A. Strong foundations - maintaining the health of the UK bioscience base

Q1 Are these the right foundations for UK bioscience? Are there other cross-cutting, underpinning capabilities that need to be developed and supported?

Sustained investment to support research and innovation will be critical to maintain and grow the UK bioscience base and must include support for the disciplines that interface with the biosciences such as chemistry.

We agree with the emphasis on people & talent, infrastructure, and collaborations & partnerships as being key underpinning capabilities to support the UK’s bioscience research base. We welcome the BBSRC recognition that there is a changing environment for biosciences research and innovation, in light of EU Exit, the formation of UK Research and Innovation and the changing industrial R&D landscape.

While it may seem obvious, we suggest that there should be explicit mention of support for research and innovation at the outset of the strategy. Importantly, this must include a joined up approach for research and translation to enable research, innovation and technology breakthroughs.

We welcome the emphasis on collaborations and partnerships between disciplines and sectors both nationally and internationally. There are many opportunities and benefits from leveraging expertise, infrastructure and technological advances from other disciplines and between sectors. Taking a broader holistic view across disciplines and sectors will minimise duplication of effort, create links and avoid a ‘silo mentality’ that can stifle innovation.

We suggest that in developing the “Collaboration and Partnership” aspect, the BBSRC include the entire biosciences ecosystem covering universities, research institutions, large companies, SMEs and spin-outs. There is also an opportunity for the BBSRC to take a lead in facilitating interactions between disciplines, for example research beyond the “conventional” biosciences as well as with disciplines that interface with the biosciences such as chemistry, engineering, materials and physics. Research in the physical sciences has enabled developments in the biosciences, for example, within the last 10 years, many of the Nobel Prizes in Chemistry have revolutionised the biological sciences. Recent examples are the 2017 Prize awarded for developing cryo-Electron Microscopy (cyro-EM) to image intricate detail of molecules and biological processes; the 2015 Prize awarded for discoveries in DNA repair, which is fundamental to our understanding of inherited genetic disorders and of diseases like cancer; and the 2014 Prize for super-resolved fluorescence microscopy that allows the visualisation of biological processes at the molecular level.

B. People and talent

Q2 How well will this approach meet the skills needs of the research base and wider economy in the coming years? Are there other considerations?

It is vital that consultation with the biosciences sector to identify emerging skills needs and/or vulnerabilities, also includes disciplines that interface with the biosciences such as chemistry.

We welcome the BBSRC’s holistic approach to the entire workforce, including postdoctoral researchers and technical specialists, as well as the emphasis on life-long learning and development.
The rapidly changing nature of the biosciences has resulted in changes in the way research is carried out, requiring additional skill sets from relatively new and evolving disciplines. In our response to the recent House of Lords Science and Technology inquiry on the Life Sciences and Industrial Strategy, we heard concerns from our community around recruiting researchers in sub-fields that are key for the UK biosciences sector, such as computational chemistry, computational biology, bioinformatics and biophysics, as well as difficulties in recruiting staff with excellent instrumentation knowledge, data and statistical skills.

We suggest that the BBSRC’s approach to people and talent also consider:

- **Supporting access to the best knowledge, ideas and people**: Building domestic capacity across the breadth of science and innovation (including new and emerging fields) will be essential to maintain excellence in biotechnology and biological sciences. However, the UK also needs to attract the best researchers from all over the world and researchers based in the UK need to be able to collaborate internationally. Conditions need to encourage the best international researchers to establish their careers in the UK, attract talented international students to study, train and work here, as well as allowing easy access for scientists at all career stages and of different nationalities to undertake international visits to collaborate or present their research as part of the global scientific community. For example, European Research Council Starting and Consolidating Grants provide flexibility and support for up-and-coming research leaders and Marie Skłodowska Curie Actions support outstanding early career researchers to work in other nations or disciplines for fixed periods of time. Similar schemes could be explored further by BBSRC, in particular in light of EU exit.

- **Supporting PhD and postgraduate researchers**: Our members highlighted the challenges in training researchers to attain competence in both chemistry and biology that is needed to work at the chemistry biology interface. BBSRC could support this via a balance of mechanisms including DTPs, joint-discipline supervision, interdisciplinary training programmes, placements and cohort training models.

- **Funding opportunities to harness all available talent**: in particular, to support early career researchers (see bullet above ‘Supporting access to the best knowledge, ideas and people’) and researchers from other disciplines or sectors. For example, several large pharmaceutical companies in UK have closed over the last decade resulting in many experienced biosciences researchers seeking new opportunities at CROs, SMEs, research institutes and universities. There may be opportunities for the BBSRC to strengthen schemes such as the “New Investigator Scheme” to support researchers returning to biosciences in academia after industrial positions or from other disciplines.

- **Supporting staff scientists and research/technology only positions**: Supporting a cadre of individuals to develop cutting edge platform technologies and pioneer new technologies underpins and enables world-class biosciences research. There is an opportunity for the BBSRC to identify mechanisms to support “staff scientist” type positions, in particular in areas where advanced technology is needed and this could complement the BBSRC’s support for Technology development in the biosciences. For example, the Broad Institute operates a “staff scientist” model that encompasses biologists, chemists, data scientists, statisticians and engineers who pioneer and advance platform technologies to benefit the institute, its collaborators and the wider research community.

The emphasis on professional and transferable skills is welcome and must include entrepreneurial and interdisciplinary skills, which are needed to be successful biosciences researchers.

Opportunities to acquire entrepreneurial and interdisciplinary skills should be developed and actively promoted to biosciences researchers. We outline mechanisms to support interdisciplinary working in question 5 on ‘Collaborations and Partnerships’. Successful examples of schemes to support development of entrepreneurial skills from across university chemistry departments are captured in our Open For Business report1 such as:

- Embed skills development in areas like communication, pitching proposals, long term strategic planning, business and entrepreneurial skills as part of undergraduate science degrees using an undergraduate skills framework, e.g. University of Reading
Provide enterprise training for academic staff to give them more confidence and awareness when considering commercialisation of their research, e.g. Medici Enterprise Training Programme, University of Birmingham

Provide business mentoring and training for post-doctoral science researchers, e.g. University of Nottingham Chemistry Business Partnership Unit

Provide Year in industry or industrial placement opportunities for undergraduate students enabling them to gain experience working in a large company or SME as part of their degree programme, e.g. Royal Society of Chemistry industrial placement grants

Support and link technology transfer professionals in universities with designated roles to support industry engagement, e.g. UCL Translational Research Office

Support staff development and training within companies, e.g. Staff development and accreditation of company training, whereby employees receive Chartered or Registered status and businesses improve staff retention and recruitment

Provide enabling funding for academic and industrial scientists to work on collaborative projects, e.g. Royal Society Industry Fellowships

C. Infrastructure

Q3 What are the biggest gaps in UK infrastructure for bioscience research and innovation?

Q4 How could the UK take a more strategic approach to the provision and use of infrastructures that are required for bioscience research and innovation?

Access to world leading infrastructure, resources and facilities locally, nationally and internationally is essential for biosciences research and innovation.

We agree that cutting-edge research, a vital element in the innovation ecosystem, requires access to a range of state-of-the-art instruments, resources and research infrastructure. The UK has strong capability in some universities and research institutions and has world leading facilities such as the Diamond Light Source and ISIS.
It is not possible for any nation to establish and maintain centres of excellence in all areas, and the number and range of experimental techniques that can be applied also varies between facility, which is why access to international facilities is essential. For example, the European Synchrotron Radiation Facility (ESRF) in Grenoble generates X-rays that scientists use to map molecules in detail, helping to uncover the causes of heart disease, as well as to understand how viruses spread. Whilst the facility itself is funded by the participating nations both within and outside the EU, access to EU programmes allows UK scientists to apply for funding to visit facilities such as this and carry out work there. This provides an important complement to domestic facilities like the Diamond Light Source as ESRF is able to offer some beamline opportunities that differ from those available at the Diamond. This is coupled with the fact that there is enormous user pressure for time at synchrotrons. The Diamond Light Source reports that between 50-70% of proposals for experiments were awarded between April 2012 and March 2016 and the ESRF reports that approximately 40% of experimental shift requests were awarded between 2013 and 2016.

The BBSRC has a role in facilitating data sharing across disciplines, for example by supporting awareness of repositories, facilitating access and usage. For example, cryo-EM has the potential to be truly transformative for biochemistry, however future challenges could relate to the size and scale of data generated that will place enormous pressure on computing power to carry out these experiments as well as to store or share the data across institutions. An option would be for the BBSRC, in collaboration with other funders, to conduct a survey to better understand the current capability and to support enhancement where needed so that biosciences can truly benefit from the wealth and breadth of data generated. Data sharing leads to major advances, for example structural biologists used small molecule data from the UK’s National Chemical Database Service to understand drug binding to human serum albumin, which is a major challenge in drug development.

Research translation often requires access to scale-up and pilot facilities to test products and technologies, along with expert technical knowledge in areas such as protocol development. Availing of this support can be particularly challenging for researchers based in academia, smaller companies or those working in emerging areas of science, for example in biotechnology or synthetic biology, who wish to move through the various stages of research translation. In preparing our response to the House of Lords Science and Technology inquiry on the Life Sciences and Industrial Strategy, we were made aware of a biotechnology company that encountered problems with adapting their large scale plant to a new business opportunity, due to a lack of expertise and infrastructure further down their (UK) value chain. The example illustrated the need for expertise that spans a breadth of disciplines, but also expertise that understands the challenges within a discipline at the different stages of translation. Whilst novel research may originate in, for example, a university biosciences laboratory, the skills and expertise to turn this into a product on a large scale requires input from chemists, physicists and engineers that have experience of working at pre-commercial technology readiness levels.

D. Collaborations and partnerships

Q5 How might opportunities for collaboration and partnership change in coming years, and how can UK bioscience make the most of these?

Collaboration and partnership between researchers in the biosciences, engineering and physical sciences should be encouraged and supported as it is critical for research and innovation.

Developing and supporting collaboration and partnership between disciplines and sectors helps to raise awareness of pressing research challenges and unmet needs and highlights technological developments. One way to do this is interdisciplinary research networks with associated pump-prime funding that aims to link research communities, e.g. the EPSRC Bridging the Gap Networks between the Engineering and Physical Sciences and Antimicrobial Resistance, the BBSRC Networks for Industrial Biotechnology and Bioenergy (NIBB) and the cross council Technology Touching Life Networks. Research networks are incredibly useful, but should be able to access follow-on investment to sustain the newly formed research community.
Supporting the bi-directional flow of knowledge and expertise can be achieved via various structures, activities and mechanisms such as:

- Joint funding calls such as the Antimicrobial Resistance Funders Forum (AMRFF) that brings together key funders to share information and coordinate shared funding schemes to tackle antimicrobial resistance.
- Multidisciplinary research institutions include the MRC Laboratory of Molecular Biology (LMB), the Francis Crick Institute, the John Innes Centre, Rothamsted Research and other BBSRC strategically funded institutes. Common features essential for success of these institutes are that they:
  - include core discipline teams working alongside interdisciplinary groups and are focused on addressing key research challenges;
  - promote mechanisms to encourage collaboration and mobility across discipline boundaries;
  - establish strong links to industry or patients; and
  - are underpinned by access to flexible and longer term funding.
- Research consortia focused on a research area or technology, e.g. the Drug Discovery Alliance and the Dementia Consortium, funded by Alzheimer’s Research UK, embed experienced drug discovery experts across three universities drawing on academic research in chemistry and biology to find new and disruptive treatments for dementia.
- Knowledge sharing agreements, e.g. Cancer Research UK (CRUK) researchers have access to Astra Zeneca’s compound library and screening tools, and AGRI-Net members (a Cross-Council network) have access to Syngenta’s compound library.
- Interdisciplinary meetings that establish a common language and catalyse interdisciplinary collaboration, an example is the Royal Society of Chemistry discussion meeting on Bio-Resources: Feeding a Sustainable Chemical Industry
- Ambassadorial positions and joint appointments in physical and biosciences departments variously encourage departmental exchanges, clarify new funding opportunities and facilitate the process of making joint funding applications

E. Pushing the frontiers of bioscience discovery

Q6 What are likely to be the ‘next generation’ of breakthroughs that will revolutionise bioscience research, or open up new opportunities for innovation?

Q7 How can the UK foster an environment in which creative, curiosity-driven research can thrive and advance the frontiers of bioscience knowledge?

Research in the physical sciences, including chemistry, will underpin developments in the biosciences in the future.

Examples of emerging trends or developments in the physical sciences that are likely to lead to novel research opportunities in biosciences include:

- **Using synthetic DNA to store data:** By 2040 the archive for instant access data is projected to exceed the likely supply of chip-grade silicon by a factor of 10 to 100. Developments in analytical and synthetic chemistry and the application of technologies such as PCR, CRISPR-Cas9 are making rapid strides towards making DNA a viable long-term data storage material of the future.\(^5\)
- **Chemical control of CRISPR:** CRISPR-Cas9 based genome editing enables rapid, accurate genetic manipulation and also significant advances in genome imaging, epigenome editing, and the control of endogenous gene expression. Recent advances now also enable precise
chemical control of the activity; opening the door to inducible genome-interrogating activities across multiple dimensions including time, dose, and specificity.6,7

- **Advances in chemical synthesis** to generate novel molecules and identify ways to make them more efficiently or with defined properties. This is relevant to molecule dependent sectors such as pharmaceuticals and agrichemicals but also for fundamental research in the biosciences where molecules are used to probe biological processes. For example, the development of selective, potent pesticides and fertilizers that do not harm the environment and ecosystem.

- **Directed biosynthesis** can generate novel or rare bioactive compounds with tailored properties and uses; helping to address emerging challenges in health, the environment and sustainability on a global scale. While this multidisciplinary field is driven by genetic and associated technological advances, chemistry remains the central focus with key input from the fields of organic chemistry, enzymology, biochemistry and ecology.

- **Miniaturisation** spanning microfluidics, microfabrication, assay platforms and molecular machines. The 2016 Nobel Prize for Chemistry was awarded for the development of molecular machines that will pave the way for new materials, drug delivery systems, sensors and energy storage systems. Examples highlighted in recent literature include organ-, body- and disease-on-a-chip systems that have the potential to transform drug development and exploiting microfluidics for single cell sequencing.

- **Sequencing technologies** offer improvement in diagnostics, as well as underpinning developments in the ‘omics’ fields. For example, metagenomic analyses of local soils will enable an understanding of the chemistry needed to maintain the health and sustainability of localised soil and ecosystems. It will also inform adequate life cycle assessment procedures to test the viability of proposed agricultural innovations at a localised or national scale.

- **New analytical techniques and visualisation tools** present opportunities for non-invasive analysis of cell/tissue/organ content (including metabolites and proteins). A major theme for the Rosalind Franklin research institute will be next generation imaging methods, including biological mass spectrometry and advanced microscopy.

- **Materials chemistry** to develop medical devices, self-healing and other smart materials especially prosthetics, implantable and delivery devices. For example, the interfaces between prostheses or biomedical implants and body tissues require the optimisation of many material properties, key amongst which are biocompatibility and softness. Satisfying such conflicting demands requires innovative molecular design to make materials that are biocompatible, hard-wearing and possess appropriate viscoelastic properties, and calls on an intimate knowledge of synthetic chemistry, polymer chemistry, the physics of macromolecules, tribology and lubrication among others.

- **Data analysis and computational tools** are vital to maximise the rigour and impact of research as well as to inform future research activities. For example, bio and chemoinformatics use statistical techniques to understand vast amounts of data to describe complex interactions of compounds and the properties of living organisms, respectively. Coupled with genetic profiles, this area is set to underpin personalised medicine and predict pharmacology of potential medicines. In addition, the use of artificial intelligence to mine ever larger data sets have the potential to change how researchers develop medicines.

- **Energy and manufacturing technologies** including catalysis, 3D printing, robotics, automation and improved energy generation and storage will support the production of medicines and medical devices with multiple classes of materials and functionality; more efficiently and with lower environmental impact.

**Funding must support curiosity-driven basic research as well as interdisciplinary and challenge-driven research; and be complemented by funding streams to support innovation and technology development.**

We support the BBSRC’s view of the synergistic relationship between research, innovation and technology development. The REF impact case studies and Research Council pathways to impact demonstrate that curiosity-driven basic research takes time to deliver impact but that these impacts can be truly transformative, opening up completely new avenues for research, innovation and technology development.
Past examples demonstrate that major advances are often made when the application of science generates further fundamental research questions, which in turn can lead to wider scientific impacts. It is therefore critical to develop opportunities to support iterative feedback in which early stage research informs later stage research and vice versa. For example, target identification studies of the immunomodulatory drugs (IMiDs) led to insights into the biological mechanisms of ubiquitination and proteasomal degradation. Subsequent chemical biology investigations into IMiD pharmacology led to the development of proteolysis targeting chimera (PROTACs) technologies that has underpinned the creation of new drug discovery companies and novel therapeutic modalities.

Attempting to secure funding to support research translation in the early stages or for high risk projects can be a particular barrier. Higher risk or completely new research areas can lack precedent or preliminary data and therefore struggle to obtain support. However, high risk projects have the potential to create entirely new industries or new ways to address strategic challenges. There is an opportunity for the BBSRC to consider how its support for research translation, including for high-risk research, is positioned within the broader innovation landscape (including Innovate UK, other funding bodies and medical charities) so that researchers are aware of the most suitable funding and mechanisms to support their cutting edge research.

We welcome joint Research Council initiatives such as Technology Touching Life, and urge the BBSRC to create or strengthen links in relevant areas with other Research Councils. Support could include opportunities for physical scientists to carry out research in the biosciences or making funding available to support collaboration between the physical and bioscientists. Funding calls must account for the differences between disciplines e.g. experiment costs, timelines and infrastructure requirements. Examples where curiosity-drive basic research in chemistry or at the chemistry biology interface has led to new avenues of biosciences research, innovation or technology development include:

- **fundamental analytical, synthetic, physical and computational chemistry** to understand the interactions between protein–protein complexes led to the development of small molecule or peptides that modulate these protein–protein interactions (PPIs). PPIs show great potential for new medicines and it is predicted that the market value of PPI small molecule modulators will exceed €600 million in the next 5 years.8

- **curiosity-driven basic research** into the sensing ability of membrane proteins carried out by Professor Hagan Bayley, University of Oxford, is being developed into a portable, low-cost, DNA sequencing device with applications in personalised medicine by Oxford Nanopore9 a company that has the largest valuation of any privately listed company in the UK, at £930 million.

- **fundamental chemical biology research** into the visualisation of single molecules being incorporated by DNA polymerase led to a new DNA sequencing technology, Solexa sequencing, that was acquired for $650 by Illumina Inc., in 2007. The technology can sequence a human genome for about $1000 in a day, a million-fold improvement on state-of-the-art at the start of the project in 1997, and is being used by the NHS for their 100,000 Genomes Project.

- **fundamental research in structural biology and organic chemistry** to better understand protein–ligand interactions provided the basis for the development of an X-ray structure guided fragment-based approach to drug discovery. This research led to the formation of a spin-out that became Astex Pharmaceuticals, which combined fragment-based drug discovery with high-throughput methods and roboticised data collection. Astex has 8 molecules in clinical trials and continues to build a rich portfolio of drug candidates. In 2013, Astex was acquired by Otsuka Pharmaceuticals for $886 million, and Kisqali, a breast cancer drug developed with Novartis was recently granted approval for use in the EU.10
F. Strategic challenges - building a more resilient, productive and secure future

Q8 Are these the right strategic challenges for UK bioscience to focus on? Are there others?

Q9 What do you see as the greatest opportunities for UK bioscience research and innovation to effect a step change in how these challenges are addressed?

Research in biology, chemistry, engineering, materials and physics is needed to unlock discovery opportunities and effect a step change in how these strategic challenges are addressed.

We welcome emphasis on the strategic priority areas including Agriculture and Food Security; Industrial Biotechnology and Bioenergy; and Bioscience for Health. Given the nature of these research areas, there is a natural overlap with challenges identified by other funders within the UK and internationally. For example, these challenges are also captured under the UN's Sustainable Development Goals and will overlap with research to support the UK Government's Industrial Strategy and the Global Challenges Research Fund.

There is an opportunity for the BBSRC to seek joint funding arrangements in areas where partnering with others can achieve greater impact. Examples to build on are the establishment of joint initiatives such as Global Food Security programme, the AMR Funders Forum and Technology Touching Life.

The BBSRC leads the UK’s involvement in the Joint Programming Initiative on Agriculture, Food Security and Climate Change (FACCE-JPI) and is involved in the JPI A Healthy Diet for a Healthy Life (JPI-HDHL). The UK can continue to participate in JPIs beyond EU Exit because participation is based on contribution to the initiative.

All of the strategic priority areas will require a multidisciplinary approach that includes biology, chemistry, engineering, materials and physics, for example:

- **Agriculture and food security** in particular in relation to crop protection or enhancement technology, minimising environmental impacts, improving water efficiency and increasing photosynthetic efficiency draws on a number of scientific disciplines such as biology, chemistry, ecology and genetics. Emerging areas of concern are the resistance to many active ingredients used in crop protection and a lack of chemical tools to understand fungal metabolism.

- **Bioscience for health** will require a range of disciplines to better understand the development of disease and accelerate the development of new therapeutics, diagnostics and alternatives. For example:
  a. the latest automated solid-phase synthesis and synthetic biology approaches to carbohydrate production could revolutionise anti-microbial vaccine development.
  b. synthetic biology also presents opportunity for the scaled production of, for example, human milk oligosaccharides, paving the way to underpin studies on infant nutrition as potential alternatives to antibiotics.
  c. medical diagnostics rely on improved and more cost-effective means of chemical measurement to provide data faster, cheaper and at the point of care. These advances in the clinic are dependent on developments in, for example, miniaturised power sources, energy storage, new materials and biomarkers.

- **Industrial Biotechnology and Bioenergy** present both challenges and opportunities across a number of sectors and disciplines. For example, there is a need to develop novel catalytic and bio-catalytic approaches for processing biomass with a view to the generation of useful chemicals, also known as chemical valorisation. This draws on basic research ranging from the development of catalysts, enzymes and new synthetic approaches to make useful chemicals from oxygen-rich starting feedstocks (e.g. lignocellulose). In addition, innovative ways to utilise a range of waste materials, separate and purify chemicals requires new
technological advances. Inter- and multidisciplinary approaches from across the physical sciences and engineering will be required at every point in different manufacturing chains.

**Any other comments?**

**Q10** Is there anything else that BBSRC should consider in developing a strategy for UK biotechnology and biological sciences that is not covered in the previous sections, including, for example, any particular risks or threats you see for UK biotechnology and biological sciences over the coming years?

As part of the development of the Strategy for UK Biotechnology and Biological Sciences, there must be an analysis of the role of the EU in supporting this sector.

In the coming years, EU Exit poses both risks and opportunities for UK biotechnology and biological sciences. The BBSRC will be a key advocate for the biosciences research community and careful consideration of the connections between the EU and UK biosciences is needed as many research areas draw upon links to EU programmes. Clearly this will depend on the outcomes of the UK’s negotiation to exit the EU and also on Government policy such as the Life Sciences Industrial Strategy and the Bioeconomy Strategy.

In relation to EU Exit, it is vital that the UK sustains and builds on our already world-class science and innovation base. For the UK to stay at the forefront of global science and innovation there are three key overarching objectives that apply equally to biosciences, as they do to research and innovation more broadly:

- Maintain access to international research and development funding programmes and research facilities, along with the collaboration opportunities these bring (See example provided to Question 3&4 on ‘Infrastructure’ and Question 8&9 on ‘Strategic Challenges’).
- Enable easy movement of skilled and talented scientists and students to and from the UK, (See example provided Question 2 on ‘People and Talent’).
- Develop a future regulatory system that achieves a balance between nurturing innovation, protecting the environment and human health and enabling the UK to trade internationally. This is also relevant to new and emerging technologies, for example CRISPR. In parallel with fostering and anticipating potential breakthroughs it is critical to be aware of and discuss ethical and regulatory implications.

**Contact**

The Royal Society of Chemistry would be happy to discuss any of the issues raised in our response in more detail. Many of the examples above were provided by members of our community and we would be delighted to provide further links with researchers whose expertise and perspective may be valuable as the strategy develops. Any questions should be directed to Dr Anne Horan, horana@rsc.org, 01223 432699.

**About us**

With over 50,000 members and a knowledge business that spans the globe, the Royal Society of Chemistry is the UK’s professional body for chemical scientists, supporting and representing our members and bringing together chemical scientists from all over the world. Our members include those working in large multinational companies and small to medium enterprises, researchers and students in universities, teachers and regulators.

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