and development of cephalosporin antibiotics from *Cephalosporium*. (Abraham/Newton; first compound, *Cephalothin*, marketed by Eli Lilly, 1964);
- The cloning of the genome of Hepatitis B virus (Murray, late 1970s) contributed to the establishment of Biogen and development of diagnostic tests for Hepatitis B. Also, over the long-term, the current vaccine which has saved millions of lives, globally;
- The pioneering use of phage Lambda to clone DNA (Murray & Murray, 1974), representing the entry point to the molecular genetic era;
- Invention of the dideoxy DNA sequencing method, and its demonstration in sequencing the first complete genome of the phage PhiX 174 (Sanger, 1977; Nobel Prize in Physiology or Medicine, 1980);
- Identification of the critical cell cycle regulator, p53 (a gene that is implicated in half of human cancers) through its interaction with SV40 T antigen (Lane/Old with Levine (US), 1979);
- Identification and cloning of antibiotic biosynthetic pathway genes, and enabling technologies for cloning, in *Streptomyces* sp. led to the first 'hybrid' antibiotic being made by genetic engineering (Hopwood *et al.*, Nature 1985). This spawned new biotech industries (e.g. Biotica in US, Kosan in the USA) in combinatorial biosynthesis which focus on the production of novel drugs from secondary metabolism pathways. The UK *Streptomyces* group at JIC (e.g. Hopwood, Chater, Bibb) have been at the heart of this work since the group was formed in 1968;
- Elucidation of the structure of *Influenza* hemagglutinin, representing the first structure of a molecular machine, and setting a paradigm for structural change in fusion proteins (Skehel, 1981).
- Discovery in yeast of the cell cycle 'master switch' *cdc2*, in the mid-1970's, and subsequent elucidation of cyclin and cyclin-dependent kinase control of cell cycle determined in the late 1980s and 1990s. This work has had wide implications for cancer biology and the development of therapeutics, and led to a diaspora of UK laboratories offering associated training. Hartwell/Hunt/Nurse shared the Nobel Prize in Physiology or Medicine, 2001;
- Work on *Eimeria* at Institute for Animal Health (Shirley) led to the development of the *Paracox* poultry vaccine (Schering-Plough Ltd., first marketed in 1989) with ~800M doses now produced annually;

<sup>8</sup> An instructive, broader view of significant global microbial science events and achievements in the 125 years from 1861 to 1995 can be obtained by viewing the chronological list compiled by the ASM. This can be found at <http://www.asm.org/MemberShip/index.asp?bid=16731>

- Insights into the critical role of DNA topology in the regulation of gene expression (Higgins, Lilley and Dorman) late 1980s to early 1990s;
- Elucidation the physiological roles of ion channels in bacteria in osmoregulation and metabolite detoxification (Booth, 1990s);
- Characterisation of extent and mechanisms of quorum sensing in a wide range of bacterial systems, controlling a diversity of bacterial phenotypes from conjugation, plant pathogenesis and symbiosis (nodulation), bioluminescence, antibiotic production and biofilm formation (Salmond, Stewart, Williams, Bycroft, Stewart Glover, Downie and others, 1990s);
- Development of signature-tagged mutagenesis and its use to identify genes in *Salmonella* required for pathogenicity (Holden, 1995). This technique has since been adopted by many other researchers to identify key pathogenesis genes in a wide range of microorganisms;
- Development of multilocus sequence typing, an early success of genomics approaches, allowing highly accurate and sensitive tagging and, therefore, cross-referencing of microbial strains for the first time, and allowing the evolution of diversity in microbial populations (especially of interest, pathogens) to be studied in unprecedented detail (Spratt and Maiden, 1998).

### Entering the 21<sup>st</sup> Century

- Emerging from the first descriptions of virus-mediated RNAi by plant virologists (Baulcombe group, Sainsbury Laboratory, late 1990s), the unforeseen prevalence of siRNA/miRNA-mediated gene regulation is being dissected in unparalleled detail by microbiologists (predominantly virologists), representing the most significant step-wise change in our understanding of genetic regulation for many years;
- Recent insights into the unforeseen scale of microbial diversity (particularly in marine systems<sup>9</sup>). Early results have revolutionised our understanding of microbial evolution and systematics and the scale of genetic diversity held by the oceans and terrestrial habitats: the number of recognised microbial classes has more than doubled in the last ten years, from around 37 to 80 at present. This work has had far-reaching implications for our understanding of ecological systems, including global contributions to climate and nutrient cycling, agricultural sustainability and habitat conservation;
- The description of general glycosylation in *Campylobacter*, from genomics approaches, and transfer of a functional N-linked glycosylation cassette to *E. coli*, opening up a wide range of research and biotechnological applications (Wren, with Aebi (Switzerland), 2002);
- Discovery of the coordination of cell division and chromosome segregation in *Bacillus subtilis* and the genetic control of endospore formation (Errington, 2003-2005);
- Identification of the key nodulation signal in nitrogen-fixing legume crops that is normally induced by *Rhizobium* (Oldroyd, 2006);
- First complete structure of a first reaction centre/light harvesting complex, from *Rhodospseudomonas palustris* (Cogdell 2003);
- The discovery of a non-homologous endjoining mechanism for DNA repair in bacteria (Doherty, 2002-2004);
- Experimental evidence for eukaryote-like DNA replication in the archaea (Bell, 2004);
- Recent characterisation of a key fungal protein involved in the economically and socially important *Magnaporthe* (Rice Blast) fungal infection, which will allow dissection of key processes of fungal pathogenicity and possibly lead to new disease prevention strategies (Talbot, 2006).

<sup>9</sup> For example, via the recent NERC Marine and Freshwater Microbial Biodiversity Programme, and the resulting *Blue Microbe* network. See [www.bluemicrobe.com](http://www.bluemicrobe.com)

## Microbial science in 2006- the state of the art and future opportunities

13. A search of the Genomes on-line database<sup>10</sup> in July 2006 revealed 403 complete genome sequences, of which 335 were bacterial, 27 archaeal. Of the 41 completed genomes from eukaryotic species, 28 were microbial. Therefore, 97% of the genome sequences from cellular organisms that have been completed to date come from microbial species. A further 932 bacterial genome and 56 archaeal genome projects were under way, as were a number of metagenome projects that will yield entirely microbial gene sequences. With the advent of high speed sequencing technologies<sup>11</sup> this number will increase dramatically in the coming years. In addition, 2,433 viral reference sequences for 1,666 complete viral genomes are currently held on the Entrez database<sup>12</sup>, including most known pathogenic viruses. Some measure of the staggering scale of microbial genetic diversity is rapidly becoming apparent. For the first time in history technological innovation offers us the opportunity to make its exploitation tractable. The development of the tools and infrastructure to mine this resource effectively represents a critical and urgent challenge.
14. It is clear that microbiologists will lead the way in understanding genome function and the diversity of gene inventories and evolutionary relationships between the major life groups on the planet, including the radiation and proliferation of prokaryotes and the evolution of eukaryotes. Harnessing the power of this unprecedented informatic resource presents a step-change in the biosciences, and must be a key theme in microbial science research for the coming decades.
15. Alongside the unprecedented opportunity afforded by high throughput 'omics methodologies for beginning to understand something of the **breadth** of microbial diversity of life on Earth, there are commensurate opportunities to achieve unprecedented **depth** of penetration in understanding biological systems. This requires the application of reductionist methods. It is important to emphasise that reductionist and genomics approaches must be viewed as complementary and not as being in competition.
16. It is increasingly obvious that microbial science will drive the first major advances in systems biology: unicellular bacteria/archaea (and their bacteriophage) represent the most reducible, tractable biological systems, and are an obvious and natural starting point for 'systems' aspirations. Yeast cells will correspondingly present the most reducible, tractable eukaryote systems. The spatio-temporal coordinates of macromolecular metabolism is already being described within individual virus infected eukaryote cells and these studies will be extended to unicellular microbes. The complete modelling of a minimal 'e-cell' represents an iconic, but realistic, goal. The pursuit of this goal will provide the intellectual framework and the technological

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<sup>10</sup> <http://www.genomesonline.org/>

<sup>11</sup> For example, the 454 technology: <http://www.454.com>

<sup>12</sup> <http://www.ncbi.nlm.nih.gov/genomes/viruses/viruses.html>

'toolkit' needed to enable exploitation for biosynthesis, bioenergy and nanotechnology, for example, and to undertake a complete description the physiological complexity of higher organisms.

17. Due to the tractability of 'model' microbial systems, microbial science offers one of the best 'all-round' training routes for bioscience and computational researchers. It provides a solid grounding in key, transferable research skills, and lends itself to integrative systems approaches and high-throughput technologies. Such training offers access to a wide diversity of career options, and the discipline of microbial science is positioned favourably to capitalise upon these advantages.

## **Overview of current funding provision for microbial science**

18. By way of background and context, we provide here a brief overview of the UK's main funders of microbial science, their level of support and principal interests. A much more detailed analysis of BBSRC's recent funding of microbial science is presented in Annex 4, with supporting datasets located in Annex 5. The microbial science portfolios and strategic interests of other leading funders are described in more detail in Annex 6.

### **BBSRC**

19. In its role as the leading UK funder of non-clinical bioscience, basic and strategic microbial science sits at the heart of BBSRC's remit. Approximately 18% of BBSRC's research budget (£47M in 2005/06) in recent years has been spent on projects with significant microbial science components. Whilst the largest proportion of microbial science is supported through the Plant and Microbial Science (PMS) committee, representing approximately 40% of the total annual spend through the committee, microbial science funding is administered relatively widely across its Research Committees<sup>13</sup>, and a significant proportion of research through most of the Committees has microbial components. These trends reflect the pervasive nature of microbial science, and a highly active and successful cohort of BBSRC-funded microbiologist investigators who affiliate themselves with a wide range of research areas. However, the overall funding of microbial science studentships has shown a recent proportional decrease, which is of cause for concern<sup>14</sup>.
20. We have attempted an analysis of research areas which, although crude, reveals some clear and informative trends<sup>15</sup>. Fundamental, core microbial science (reductionist cell biology, physiology, biochemistry and molecular genetics) represents the greatest subset of funding relevant to microbial science, in accordance with BBSRC's role in funding such science. However, funding in this area has been in marked decline, from

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<sup>13</sup> See Annex 4, Fig. 2 for detail.

<sup>14</sup> See Annex 4, Fig. 1 for detail.

<sup>15</sup> See Annex 4, Fig. 6, and Annex 5, Table 7, for further information.

almost 8% of BBSRC's research funding in 2000-01 to approximately 5.5% in 2005-06 at a time of considerable increases<sup>16</sup> in the total research budget.

21. This trend has been concomitant with a marked (and unsurprising) increase in funding of projects based on high-throughput 'omics techniques, which probably partly explains and offsets this trend. In combination, these areas account for a steady ~50-60% of BBSRC's microbial science portfolio. However, projects using high throughput techniques have extended considerably beyond the basic research core, and do not replace reductionist studies, but are complementary. The apparent steep reduction in the funding of reductionist, core microbial science areas is therefore of considerable concern.
22. Relating to more strategic and applied microbial science areas, animal/microbe interactions (microbial focused projects only) is an area of marked growth, in line with strategic priorities in animal health and welfare. In contrast, funding for work on plant/microbial interactions (microorganism-focused projects only) experienced a 25% decline from 2003-04, from ~1.6% to 1.2% of the BBSRC research budget. Applied microbiology also stands out as an area that received steadily decreasing proportions of funding over the reporting period, with rhizology following a similar, if less marked, trend. Research on vaccine development, antimicrobial research and other pharma applications (when disentangled) have all received steady support in the region of £1M per annum.
23. Of the microbial divisions, work on bacteria represents the area that has received the greatest proportion of BBSRC funding<sup>17</sup>. This is unsurprising given the pre-eminence of bacterial systems in fundamental bioscience research. Interestingly, work involving archaea represents an area of contrastingly low investment, as does mycology. Of concern, especially when taken together with the apparent steep decline in reductionist core microbial areas, the real-terms quantity of bacterial research being funded has also shown marked signs of decline in the last 3 financial years.
24. The BBSRC-sponsored Institutes are centres of significant critical mass for microbial science activity. JIC and IAH were within the top five institutions in receipt of BBSRC funding for microbial science from 2000-2006 (positions 1 and 3 respectively<sup>18</sup>), and RRes was within the top ten. IFR (ranked at position 29) and IGER (36) have important microbial science strategic interests, although funding in these cases has been more modest.
25. Leading HEI recipients of BBSRC microbial science funding included the Universities of Manchester (2), Cambridge (4), Warwick (5), Oxford (7), Sheffield (8) and Birmingham (9), and Imperial College London (6). Overall, 83 HEIs received funding from BBSRC to undertake microbial science between 2000 and 2006 and funding was well distributed, with in excess of half of these institutions receiving

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<sup>16</sup> 46%, non-inflationary adjusted.

<sup>17</sup> See Annex 4, Fig. 4 for further information.

<sup>18</sup> See Annex 5, Table 4 for details.

funding during this period in excess of £1M. This provides an indication of the wide geographical dispersal of BBSRC-funded microbial science.

### **Other Research Councils**

26. MRC, NERC and EPSRC all have significant funding streams for microbial science, and represent critical interfaces for BBSRC microbial science. Key aspects of these investments are highlighted below, with further detail provided in Annex 6.
27. **MRC** funding for microbial science is primarily directed through the Infections and Immunity Board (IIB)<sup>19</sup>, which had a budget of ~£20M in 2005-06 (infections:immunity funding split approximately 2:1, the former including pathogen-specific immunity). Research is heavily focused on research areas of UK strength, notably in HIV, malaria, TB and, of particular recent focus, influenza; the Council committed to a £10M (plus fEC uplift) initiative in pandemic Influenza in Dec. 2005.
28. There have been deep community concerns raised that non-TB bacteriology is highly underrepresented in pre-clinical and clinical studies funded by MRC, representing < 5% of the IIB funding in 2004/2005. This is an issue which has been examined by MRC (Dec. 2005), and is being monitored. We have also identified community perceptions that clinical researchers are not being encouraged as much as they could be to recognise and exploit synergies with other infectious disease areas.
29. **NERC** has made significant investments in microbial ecology and microbial aspects of environmental research, spending in the region of £6-8M PA in the area. The Council has funded a number of programmes in the last 10 years with significant microbial science components (e.g. Environmental Genomics; Gene-flow in plants and microorganisms) including the microbiology-targeted, £7M Marine and Freshwater Microbial Diversity programme of 2000-2005, joint with BBSRC. Environmental metagenomics represents an area of NERC leadership for microbial research.
30. **EPSRC** has increasing investments relevant to microbial science, commitments amounting to at least £5M in 2006-07, more than doubling that invested in 2002-2003. Key investment areas include physical science and engineering for antimicrobials (e.g. antimicrobial surface coatings), bioenergy, bioremediation, process technology and enzyme engineering. EPSRC is also taking a notable lead in the development and exploitation of the emerging power of nanotechnology, and has contributed to BBSRC's recent investment in systems biology centres.

### **Government**

31. Several Government agencies have significant research interests in basic microbial science and the extension of the basic science pipeline for policy needs and societal benefit. Leading interests and investments are summarised below, with further detail provided in Annex 6.

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<sup>19</sup> Clinical trials and public health research relating to infections is directed through the Health Services and Health Research Board.

32. **Defra** has had significant research interests relevant to microbial science, funding projects with some relevance to microbial science at around £20M PA. A significant proportion of this funding has been allocated to animal and plant disease research areas, and the Department has funded relevant programmes at IAH, IGER, RRI, in addition to notable investments at the Veterinary Laboratories Agency, Central Science Laboratory and Warwick-HRI. The Agency's strategic interests are shifting away from agricultural productivity towards environmental sustainability and climate change. There are, therein, important implications, which BBSRC Strategy Board will be aware of, for the balance of support of microbial science in animal health, agricultural and environmental ecology areas.
33. **DTI** funds two Knowledge Transfer Networks, *BioProcessUK* (biopharmaceuticals and bioprocessing area) and *BioScience for Business* (biocatalysis area; previously Pro-Bio Faraday), which operate in areas with relevance to microbial research industrial applications.
34. **FSA** funds a significant amount of microbial research and survey work relevant to food safety and standards. This amount is variable on an annual basis, at between £2.5 and £3.9M PA between 2002 and 2005.
35. **DfID** directs £4M PA through the MRC for poverty-related diseases, a significant proportion relating to infections.
36. **SEERAD** invests in the region of £11M PA through the Science and Analysis Group to projects with relevance to microbial science, cutting across infectious disease of animals (especially ruminants), gut health, rhizosphere ecology and crop pathology and ecological interactions. Much of this funding is directed to the SABRIs<sup>20</sup>, complementary to BBSRC's investments in microbial interactions with plants and animals. In addition, £0.5-1.0M PA is spent on research relevant to fish disease, via the Fisheries Research Service.

#### **NGOs**

37. **The Wellcome Trust** is a key UK funder of medical microbial science, and represents an important funding interface for BBSRC. The Trust's investments are Global, and very considerable, with £260M of microbial science commitments (full life cycle) being made in the three years from 2002 to 2005, including a full range of directed programme and responsive project grants, Fellowships, Studentships and equipment awards. A significant proportion of this funding was awarded to UK researchers. Researchers in Africa and India also received funding for work on diseases of relevance to Developing World nations.
38. Although it has proved difficult to obtain indications of investment levels, other relevant funders of importance include the Royal Society (funding fellowships in the biosciences) and the cancer charities.

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<sup>20</sup> See Annex 6, Table 13 for details.

## Industry

39. The pharmaceutical industry has been historically strong in UK, but much of the research activity of leading companies is now undertaken abroad. Industrial Vaccine R&D is now poorly represented in the UK: of the big 5 companies that share >90% of global market<sup>21</sup> none have significant R&D centres in the UK. Recent further examples of erosion are the sale of *Powderject* to *Chiron/Novartis* and the consolidation of *Acambis R&D* to Boston, USA.
40. This emigration of microbiological R&D has occurred in an era in which vaccine sales, and medical needs, are increasing rapidly (19% compound annual growth rate over the past decade) and where international NGO effort in research and application is being galvanized<sup>22</sup>. Set in a context of wider market trends for large-scale UK biotechnological industry, this is clearly of great concern with respect to UK private sector investment in biomedical microbiology and, more broadly, the UK Government's ambitions to drive up industrial R&D investments<sup>23</sup>.

## International

41. The US, EU and IndoChina have leading investments in microbial science R&D and, as for much of the broad sweep of bioscience, represent leading opportunities for collaboration and bringing added value to UK-based research. For example the EBI represents an important international (but UK-based) strategic partner, bringing post-genomics expertise that could be drawn upon to maximise the useful outputs from UK genomics investments. Conversely, strong international investments represent a threat to UK research if opportunities for complementarity, collaboration and integration are not converted.
42. With respect to vaccine R&D, in particular, India and China are investing heavily to address their needs and those of other emerging markets. Whilst the UK contributes strongly to underpinning basic research in this area, it is widely considered to be weak in promoting focused translational R&D or active promotion of biotechnology via substantial grants as compared to the US (e.g. for avian influenza research facilities).

## US

43. US strategy for microbial science research is in a highly advanced state compared to that of the UK. In particular, the American Academy of Microbiology has produced an ongoing series of influential, high-level and forward-looking colloquia reports on microbial science issues<sup>24</sup> including *Microbiology in the 21<sup>st</sup> Century (where are we and where are we going?)*; *Systems Microbiology: Beyond Microbial Genomics*;

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<sup>21</sup> *Sanofi Pasteur, GlaxoSmithKline, Merck, Wyeth and Chiron/Novartis.*

<sup>22</sup> For example, the Gates Foundation, the Wellcome Trust, Global Alliance for Vaccines and Immunization, International AIDS Vaccine Initiative.

<sup>23</sup> As expressed in the Science and innovation investment framework 2004 – 2014 (2004) HM Treasury: [http://www.hmtreasury.gov.uk/spending\\_review/spend\\_sr04/associated\\_documents/spending\\_sr04\\_science.cfm](http://www.hmtreasury.gov.uk/spending_review/spend_sr04/associated_documents/spending_sr04_science.cfm)

<sup>24</sup> Further details and downloads at <http://www.asm.org/Publications/index.asp?bid=1358>

*Research Opportunities in Food and Agriculture Microbiology; The Global Genome Question: Microbes as the Key to Understanding Evolution and Ecology; and Vaccine Development: Current Status and Future Needs.* Microbial science in the US has seen great recent increases in funding through investment by the Dept. Homeland Security, for example.

## **EU**

44. Several themes under the Framework Programme 6 include thematic areas of relevance to microbial science, including:

- Life sciences, genomics and biotechnology for health theme;
- Food quality and safety theme;
- Sustainable development, global change and ecosystems theme;
- Nanotechnologies theme.

In addition, Marie Curie fellowships are available to these areas of potential microbial science activity.

## **Potential Barriers to Success**

45. A significant element of the Terms of Reference for this review was not only to consider the future opportunities and priorities for BBSRC-funded microbial science but also to consider what barriers there are to realising the opportunities and how they might be addressed. To aid in our analysis we undertook a wide consultation (further information on this can be found at annex 3). Based on the funding and contextual information as summarised above, and on our consideration of community concerns, we perceive three main issues that need to be addressed (see section 2 for more detail and key recommendations to reduce or remove the barriers).

### **1. Improving critical mass, coherence and focus of microbial science in the UK**

46. Whilst there is a large and relatively healthy diversity of microbial research funded in the UK, there is widespread concern that there is a lack of coordination and focus, particularly relating to core microbial research areas. This comment applies in particular to bacteriology. Fundamental microbial physiology sat centrally within a historical critical mass of microbiology HEI departments, but with the almost universal consolidation of these departments into larger bioscience structures or life science schools over recent decades, core microbial skills have been eroded and geographically dispersed. Whilst we can foresee no return to the stand-alone microbiology department, new ways of generating critical mass in core microbial science areas must be found if we are to maintain a skilled workforce to meet current and future opportunities in the basic and applied analysis of microbes and microbial communities in both academia and industry.

47. Additionally, there is widely perceived to be a deficiency in coherence and focus on microbial science areas that span the remit boundaries of the Research Councils, and their interactions with Government departments and NGOs. Correspondingly, there are concerns that the development of important synergies of strategic importance to both BBSRC and the UK is currently sub-optimal. It is widely considered that there is

considerable room for improvement in the coordination of the pool of expertise that the UK is able to engage in response to research issues of great strategic importance; for example, emerging human, animal and plant diseases, multilateral microbial surveillance needs, and the pressing strategic drivers of bioenergy research.

## **2. Increasing the supply of skilled people – repairing the Skills Pipeline**

48. There are grave community concerns, highlighted in the consultation, about the loss of microbiology teaching (especially practical-based teaching) at undergraduate level in the universities. Concern was also expressed about the representation of microbiology in the secondary school curriculum. The panel notes efforts made by SGM to address this issue by engaging in school curriculum development and through the appointment of a full-time school liaison officer, but much remains to be done. In the eyes of the research community, the skills pipeline is not being adequately fed. Whilst there is a limit to BBSRC's ability to affect change in these areas, the Council must be aware of these concerns, which will impinge on the UK's future ability to deliver microbial research priorities.

## **3. Providing the tools and resources for world class microbial science – Capitalisation and Future Development**

49. There are also wide concerns about a current lack of investment in post-genomic exploitation/annotation in particular comparative/evolutionary genomics. A great deal of genome sequence information is being generated, and much more is on the horizon, but it is not clear from where informatics and software infrastructure for annotation, analysis and exploitation will emerge, especially for non-clinical microbial science.

## **Section 2: Facilitating world-class UK microbial science**

50. Having set out the high level ‘state of play’ for microbial science in Section 1, including grand opportunities and potential barriers to success, in Section 2 we develop the ‘grand opportunities’ into a series of suggested scientific and underpinning resource priorities for BBSRC, with the aim of improving visibility, vision and focus for fundamental microbial science research. We also address how potential barriers might be reduced or removed, provide recommended options to improve the ability of UK researchers to respond to these headline challenges.

### **Basic research priorities**

51. It is clear that, on a 5-10 year time frame, and probably beyond, there are some exciting headline challenges for fundamental microbial science, driven by the enabling toolkits of high throughput ‘omics and informatics. BBSRC is centrally placed to help to address these challenges. Though the consultation, we are aware of an element of suspicion from some parts of the community about what is seen as the inexorable march of ‘omics and systems biology. But it is our view that these are opportunities and represent a step-change for microbial science that should not be ignored. Researchers must be enabled to embrace systems biology in much the same way as they have been doing with ‘omics’ methodologies. It must cascade throughout the entire microbial research community, and not be limited primarily to flagship centres of excellence.

52. While this step-change must and will proceed, the core skills required to solve problems and capitalise on new opportunities need constant development and should not be neglected. An over-enthusiasm for systems biology at the expense of core disciplines carries inherent risks for the health of microbial science. One can not generate a broad-based systems-level understanding of a cell or microbial community without ultimately deriving a deep analysis of its core components. Consequently, a careful marriage of systems biology and core microbiology skills is required if UK microbial science is to seize the opportunities and meet the challenges ahead.

53. The level of complexity to be unravelled so as to fully model even the most reducible molecular-cellular systems is highly sobering and must not be underestimated, demonstrated aptly by the relatively advanced experiences of virologists, working with viral systems containing as few as eight proteins. Even at this comparatively simple level of complexity, one viral protein may have multiple functions (many of which may still be obscure) through multiple and, perhaps, unrelated interactions with cellular components, modulated by post-translational modification, glycosylation and small ubiquitin-like modifier (SUMO)-modification. Additionally, single amino acid changes can have profound multifunctional implications. The system’s input, output and sensitivity parameters are often unknown or unaccounted for. ‘Omic techniques currently only offer relatively crude analysis in many respects- for example

proteomes may not differentiate between active and inactive protein forms, or even degradation products, or relate this information to subcellular locations. Therefore, there are considerable conceptual and experimental challenges to be faced in achieving effective modelling of even those systems that on the surface seem to represent tractable challenges, and ambitions for systems approaches must both be firmly tethered to core physiology skills and be tempered and informed by a growing body of experience.

## **Guiding lights - Breath and Depth**

54. As described in Section 1, the tremendous growth in the description of microbial genomes is enabling researchers, for the first time, to address microbial science questions in unprecedented **depth** (modelling the physiology of key microbial models, particularly towards the minimal bacterial cell) and **breadth** (microbial diversity). These opportunities must, in our view, represent the twin guiding lights for the medium-term outlook of much of fundamental microbial research.
55. In making this broad statement, we must also recognise that not all branches of microbiology are at equivalent stages with respect to these challenges. An understanding of virological diversity, for example, is comparatively well advanced, and virologists are at the forefront of attempts to undertake early modelling of discrete cellular processes and unravelling the inherent challenges therein.

### **Modelling important model microbes, towards the minimal microbial cell**

56. To achieve sufficient depth of penetration, systems microbiology must be driven forward utilising a few, key microbial systems. Obvious candidates might include *E. coli*, *Bacillus subtilis*, *Streptomyces coelicolor*, certain filamentous fungi such as *Aspergillus nidulans*, *Neurospora crassa* and *Magnaporthe grisea* budding and fission yeast, and important, tractable pathogens (e.g. *Mycobacterium tuberculosis*, malaria, trypanosomes, HIV), but there are others that might usefully be taken forward (Influenza, Meningococcus, photosynthetic bacteria, to name a few). Bacteriophage or other types of viral assembly may arguably provide the simplest, most tractable system for researchers first attempts at modelling a cellular process in its entirety, and the first steps towards the complete physiological description of a microbial cell and its interactions with the environment: the iconic predictive *e-cell*.
57. Systems biology is currently a very high profile area, yet current provision remains insufficient given the scale of the challenges. Six high profile BBSRC centres<sup>25</sup> have been created, but there is a need to embed systems approaches and capability more widely in the research community alongside the core disciplines necessary to test

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<sup>25</sup> These centres are: The Centre for Integrative Systems Biology at Imperial College (CISBIC); Manchester Centre for Integrative Systems Biology; Centre for Integrative Systems Biology of Ageing and Nutrition (CISBAN; at Newcastle); Centres for Systems Biology at Edinburgh, Nottingham and Oxford (announced in April 2006).

modelling predictions. Additionally, genomic annotation/functional reconstruction is a major resource bottleneck, and the infrastructural developments in this area should be driven by the bottom-up needs of researchers for knowledge management and integration, informatics and computational infrastructure.

58. The need to marry effective exploitation of functional genomics and its associated high-throughput technologies with core bacteriology lies at the heart of the *predictive-cell* ambition. There is a significant danger that leading research opportunities could be missed or not fully realised if the growing deficit in bacterial, yeast and fungal physiology and metabolism (formerly strong in the UK) is not made good, and properly integrated with high-throughput technologies.
59. The tractability of complete physiological networks within a cell will benefit from a much-improved understanding of the physiology of cells under stress, in their natural environment or in the quiescent state (e.g. those stresses that result in stationary phase, sporulation etc). Therein lies the likely route to unravel the role/expression of cryptic functions encoded in genomes, genetic redundancy, and genes with no known functions. Toolkit innovation in this area will be essential for significant progress to be made.

### **Tractability of Microbial Diversity**

60. An improved understanding of microbial diversity, and of the relationships between sequence similarities and divergences in varied microbial genomes, will be central to driving forward our understanding of the evolution of prokaryotes and eukaryotes; including the evolution of endosymbionts, the eukaryotic cell (flagellated and non-flagellated forms), and the role that horizontal gene transfer has played and is continuing to play in the lives of microbes.
61. Metagenomic studies of microbes that have not previously been analysed or cultured is beginning to provide our first window on the astounding 'real-world' scale of genetic diversity among microbes. Non-culturable organisms probably represent the vast majority of all microbes, yet a large-scale investigation of their biology has barely begun. The development of both metagenomic techniques and new routes to making non-culturables tractable are important technological challenges that require focus and innovation. Provision of genomic resources (particularly for non-pathogens), sequence annotation and informatics are key challenges to be met. Metagenomics will profoundly improve our knowledge of microbial diversity and evolution; providing that appropriate research structures are built to exploit it: metagenomic interrogations require novel theoretical and computational approaches for genomes functional reconstruction and predictive modelling. Ultimate exploitation of metagenomic libraries will also depend on their manipulation and expression in known, culturable hosts.
62. Research aimed at understanding microbial diversity will provide a driving force for strengthening the microbial science research base in the UK. Meeting the intellectual

and technical challenges associated with this research activity will be a prerequisite for a satisfactory understanding of the fullness of microbe-microbe interactions (mixed microbial communities), microbe-host interactions (pathogenic, parasitic, beneficial or commensal) and microbe-environmental interactions.

**Recommendation 1: BBSRC should consider the leading scientific priorities for fundamental/basic microbial science to be:**

**1. understanding microbial diversity from genomics to physiology, encompassing the challenges arising from metagenomics and overcoming the current experimental intractability of ‘unculturable’ microbes;**

**2. using a balance of reductionist and systems approaches to achieve a complete systemic description of the minimal microbial cell and its fundamental environmental interactions.**

## **Strategic Research Priorities**

63. An important systems biology challenge will be to move away from studying single strains under highly contrived *in vitro* conditions and to start to attempt to set the behaviour of microorganisms in the context of their *in vivo* environmental contexts. Many practical challenges will probably only be met in this way. Harnessing the power of both comparative genomics and a systems understanding that extends to microbial ecology will be critical in making tractable the ‘deep’ mechanisms of pathogenesis and other microbial interactions with higher organisms and the environment.
64. Emerging diseases of animals and plants (particularly zoonoses) linked to climate change and threats associated with the altered behaviour of the vectors of such diseases are major challenges for UK (and global) health and wealth. Effective responses will depend on high-quality, underpinning basic research. For example, improved molecular and cellular knowledge is necessary to understand why microbes that infect the wild flora and fauna are non-pathogenic. In virology especially, chronic and persistent, apathogenic infections in animals of today have shown able to become tomorrow’s human and agricultural disasters.
65. It will be important to capitalise on knowledge gained in the nascent modelling attempts using simple biological systems (e.g. bacteriophage) and extend these to pathologically relevant systems, describing microbial interactions with eukaryote host cell compartments, defence systems (e.g. the various facets of human/animal immune systems) and genetically diverse host populations. Basic science and innovation are also badly needed in the area of antimicrobials; new targets and strategies are needed for the development of novel or improved vaccines, therapeutics and probiotics.
66. A better understanding microbial diversity will drive innovation in areas of high strategic importance. Research in the areas of bioenergy and biocommodities

(encompassing petrochemical replacements, industrial raw materials and *pharming*) represent critical emerging 21<sup>st</sup>-Century strategic priorities. Climate change and diminishing supplies of fossil fuels may be the two forces that most affect human society in the foreseeable future. Microbial bioscience has a critical role to play in unlocking the potential of energy crops (improving energy conversion), and may have more radical applications in microbial fuel cells. BBSRC must ramp its investments in this area to meet these challenges<sup>26</sup>.

67. In line with petrochemical replacement strategies for energy, there will be considerable demand for biochemicals/commodities from biorefinery, metabolic engineering or synthetic biology routes. Microbial science challenges lie at the heart of these emerging strategic priorities but capitalising on these opportunities requires a deep understanding of the metabolic and regulatory underpinnings of appropriate microbial catalysts<sup>27</sup>.

**Recommendation 2: In seeking to extend and reinforce the fundamental microbial science pipeline, BBSRC should consider leading strategic priorities for microbial research to be:**

- 1. effective exploitation of basic science opportunities to gain new insights into the complex cellular-molecular-genetic webs determining microbial pathogenesis;**
- 2. to provide leadership in driving forward research in emerging and re-emerging infectious disease of animals, plants and humans, and exposing and developing the synergies between these research areas;**
- 3. new antimicrobial therapeutics and immunological strategies;**
- 4. the generation of high-quality critical mass in microbial research underpinning bioenergy and biocommodities applications.**

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<sup>26</sup> The recent Review of Bioenergy Research recommended that BBSRC consider this area to be of high strategic importance. The report can be downloaded from [http://www.bbsrc.ac.uk/about/pub/reports/06\\_may\\_bioenergyreview.html](http://www.bbsrc.ac.uk/about/pub/reports/06_may_bioenergyreview.html)

<sup>27</sup> Including those facilitating biomass production (e.g. maximising crop nutrient capture and biomass accumulation) and processing (e.g. maximising the conversion of complex carbohydrates to fermentable sugars), in addition to direct microbial energy capture and conversion strategies.

## **Delivering the priorities, overcoming the barriers**

68. In order to seize the opportunities, and to ensure that UK microbial science continues to be fit for purpose into the future, it is essential that:

- **funding mechanisms and models** are fit for their intended purposes;
- we have **skilled researchers sufficient both in quality and quantity** (including bright young people) coming through the system;
- we have the right **research infrastructure, tools and resources**;
- we are able to **increase the economic and social impact of microbial science**;
  - to improve **industry/academic interaction**;
  - to better translate **microbial science needs and priorities into policy**.

69. Over the following pages, we set out leading issues in these areas, as we see them, and recommend options for BBSRC to facilitate delivery of priorities. In particular, we examine how potential barriers to future success, as identified in Section 1 (insufficient critical mass, coherence and focus, weakened skills pipeline, and access to appropriate tools and resources), might be addressed.

## **Improving critical mass, coherence and focus of microbial science in the UK**

### **BBSRC Funding**

70. Microbial science currently has access to a number of funding routes, both within and external to BBSRC. There are considerable advantages to this diversity, offering more ‘bites at the cherry’ than are available to researchers in other bioscience fields. It also reflects the widely pervasive nature of microbial science and the success of investigators in promoting the microbial aspects of their research.

71. However, we note that some important issues persist under current BBSRC funding arrangements; the diversity of funding routes BBSRC also diffuses focus, and militates against concerted activity and the seizing of grand challenges. From the consultation, there was a prevalent view that current Scientific Committee structures may not be encouraging growth in basic microbial science areas, and this certainly seems consistent with the captured data trends<sup>28</sup>. We note and concur with community concerns that there is an absence of ‘around the table’ critical mass in microbial expertise and strategic awareness in microbial science across the Scientific Committees, and a resulting lack of focus on microbial issues to inform both current peer review and forward strategy. This is a matter of particular concern among animal virologists.

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<sup>28</sup> See Annex 4, Table 6, showing decline in reductionist basic science areas from 2000-2006.

72. It is clear that the leading opportunities and challenges for microbial science, as set out earlier in this chapter, will require much improved coordination and focus from both funding body and research provider perspectives, and it may be that current funding structures do not best serve this purpose. BBSRC is currently reviewing its Research Committee structures<sup>29</sup>, and we strongly encourage the Council to give careful consideration as to how focus on basic microbial research might be improved in order to position the UK to take advantage of the impending microbial revolution.
73. Aligned to these concerns, we note strong views from some quarters of the microbial research community that microbial science would be best funded via a dedicated BBSRC Committee. Recognising the apparent attractiveness of this proposal, we also note a compelling counter-argument that such a move would ring-fence and, therefore, inevitably constrain funding available for microbial science. We foresee that such a move would be counter-productive, and possibly detrimental to the field. We therefore encourage BBSRC to seek more holistic routes to improving the coordination of microbial science funding whilst recognising and continuing to foster the strengths provided by the current funding system.

**Recommendation 3: Noting that BBSRC is currently reviewing its funding committee structures, it is timely that the Council should develop mechanisms that will bring coherence to fundamental microbial science funding, and promote the necessary culture change and coordination of research effort that will be needed to meet the existing and emerging opportunities and challenges for the field.**

### **Bridging disciplines to meet systems objectives**

74. BBSRC has made important and substantial investments to date in systems biology, creating six high profile centres (see footnote 25), with the study of microorganisms featuring prominently. BBSRC has also made highly relevant commitments to systems microbiology in Europe (SYSMO). However, there is a need to extend the ethos and benefits of these highly focused investments; further afield, there has been little tangible effort directed at bridging the gap between well-advanced molecular genetic studies, biochemical analysis of enzyme and protein function, proteomics, cellular physiology, metabolomics, high resolution cell biology, and initial mathematical modelling of discrete cellular signalling events. Particularly given the scale and timeliness of the challenges to be met, the development of this area would benefit substantially from additional targeted funding; we envisage that this would form the basis of a useful initiative centered upon **cellular microbiology**. It is important to note that some data may need to be re-acquired to meet the needs of systems approaches for data that has come from a single source.

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<sup>29</sup> A community consultation on this issue has been undertaken, closing on 30<sup>th</sup> Sept. 2006. See <http://www.bbsrc.ac.uk/society/dialogue/consultations/committees/Welcome.html> for details.

**Recommendation 4: Acknowledging BBSRC's recent, focused investments in systems microbiology, there is a clear methods gap to be bridged between data acquisition (through biochemical investigations, molecular genetic studies cell physiology, and high resolution cell biology) and initial mathematical modelling of discrete cellular events. This represents a broad-scale challenge for UK microbiologists, and BBSRC should seek to further stimulate innovation in this area, which has the potential to drive forward the state of the art for systems microbiology and set the ground rules for systems analysis of more complex biological systems.**

#### **Co-ordination of funding interfaces**

75. BBSRC-funded microbial research has important interfaces with MRC, NERC and EPSRC, and there is a major challenge is to ensure that there are no gaps. We are aware of a wide body of opinion within the microbial science community that better cross-Council co-operation is needed to serve strategically important areas of microbial science. This is particularly relevant for research on pathogenesis of higher organisms, where there is a perceived disconnection between the activities of BBSRC, MRC and the Wellcome Trust.
76. The European Research Council (ERC) will be critical funder of microbial science, and can be expected to join up microbial science funding in continental Europe. It will be critical to ensure that microbial science supported by BBSRC is also effectively linked into this activity.
77. It is extremely important to emphasise that strong synergies that exist between studies of pathogens that infect humans, animals and plants. There are currently perceptions of a highly undesirable 'intellectual apartheid' in some areas of microbial science (particularly relating to bacteriology) with divisions reinforced by rigidly separate Research Council (and charitable) funding streams or historical events<sup>30</sup>. Such a situation has the potential to reduce the impact of work supported by all funders and must be guarded against strongly.
78. Promoting the potential synergy between human and animal pathology was an issue raised in the previous Farm Animal Genomics Review<sup>31</sup>. This review recommended that BBSRC should encourage more interaction between the animal and human bioscience research communities Suggested options included joint workshops or networking activities, studentships and fellowships, and a targeted initiative specifically aimed at translational studies would be a positive move by the Council to establish collaborative research<sup>32</sup>.

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<sup>30</sup> For example the parallel investigation of type III secretion systems in bacterial pathogens of plants (supported by BBSRC) and in pathogens of humans (supported by other agencies).

<sup>31</sup> Chaired by Professor Cheryl Tickle. The report can be downloaded from the BBSRC website, at: [http://www.bbsrc.ac.uk/about/pub/reports/fagr\\_11\\_10\\_05.html](http://www.bbsrc.ac.uk/about/pub/reports/fagr_11_10_05.html)

<sup>32</sup> Recommendation 8 of the Farm Animal Genomics Review. Strategy Board is currently working with the Sustainable Agriculture and Healthy Organism Strategy Panels to take this recommendation forward in the wider context of BBSRC's animal health and welfare priority.

79. It is vitally important for the ongoing health of infectious disease research that there is a strong, unbroken pipeline back to the basic microbial science *catalyst for change*. The strong perception of the research community is that this linkage is not being forged with sufficient strength, particularly relating to research on emerging and re-emerging diseases.
80. Acknowledging BBSRC's strategic focus and commitments in the areas of animal and plant disease research, it is our view that the Council should seek to maximise the synergies of UK infectious disease research. This is particularly the case in the context of the present and future challenges presented by emerging and re-emerging disease, especially zoonoses. These challenges can be expected to be significantly exacerbated by global climate change. In tune with the findings of the Farm Animal genomics Review it is our view, as expressed in Recommendation 2, that there are particularly compelling reasons to foster cross-Funder synergies in emerging and re-emerging disease research, with an emphasis on zoonoses.
81. The large scale of Wellcome Trust investments in medical microbiology results in a critical distortion of the opportunities to advance the non-medical microbial science agenda. If we are serious about the need to tackle the basic science challenges of microbial diversity, there will be a need to address the imbalance that results in an almost irresistible tendency for microbial science expertise to be diverted towards medical research.
82. It will also be critical for BBSRC to forge microbial research links with Defra's sustainability agenda. Important fundamental science, underpinning this activity, lies firmly within BBSRC's remit. However, as a consequence of Defra's redefined priorities, it is our view that a national UK strategy for research on infectious diseases of animals may have to be led by BBSRC in the future.

**Recommendation 5: BBSRC must engage with other key funders of UK microbial science (including MRC/NERC/Defra/Wellcome Trust/EBI/ERC) to develop research synergies, to remove artificial barriers where they persist and, in particular, to ensure that an unbroken R&D pipeline exists from basic microbial science to medical and environmental microbial science applications. BBSRC should consider *microbial diversity* and *emerging and re-emerging disease* to represent, respectively, basic and strategic areas of high priority for which effective multilateral synergy will be critical to meet research challenges.**

## **Increasing the supply of skilled people – repairing the skills pipeline**

83. If UK microbial sciences are to remain healthy and be able to deliver the research priorities (above) then an adequate **quantity and quality of trained microbiologists** will be essential. The particular challenge here is to generate critical mass in key areas of expertise, especially relating to core skills in microbial physiology/biochemistry.

### **Potential role for dynamic networks**

84. We note several models by which critical mass could be developed in vital core areas of microbial science including the promotion of new centres of excellence ('virtual' or 'real'). However, given limits on BBSRC funding and the Council's limited ability to influence HEI organisation and/or priorities, it is our view that BBSRC might most successfully catalyse the development of improved core skills through the funding of *dynamic networks*.

85. Many of the best microbiologists in a given area are dispersed across the UK, whether that area is defined by system (e.g. metabolism and microbial products, bacterial wall biochemistry), or organism (model system or pathogen) or area (e.g. host-pathogen/symbiont interface), or cross disciplinary area (e.g. evolution of eukaryotic cells). These groups could be linked into dynamic networks through the development of a new form of grant that funds the collaborating members of the intranational network regardless of geographical location.

86. This type of grant could be structured around the research, additive to both the single grants of some of the individual participants, and training provision funded by BBSRC through the local Doctoral Training Accounts (DTAs). In this manner the health of a subject can be maintained and training enhanced in areas of BBSRC and community priority. It would allow geographically separated researchers to join groups and serve as a mechanism to maintain intellectual cohesion in a diversity of organisms. As a possible model, this form of funding could cover:

- research programmes involving two or more principal investigators working in complementary areas but based at different UK locations;
- integrated training grants with support for undergraduate internships, graduate students, and associated postdoctoral fellows working in a coordinated effort;
- short joint projects;
- extension of DTA money to fund a collaborative year for a student in a partner lab;
- funds for a new researcher to join the network;
- small meeting funds;
- joint and joined-up training in core skills.

87. Such a mechanism<sup>33</sup> would facilitate the formation of dynamic networks in both bottom-up and top-down modes of engagement, and we encourage Strategy Board to consider its merits in improving coordination and critical mass in fundamental microbial science areas in fundamental microbial science areas.

### **Graduate training**

88. Experience at undergraduate level affects subsequent postgraduate career choices, and can influence high quality candidates to take up PhD studentships. BBSRC has no brief to influence undergraduate teaching, but the Council can help to attract individuals to research careers. BBSRC has an existing scheme of Vocational Bursaries to give undergraduates a taste of research so that more are likely to see research as an attractive career option. This is a very positive tool that could be reinforced. BBSRC might also consider the creation of a Summer Schools Scheme, perhaps running the initial trials in the microbial science area. There is also a possibility that the BBSRC Institutes could play significant training roles here.

89. Training aspects of PhDs are of concern to PIs. There is a perception that PhD students in the microbial research area require increasing amounts of remedial training. This is thought to be due to reduced undergraduate-level exposure to the practical aspects of the subject (likely related to the loss of distinct university microbiology departments). PIs also report that, in recent years, PhD training does not expose trainees sufficiently to an interdisciplinary grounding in bioscience techniques as required for modern research modes. In our view, BBSRC's DTAs are a positive move forward in postgraduate support. The flexibility of institutions discretionally to tailor postgraduate packages may also assist in attracting better students to priority areas. It is important, in our view, that the leading centres of excellence for microbial research bid strongly for quota Doctoral Training Grants.

90. More radical and holistic mechanisms of capacity building and training in core microbial science could be engaged such as that recently for Integrative Mammalian Physiology. This is widely considered to be a progressive example of best practise that engages all stakeholders (notably including the private sector) reinvigorates identified priority areas and utilises the joint funds to maximum advantage. Such schemes may represent the future for targeted funding.

**Recommendation 6: Strategy Board should seek to reinvigorate core microbial science capability in the UK, and foster the necessary critical mass of core microbial skills to meet identified strategic priorities. BBSRC should carefully consider targeting mechanisms such as dynamic networks and cross-funder capacity awards to achieve this aim, and seek imaginative ways of working with stakeholders to improve the attractiveness of graduate training opportunities in core microbial science areas.**

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<sup>33</sup> The Scottish Pooling Initiatives, commencing this year for cell biology, translational biology and systems biology, address similar aspects of 'dynamic network' formation.

### **The BBSRC-sponsored Institutes**

91. Those BBSRC-sponsored Institutes that have microbial science interests play critical roles in building national research skills capacity in areas of high strategic importance, particularly relating to the interactions of microbes with other organisms and with the environment. IAH is a leading centre for basic and strategic research on endemic and exotic pathogens of animals. It is internationally pre-eminent and provides a critical mass of core underpinning microbial science expertise. This national and international leadership role must be strongly supported and encouraged.
92. In addition, JIC represents the pre-eminent national centre for plant and plant/microbial research, with expertise in a broad range of microbial areas (focused on actinomycete and filamentous fungal molecular biology and plant-microbe interactions). We note that the recent Institute Assessment Exercise<sup>34</sup> recommended that JIC must set out strong strategic ambitions for its microbial science remit. We concur that this is an urgent necessity, given the unique position of JIC researchers in providing unprecedented focus and leadership for the field.
93. Microbial science at RRes links research on crop sustainability, insect vectors of disease and the rhizosphere. RRes research, particularly given its strong commitment to informatics and the associated strength of expertise at the Institute, represents an important test-bed for extending the scope of microbial systems biology to the ecosystem level, driving forward an improved holistic and predictive understanding of microbial communities on plants and in the soil.
94. IFR and IGER also have important underpinning roles in driving forward the understanding of complex microbial communities, allied to areas of strategic importance (microbial ecology at environmental and rumen level (IGER) and the human gut (IFR)). These areas encapsulate significant challenges for expanding systems biology approaches to microbial community and ecology scales. The investment at IFR in studies of food-borne pathogens using systems biology methods is particularly noteworthy in this regard.
95. The Institutes working in the plant/microbial research area have a clear role, which should be seized, in providing critical mass and leadership in emerging areas of strategic opportunity (bioenergy and biocommodities) that will benefit from long-term strategic investment.

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<sup>34</sup> Reports can be viewed at [http://www.bbsrc.ac.uk/about/pub/reports/06\\_feb\\_visitinggroups.html](http://www.bbsrc.ac.uk/about/pub/reports/06_feb_visitinggroups.html)

**Recommendation 7: BBSRC should strongly support the strategic positioning of appropriate BBSRC-sponsored Institutes as centres of underpinning critical mass for core microbial research at the animal:microbe, plant:microbe and environment:microbe interfaces, with commensurate leadership and training roles. The Institutes are the ideal environments in which to develop the skills to meet the long-term challenges associated with strategic demands for bioenergy and biocommodities research in the 21<sup>st</sup> Century. The relevant Institutes should develop clear strategies and appropriate critical mass to meet the microbial research challenges therein.**

## **Providing the tools and resources for world class microbial science – Capitalisation and Future Development**

### **Sequencing and Functional Genomics**

96. Despite initial progress, there is now an enormous backlog of microbial genome sequence data to be mined before researchers can begin to claim to have a broad knowledge base. Whilst technological advances result in ever-increasing speed and accessibility of genome sequencing, this represents a highly significant challenge for resources and infrastructure that must not be underestimated. In particular, reliance on the WTSI as the only large resource for microbial genomics is a long-term issue of community concern, particularly with respect to service provision for the sequencing and annotation of non-pathogenic microbes. There is a need for more resources and skilled people for microbial genomics and informatics and, recognising both likely infrastructural realisms and the diverse local needs of researchers, this might possibly be best organised in a coordinated but geographically dispersed way.

97. There is a particular urgency to reduce the annotation/functional genomics bottleneck so as to realise the full potential of microbial genome sequences. This bottleneck currently acts against effective use of those genomics resources that are already available. Given the number and size of microbial genome data sets likely to emerge in the immediate future, effective annotation will increasingly represent a critical issue for the field.

### **Development of critical new toolkits**

98. Microbes are unique in their unprecedented diversity and metagenomics projects help to reveal this, but the majority of microbes are yet to be cultured. At the other end of the technology spectrum there are challenges to imaging inside cells to understand their organisation and function. Technological innovation is therefore essential to increase the tractability of:

- The quiescent cell and current unculturables;
- Advanced optical imaging and electron microscope tomography at the scales of bacterial cells and imaging analysis of single molecules.

99. These challenges are likely to require cross-disciplinary research, and BBSRC has a role in facilitating this through a range of actions such as cross-disciplinary workshops and ‘sandpits’. In particular, relating to imaging, there is a strong need for innovation at the interface of BBSRC and EPSRC-funded research.

### **Culture collections**

100. The funding, curation and use of microbial culture collections is an ongoing issue for the UK research community, which has been the custodian historically of numerous collections of different sizes. The current funding position of large, **national** culture collections is currently only ‘metastable’, and the curation of smaller, localised collections is increasingly reliant on diminishing pots of ‘soft money’. This is an issue which must clearly be tackled soon.

101. We are aware of views that culture collections should ‘sink or swim’ based on current need. However, we also acknowledge strong counter-arguments based on ‘tomorrow’s need’, which may be both critical and perhaps unforeseen. We perceive too that in several cases, there is a strong requirement to maintain large, centralised collections, not least because they serve as invaluable standard reference libraries.

102. Our view is that rationalisation and curation of important major culture collections must be undertaken at international level for the future, and probably at a European level with respect to primary UK rationalisation and access. Requirements need to be identified, audited and funded properly. We encourage BBSRC to engage with other national and international stakeholders to work towards sustainable multilateral solution for major UK funding collections, with emphasis on strong governance and curation, reasonable accessibility (costs and timeframes) and high standards of quality assurance for samples.

**Recommendation 8: BBSRC should seek to facilitate, unilaterally and multilaterally as appropriate, the provision of appropriate tools and resources in the following areas, which will be of critical importance in realising the leading scientific challenges as set out in Recommendation 1:**

- **appropriate infrastructure investment for functional genomics of non-pathogenic microbes;**
- **tools that facilitate accurate and reliable annotation of genomic sequence data and that protect the integrity of such data;**
- **new tools to improve the tractability of genes with functions in the quiescent cell and to provide access to the enormous variety of microbes that currently are ‘unculturable’;**
- **reinvigorated innovation in optical imaging and electron microscope tomography of microbial cells, working at the interface of EPSRC and BBSRC;**
- **sustainable, high quality curation of important UK microbial culture collections.**

103. Much of our attention has been focused on the need to protect and reinvigorate core skills in microbial science, which serves as the central ‘hub’ from which spokes

of more strategic and applied research extend. There is also a need to ensure that these spokes extend appropriately beyond the boundaries of BBSRC science; that economic opportunities arising from BBSRC science are exploited, and that UK policy is appropriately informed by the knowledge generated. The remaining sections of the report focus upon these issues.

## **Economic and social impact of microbial science**

### **Improving industry/academia links**

104. There are few areas of microbial science that are not relevant to industry, but it seems to us that this fact is not embedded in the general outlook of the field. Microbial science is a deep source of opportunity for industrial innovation, but currently under-exploited on almost all fronts. Particular emerging opportunities include bioenergy, industrial remediation, biofilms, probiotics, new routes to antimicrobials/vaccines/therapeutics, and synthetic biology to generate commodity chemicals in microbial biorefineries.
105. There is widespread concern in the community that the UK is slow to capitalise and invest appropriately, and that early and concerted foreign investments will reap the greatest dividends. Recognising that the issues for industrial microbiology have commonality across bioscience research areas, there is nevertheless a clear need for UK academic and industrial researchers to find new ways to exchange ideas, expertise and personnel, and work together to remove barriers to the application of the UK's excellent fundamental microbial science outputs.
106. There is a need for better dialogue, and *different* modes of dialogue. KTNs have an important role here in facilitating cultural cross-fertilisation, and the Bioscience for Business KTN<sup>35</sup>, has microbial science-relevant remit. Mechanisms such as bio-partnering events should be fully engaged. We also envisage a stronger role for the SGM in improving the relevance of their networking activities to industry and engaging industrial Council members.
107. Such mechanisms would help to erode barriers which militate against the best new-blood researchers gaining industrial awareness and experience: high-flying microbial science fellows exhibit a near-universal lack of exposure to industrial research, and a commensurate level of antipathy towards industrial research collaboration and careers. This culture must be addressed in haste if it is not to become embedded in the next generation of microbial research leaders. BBSRC's Industry Interchange Programme (launched in 2005) is a welcome mechanism which should be strongly promoted.

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<sup>35</sup> formerly Pro-Bio Faraday.

108. **Implications of Full Economic Costing:** Whilst a positive step forward in principle, there are potential negative impacts of full economic costing (fEC) on the attractiveness of the UK as a base for industrial biomedicine/biotechnology. Whilst we acknowledge that this funding shift is in the early stages of embedding, there are implications of widespread concern. If fEC is applied within the UK but not in other European countries (in particular, and as seems likely for the foreseeable future) then UK research will be placed at a significant competitive disadvantage. It is vital that BBSRC (and others) should monitor the situation carefully as fEC conditions become established. As part of its Bioscience for Industry spectrum of activities, we suggest that the Council should work closely with DTI to identify mechanisms to improve attractiveness of UK collaborations, with emphasis on key areas of priority and concern, such as antimicrobials/therapeutics/vaccines.
109. If UK innovation in the areas of antimicrobial therapeutics and immunity is to be developed sustainably for the future, strong academic/industrial partnerships will be essential, and the UK needs to strategies to attract back expatriate companies working in these areas. We are aware that UKTI is working on mechanisms to attract overseas investment, and in dialogue with DTI, BBSRC should seek to promote needs of the biotech sector. BBSRC should also seek to improve awareness of existing mechanisms by which international industry and UK academia can collaborate (for example, CASE studentships).

#### **Facilitating a microbial science-informed UK culture**

110. Microbial science needs to be more embedded and prominent in society and Government policy, particularly given high profile of current infectious global disease challenges, the impact of microbes and microbial activities on this planet, the needs for new biotechnology (e.g. renewable energy sources), and the undeveloped synergies across these challenges.
111. In particular, BBSRC should take a lead in working with Government, other funders (e.g. MRC, Wellcome, Defra) and supported researchers to address how best to meet, at a high multilateral level, the needs of global infectious disease challenges and markets and provide focus on key issues (e.g. surveillance of human and animal infectious disease).
112. We applaud SGM on its recent efforts to influence Parliament and other assemblies throughout the UK and encourage it to build on its successes in the future. BBSRC can assist and influence this process through more formal contact with SGM Council. Similar approaches could be taken with the Royal Society, the Biosciences Federation and the Institute for Biology.
113. Bioterrorism and misuse of research represent issues of high Government and media interest. Whilst we do not wish to overplay this issue, it is clearly the case that BBSRC, as the principle UK funder of basic microbial science, has an essential role to play in engaging the media and policy makers and helping to ensure, as far as possible, that policy and media activity is scientifically balanced and informed.

114. Whilst we must not be complacent regarding the potential misuse of microbial science, it is also vital that regulatory frameworks designed to guard against research misuse and to protect against health and safety risks are relevant and proportional, and responsive to the state of the art. We note and agree with the considerable community concerns that current HSE regulations governing the use of microorganisms are often overzealous, and do not bear sufficiently close relation to actual risks or real-world contexts; there are sometimes considerable discrepancies resulting, for example, in harmless or near-harmless organisms being treated with the same restrictions as pathogens.
115. This has considerable implications for research and teaching. In particular, current HSE regulations are widely perceived to be discouraging the incorporation of microbial laboratory work into coursework at school and universities, contributing to the lack of visibility of microbiology at the school and undergraduate bench. This has clear implications for the microbial science skills pipeline. It is vital that funding bodies such as BBSRC should seek to maximise their influence with HSE and other relevant regulatory bodies to ensure that regulatory frameworks are based upon rigorous scientific principles and risk contexts.

**Recommendation 9: BBSRC should strive to use the full range of mechanisms at its disposal to ensure that the world-class knowledge and innovation generated by basic and strategic microbial science is fed forward strongly into increased industrial innovation, appropriate public services, national security and strong policy making.**

## **Annex 1: Terms of Reference for the Review Group and membership of the Review Panel**

### **Terms of Reference**

1. To review current research sponsored by BBSRC through responsive mode, core strategic grants to Institutes and other funding relevant to microbial science, encompassing research on all microbial divisions (i.e. viruses, bacteria, archaea, fungi and protista) and associated technology outputs, including pharmaceuticals (e.g. antimicrobials and vaccines), processing and production.
2. To analyse research strengths, weaknesses, opportunities and threats, in the context of a medium to longer-term (i.e. 5-10 years) strategy for microbial research.
3. To consider how BBSRC's research priorities in this area relate to those of other Research Councils (in particular to MRC and NERC), Government Departments, and other stakeholders, and to the outlook and needs of industry, all in an international context.
4. To advise BBSRC on priorities for future research in microbial science and how the high priority areas should be developed and to recommend options that:
  - a. promote collaborations as appropriate:
    - within and between BBSRC Institutes
    - between BBSRC Institutes and the Universities
    - between BBSRC and other funders nationally and internationally;
  - b. incorporate the most appropriate funding and training arrangements/mechanisms to sustainably support microbial science research in Institutes and Universities;
  - c. that optimises the transfer of the outputs of basic research (including that on model systems and species) into application.
5. To report to Strategy Board by September 2006.

## **Panel membership**

### **Professor Charles Dorman, Trinity College Dublin (Chairman)**

Bacterial virulence gene transcription and regulation. SGM Council member.

### **Dr Aileen Allsop, VP, AstraZeneca**

Yeast biology.

### **Professor Jeffrey Almond, Senior VP, Sanofi Pasteur MSD, France**

Human vaccine development.

### **Professor Michael Danson, University of Bath**

Structural basis of extremophile enzyme stability and catalytic activity.

### **Professor Tim Donohue, University of Wisconsin, USA**

Metabolic and regulatory pathways of *Rhodobacter sphaeroides*.

### **Professor Steve Edwards, CE, Defra's Veterinary Laboratories Agency**

Veterinary virology. BBSRC Sustainable Agriculture Strategy Panel.

### **Professor Jeff Errington, University of Newcastle/ Prolysis Ltd**

Cell division, chromosome segregation and control of cell shape in bacteria. SGM Council member.

### **Professor Mike Gasson, Institute of Food Research**

Molecular microbiology of Gram-positive bacteria and GI tract microbial communities.

### **Professor Igor Goryanin, University of Edinburgh**

Whole cell modeling of microorganisms; informatics and systems biology.

### **Professor Keith Gull, University of Oxford**

Cytoskeleton, cell cycle and cell differentiation in Trypanosomes.

### **Dr Joel Milner, University of Glasgow**

Plant virology, plant-microbe interactions. BBSRC PMS Committee member.

### **Dr Clive Price, University of Lancaster**

Cell division, cytokinesis and cell separation in yeast. BBSRC GDB Committee member.

### **Professor Richard Randall, University of St Andrews**

Protective immunity to viruses (human/animal). SGM Council member.

### **Professor Bert Rima, Queens University Belfast**

Molecular virology (human/animal), attenuated viral vaccines. SGM Council member.

### **Professor Katherine Smart, University of Nottingham**

Brewing science, fermentation, yeast cell biology. SGM Council member, IUMS Council Member.

### **Professor Maggie Smith, University of Aberdeen**

*Streptomyces* biology/genetic engineering.

### **Professor Nicholas Talbot, University of Exeter**

Fungal pathogenesis of plants. BBSRC PMS Committee member.

### **Professor Liz Wellington, University of Warwick**

Characterisation of microorganisms in soil; survival of pathogens in soil.

## **BBSRC Secretariat**

**Dr Jef Grainger**

**Strategic Planning Unit, Review Secretary**

**Dr Paul Burrows**

**Strategic Planning Unit, Head**

**Peter Hurrell**

**Strategic Planning Unit**

## Annex 2: Main abbreviations used in the report

AF	Agri-Food (BBSRC grant awarding Committee)
AIDS	Acquired Immune Deficiency Syndrome
AS	Animal Sciences (BBSRC grant awarding Committee)
BBSRC	Biotechnology and Biological Sciences Research Council
BCB	Biochemistry and Cell Biology (BBSRC grant awarding Committee)
BMS	Biomolecular Sciences (BBSRC grant awarding Committee)
CSG	Core Strategic Grant (used to support long-term research in BBSRC Institutes)
Defra	Department for Environment, Food and Rural Affairs
DfID	Department for International Development
DTG	Doctoral training grant (recently introduced BBSRC PhD funding scheme)
DTI	Department of Trade and Industry
EBS	Engineering and Biological Systems (BBSRC grant awarding Committee)
<i>E. coli</i>	<i>Escherichia coli</i>
EPSRC	Engineering and Physical Sciences Research Council
EU	European Union
fEC	Full economic costing
FRS	Fisheries Research Services (SEERAD-sponsored)
FMD	Foot and mouth disease
FSA	Food Standards Agency
GDB	Genes and Developmental Biology (BBSRC grant awarding Committee)
HEI	Higher education institution
HIV	Human Immunodeficiency Virus (etiological agent of AIDS)
HSE	Health and Safety Executive
IAH	Institute for Animal Health (BBSRC-sponsored)
IGER	Institute for Grassland and Environmental Research (BBSRC-sponsored)
IPA	Industrial Partnership Award
JIC	John Innes Centre (BBSRC-sponsored)
MRC	Medical Research Council
MRSA	Methicillin-Resistant <i>Staphylococcus aureus</i>
NERC	Natural Environment Research Council
OSI	Office of Science and Innovation (an office of the DTI)
PA	Per annum
PI	Principle Investigator
PMS	Plant and Microbial Sciences (BBSRC grant awarding Committee)
R&D	Research and development
RRes	Rothamsted Research (BBSRC-sponsored)
SARS	Severe acute respiratory syndrome
SCRI	Scottish Crop Research Institute (SEERAD-sponsored)
SEERAD	Scottish Executive Environment and Rural Affairs Department
SME	Small to medium enterprise
TB	Tuberculosis
TSE	Transmissible spongiform encephalopathy

### **Annex 3: Summary of consultation exercise process**

A consultation was disseminated to a very broad range of academic, industrial, Societal and NGO stakeholders in December 2005, accordingly designed to be accessible to a wide range of potentially interested parties. The document consisting of 27 questions divided into four sections: *research and its implications; utilisation of research; resources and facilities; funding*. This document<sup>36</sup> was sent to over 600 identified potentially interested parties, including academic researchers, Government Departments, industry, unions and societies, consumer groups and NGOs.

We received 159 contributory replies to the consultation document, largely from the academic research sector. The replies will be published on the BBSRC website concurrently with this report. The consultation responses were considered by the Review Panel, and the key messages returning from the questions posed were extracted. A very wide range of views was returned on most issues raised. In some cases, very clear majority views emerged whereas a wider range of opinion was expressed in other cases. Answers to some questions posed revealed a considerable diversity of opinion and, in some cases, strongly held opposing viewpoints.

The Panel firmly incorporated the messages emerging from the consultation process in the formulation of their arguments and conclusions: key messages emerging from the consultation are referenced at the appropriate junctures within the main body of the report. All views represented were carefully considered by the Panel and although, we might respectfully disagree with some views, particularly given the diversity of opinions voiced on many issues, our conclusions were based on an understanding of the balance of opinions returned by stakeholders, and our own considerations of the issues and responses received. We would like to thank once again all who submitted questionnaires for providing high-quality responses and a strong depth of opinion upon which the Panel could draw during its discussions.

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<sup>36</sup> The consultation document can be viewed at <http://www.bbsrc.ac.uk/society/consult/microbial/Welcome.html>

## **Annex 4: BBSRC microbial science funding portfolio (A) - Trends in Detail**

Here we set out a broad summary of BBSRC's funding for microbial science, derived from a comprehensive interrogation of BBSRC's grants database. Broad trends of interest are highlighted here, but the detailed information arising from this search is tabulated in Annex 4, in a number of different derivations; relevant cross-references are provided here.

### **Overall funding mode trends**

BBSRC allocates in the region of a steady 18% of its research budget to projects with significant microbial research content (2000-2006)<sup>37</sup>. This figure increases to around 22%) when structural research elements, perhaps not usually considered within the spectrum of microbial science, are included<sup>38</sup>. As shown in Fig. 1<sup>39</sup>, funding streams for microbial science have remained relatively stable over the reporting period, increasing in line with BBSRC's total research budget, and therefore benefiting from the significant expansion in BBSRC's total research budget over the reporting period<sup>40</sup>. CSG allocations and studentships both show slight decreases in proportional terms, the latter in particular representing cause for concern. BBSRC has funded 22 fellowships in microbial science areas between 2000 and 2006<sup>41</sup>.

The following BBSRC initiatives have provided funding streams of significance for microbial research over the last 10 years:

- 2006 – Transnational Research Projects on Systems Biology in Micro-Organisms (SysMO);
- 2005 – Plant and Microbial Metabolomics;
- 2004 – Proteomics and Cell Function;
- 2001 – Biological Interactions in the Root Environment;
- 2001 – Exploiting Genomics;
- 2000 – Prokaryote Responses to Environmental Stress;
- 2000 – Gene Flow in Plants and Microorganisms (joint with NERC);
- 2000 – Functional Genomics Toolkit;
- 1999 – Biology of Foodborne Pathogens;
- 1999 – Investigating Gene Function (*Streptomyces* consortium funded);
- 1998 – Mathematical Modeling;
- 1997 – Acquisition of Microbial Genomics (*Streptomyces coelicolor* genome);
- 1996 – Cell Commitment and Determination.

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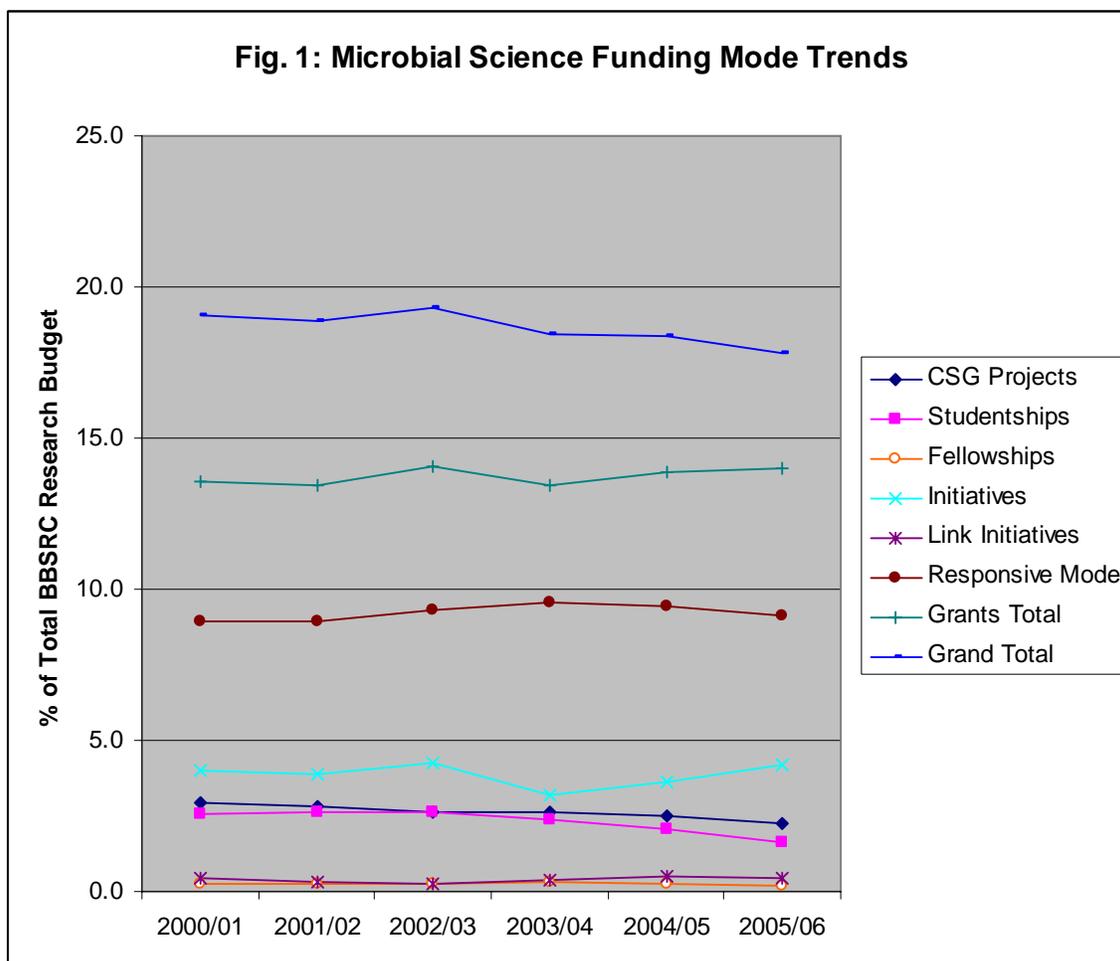
<sup>37</sup> Detail in Annex 5, Table 1.

<sup>38</sup> e.g. crystallographic characterization of microbial proteins. Typically funded by the BMS committee. See Annex 5, Table 7 for data.

<sup>39</sup> Data derived from Annex 5, Table 1.

<sup>40</sup> Total research budget has increased 46% from £182-266M between 01 April 2000 and 31 March 2006.

<sup>41</sup> See Annex 5, Table 8, for details.



### Funding by the Scientific Committees

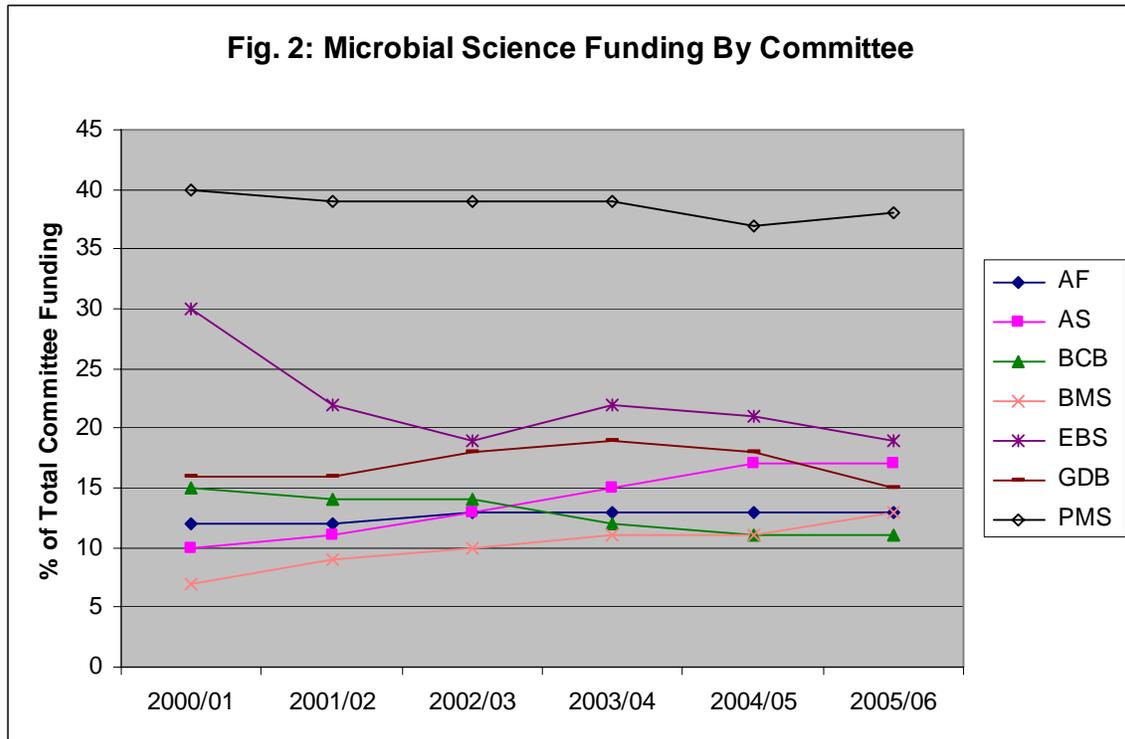
Microbial research represents a significant proportion of the funding of all of the BBSRC scientific committees, as shown in Figure 2<sup>42</sup>. As expected, PMS represents the most significant funding stream for microbial science, and microbial research has represented a generally stable 37-40% of the committee's funding, perhaps dipped slightly in the last couple of years in proportional terms.

It is revealing that in addition to PMS, microbial research is also funded at a significant level through the other research committees. In particular, both the overall amount and proportion has increased rapidly for AS and BMS<sup>43</sup>, representing sizeable absolute increases over the reporting period. The increasing proportion of animal pathogen work represented in the AS committee's portfolio probably reflects the increasing priority of the animal health research area.

<sup>42</sup> Data derived from Annex 5, Table 2.

<sup>43</sup> Not including the significant volume of structural analyses of microbial macromolecules, largely also funded through BMS.

In contrast, proportion of microbial research funded by the BCB and EBS committees has declined. This decline has been notable in the case of EBS (from 30% to 18%). However, the apparent decline may not be a significant trend, possibly reflective of the strong representation of microbial science in the Functional Genomics Toolkit Initiative (awards in 2000) and the fact that a very significant responsive award (>£1M) of relevance was also made at this time.

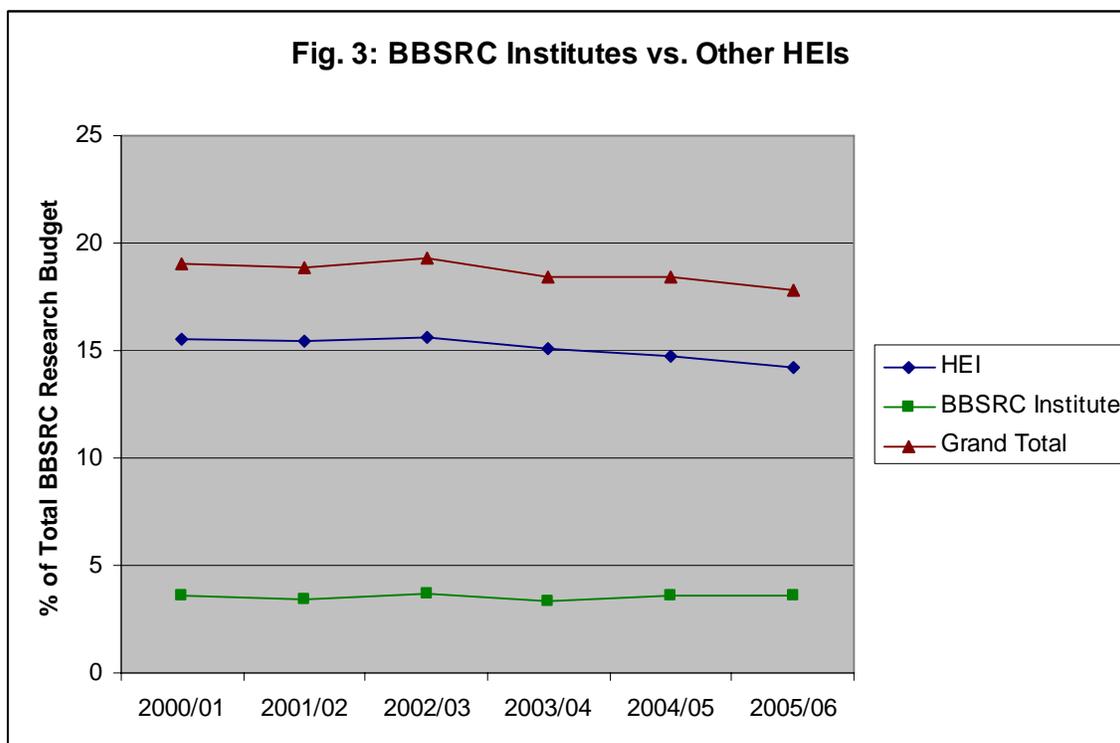


### Funding of HEIs and BBSRC Institutes

UK HEIs and BBSRC Institutes received BBSRC microbial research funding in an approximate 4:1 ratio between 2000-2006. Levels remained generally stable with respect to total BBSRC research funding as shown in figure 3<sup>44</sup>. Of the BBSRC-sponsored institutes, JIC, IAH and RRes have the most significant research interests in microbial science, with moderate investments at IFR and IGER (the latter reducing in recent years). JIC received the most microbial science funding of all UK institutions between 2000 and 2006, followed by the University of Manchester, IAH, University of Cambridge and Imperial College London. All of these institutions received in excess of £14M to fund microbial research within this period<sup>45</sup>.

<sup>44</sup> Data derived from Annex 5, Table 3.

<sup>45</sup> HEI rankings for BBSRC microbial science funding are presented in Annex 5, Table 4.

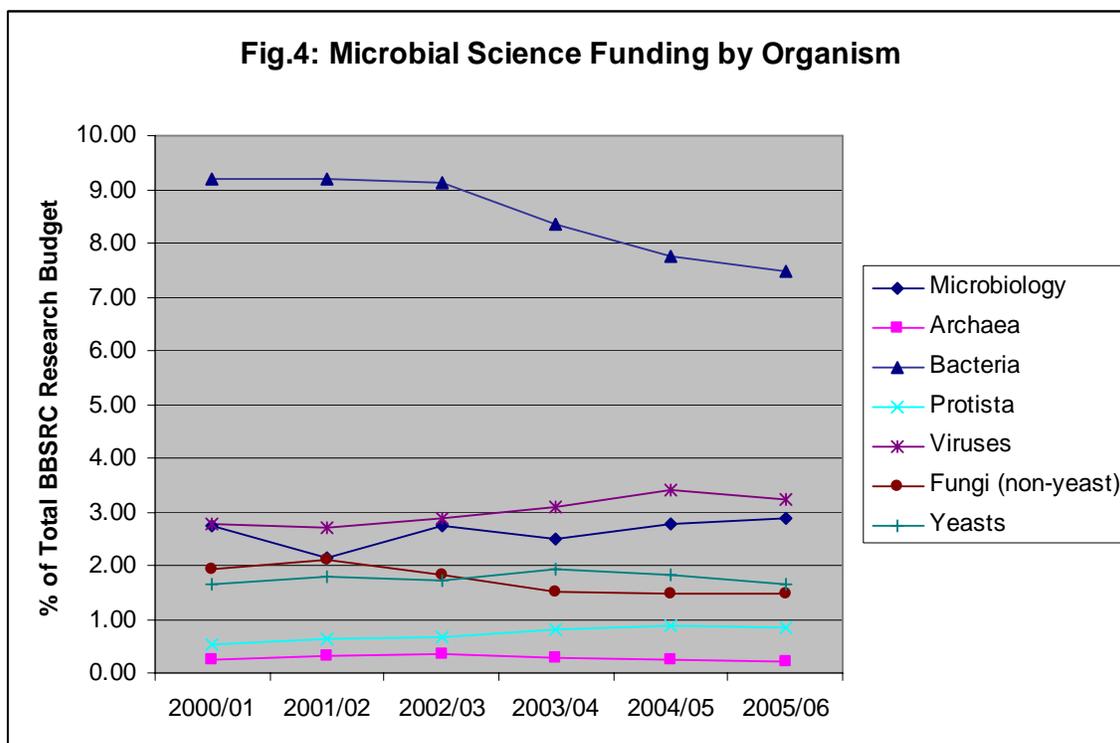


### Funding by organism categories

Of the major microbiological organism categories (Fig. 4<sup>46</sup>), bacterial research has represented by far the largest area of microbial science funding for BBSRC, in line with BBSRC's niche in basic microbial science. The real-terms proportion of this research, however, has also seen the most marked decline over the reporting period, which represents cause for concern.

Interestingly, sub-division of fungal projects into those focused on yeasts or filamentous types suggests that these categories have received approximately equal funding from BBSRC. This is contrary to some anecdotal suggestions that the former have been better funded than the latter. Protista- and archaea-focused research received less funding than other areas, as anticipated, at around 3-4% and 1-2%, respectively.

<sup>46</sup> Derived from data in Annex 5, Table 5.

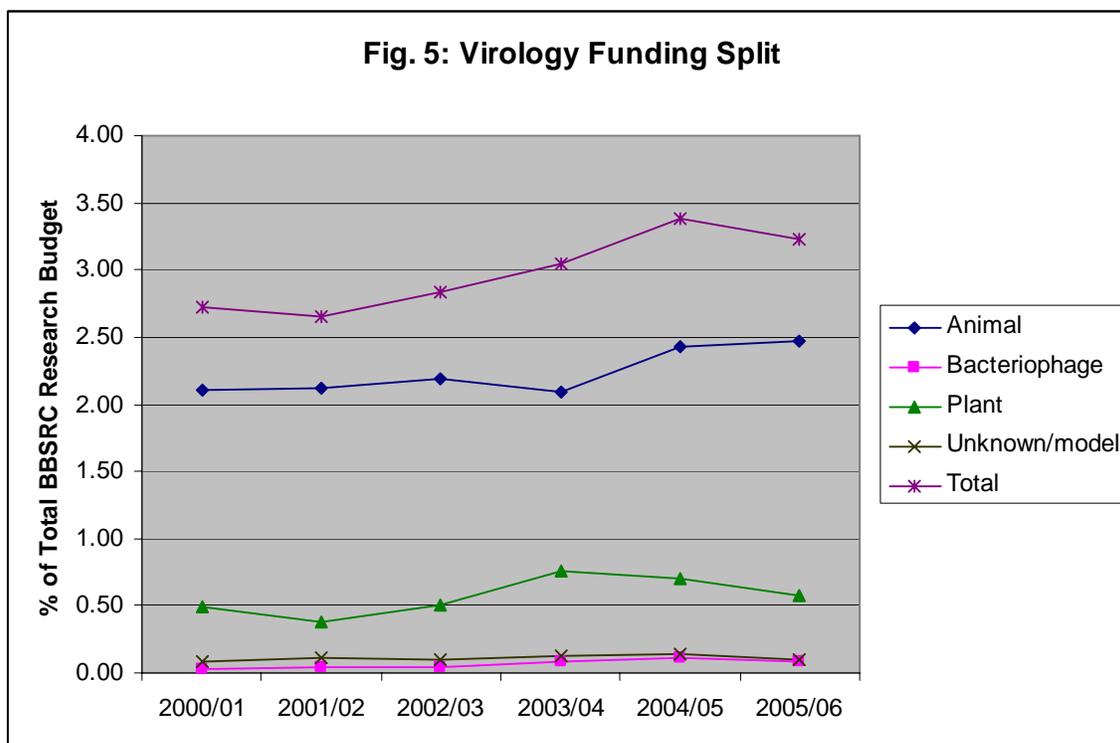


### Funding of Virology

Particularly in light of some community concerns raised in the consultation, we looked in more detail at the proportions of virus research categories (plant, animal, bacteriophage and model/unknown) funded across the Scientific Committees. The summarised cross-Committee split is presented in Figure 5<sup>47</sup>. Animal virus research represents the area of greatest investment, and has exhibited growth during this period; a reflection of BBSRC's increasing commitments to animal health (identified as a SR2004 priority). Animal virology has been funded primarily by AS, but significant numbers of animal virology projects (17-80 projects each within 2000-2006 period) have also been funded through all of the other Committees, with the exception of AF (2 projects). This suggests that animal virology is being well supported, with a diversity of potential funding streams.

By comparison, spending on plant virology projects has been at lower level (almost an order of magnitude), largely through PMS (some also through GDB and BMS). Funding peaked in 2003-2004, and has diminished slightly in relative terms since this point. By comparison to animal and plant virology, Research relevant to bacteriophage and uncategorised (e.g. model) viruses has been consistently funded at relatively basal levels, focused towards the structural and technological ends of the research spectrum (primarily BMS and EBS-funded).

<sup>47</sup> Data presented in Annex 5, Table 6.

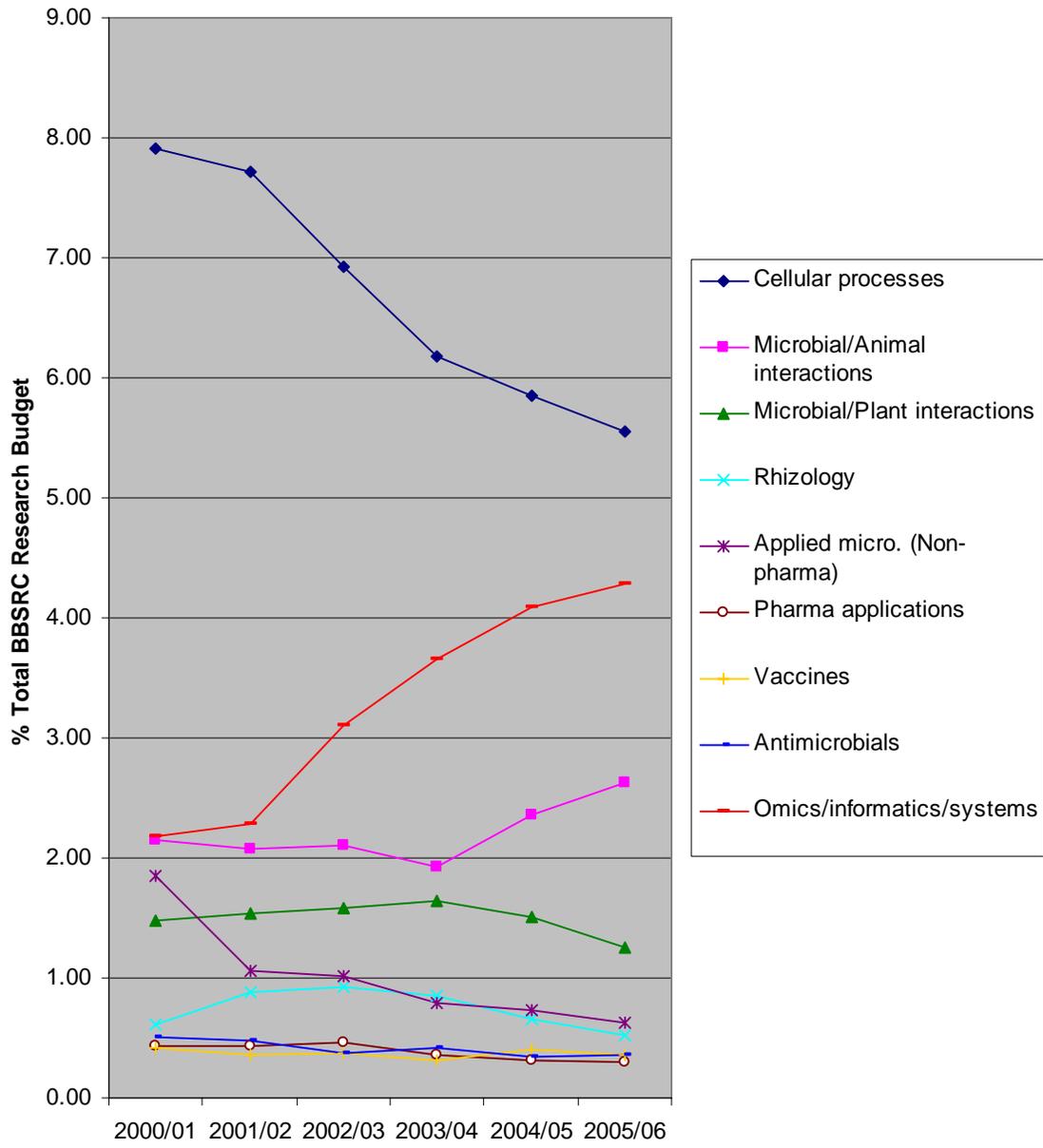


### Funding by research areas

Whilst it is a particularly fraught exercise to assign research area identifiers to projects (they can be invariably mapped to multiple categories) we have attempted to do this crudely, and useful trends can be seen. Fig 6 displays funding trends for the more significant categories<sup>48</sup>. Fundamental research focused on elucidating cellular processes represents the area of greatest investment, at almost £15M in 2005-2006, underlining the central importance of fundamental molecular cell biology to BBSRC's remit. However, this research (excluding 'omics approaches) has diminished significantly over the reporting period. Part of this is probably explained by wide adoption of high throughput technologies, categorised separately here, and displaying an unsurprising marked increase in prevalence over the same period. However, these data nevertheless point to a possible area of concern. Animal/microbe interactions (microbial focused projects only) represented an area of marked growth, in line with strategic priorities in animal health, whereas, in contrast, funding for work on plant/microbial interactions (microbial focused projects only) experienced some decline from 2003-04. Applied microbiology also stands out as an area that received steadily decreasing proportions of funding over the reporting period, with rhizology following a similar, if less marked, trend. Research with pharma applications, vaccine development, and antimicrobial research (when disentangled) have all received steady support in the region of £1M PA. Of the areas funded at lower levels (not represented on Fig. 5), of particular note, resource investments for culture and library collections has remained very low throughout the new Century.

<sup>48</sup> See Annex 5, Table 7 for full dataset, including an indication of funding of structural biology work on microbial macromolecules, and explanation of categories on the next page.

**Fig. 6: Microbial Science Funding by Research Area**



## Annex 5: BBSRC Microbial Science Funding Portfolio (B) – Supporting data

The following data were compiled from a detailed search and series of categorisations of BBSRC's funding database. Figures presented must be considered to be approximations. Rigorous distinction between categories of research is difficult in many cases, and many projects may include non-microbial aspects to the research. However, projects have only been included where microbial research represents a significant part of the research (estimated as 50% or more for hypothesis-led projects, or 30% or more for resource provision).

**Table 1: Microbial Science Funding Breakdown by type of award**

Type of award		No. projects live 2000-06	Estimated Total Spend in £k (% Total BBSRC Research Budget)					
			2000/01	2001/02	2002/03	2003/04	2004/05	2005/06
CSG <sup>49</sup> projects		382	5,301 (2.9)	5,451 (2.8)	5,474 (2.6)	6,037 (2.6)	5,868 (2.5)	5,930 (2.2)
Studentships		1068	4,701 (2.6)	5,185 (2.7)	5,460 (2.6)	5,525 (2.4)	4,861 (2.1)	4,273 (1.6)
Grants	Fellowships	17	427 (0.2)	524 (0.3)	480 (0.2)	699 (0.3)	655 (0.3)	482 (0.2)
	Initiatives	284	7,260 (4.0)	7,630 (3.9)	8,784 (4.2)	7,308 (3.2)	8,621 (3.6)	11,147 (4.2)
	Link <sup>50</sup> initiatives	36	763 (0.4)	596 (0.3)	482 (0.2)	886 (0.4)	1,175 (0.5)	1,238 (0.5)
	Responsive mode	848	16,229 (8.9)	17,483 (8.9)	19,335 (9.3)	21,961 (9.6)	22,325 (9.4)	24,359 (9.1)
	<b>Grants Total</b>	<b>1185</b>	<b>24,679 (13.6)</b>	<b>26,234 (13.4)</b>	<b>29,081 (14.0)</b>	<b>30,854 (13.4)</b>	<b>32,776 (13.8)</b>	<b>37,227 (14.0)</b>
<b>Grand Total</b>		<b>2635</b>	<b>34,681 (19.1)</b>	<b>36,870 (18.9)</b>	<b>40,016 (19.3)</b>	<b>42,416 (18.4)</b>	<b>43,505 (18.4)</b>	<b>47,430 (17.8)</b>
<b>BBSRC Research Funding Total<sup>51</sup></b>			<b>181,800</b>	<b>195,500</b>	<b>207,100</b>	<b>229,900</b>	<b>236,730</b>	<b>266,330</b>

<sup>49</sup> CSG = Core strategic grant. Awarded to BBSRC-sponsored institutes to deploy as best suits strategic aims. In addition, the institutes may bid for responsive grant funds.

<sup>50</sup> Government wide initiative aimed at promoting academic/industrial research collaboration in a pre-competitive research area. The initiative stimulates collaboration between partners from industry and the research community by providing up to 50% of the funding for collaborative projects in key scientific areas.

<sup>51</sup> Includes CSG, responsive research grants, studentships and fellowships, but does not include non-responsive equipment and facilities, capital and buildings, administration, depreciation and restructuring.

**Table 2: Projects relevant to microbiology: breakdown by BBSRC Committee**

**Estimated spend, in £k (+ % Total BBSRC Research Budget)**

<b>Committee *</b>	<b>No. projects live 2000-06</b>	<b>2000/01</b>	<b>2001/02</b>	<b>2002/03</b>	<b>2003/04</b>	<b>2004/05</b>	<b>2005/06</b>
<b>AF</b>	402	4,308 (12)	5,061 (12)	5,553 (13)	5,333 (13)	5,220 (13)	5,537 (13)
<b>AS</b>	401	2,426 (10)	3,111 (11)	3,977 (13)	4,645 (15)	5,854 (17)	7,203 (17)
<b>BCB</b>	304	3,321 (15)	3,787 (14)	4,324 (14)	4,046 (12)	3,992 (11)	4,176 (11)
<b>BMS</b>	172	1,502 (7)	2,145 (9)	2,530 (10)	2,821 (11)	3,229 (11)	3,963 (13)
<b>EBS</b>	268	4,703 (30)	3,698 (22)	3,625 (19)	4,411 (22)	4,615 (21)	5,071 (19)
<b>GDB</b>	305	5,615 (16)	5,665 (16)	6,820 (18)	8,029 (19)	7,978 (18)	7,470 (15)
<b>PMS</b>	773	12,767 (40)	13,323 (39)	13,082 (39)	13,029 (39)	12,566 (37)	13,995 (38)
<b>EQP*</b>	10	39	80	106	103	52	16

\* Figures do not include a small amount (<£100k PA) of relevant scientific equipment funding, which cross-cuts the committees (now under the stewardship of the Tools and Resources Strategy Panel).

**Table 3: Breakdown by HEIs/BBSRC Institutes**

**Estimated spend, in £k (+ % Total BBSRC Research Budget)**

	<b>No. of live projects (2000-06)</b>	<b>2000/01</b>	<b>2001/02</b>	<b>2002/03</b>	<b>2003/04</b>	<b>2004/05</b>	<b>2005/06</b>
<b>HEI</b>	2144	28,184 (15.5)	30,222 (15.5)	32,376 (15.6)	34,689 (15.1)	34,967 (14.8)	37,949 (14.2)
<b>Institute</b>	491	6,496 (3.6)	6,648 (3.4)	7,640 (3.7)	7,727 (3.4)	8,538 (3.6)	9,482 (3.6)

**Table 4: Projects relevant to microbiology, split by HEI (ranked by combined value of funding, 2000-2006)**

Institution name (BBSRC-sponsored Institutes highlighted)	No. live projects 2000-06	Estimated spend, (£k).						
		2000/ 01	2001/ 02	2002/ 03	2003/ 04	2004/ 05	2005/ 06	2000 -06
John Innes Centre (JIC)	133	2,978	2,504	2,663	3,093	3,205	3,327	17,768
University of Manchester	133	2,445	2,261	2,259	2,510	3,085	3,568	16,129
Institute for Animal Health (IAH)	251	1,387	1,814	2,348	2,479	3,120	3,432	14,579
University of Cambridge	147	1,850	1,974	2,095	2,742	2,754	2,607	14,023
University of Warwick	116	1,801	2,046	1,852	2,328	2,686	2,362	13,074
Imperial College London	110	1,315	1,622	1,773	2,159	2,294	2,189	11,353
University of Oxford	115	1,571	1,637	1,789	2,024	1,867	2,051	10,940
University of Sheffield	114	1,541	1,490	1,683	1,886	1,885	1,868	10,353
University of Birmingham	112	1,731	1,870	1,934	1,496	1,295	1,320	9,646
Rothamsted Research (RR)	31	1,167	1,444	1,678	1,412	1,473	2,033	9,208
University of East Anglia	111	1,242	1,202	1,249	1,365	1,139	1,316	7,513
University College London	80	2,050	1,124	1,054	1,455	776	635	7,092
University of Aberdeen	78	860	864	962	1,038	1,205	1,453	6,383
University of Newcastle upon Tyne	64	852	763	640	866	1,234	1,494	5,850
University of Edinburgh	75	636	699	826	1,049	1,247	1,349	5,805
University of Reading	51	560	723	1,063	890	1,106	1,313	5,656
University of Nottingham	77	768	785	725	651	799	1,129	4,858
University of Wales, Aberystwyth	34	779	1,249	1,145	687	425	426	4,711
University of Glasgow	49	664	856	1,092	870	614	548	4,644
University of Liverpool	38	323	553	835	767	956	1,067	4,501
University of Leeds	52	388	523	611	709	598	704	3,534
University of St Andrews	36	304	397	446	511	690	1,070	3,417
University of York	32	211	381	549	633	606	779	3,160
University of Bristol	64	495	590	560	497	440	505	3,086
University of Bath	27	298	472	669	578	436	584	3,038
University of Dundee	33	388	419	478	389	531	757	2,962
CCLRC	3	50	375	520	520	520	520	2,506
London School Hygiene & Trop Medicine	17	330	386	288	385	419	579	2,387
Institute of Food Research (IFR)	50	536	326	293	391	419	372	2,337
The Wellcome Trust Sanger Institute	9	399	14	619	646	332	301	2,311
University of Leicester	31	505	459	341	289	301	206	2,100
University of Surrey	25	163	183	188	479	454	587	2,053
University of Kent	26	424	346	283	301	333	340	2,027
University of Wales, Bangor	21	481	549	434	291	132	123	2,011
University of Exeter	30	292	417	325	347	300	283	1,964
Institute of Grassland and Environmental Research (IGER)	11	405	489	561	149	131	94	1,829
University of Sussex	25	35	266	227	294	377	428	1,628

Cardiff University	18	174	189	330	369	276	180	1,518
University of Southampton	22	242	283	178	173	129	185	1,190
University of Wales Swansea	8	274	181	203	136	123	124	1,040
Durham University	9	12	33	303	179	195	303	1,025
Queen's University of Belfast	9	236	281	150	56	106	178	1,007
Lancaster University	12	96	105	114	241	294	151	999
St George's University of London	6	12	26	151	181	251	147	767
The Edward Jenner Institute for Vaccine Research (EJIVR)	5	96	121	138	148	144	91	737
Royal Holloway, Univ of London	6	24	130	143	165	83	160	704
Oxford Brookes University	6	6	0	11	207	246	200	670
Roslin Institute (RI)	6	0	25	44	134	146	216	564
The Animal Health Trust	4	85	85	74	64	93	123	524
Kings College London	10	71	73	53	50	96	168	510
Queen Mary, University of London	6	173	167	13	6	13	113	485
Heriot-Watt University	8	189	160	65	14	13	31	472
University of Essex	4	112	92	78	71	66	44	463
University of the West of England	3	39	14	55	135	121	80	443
Royal Veterinary College	8	23	31	54	108	119	99	434
University of Stirling	6	29	32	13	22	56	236	387
Cranfield University	4	65	71	77	20	52	80	365
University of Abertay Dundee	4	0	0	0	23	125	169	317
Brunel University	2	0	37	46	90	81	53	308
Scottish Crop Research Institute	2	63	79	79	79	7	0	307
Royal Free & University College Medical	2	0	102	102	102	0	0	306
Marine Biological Association	2	0	38	64	80	74	48	304
NERC Centre for Ecology & Hydrology	3	29	0	0	0	81	166	276
GKT School of Medicine Weston Education	2	26	71	58	58	39	0	252
University of Portsmouth	4	12	27	108	61	14	16	238
Birkbeck College	10	46	44	47	32	14	45	229
University of Strathclyde	7	36	55	41	40	22	32	227
Sheffield Hallam University	2	0	0	0	21	84	104	210
Aston University	3	45	6	0	44	44	44	184
Silsoe Research Institute (SRI)	7	12	37	40	56	31	8	183
University of Greenwich	1	0	0	0	35	69	69	173
Moreun Research Institute	1	42	42	42	0	0	0	126
NERC Institute of Terrestrial Ecology	1	14	34	34	20	0	0	103
CABI Bioscience UK Centre	1	46	34	0	0	0	0	80
University of Brighton	1	0	47	23	0	0	0	70
Keele University	1	54	13	0	0	0	0	67
Babraham Institute (BI)	2	12	9	13	14	14	0	62

University of Sunderland	1	41	7	0	0	0	0	48
Natural History Museum	1	0	0	0	0	0	41	41
Open University	1	6	12	13	7	0	0	38
GKT School of Medicine (Guys Campus)	1	37	0	0	0	0	0	37
School of Pharmacy	2	6	0	0	0	0	8	14
Napier University	1	13	0	0	0	0	0	13
<b>Grand Total</b>	<b>2,635</b>	<b>34,681</b>	<b>36,870</b>	<b>40,016</b>	<b>42,416</b>	<b>43,505</b>	<b>47,430</b>	<b>244,918</b>

**Table 5: Spend on research grants, CSG projects and studentships between 2000/01 and 2005/06 by type of organism**

Organism	No. live projects 2000-06	Estimated spend, in £k (% Total BBSRC Research Budget)					
		2000/01	2001/02	2002/03	2003/04	2004/05	2005/06
Microbiology <sup>52</sup>	353	4984 (2.7)	4193 (2.1)	5645 (2.7)	5744 (2.5)	6640 (2.8)	7713 (2.9)
Archaea	52	417 (0.2)	592 (0.3)	701 (0.3)	637 (0.3)	604 (0.3)	605 (0.2)
Bacteria	1185	16,694 (9.2)	17,991 (9.2)	18,925 (9.1)	19,187 (8.3)	18,342 (7.7)	19,898 (7.5)
Protista	116	988 (0.5)	1,210 (0.6)	1,398 (0.7)	1,829 (0.8)	2,061 (0.9)	2,286 (0.9)
Viruses	485	5,071 (2.8)	5,267 (2.7)	5,989 (2.9)	7,100 (3.1)	8,042 (3.4)	8,584 (3.2)
Fungi (non-yeast)	245	3,526 (1.9)	4,109 (2.1)	3,761 (1.8)	3,442 (1.5)	3,499 (1.5)	3,959 (1.5)
Yeasts	199	3,002 (1.7)	3,508 (1.8)	3,597 (1.7)	4,477 (1.9)	4,317 (1.8)	4,384 (1.6)

<sup>52</sup> Includes all projects relating to more than one microbial category, or where the category is not explicitly stated or obviously inferable.

**Table 6: Spend on virology, subdivided by virus type and awarding Committee**

Estimated spend, in £k								
Type Of Virus	C'ttee	No. live projects 2000-06	2000/01	2001/02	2002/03	2003/04	2004/05	2005/06
Animal	AF	2	12	12	13	21	14	16
	AS	242	1,440	1,683	1,965	2,502	3,375	4,332
	BCB	79	849	940	888	770	973	938
	BMS	20	189	193	151	84	72	190
	EBS	17	229	177	310	267	453	405
	GDB	26	618	699	763	660	502	337
	PMS	19	483	436	450	499	345	351
<b>Animal Total</b>		<b>405</b>	<b>3,819</b>	<b>4,140</b>	<b>4,542</b>	<b>4,803</b>	<b>5,735</b>	<b>6,568</b>
Bacteriophage	AF	3	6	12	13	14	54	74
	AS	2	40	38	3	-	-	-
	BCB	1	-	-	-	49	54	54
	BMS	3	12	12	7	7	22	31
	GDB	2	-	5	62	62	62	65
	PMS	2	6	12	13	50	86	14
<b>Phage Total</b>		<b>13</b>	<b>63</b>	<b>80</b>	<b>98</b>	<b>182</b>	<b>277</b>	<b>239</b>
Plant	AF	5	12	22	79	144	121	70
	BMS	2	-	1	20	28	28	8
	GDB	4	100	21	13	4	-	-
	PMS	30	793	686	937	1,558	1,510	1,455
<b>Plant Total</b>		<b>41</b>	<b>905</b>	<b>730</b>	<b>1,050</b>	<b>1,734</b>	<b>1,658</b>	<b>1,533</b>
Unknown/model	BCB	2	12	6	-	-	7	16
	BMS	2	6	12	13	60	64	64
	EBS	12	124	165	118	159	220	141
	GDB	1	-	38	56	56	28	-
	PMS	3	12	7	7	14	20	24
<b>Unknown Total</b>		<b>25</b>	<b>324</b>	<b>441</b>	<b>300</b>	<b>345</b>	<b>436</b>	<b>303</b>
<b>Grand Total</b>		<b>527</b>	<b>5,854</b>	<b>6,060</b>	<b>6,639</b>	<b>8,248</b>	<b>8,879</b>	<b>9,482</b>

**Table 7: Spend on research grants, CSG projects and studentships between 2000/01 and 2005/06 by type of research**

Categorisation (see explanation of terms below)	No. projects 2000-06	Estimated spend (£k)					
		2000/01	2001/02	2002/03	2003/04	2004/05	2005/06
Cellular processes	959	14,374	15,080	14,333	14,194	13,853	14,778
Microbial/Animal interactions	488	3,919	4,070	4,361	4,414	5,590	6,990
Microbial/Plant interactions	128	2,698	2,996	3,290	3,780	3,586	3,349
Rhizology	106	1,116	1,714	1,925	1,939	1,564	1,383
Pharma applications	58	778	853	962	810	749	789
Vaccines	44	756	699	772	722	941	949
Antimicrobials	127	925	940	777	966	826	957
Applied micro. (Non-pharma)	156	3,363	2,058	2,114	1,802	1,721	1,659
Ecology/evolution	62	515	638	625	732	789	823
Food production/safety/standards	58	473	447	601	802	453	522
Gut/rumen interactions	47	632	810	915	784	712	524
Bioenergy	4	0	0	65	87	87	187
Bioremediation/degradation	46	927	1,119	899	674	549	453
Other (not captured above)	6	0	12	306	356	347	335
<b>Sub-total</b>	<b>2289</b>	<b>30,476</b>	<b>31,436</b>	<b>31,945</b>	<b>32,062</b>	<b>31,767</b>	<b>33,698</b>
<b>Resources</b>							
Resource – culture/library	5	26	43	43	14	7	16
Resource – lab	31	190	387	699	668	558	390
Resource – omics/informatics	24	34	529	887	1,262	1,510	1,918
<b>Resource total</b>	<b>75</b>	<b>446</b>	<b>1178</b>	<b>1831</b>	<b>2024</b>	<b>2214</b>	<b>2744</b>
<b>Omics/informatics/systems</b>	<b>286</b>	<b>3,952</b>	<b>4,473</b>	<b>6,441</b>	<b>8,409</b>	<b>9,664</b>	<b>11,407</b>
<b>Sub-total</b>	<b>2635</b>	<b>34,681</b>	<b>36,870</b>	<b>40,016</b>	<b>42,416</b>	<b>43,505</b>	<b>47,430</b>
Structural biology	333	5,547	6,228	6,387	6,943	7,380	8,296
Resource – structural	15	196	219	202	80	139	420
<b>Grand Total</b>	<b>2983</b>	<b>40,423</b>	<b>43,316</b>	<b>46,604</b>	<b>49,440</b>	<b>51,024</b>	<b>56,147</b>

<b>Explanation of categorisations in Table 7*</b>	
Cellular processes	Includes microbe-focused cellular physiology, metabolism, genetics, protein functionality/localisation/interactions (non-structural studies only), differentiation, reproduction, persistence, cellular dissection of action for antimicrobial resistance/sensitivity (development of new/improved compounds is under 'antimicrobials'), quorum sensing
Microbial/Animal interactions	Includes studies focused on microbial interactions (pathogenic/commensal) with animals, where the work is focused on the interactions, pathogenicity, host immune responses. N.b. Work is only included if the study will inform understanding of the microbe; where the study will only inform understanding of the host (i.e. the microbe serves as only as a characterised elicitor) such projects have been excluded.
Microbial/Plant interactions	Includes studies focused on microbial interactions (pathogenic/commensal) with plants, where the work is focused on the interactions, pathogenicity, host responses. N.b. Work is only included if the study will inform understanding of the microbe. Processes involved in pathogenicity that are microbe-specific cellular process categorisations (e.g. transcription/regulation for appressorium formation in rice blast fungus) have been categorised under 'cellular processes'. Rhizological interactions with plants are included here.
Rhizology	Microbial studies focused on the processes of the rhizosphere, with the exception of studies focused on interactions with plant roots (mycorrhizae, nodule formation).
Pharma applications	Studies with pharma applications- e.g. gene therapy vectors, not including antimicrobials & vaccines (separated).
Vaccines	Studies where the development of new/improved vaccines are DIRECT outputs of the project (i.e. not far-down-stream potential outcomes of the work)
Antimicrobials	Studies where the development of new/improved antimicrobials are DIRECT outputs of the project (i.e. not far-down-stream potential outcomes of the work)
Applied micro. (non-pharma)	Studies for non-pharma industrial applications, and development of new laboratory tools (e.g. vector development/purification).
Ecology/evolution	Studies where ecological interactions or evolutionary/phylogenetic considerations are the focus of the work
Food production/safety/standards	Studies where understanding of food production, safety or standards is the explicit strategic outcome.
Gut/rumen interactions	Studies where processes of, and interactions with the gut or rumen are the focus of the work (including pathogenic and commensal interactions).
Bioenergy	Studies explicitly associated with strategic bioenergy outcomes.
Bioremediation/degradation	Studies explicitly having bioremediation/degradation outcomes (diagnosis tools only excluded- 'Applied micro.')
Omics/informatics/systems	'Omic' scale studies. These will be subdivided into functional categories in due course.
Resource – culture/library	Resource provision associated with development/maintenance of microbial cultures and libraries.
Resource – lab	Resource provision associated with general lab use (e.g. optical/confocal microscopy, PCR, culture facilities)
Resource – omics/informatics	Resource provision associated predominantly with 'omic', informatic and systems biology investigations.
Structural biology	Structural studies of microbial proteins, nucleic acid and carbohydrates, and complexes of these molecules.
Resource – structural	Resource provision associated predominantly with structural microbiology.
Other (not captured above)	e.g. Includes analysis of microbial propagation on farms, via manures.

**\*Individual projects have been assigned to the single category which best describes the research (no financial overlap in data).**

**Table 8: BBSRC Fellowships in the microbial sciences**

Type of fellowship	Name of fellow	Institution	Title	Start date	End date
Advanced Fellowship	Buchanan S	NIH	"Structure determination of bacterial membrane proteins involved in active transport by x-ray diffraction analysis"	28/05/1998	28/05/2001
David Phillips Fellowship	Baldwin G	Imperial College London	"Functional studies on the Herpes-Simplex virus uracil-DNA glycosylase"	01/10/1997	28/10/2002
David Phillips Fellowship	Barrett T E	Birkbeck College	"Structural analysis of the bacterial MutHLS and UvrABC DNA-repair complexes"	01/10/1998	01/10/2003
David Phillips Fellowship	Chong JP	University of York	"Characterisation of DNA replication in Archaea"	01/01/2004	31/08/2005
David Phillips Fellowship	Chong JP	University of York	"Characterisation of DNA replication in archaea"	01/08/2000	31/12/2003
David Phillips Fellowship	Dyer PS	University of Nottingham	"BBSRC David Phillips Research Fellowship: Isolation of fungal hormones and assessment of their use as novel agrochemicals"	01/10/1996	31/12/2001
David Phillips Fellowship	Fray RG	University of Nottingham	"In planta expression of bacterial autoinducer and receptor genes to manipulate plant/microbe interactions"	01/10/1997	01/10/2002
David Phillips Fellowship)	Hodge A	University of York	"AM fungi as determinants of plant resource capture from organic patches followed by isotopic and molecular techniques"	01/02/2000	30/09/2006
David Phillips Fellowship	Hurst G	University College London	"A study into the interaction between bacterial parasites and the insect immune system"	01/09/1997	01/09/2002
David Phillips Fellowship	Mulvihill DP	University of Kent	"BBSRC David Phillips Fellowship A study into the physical properties of the fission yeast myosins"	01/10/2003	30/09/2008
David Phillips Fellowship	Sesma A	University of East Anglia	"BBSRC David Phillips Fellowship: Dissection of distinct pathogenesis-related developmental processes in the rice blast fungus <i>Magnaporthe grisea</i> "	01/07/2005	30/06/2010
David Phillips Fellowship	Spring D	University of Cambridge	"BBSRC David Phillips Fellowship Discovery of antibacterial small molecules with novel modes of action"	01/08/2001	31/07/2006
David Phillips Fellowship	Stanley-Wall N	University of Dundee	"BBSRC David Phillips Fellowship: Environmental regulators and the genes required for biofilm formation by <i>Bacillus subtilis</i> "	01/09/2005	31/08/2010
Professorial Fellowship	Dell A	Imperial College London	"BBSRC Professorial Fellowship Structural glyco-biology: applications of ultra-high sensitivity mass spectrometry"	01/10/2002	30/09/2007
Professorial Fellowship	Errington J	University of Newcastle upon Tyne	"Molecular biology and biochemistry of mitotic-like chromosome partitioning system in <i>Bacillus subtilis</i> "	01/10/1997	01/10/2002
Professorial Fellowship	Grenfell B	Penn State University College of Medicine	"Phylogenetics: Synthesizing the population dynamics and phylogenetics of animal pathogens"	01/10/2003	30/09/2004
Professorial Fellowship	Leadlay PF	University of Cambridge	"Structure, function and protein engineering of antibiotic-producing polyketide synthases"	01/01/1999	01/01/2004

Research Development Fellowship	Parker D	University of Newcastle upon Tyne	"Research Development Fellowship: Dr T P Curtis Theories of community assembly and change in open microbial systems"	01/01/2004	31/12/2006
Research Development Fellowship	Parkin DT	University of Nottingham	"Research Development Fellow: Dr M C M Smith; Characterisation and exploitation of a novel group of site-specific recombinases"	01/10/2000	01/10/2003
Research Development Fellowship	Rice DW	University of Sheffield	"Research Development Fellowship: Dr P A Bullough. The structure, function and assembly of membrane transport systems determined by electron microscopy"	01/01/2002	01/01/2005
Research Development Fellowship	Sanders D	University of York	"BBSRC Research Development Fellowship: Professor A E Douglas. The molecular basis of symbiosis function in an animal- microbial association"	01/10/2005	30/09/2008
Research Development Fellowship	Taylor GL	University of St Andrews	"Research Development Fellow: Dr J H Naismith. Carbohydrate synthesis in pathogenic bacteria"	01/01/2002	31/12/2006
<b>Total</b>	<b>22</b>				

## **Annex 6: Other funders' portfolios and stated strategies in detail**

### **Other Research Councils**

#### **MRC**

The Infections and Immunity Board (IIB)<sup>53</sup> is responsible for the strategy, portfolio and funding of MRC research into viral, bacterial and parasitic pathogens and diseases, immunity and immunology. The IIB portfolio was worth £37M PA in the 2004 and 2005 financial years, including intramural and extramural expenditure. Infectious disease and immunology research was funded in approximately a 2:1 ratio, with approx. £25M PA for infectious disease research (corresponding therefore to approx. (£12.5M PA). HIV (~£5M), other viruses (~£6.5M), malaria (~£4.2M) and TB (~£2.2M) research accounted for a significant proportion of the 'infections' part of the portfolio. Overall, the approximate distribution of recent IIB infections investment has been 53% viruses, 20% bacteria, 20% bacteria, 6% general and 1% fungi.

Funding of non-TB bacteriology is very low at < 5% of the IIB funding in 2004/2005. MRC has reviewed this issue and not identified systemic failures but is monitoring. But concern has been expressed by the community about the structure of the Infection and Immunity panel – there is a perception that the interests of bacteriology in particular are not being served well.

The Health Services and Public Health Research Board (HSPHRB)<sup>54</sup> takes responsibility for clinical trials and public health research in relation to infections. The HSPHRB manages a joint programme on Sexual Health with the Department of Health<sup>55</sup>, which includes public health research on HIV and sexually transmitted diseases.

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<sup>53</sup> [http://www.mrc.ac.uk/about-boards-iib\\_membership.htm](http://www.mrc.ac.uk/about-boards-iib_membership.htm)

<sup>54</sup> <http://www.mrc.ac.uk/about-boards-hsphrb.htm>

<sup>55</sup> [www.mrc.ac.uk/funding-sexual\\_health\\_2004.htm](http://www.mrc.ac.uk/funding-sexual_health_2004.htm)

## NERC

NERC has made significant investments in microbial ecology and microbial aspects of environmental research, spending £6-8M PA, as summarised briefly in Table 9.

**Table 9: NERC spend (£k) on projects with a significant microbial science component, 2002-2006**

	2002-2003	2003-2004	2004-2005	2005-2006
Grants	5,418	4,796	5,550	6,285
Studentships	527	722	1,215	1,834
Fellowships	182	154	157	185
<b>Total</b>	<b>6,127</b>	<b>5,672</b>	<b>6,922</b>	<b>8,304</b>

Since 2000, the Council has run several programmes incorporating microbial research elements. Of greatest significance, the Marine and Freshwater Microbiology (M&FMB) provided £7M of targeted microbial science funding, over 5 years (2000-2005)<sup>56</sup>

Other programmes with significant microbial science components have included:

- Marine Productivity (1998-2005)
- Global Nitrogen Enrichment (1999-2006)
- Environmental genomics (2000-2006)
- Gene-flow in plants and microorganisms (2000-2006; joint with BBSRC)
- UK Surface-Ocean / Lower Atmosphere Study (2003-2009)
- Post-genomics and proteomics (new call)

## EPSRC

EPSRC has funded an increasing amount of research relevant to microbial science in recent years, with the annual value of the portfolio doubling between 2003 and 2006, to around £5M (see table 10).

**Table 10: EPSRC minimum spend on projects with a significant microbial science component<sup>57</sup>**

	2002-2003	2003-2004	2004-2005	2005-2006	2006-2007*
Total Spend PA (£M)	2,336	2,566	3,148	3,457	5,095*

\*includes all projects awarded by May 2006.

<sup>56</sup> This included support for a research cruise (2001), data management costs and the programme's contribution to the Small Business Research Initiative (SBRI) scheme.

<sup>57</sup> A total of 73 projects contribute to the figures set out in Table \*. These data do not include projects focussed on the chemical total synthesis of characterised antimicrobial compounds.

Significant research themes and/or sizeable EPSRC investments of relevance have included:

- Biological fuel cells (£2M SUPERGEN consortium funding commenced in 2006);
- Mathematical modeling (e.g. viral capsid assembly and bacterial colonisation);
- Antimicrobials (synthesis and biological activity; structural studies of modes of action);
- Antimicrobial strategies for food, medical and dental equipment safety, and prevention of biofouling;
- Bioremediation, and remediation of organic soil contaminants;
- Structural analyses and manipulation of microbial enzyme activities.

## **Government**

### **Defra**

Defra has had significant research interests relevant to microbial science, funding projects with relevance to microbial science at around £20M PA. A significant proportion of this funding has been allocated to animal and plant disease research areas, and the Department has funded relevant programmes at IAH, IGER, RRI, in addition to notable investments at the VLA, CSL and Warwick-HRI.

Defra has diminishing strategic interests in agricultural research areas, and increasing strategic interests in environmental and climate science. BBSRC will be fully aware of the implications of this strategic shift for bioscience research, particularly at its sponsored Institutes.

### **DTI**

As part of the DTI's Technology Programme, it funds a series of Knowledge Transfer Networks (KTNs) which aim to bring together organisations working in a specific field of technology, such as businesses (suppliers and customers), universities, research and technology organisations, the finance community and other intermediaries, who will provide a range of activities and initiatives to enable the exchange of knowledge and stimulation of innovation amongst this community. Two of these KTNs, *BioProcessUK* (biopharmaceuticals and bioprocessing area) and BioScience for Business (biocatalysis area; previously Pro-Bio Faraday) operate in areas with relevance to microbial research industrial applications.

### **FSA**

The FSA funded 96 microbiology-relevant review, survey and research projects between 2002 and 2005. Summarised funding totals are shown in Table 11. Areas of significant investment included the diagnosis, monitoring and control of food-borne *Salmonella*, *Campylobacter*, *Listeria*, *E. coli*, *Clostridium*, and viruses and microbial toxins in shellfish.

The FSA does not set annual budgets for research and survey work, which provides it with greater flexibility to target the necessary programme activities (including research and surveys) against Strategic Plan targets, though typically it commits somewhere

between £20m and £30m per year across its research and survey portfolio. Commitments in any particular area will fluctuate year on year which can depend on a range of variables such as the life cycle of research programmes and whether the area is under review, whether there are other programme activities needed which are more closely related to delivery in an area e.g. campaigns etc, as well as changes in priorities/emphasis.

In 2004, the FSA launched a Postgraduate Scholarship Scheme. The aim is to offer 3-4 scholarships a year with calls made in areas relevant to Agency interest areas. To date, 4 scholarships have been offered in the microbial sciences area.

The Agency retains IP but encourages contractors to request transfer, subject to the Agency being able to retain certain rights e.g. if the outputs are needed for policy/regulatory work. In relation to microbial sciences work, the Agency has negotiated one such request between 2002 and 2005.

**Table 11: FSA annual spend relevant to microbial science**

<b>Financial year</b>	<b>2002/03</b>	<b>2003/04</b>	<b>2004/05</b>
Microbiology funding (£M)	3,838	3,498	2,539
Total FSA research and surveys (£M)	26,340	26,940	24,790

## **SEERAD**

Most of SEERAD's microbial science funding is administered through the Science and Analysis Group, through core grants to the Scottish Agricultural and Biological Research Institutes<sup>58</sup>, Scottish Agricultural College and Royal Botanic Garden Edinburgh as well as through the Flexible Fund by competitive tender. Overall funding of research with a significant microbial aspect is around £11M PA (Table 12). Microbial science funding cuts across several key research themes, including infectious diseases animals, especially ruminants (Scottish Agricultural College; Moredun Research Institute), gut health (Rowett Research) Institute, rhizosphere ecology (Macaulay Land Use Research Institute), plant pathology and plant environmental interactions (Scottish Crop Research Institute). A more detailed description of SEERADs investments is set out in Table 13. Funding of fish microbiology, as directed through FRS, is detailed separately. SEERAD currently also funds one Fellowship in the field of microbial science.<sup>59</sup>

<sup>58</sup> Includes the Macaulay Land Use Research Institute, Moredun Research Institute, Rowett Research Institute and Scottish Crop Research Institute.

<sup>59</sup> entitled '*Functional genomics of pathogenicity host-specificity and avirulence in plant- phytophthora infestans interactions.*'

**Table 12: SEERAD Science and Analysis Group spend relevant to microbial science**

Financial Year	2002-03	2003-04	2004-05
Microbiology funding (£M)	10,748	11,298	11,171
% total allocation	23	24	25
Number of live projects*	87	90	84
% total projects	19	21	20

\*160 projects funded in total within reporting period.

**Table 13: Major SEERAD Science and Analysis Group research investments in microbiology-relevant areas**

Institution	Key research areas of relevance	2002-03	2003-04	2004-05
Macaulay Land Use Research Institute	<ul style="list-style-type: none"> <li>• Soil, plant and microbial interactions (rhizosphere ecology)</li> <li>• Biodiversity (e.g. of fungi).</li> </ul>	1,107	1,231	1,184
Moredun Research Institute	<p>Infectious diseases of sheep and other ruminants:</p> <p><b>Bacterial:</b> long-standing issues (<i>Mycobacterium avium</i>; <i>paratuberculosis</i>, <i>Chlamydothyla abortus</i>), and emerging pathogens (<i>Pasteurella multocida</i>, <i>Caseous lymphadenitis</i>);</p> <p><b>Viral:</b> Ovine Orf virus and herpesvirus-2.</p> <p>Virology &amp; histopathology for disease surveillance.</p>	2,140	2,909	2,877
Rowett Research Institute	<p><b>Gut health.</b></p> <p><b>Microbial ecology:</b></p> <ul style="list-style-type: none"> <li>• roles of anaerobic bacteria in the human gastrointestinal tract;</li> <li>• microbial colonisation and utilisation of insoluble substrates in the gut;</li> <li>• extend advances in microbial genomics to dominant groups of commensal and symbiotic gut bacteria.</li> </ul> <p><b>Microbial biochemistry:</b></p> <ul style="list-style-type: none"> <li>• Identification of microorganisms, enzymes and genes involved in metabolism of health-promoting fatty acids in the rumen;</li> <li>• hydrogen metabolism in gut microorganisms;</li> <li>• development of natural plant-based feed additives that can replace growth-promoting antibiotics in animal feeding;</li> <li>• gene transfer in rumen ciliate protozoa;</li> <li>• improving the healthiness of food from animal production .</li> </ul>	1,849	1,760	2,573
Scottish Agricultural College	<p><b>Crops and Soil</b></p> <ul style="list-style-type: none"> <li>• Epidemiology</li> <li>• Maximising host defence</li> <li>• Organic systems</li> </ul> <p><b>Animal Health</b></p> <ul style="list-style-type: none"> <li>• Epidemiologically-based research on major animal-related problems that pose a significant threat to human health:</li> </ul>	1,316	1,382	1,516

	<ul style="list-style-type: none"> <li>• Endemic animal disease and possible controls</li> <li>• The interaction between nutrition and health for sustainable and organic systems</li> </ul> <p><b>Other</b></p> <ul style="list-style-type: none"> <li>• Animal carcass and byproduct safety</li> </ul>			
Scottish Crop Research Institute	<p><b>Environmental Plant interactions</b></p> <ul style="list-style-type: none"> <li>• Plant and Plant-Soil interactions (soil microbes)</li> <li>• Functional Ecology (environmentally friendly disease management).</li> <li>• Ecosystem upscaling (plant and microbial ecology).</li> </ul> <p><b>Plant Pathology</b> durable resistance &amp; sustainable disease control strategies, particularly for potato, barley and soft fruit. Microbial emphases are on pathogen genomics &amp; disease management.</p>	3,662	3,106	2,553

The Fisheries Research Services, an agency of SEERAD, also funds microbiology research relevant to fish disease. Key areas include disease susceptibility, transmission and epidemiology. The annual spend is variable (£0.5M to £1M), representing around 10% of the FRS budget.

## NGOs

### The Wellcome Trust

The Wellcome Trust has made highly significant global investments in wide range of projects of relevance to preclinical microbiology, largely through *immunity and infectious disease* funding stream, and additionally through the Cells and Genes panel. The global value of Wellcome Trust projects awarded in the three financial years from 2003-2006 and of relevance to microbial research was in the order of £260M.

As with MRC, there is growing disquiet in the community about perceived lack of bacteriological expertise on these panels.