***TECHNOLOGY TOUCHING LIFE* - JOINT BBSRC, EPSRC, MRC CONSULTATION**

INTRODUCTION

Building on our track record of working together to support interdisciplinary research across the physical, life and biomedical sciences, BBSRC, EPSRC and MRC are at an early stage in scoping a joint strategy to foster more diverse, fundamental, interdisciplinary technology development research. This is a new theme provisionally titled '*Technology Touching Life*' (*TTL*). As part of the initial scoping exercise this consultation is being sent to universities/institutes, individual researchers, learned society contacts and industry representatives to garner views from the scientific community in order to inform the development of the *TTL* theme.

Discussions on *TTL* across the three Research Councils were initially stimulated by the EPSRC report 'The importance of engineering and physical sciences research to health and life sciences', published in May 2014. Fundamental breakthroughs in the life and biomedical sciences are often based on new physical science-based research technologies, which in turn often open up longer term opportunities for the economy and society. The *TTL* strategy aims to stimulate and support interdisciplinary collaborations to explore novel technologies and approaches that address application-driven challenges. By enabling joint working and two-way flow of ideas between life scientists and engineers/physical scientists we expect that *TTL* will ensure the UK leads future waves of foundational technology discovery for the life and biomedical sciences, and create new opportunities for commercial development.

HOW TO COMPLETE THE CONSULTATION

The consultation consists of six free-text response questions. You have been provided with a unique link to capture your response; please note only a single response can be submitted using this link. Your response may be returned to and edited at any point prior to submission. The deadline for submissions is Friday 28 March 2015.

Alternatively, your response can be submitted as a Word document to peter.burlinson@bbsrc.ac.uk.

CONTACTS

If you have any queries please feel free to contact:

BBSRC	EPSRC	MRC
Peter Burlinson	John Hand	Heike Weber
Peter.burlinson@bbsrc.ac.uk;	John.Hand@epsrc.ac.uk	Heike.Weber@headoffice.mrc.ac.uk
01793 413393	01793 444164	01793 416200

BBSRC, EPSRC and MRC thank you in advance for your time and input.

'*TECHNOLOGY TOUCHING LIFE*' CONSULTATION QUESTIONS

CURRENT AND FUTURE RESEARCH OPPORTUNITIES AND TRENDS

Within the broad scope of '*Technology Touching Life*':

1. What are the 'sweet spot' areas where there is high potential for closer alignment across physical sciences and life sciences to lead to major advances?

There are many areas where development and application of physical science techniques and understanding will lead to advances in life sciences research. Fundamental developments from the physical sciences promise to advance the following areas among others:

(i) The drive for better molecular understanding of biological processes means that **making molecules** will become ever more important. Generating new probes and lead compounds is dependent on advances in synthetic chemistry to deliver novel molecules and to find more efficient ways to make them. Physical and *in silico* compound collections of structurally diverse molecules, coupled with high throughput screening technologies, will accelerate research in molecule-dependent sectors such as pharmaceuticals, materials and agrichemicals. For example, wide screening of biological targets is now feasible due to miniaturisation of assays, increased computational power and precise biological analysis. Clearly, organic chemistry is a key discipline and was recently identified in a Department for Business Innovation & Skills economics paper as the area where the UK has the greatest revealed technological advantage.[1]

(ii) Ever-improving **chemical understanding** will drive more specifically targeted interventions at the genetic, metabolic, cellular and organ levels, ranging from nanoscale drug delivery and gene therapy to stratified medicine and tissue engineering. Modelling and computational approaches will be required to complement these endeavours in, for example, systems biology research and its applications in personalized medicine.

(iii) The past decade has witnessed spectacular advances in **spectroscopy, imaging and other analytical techniques**, including DNA sequencing, real time PCR and single molecule studies. The latter was recognised by the 2014 Nobel Prize in Chemistry.[2] Such advances, in particular from the physical sciences, will continue to accelerate, and impact on, the now more routine fields of proteomics, genomics, metabolomics but also emerging areas such as metagenomics and in the elucidation of an individual's microbiome. There is an ever growing demand for new chemical probes and highly site-specific, low cost contrast agents which will facilitate higher resolution and more selective imaging of, for example, tumours, ischaemia and neurodegeneration.

(iv) **Advanced materials** will enhance diagnostic capabilities and accelerate the development of self-healing and other smart materials for medical applications such

[1] BIS Economics paper No. 18: Industrial Strategy: UK Sector Analysis, Department for Business, Innovation and Skills, September 2012

[2] http://www.nobelprize.org/nobel_prizes/chemistry/laureates/2014/

as delivery devices and prosthetics. For example, haptic (sensing) materials comprise a touch response facility interfacing with novel electro-active or piezoelectric polymers. Further innovative chemical design to advance haptic materials is strongly needed, especially at the microdomain level. As a further example, the interfaces between prostheses and body tissues, or biomedical implants 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.

(v) Physical sciences are also intimately involved in many **developments across the agri-sciences**. Apart from the obvious relevance of the chemical sciences to the development of selective, potent pesticides and fertilizers that do not harm the environment and ecosystem, the chemical sciences also strongly contribute to other areas. For example, soil science, crop protection and efficiency in nutrient use are all areas underpinned by chemical sciences research. Routine application of the results of metagenomic analyses of local soils will enable a proper understanding of the important chemistry that needs to be put in place 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.

2. What trends or developments in engineering and physical science technologies are already emerging which you think will have impact in the life and biomedical sciences?

The UK Government identified priority areas for technological advancement ('eight great technologies').[3] Of those, the engineering and physical sciences will be play a vital role in driving forward advances in energy storage, synthetic biology, regenerative medicine, advanced materials and agri-sciences.

No list of current emerging technologies is likely to be exhaustive, but some specific emerging technologies for use, or that will have impact, in life and biomedical sciences are:

(i) **Miniaturisation** and new assay platforms for analysis and biological interventions will continue to offer improved diagnostics and therapies – facilitating point-of-care testing and more targeted therapies from better and faster diagnosis which have the potential to be used by non-experts 'handheld' in the field or in the clinic.

(ii) **High throughput screening** and spectroscopic techniques are already being employed in life sciences fields including 'omics' and imaging, and these trends will surely accelerate.

(iii) Separation and detection techniques for **single cell analysis** and identification of multiple biomarkers (particularly of major diseases such as cancer and Alzheimer's).

(iv) Advances in **modelling and visualisation** tools including new contrast agents and refinement of imagining techniques.

[3] Eight great technologies, Department of Business, Innovation & Skills, October 2013

(v) **Molecule-driven research** and **advances in synthesis** will enable development of DNA assemblies, chemically modified nucleotides, artificial proteins and enzymes, nano-science and natural products.

(vi) **Materials chemistry** for medical devices, especially prosthetics (see also 1(iv) above).

(vii) **Nanotechnology** for chemical agent delivery in human health, agriculture and in the environment (e.g. bubble shell technology for the delivery of active ingredients).

(viii) **Data analysis and statistical methods** are vital tools that cut across all disciplines and are essential to maximising the rigour and impact of excellent and well-informed research. High quality interactions between the disciplines must be facilitated by encouraging proper data handling/analysis skills. For example, the *Dial-a-molecule* ESPRC Grand Challenge network recently ran a workshop aimed at informing chemists of the power of statistical methods in design of experiment and the need to link with statistical scientists.

(ix) **Energy and manufacturing technologies** (e.g. photovoltaics, 3D printing and improved energy storage) will serve to power medical devices and facilitate developments in personalized medicine impacting on low resource, point-of-care settings and so present opportunities to develop bespoke biomedical solutions.

(x) **Renewable materials** as alternatives to fossil fuel-derived chemicals and fuels will increasingly provide an industry 'pull' for research in this area. The increased use of more environmentally friendly processes, known as 'green chemistry', highlights the contributions that the chemical sciences make to manufacturing. An example is the scale up in the synthesis[4] of Pregabalin, a drug used to treat neuropathic pain. New catalysts will, in their own right, enable previously impossible chemical transformations relevant to bioprocessing renewable chemistry and across the pharmaceutical research landscape.

3. What important areas in the life and biomedical sciences are currently limited by existing technologies and require new technology developments to 'unlock' discovery opportunities and deliver a 'step change' in understanding?

Some illustrative examples where further developments would unlock discovery opportunities and increase understanding are given below:

(i) **-omics** (including genomics, proteomics, metabolomics, glycomics etc.) require chemical expertise to deliver a better understanding of the mechanisms that drive cellular processes. This will come through further improvements to high-throughput analytical technologies and an improved appreciation of the molecular interactions which link changes within any biological system. Genomic advances are reliant on improved and affordable sequencing technologies which will facilitate application towards increased understanding of the relationships between gene expression and cellular differentiation.

(ii) **Precision medicine** using molecular understanding to redefine diseases based on individual genetic and molecular causes. This will help to target delivery of molecules to specific cell-types and organs as well as examine metabolic pathways to increase our understanding of complex interrelated biological processes.

(iii) **New relevant drug target identification** is a key challenge which will draw on both predictive and "wet" lab approaches. Many of the new target classes being tackled by UK-based research groups are less well understood. For example modulators for protein-protein interactions (PPI) show great potential and it is predicted that the market value of PPI small

[4] Organic chemists reducing impact on the Environment, 2012

molecule modulators will exceed €600 million in the next 5 years.[5] Advances were initially made by attempting to probe the fundamental chemistry involved in protein-protein complexes using analytical, structural and computational chemistry. Using synthesis and peptide chemistry, small molecule and peptide interventions of protein-protein interactions were identified.

(iv) **Tackling antimicrobial resistance** will require a range of disciplines to better understand the development of resistance and accelerate the development of new therapeutics, diagnostics and alternatives, and in particular to exploit information provided by the microbiome. For example, medical diagnostics rely on improved and more cost-effective means of chemical measurement to provide data faster, cheaper and at the point of care. However such advances in the clinic are dependent on developments in for example, miniaturized power sources (energy storage), new materials and biomarkers.

(v) **Support for agri-sciences** in particular in relation to crop protection technology, minimising environmental impacts, improving water efficiency and increasing photosynthetic efficiency. Resistance to many active ingredients used in crop protection is a major issue, for example there are a lack of chemical tools to understand fungal metabolism. Addressing these challenges will draw on a number of scientific disciplines such as biology, chemistry, toxicology, ecology and genetics.

(vi) **Industrial Biotechnology** already presents 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.

INTERDISCIPLINARITY

4. What do you see as the key features of successful models of close working between physical sciences and life sciences in fundamental discovery research? Please use specific examples, national or international, where possible. You views on unsuccessful as well as successful models are welcome.

Close, direct collaboration between physical and life sciences, including chemistry, is essential for fundamental discovery research and to address many of the pressing and complex questions in life sciences. Achieving increased interactions between the physical and life sciences research community can be addressed through a variety of mechanisms such as networking events, scientific meetings, specific training programmes and targeted research funding schemes.

There are many examples of successful models of close working between the physical sciences and life sciences. One example is collaborative screening agreements which provide discovery researchers with access to both physical samples and virtual libraries of compounds. Examples are

[5] L. Nevola and E. Giralt, *Chem. Commun*., 2015, 51, 3302

the arrangement where **AGRI-net members have access to Syngenta's compound library** and **CRUK researchers have access to Astra Zeneca's compound library and screening tools**.

Another example is the **MRC Laboratory of Molecular Biology** where many techniques were pioneered, including DNA sequencing, methods for determining the three-dimensional structure of proteins and the development of monoclonal antibodies. These were underpinned by developments in the physical sciences, exploited through close interaction with the life sciences disciplines. The work of LMB scientists has achieved considerable impact including ten Nobel prizes and generated over £330 million from technology transfer activities.[6]

Other notable UK examples include the **Institute of Cancer Research**, the **Structural Genomics Consortium**, **Dundee Signal Transduction Institute** and **BBSRC's multi-site Sustainable Bioenergy Centre (BSBEC).** Examples in the US include the **Broad Institute** and the **Scripps Research Institute**. A common feature of these institutes is that they include core discipline teams alongside interdisciplinary groups/platforms, importantly providing mechanisms that encourage experts to collaborate across disciplinary boundaries and include a strong link to the end-user such as the clinic or industry.

We have previously called for the establishment of **therapeutic centres of excellence** as a model that would embed experienced drug discovery scientists and link to biomedical research units and centres drawing on a variety of expertise from fundamental physical sciences research to clinical application. A recent example is the **Drug Discovery Alliance**[7] funded by Alzheimer's Research UK which will draw on academic research in chemistry and biology to search for new dementia treatments.

Key features of successful models include:

- Programmes built around key fundamental or applied challenges with clear objectives
- Cultures that encourage researchers to cross and challenge traditional disciplinary boundaries
- Increasing awareness and visibility of technology developments and new approaches guided by close involvement with end-users (industrialists, clinicians, biologists, chemists etc.)
- Access to flexible and long term levels of funding to facilitate and encourage fundamental and speculative research
- Mechanisms to enable knowledge transfer and iterative feedback between scientists regardless of discipline

Perceived barriers or challenges to interdisciplinary research include:

- Uncertainty about where to submit grant proposals or how they will be reviewed, in particular for proposals that fall within the gaps (e.g. if perceived to be "too physical, biological or medical")
- Lack of funding for interdisciplinary research, smaller grant projects and poor support for follow-on investigative studies
- Cultural challenges including language or jargon specific to particular scientific disciplines
- Logistical challenges in terms of supervision of PhD students and research projects (proximity, administration and time).

[6] http://www2.mrc-lmb.cam.ac.uk/about-lmb/

[7] http://www.alzheimersresearchuk.org/alzheimers-research-uk-launches-three-drug-discovery-institutes/

5. What structures, activities and mechanisms help establish a culture of interdisciplinary research and strong interdisciplinary leadership in universities, institutes and centres?

Institutional vision and culture contribute to successful interdisciplinary teams by ensuring goals are meaningful and not too granular. Time needs to be allocated to management and coordination which facilitate knowledge exchange across the disciplines. Participants from different disciplines must ensure that they understand the aims of any research collaboration, what each can offer and how the findings will be disseminated (including publication authorship and joint thesis supervision). Creating an interdisciplinary environment needs to account for differences in specific research areas ("jargon"), laboratory infrastructure required, administrative arrangements and differences in organisational structure. In cases where the interdisciplinary collaboration is established between researchers from different institutions, individual institutional research requirements need to be considered, and so it is likely that different models will be created.

Ambassadorial positions and joint appointments in physical and life sciences departments variously encourage departmental exchanges, clarify new funding opportunities and facilitate the process of making joint funding applications. A concerted drive to support and fund the bi-directional flow of staff (e.g. through secondments) is vital as a route to providing direct exposure to a new discipline and as a means of identifying new collaboration opportunities. Institutions and centres with specific discipline expertise need to be encouraged to be proactive in forging relevant interdisciplinary initiatives as well as sharing instrumentation.

Networks build links between researchers and have been successful in stimulating exchange of ideas and closer working. Networks are useful, but must be followed by real investment to sustain the newly formed research community. Scientific meetings and stakeholder workshops that bring together the physical, life and biomedical sciences research community facilitate research opportunities and knowledge exchange. The recently established BBSRC Networks for Industrial Biotechnology and Bioenergy (NIBB)[8] are a good example aimed at linking research communities. The Research Councils should aim to strengthen these types of programmes, including in areas that are not currently covered.

Interdisciplinary working can be fostered at all stages from the early research phase through to the more advanced and applied stages. There is an opportunity to introduce **iterative feedback** in which early stage research continues to inform later stage research and *vice versa*. Major advances are often made when the application of science generates further fundamental research questions, which in turn can lead to wider scientific impacts.

STRENGTHENING SCIENTIFIC PERFORMANCE AND IMPACT

6. How might the Research Councils working with research organisations (e.g. universities and institutes), industry and other stakeholders help address the issues raised in response to the questions above? Please provide examples of successful approaches (both national and international) where applicable.

A joined-up approach from Research Councils is important in accelerating both discovery and challenge research within and across disciplines. It is vital to provide funding for fundamental blue-skies physical sciences research, which will enable and transform life sciences research in both the short and the long term. It is also important to **link with other research and innovation funders** such as charities and government departments and agencies.

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[8] Networks in Industrial Biotechnology and Bioenergy (NIBB), 2013

For example, the Antimicrobial Resistance Funders Forum (AMRFF) brings together key funders to share information on activities and funding schemes relevant to the challenge of Antimicrobial Resistance. RCUK Cross-Council Programmes such as the Energy Programme also have the potential to link research at different stages and across disciplines based on a technology challenge area.

Regular consultation with the research and innovation community, for example through meetings or surveys will be fertile way of identifying future gaps, challenges and solutions. For example, IMI EMTRAIN,[9] the European Medicines Research Training Network recently asked researchers to identify "the next big thing" in biomedical sciences. Early in 2015 this survey will be extended to a number of IMI partners including SMEs and large pharmaceutical companies in order to identify gaps in training.

Funding and specific initiatives to support interdisciplinary collaborative research are also essential. A risk for interdisciplinary research is that topics at the boundaries between two funding bodies may be under-supported by both. **Interdisciplinary proposals should be reviewed by interdisciplinary review panels.** For example, the use of a 'chemical sciences' and a 'biology' peer reviewer does not necessarily capture the expertise of the chemistry-biology interface. A survey of the chemistry-biology interface community highlighted the importance of providing clarity on the remit and procedures of Research Councils especially in connection with proposals that are interdisciplinary or a series of proposals which straddle more than one Research Council as research evolves.[10]

Educating and supporting the next generation of interdisciplinary researchers will be crucial. Postgraduate research programmes, while developing expertise in core disciplines, can also provide PhD students with opportunities to develop the language, skills and knowledge to embark on interdisciplinary research careers. Examples of such opportunities are: joint supervision of postgraduate researchers, for example with supervisors in different disciplines or with one in academia and one in industry; training courses and industrial placements.

There is a perceived lack of funding for **proof of concept or larger scale tests** aiming to gather sufficient evidence to drive development and adoption of new technologies. For example the potential of vibrational spectroscopy[11] for disease diagnosis has been well demonstrated but translation into clinical practise is slow. Relevant networks (e.g. EPSRC Network CLIRSPEC and EU COST Action Raman4Clinics) can play a significant role in increasing the uptake of new technologies by end-users. Along with funding for proof of concept studies, examples of other mechanisms to support the use of technology across sectors and disciplines are multi-institutional collaborative grants, knowledge transfer partnerships and training programmes for technology end-users. There are opportunities to link with Innovate UK and with Horizon 2020 platforms and programmes such as SusChem and SPIRE.

More generally, researchers need support for the **translation of their research into treatments, technologies and products**. Examples of models to facilitate translation are R&D clusters that link universities, research institutes and local companies (SMEs, CROs and multinational companies) and researcher mobility schemes such as the Royal Society of Chemistry Researcher Mobility Grants and the Royal Society Industry Fellowship Scheme. Wider barriers identified by the Wellcome Trust[12] that are inhibiting translation and commercialisation of life sciences research are:

[9] https://www.on-course.eu/knowledge-area/demand-areas/
[10] Face to Face: The UK Chemistry Biology Interface, Royal Society of Chemistry. 2008.
[11] H. J. Byrne, M. Baranska, G. J. Puppels, N. Stone B. Wood, K. M. Gough, P. Lasch, P. Heraud, J Sulé-Susoj and G. D. Sockalingumk, *Analyst*, 2015, 140, 2066
[12] The UK's innovation ecosystem, Wellcome Trust,2014

- an academic culture that does not facilitate translation of research
- prioritisation of revenue over innovation by university technology transfer offices
- insufficient support and funding for concept testing
- a lack of long term investment to underpin commercialisation

WRAP UP

Finally, we would welcome any other comments you have on developing the 'Technology Touching Life' theme.

We welcome this Cross-Council 'Technology Touching Life' initiative. The UK already benefits hugely from its many strengths and research achievements in life sciences, biomedicine, physical sciences and in engineering. In 2009 an MIT white paper[13] highlighted how "convergence" between engineering, physical sciences and the life sciences is the next revolution in biomedical research leading to major healthcare advances and economic prosperity. Our answers to questions 1-3 above demonstrate existing UK capability and a fertile interplay between the physical and life sciences which, in an increasingly competitive global environment, we must seize the opportunity to develop.

The Royal Society of Chemistry welcomes the opportunity to contribute to this consultation and we are keen to add to the development of the 'Technology Touching Life' theme. 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 will be valuable as the theme develops. We have a variety of activities to advance research and innovation across chemistry and the disciplines with which it interfaces. We work with many partners - including Research Councils and sister societies as well as research networks and consortia - and are very open to exploring new opportunities for collaboration. Our activities include:

- Our Divisions and Interest Groups are networks of researchers and include the Chemistry Biology Interface Division.
- Our portfolio of conferences and symposia focus on cutting-edge research.
- The National Compound Collection aims to capture and enable exploitation of the structural diversity contained within UK synthesis PhD theses.
- Our Researcher Mobility Grants provide flexible support for early career researchers and recent appointees for scientific visits nationally and internationally, and between academia and industry.
- Our upcoming Researcher Mobility workshop organised as part of our partnership with the cross Learned Society *Drug Discovery Pathways Forum*. Previous workshops have been successful in bringing researchers from different disciplines together, and providing mentoring alongside opportunities for academics, industrialists and clinicians to work together on challenge scenarios.
- Our Emerging Technologies Competition aims to accelerate the commercialisation of chemistry-based technologies from small companies and universities.
- A number of our Prizes and Awards recognise excellence for work at the interface between chemistry and other disciplines.

[13] The Third Revolution: The Convergence of the Life Sciences, Physical Sciences, and Engineering, MIT, 2009

- Our journals and books disseminate knowledge across the chemical and other sciences: examples of recent themed web collections include optical diagnosis and epigenetics.
- The Chemical Sciences in Society Summit brings together eminent researchers from the UK, US, Germany, Japan and China to articulate current challenges in frontier chemistry research related to global challenges such as energy, water, agriculture and health.

Summary of recommendations:

1. **Funding for fundamental blue-skies physical sciences research must be an integral part of the Technology Touching Life theme.** The timescales for a "return on investment" cannot be predetermined. There are many examples in our response to questions 1-3.
2. **There must be a joined-up approach across Research Councils to ensure that excellent research across the boundaries between Councils is supported.**
3. **Mechanisms to ensure that excellent interdisciplinary research is supported are crucial**. These include appropriate interdisciplinary expertise on assessment panels and minimising any barriers due to the remit of each Council.
4. **More initiatives are needed to facilitate interactions and collaboration, between physical and life scientists**. Examples include research networks, workshops and meetings focused on current and future challenges, researcher mobility schemes, and grant schemes that are structured to encourage collaboration across disciplines and sectors.
5. **More initiatives are needed to facilitate collaboration between academia and industry.** There are opportunities to partner with other organisations such as research charities, government departments and Innovate UK. See examples in 4

We would be very pleased to discuss any aspect of this response further.
Please contact Dr Anne Horan, Life Sciences Programme manager, at horana@rsc.org