Government Science and Innovation Strategy

Input from the Wellcome Trust - July 2014

Key messages

- **Long-term commitment and funding for science is essential**, and will leverage support from charities, industry and investors.
    - A vision for science should be cross-governmental with an investment plan spanning at least 10 years to strengthen our world-leading research base.
    - The balance of the dual funding system must be maintained and the Charity Research Support Fund should be grown in line with charity investment.
- Sustainable **investment in infrastructure is at the heart of scientific excellence**.
    - While we are pleased to see a capital commitment to 2021, operational funding for world-class laboratories and national facilities is crucial.
- It is **critical that barriers to translation are removed** to promote innovation.
    - Academics should be able to access training and mentorship to equip them with the skills they need to collaborate with commercial partners.
    - Entrepreneurship should be rewarded and supported, with metrics and incentives that recognise the range of behaviours needed for translation.
    - Government must work with universities to ensure that Technology Transfer Offices focus on exploiting knowledge for public good rather than revenue.
    - We must address the lack of long-term 'patient' capital that companies need to develop research ideas into treatments, technologies and products.
    - The NHS should be 'research-friendly' and improve the uptake of innovation.
- The importance of the **underpinning research environment cannot be ignored**.
    - Today's grand challenges in health require collaboration across disciplines. Appropriate skills, platforms and networks are needed to facilitate this, particularly in the areas of genomics and 'big data'.
    - The regulatory environment must promote proportionate standards and safeguards, while protecting research participants and ensuring public trust.
    - The use of animals in medical research is essential and the Government must be explicit about its importance.
    - The outputs of research — including data and publications — should be freely accessible and used to advance knowledge and drive societal benefits.
    - It is vital to invest in public engagement to create an environment of trust, support and interest in science and its application.
- The **shortfall in the STEM workforce must be addressed**.
    - The STEM pipeline starts early and we must ensure that all young people have a high-quality and inspirational science education.
    - Researchers should be recognised as a core part of an organisation's workforce, and diversity and equality must be promoted.
    - Immigration policies should signal that the UK is 'open for business' and supportive of international science.

Introduction

1. The Wellcome Trust is a global charitable foundation dedicated to achieving extraordinary improvements in health. This year, we are planning to invest £750 million in biomedical research and the medical humanities. The majority of this will be spent in the UK as a direct result of both the excellence of the research base and the Government's commitment to science.

2. We are pleased to input into the Science and Innovation Strategy. For UK science to flourish, there must be an ambitious, overarching vision with strategic oversight of the UK's capabilities and areas of strength. This will also help ensure that we are the location of choice for international scientists, industry and investors.

A strategy to underpin scientific excellence

The importance of long-term, coordinated funding

3. The strategy must focus on delivering a long-term, coordinated and stable approach to research. The estimated time lag between research expenditure and realisation of health benefits is 15 years[1] — science is a 'long game' and Government support must reflect this. Critically, the strategy should include an investment plan spanning at least 10 years. This will underpin the delivery of health, societal and economic benefits, and is essential to drive economic growth.

    - The 2014 *Medical Research: What's it worth?*[1] study — commissioned by the Trust, the Academy of Medical Sciences, Cancer Research UK and the Department of Health — found that each pound of public or charitable investment in cancer research returns around 40 pence to the UK every year.

    - This builds on a 2008 study which found that every pound spent on cardiovascular and mental health research generates benefits equivalent to an annual return of 39 pence and 37 pence respectively[2].

4. Public expenditure in science achieves huge leverage and sustained Government funding will ensure continued confidence, partnership and investment from universities, medical research charities and industry (see **case studies 1 and 2**).

    - Every pound spent by the Government on research increases private sector R&D output by 20 pence per year in perpetuity[3].

    - Between 2003 and 2013, the Trust partnered with the Government to commit nearly £1.5 billion to medical research, training, education and innovation.

    - Between 2006 and 2013, Medical Research Council funding of £3.5 billion led to a further £1.5 billion commitment from charitable organisations[4].

5. The Government must maintain the balance of the dual support system given the complexity of the research funding ecosystem. The combination of Research Council grants alongside Funding Council block support allows institutions to take strategic decisions about their research activities, and provides flexibility to undertake blue skies research and respond to new opportunities. It also enables a range of organisations to invest in university research, contributing to the diversity and strength of the UK science base.

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[1] Matthew Glover, Martin Buxton, Susan Guthrie, Stephen Hanney, Alexandra Pollitt and Jonathan Grant (2014) *Estimating the returns to UK publicly funded cancer-related research in terms of the net value of improved health outcomes. BMC Medicine,* 12:99 http://www.biomedcentral.com/1741-7015/12/99

[2] Health Economics Research Group, Office of Health Economics, RAND Europe (2008) *Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK* www.wellcome.ac.uk/economicbenefits

[3] Campaign for Science and Engineering (2014) *The Economic Significance of the UK Science Base* http://sciencecampaign.org.uk/CaSEUKScienceBaseReportBriefing.pdf

[4] Data gathered by a system called Researchfish which collects information about the outputs and outcomes of MRC research that have arisen since 2006.

6. The Charity Research Support Fund (CRSF) is a particularly important element of quality-related (QR) funding, enabling charity investment to be leveraged and encouraging donations by giving the public confidence that their money will be spent directly on research. While there has been a significant increase in charity funding for research in recent years, the CRSF has been maintained at £198 million until 2015 — this must be grown and protected against inflation.

7. There is a role for both curiosity-driven and applied funding in the UK science portfolio, and the strategy must recognise the importance of pursuing research to expand knowledge as well as for potential health and societal benefit. Nobel laureate Professor Lord Porter famously commented that "pure research was merely that research which has not yet been applied". This still holds true today.

8. While the Government has an important role in deciding strategic areas of importance, identifying grand challenges for research, and setting broad priorities for funding, it should be informed by expert advice. Ultimately, funding decisions should be based on excellence and not politicised. Funding agencies also play a key role in identifying areas of unmet need, but should not be too directive — researchers need the flexibility to ask the right questions and put forward the best ideas.

9. It is essential that the strategy is cross-governmental and coordinated across all of the departments that support the research base. The multidisciplinary research funded by the Department for Business, Innovation and Skills (BIS) ensures the quality, diversity and breadth of UK science. Clinical research funded by the National Institute of Health Research via the Department of Health is a critical element of the system, and the NHS is an important location for research and innovation. The Department for Environment, Food and Rural Affairs, the Department of Energy and Climate Change, the Department for International Development and the Ministry of Defence are also key research funders, and the Department for Education plays a vital role in ensuring that all young people have an inspirational science education.

Ensuring world-class infrastructure

10. We welcome the Government's long-term commitment to capital to 2021 and recently responded to the BIS consultation *Science and research: proposals for long-term capital investment*[5]. World-class research requires state-of-the-art facilities and cutting-edge equipment. Sustainable investment in capital is at the heart of scientific excellence, and will help attract scientists, industry and funding to the UK.

11. Investment in infrastructure can only realise its full potential with appropriate operational funding and provisions to support a highly skilled workforce of researchers and technical staff. There must be mix of support at the project, institutional, national and international level to ensure that the UK's 'well-found laboratories' and large-scale facilities are sustainably operated, upgraded where necessary and have access to cutting-edge technologies and equipment. Existing capital capability should be maximised wherever possible (see **case study 3**).

12. It is becoming increasingly important to plan for the infrastructure and technology needed to support the storage and analysis of very large quantities of data — an issue which cuts across almost all research disciplines. 'Big data' requires us to think about capital in a new way, focusing on hardware, software, data curation and efficient networks. A highly skilled workforce will be essential to underpin this, bringing together bio-informaticians, mathematicians and data scientists. A high degree of coordination in funding, joint initiatives and policy formulation will be essential to ensure the UK maintains its competitive advantage.

[5]Wellcome Trust response to the BIS consultation *Science and research: proposals for long-term capital investment*
http://www.wellcome.ac.uk/stellent/groups/corporatesite/@policy_communications/documents/web_document/wtp056979.pdf

Catalysing innovation and technology transfer

13. It is critical that barriers to research translation are removed. As a first step, we must ensure that there is an awareness and understanding of the commercialisation process across the research community, including the different players involved. Researchers must be able to access training and mentorship to equip them with the skills they need to collaborate with commercial partners. Entrepreneurship should be celebrated, rewarded and supported. Funding and incentives should also encourage a 'revolving door' between universities and companies.

14. While publication outputs are an important metric for scientific success, it is important to recognise the range of behaviours that contribute to a flourishing research environment. This includes collaborative, cross-disciplinary and cross-sector working, advisory roles, entrepreneurship, and mentoring activities. The Higher Education Funding Council for England should also consider how it can incentivise collaborative working and translation through the Research Excellence Framework.

15. Government should give universities a clear steer on the appropriate mission and purpose of Technology Transfer Offices (TTOs) — their principle focus should be to exploit knowledge for public good rather than generate revenue. This lack of mission clarity impacts on their ability to meet the needs of their very different customers: academics, industry and investors. Part of their remit should be acting as a 'broker' between businesses and universities, catalysing successful collaborations and helping companies of all sizes to access academic expertise. They should also better consider the decision to spin out companies versus incubating research to a point where it is less risky and more attractive to follow-on investors.

16. In the UK, there is a need for increased concept funding to enable researchers to develop innovative or high-risk ideas which could then go on to compete for larger awards. Ultimately, long-term capital underpins the translation of medical research. Traditional venture capital has underperformed in the UK and Europe, and there is a pressing need for additional incentives that will attract alternative sources of 'patient' funding. One example is 'evergreen' investment company Syncona Partners, which was founded in 2012 as an independent subsidiary of the Wellcome Trust, and takes a long-term view that focuses on the creation of sustainable healthcare businesses (see **case study 4**).

17. Research and innovation uptake across the NHS must be improved. The Association of Medical Research Charities' *Vision for research in the NHS*[6] sets out a helpful framework in this area and describes how the Health Service can better support research, offer patients the opportunity to be involved in research, and improve the adoption of new treatments. Academic Health Science Networks should also play a key role in promoting the adoption of innovations across the NHS by bringing together academic and clinical expertise to develop and share best practice.

Creating an environment that supports research

18. Today's grand challenges in health will only be solved with multidisciplinary working across sectors, including the humanities and social sciences. We must ensure that effective networks, platforms and facilities are in place to bring people from diverse areas together (see **case study 5**). R&D clusters provide one way to facilitate collaboration, promote knowledge sharing, accelerate innovation and foster local economic growth. They create an environment that helps cross-sector partnerships to flourish and the close proximity of organisations gives people a degree of career flexibility.

19. The regulatory environment must promote proportionate standards and safeguards that facilitate research and innovation, while protecting research participants and

[6] Association of Medical Research Charities (2013) *Vision for research in the NHS* http://www.amrc.org.uk/blog/our-vision-research-nhs

maintaining public trust. This is necessary to ensure we deliver benefit to patients as efficiently as possible and provide a competitive research environment by limiting costly regulatory requirements and delays. The establishment of the Health Research Authority has been an important first step in streamlining the regulatory framework. Effective European legislation is also a priority given its impact on the UK.

20. Research using animals has enabled major advances in our understanding of disease and led to the development of nearly every type of drug, treatment or surgical procedure in contemporary medicine. We welcome Government moves towards greater transparency, particularly its review of Section 24 of the Animals (Scientific Procedures) Act. The strategy must be explicit about the importance of animal research and maintaining an open dialogue between researchers and the public in this area, whilst ensuring proportionate and appropriate protection.

21. It is vital that the outputs of research are made freely available so that they can be accessed and used to advance knowledge, further our understanding of disease and drive societal benefits. Enabling greater access to research datasets can also spark economic growth and improve public services. The Government has taken a global leadership role in promoting open access to research publications and data. We look forward to continuing to work in partnership in this area.

22. The strategy must promote a culture of public engagement, increasing people's trust, support and interest in science and its application, and fostering a shared sense of ownership about its contribution to quality of life, society and economic development. The Trust strives to be a leader in our approach to engagement, working in partnership with science and research, arts and other cultural groups to create inclusive and wide-ranging opportunities. We also support the Government's *Charter for UK Science and Society*[7] and the *Concordat for Engaging the Public with Research*[8].

Securing the STEM workforce and inspiring tomorrow's scientists

23. A recent Campaign for Science and Engineering report[9] highlights that the UK has an estimated annual domestic shortfall of around 40,000 new STEM skilled workers. Sustainably growing the workforce must be a key priority. The STEM pipeline starts early, and well-equipped and inspired students will form the next generation of science leaders, innovators, researchers, technicians and healthcare workers. For this reason, the Trust has a long-standing commitment to supporting high-quality, stimulating science education for young people. This will also enable all students to obtain the skills and knowledge needed to live in an increasingly technological world.

24. Science teachers should have annual entitlement to subject-specific, high-quality professional development. This enhances teacher knowledge, confidence, progression and retention, and boosts student performance. Primary teachers should also have access to professional development to help increase science expertise at this stage, and science graduates should be incentivised to train as primary teachers.

25. The Government must ensure that all students study a balance of biology, chemistry and physics up until the end of Key Stage 4. Schools should also be accountable for the quality of their practical science provision — this is an essential part of training for university study, higher apprenticeships and jobs in science and engineering. This broad and rich knowledge is essential for progression in any particular science post-16 and will facilitate future 'discipline-hopping'. It also enables people to make more informed decisions in their lives, from healthcare to choices about new technologies or sustainable diets.

[7] BIS (2014) *UK Charter for Science and Society* https://scienceandsociety.blog.gov.uk/uk-charter-for-society/
[8] Research Councils UK (2010) *Concordat for Engaging the Public with Research* http://www.rcuk.ac.uk/Publications/policy/perConcordat/
[9] Campaign for Science and Engineering (2014) *Improving Diversity in STEM* http://sciencecampaign.org.uk/CaSEDiversityinSTEMreport2014.pdf

26. Careers guidance needs to be improved across schools and colleges so that all students appreciate the breadth of opportunities in science, and are not limited by their background or schooling.

27. We are a signatory of the *Concordat to Support the Career Development of Researchers*[10] and expect organisations that hold our grants to adopt its principles. This sets out a vision to improve the attractiveness and sustainability of research careers, including the need for transparent recruitment procedures, recognising researchers as an essential part of the workforce, encouraging adaptability and flexibility, supporting development, and promoting diversity and equality.

28. Science is a global endeavour and it is critical that the UK's immigration policies attract and retain the very best researchers. While we have been pleased to see a streamlined endorsement process for the Tier 1 Exceptional Talent and Exceptional Promise visas, we are aware of a number of occasions when researchers from outside of the EU have had problems obtaining visas for team or family members, or have been refused visitor visas to attend scientific meetings and interviews in this country. This is detrimental to science and does not signal that the UK is 'open for business' or supportive of international research.

Conclusion

29. We look forward to seeing the Government's Science and Innovation Strategy at Autumn Statement. It is important that this vision sets out the direction of travel for UK research and outlines a plan for investment as economic conditions improve. We would be happy to give further input as it develops over the coming months, and would be pleased to discuss any of these points in more detail.

Case study 1: Progress through partnership: the Health Innovation Challenge Fund

The Health Innovation Challenge Fund is a partnership between the Wellcome Trust and the Department of Health. The scheme offers translational funding to progress innovative healthcare ideas from proof-of-concept to early clinical studies in man.

The Health Innovation Challenge Fund focuses on stimulating the creation of innovative healthcare products, technologies and interventions, and facilitates their development for the benefit of patients in the NHS and beyond. It has a succession of thematic calls for proposals that focus on unmet healthcare needs, ranging from innovative diagnostics to surgical technologies.

One project supported by the initiative is led by Professor Robert MacLaren at the University of Oxford. His team is conducting a multicentre programme to develop a gene therapy for choroideremia — an incurable degenerative disease that causes progressive loss of vision. Affecting 1 in 50,000 people worldwide, it is caused by the deficiency of a specific protein encoded by the choroideremia gene (CHM).

Professor MacLaren's group has developed a procedure that allows defective copies of CHM to be replaced in cells in the eye. Phase I safety trials have shown very promising early results and if the degeneration can be slowed, this procedure would represent the first treatment for choroideremia and the first successful application of a gene therapy targeting a photoreceptor disease.

[10] Vitae (2008) *Concordat to Support the Career Development of Researchers* https://www.vitae.ac.uk/policy/vitae-concordat-vitae-2011.pdf

Case study 2: Producing a more stable vaccine for foot and mouth disease

The outbreak of foot and mouth disease (FMD) in 2001 cost the UK economy over £8 billion. Now scientists from the Pirbright Institute, the Universities of Oxford, Reading and Dundee, and MSD Animal Health are developing a new vaccine which overcomes many of the previous limitations. The research is currently funded by the Trust, but has also been funded by the Biotechnology and Biological Sciences Research Council and the Department for Environment, Food and Rural Affairs.

Current vaccines against FMD are based on a live but inactivated virus and have serious drawbacks. They have to be produced in expensive facilities with extremely high levels of containment and are unstable, needing to be refrigerated during storage and transport.

This new method uses the outer shell of the virus — the 'capsid' — without any of the genetic material that enables it to cause an infection. Working at the UK's Diamond synchrotron, which allows the FMD virus to be visualised at the atomic level, the team was able to engineer the empty capsids, atom-by-atom. This improves their stability and keeps their structure as close to the original virus as possible.

The new 'synthetic' capsid is more stable than existing vaccines. Because it does not use the live virus it is safer and cheaper to produce, and is easier to transport and store. Importantly, because the new vaccine does not include all the proteins of a live virus, it should also be possible to distinguish between vaccinated and infected animals, enabling farmers to continue to export cattle globally.

An affordable vaccine that does not require a cold storage chain will help to control FMD in Asia and Africa where it is currently endemic. Not only does the disease place a huge economic burden on low-income countries, but it also increases the threat of reintroducing the disease in other locations. An initial vaccine efficacy trial has been successful and the commercial version should be available within six to eight years. The vaccine development technology should also be transferable to other viruses from the same family which includes polio and hepatitis A.

Case study 3: Maximising UK infrastructure to support informatics research

The Farr Institute of Health Informatics Research brings together researchers from across the UK to build capability and enable linkage and analysis of anonymised health and health-related datasets. It was established by a consortium of funders which includes the Trust.

Electronic patient records offer real potential to improve healthcare and advance biomedical research, and NHS cradle-to-grave records of the entire population give the UK a unique advantage. Cutting-edge research using large health datasets enables a wide range of impacts, from the development of more effective treatments, to improved drug safety and the identification of public health risks.

In 2012, ten UK funders invested £19 million to strengthen the UK's capability and competitiveness in this field, and four centres of excellence in e-health informatics research were established in Dundee, London, Manchester and Swansea. In 2013, the Medical Research Council invested a further £20 million of capital to create the overarching Farr Institute of Health Informatics Research.

The Farr Institute aims to deliver high-quality, cutting-edge research linking electronic health data with other forms of research and routinely collected data. Although work is led from Dundee, London, Manchester and Swansea, Farr brings together 24 academic institutions and two MRC units based across the UK. It also facilitates collaborations by providing a physical structure to co-locate NHS organisations, industry, and other UK centres. Capacity Building activities across Farr will also train a new cadre of health informaticians and related methodologists, with coordinated training that is open to researchers at all stages of their career.

Case study 4: Syncona's approach to long-term healthcare investment

Launched in 2012 as an independent subsidiary of the Wellcome Trust, Syncona Partners is an 'evergreen' investment company. It supports the creation of sustainable healthcare businesses, backing partner companies over the long-term to enable them to grow and succeed. It will invest globally and at any stage, funding both start-ups and established businesses.

In March 2014, Syncona invested £12.8 million in newly-formed company Blue Earth Diagnostics, who focus on developing imaging agents for use in positron emission tomography (PET) scanning — this produces detailed three-dimensional images of the body and is an important diagnostic tool. Blue Earth's lead agent is fluciclovine which can be used to image recurrent prostate cancer. Prostate cancer is the second leading cause of cancer in men worldwide and approximately 35% of patients who receive radical first line treatment will subsequently experience recurring disease which is not detected by conventional imaging. Clinical studies have shown that fluciclovine can detect local or metastatic cancer, and could stratify patients, direct therapy choices and improve outcomes.

Syncona has also supported Professor Robert MacLaren's work to develop a gene therapy for choroideremia (see **case study 1**), funding £12 million to support phase II clinical studies and further develop this treatment through the creation of a spin-out company called NightstaRx.

Case study 5: Innovation at the interface between disciplines

The Medical Engineering Initiative is a £41 million collaboration between the Trust and the Engineering and Physical Sciences Research Council. It has funded four new centres of excellence since 2009, which together have leveraged over £140 million of funding and filed 29 patents.

Engineers have made a huge contribution to medical innovation and millions of people have benefited from their inventions, which include implants and prosthetic limbs, devices to monitor patients, and instruments to maintain the body's functions. Interdisciplinary working across medicine and engineering can revolutionise healthcare, and the centres support this by bringing together mathematicians, physical scientists, engineers and medical researchers.

Imperial College London's Medical Engineering Solutions in Osteoarthritis Centre of Excellence uses emerging technologies to improve the management of osteoarthritis — the most common cause of chronic pain in the UK. Its inventions include new surgical implants, an artificial knee joint meniscus, a novel neck of a replacement femur and a total shoulder replacement implant. It has also generated significant IP for lower limb modelling which will increase our understanding of the changes that occur as osteoarthritis progresses.

The **King's College London Medical Engineering Centre** focuses on medical imaging. Its key achievements include the development of a steerable catheter, a novel imaging agent for the detection of plaques and aneurysms to aid cardiovascular disease diagnostics, and *in vitro* mineralisation and blood vessel formation using bone, endothelial and stem cells. It has also spun-out a company to commercialise a tool that enables surgeons to align preoperative CT images with real time fluoroscopy during aneurysm repairs.

The **University of Leeds WELMEC Centre of Excellence in Medical Engineering** focuses on developing new ways to extend human joint and cardiovascular health. It has produced the world's first natural knee joint simulation system in collaboration with industry, and its new technologies include low wear bearings for use in knee joints, scaffolds for pulmonary and aortic valve replacements, and a patented peptide for faster repair of damaged teeth. Its dCELL® vascular repair products are also being co-developed for ligament, tendon and meniscus repair.

The **University of Oxford's Centre of Excellence in Personalised Medicine** is developing techniques and strategies to measure an individual's response to their condition and treatment. Its achievements include the development of a new image-based biomarker for growth restricted babies in the womb, a technology that enables ultrasound-mediated localised drug delivery, and the creation of a spin-out to monitor heart rate, respiratory rate and oxygen saturation using a standard webcam.