# House of Commons Select Committee on Science and Technology: Inquiry into genomics and genome-editing

## Response by the Wellcome Trust, Association of Medical Research Charities and Cancer Research UK

30 January 2017

### Key messages:

- Genome editing and genomics have huge potential for research and ultimately to improve human health. We support the use of genome editing in a research context when the studies are legal and ethically and scientifically justified.
- The UK provides a robust but supportive environment for the use of genome editing in health. As genome editing technologies develop, regulation will need to keep pace to maximise health benefits while managing social and ethical concerns.
- It is crucially important that public engagement is embedded as the science progresses and throughout the process of developing regulation.
- Combined with its strong science base in genomic technologies, The UK is in a strong position to be a global leader in the development and proportionate regulation of genomic and genome editing technologies. There is an opportunity with the upcoming Industrial Strategy to capitalise on this existing strength.

We welcome the opportunity to respond to this inquiry, though we note that the criteria are incredibly broad and the two topics are too large in scope to be considered together in any detail. We are willing to provide further evidence to the Committee to expand on any of the points raised here.

### 1. The impact of genomics and genome-editing on:
### a. wildlife and ecosystems, including potential uses in relation to infectious disease, re-introducing extinct species and controlling predator populations;

Genome editing

1. Gene drive research is a form of genome editing which can influence particular genetic characteristics to spread rapidly through a population; one application is to control the spread of some infectious diseases. It is a technology with many promising applications in public health, particularly in addressing vector-borne diseases such as Zika, Malaria or Dengue. The applications in the UK of such infectious disease research are limited, but with its excellent science-base the UK has a significant role to play internationally in ensuring a supportive environment for gene drive research that may have significant benefits for human health.

2. The House of Lords Science and Technology Select Committee[1] points to principles of a constructive path forward in developing applications of gene drive technology by ensuring the EU regulatory regime does not hold back new GM technologies. We support its recommendations that the government invest in scientific trials to test the science, regulatory processes and policies behind GM insects and catalyse a comprehensive public engagement exercise.

[1] Science and Technology Committee 'Genetically Modified Insects' http://www.publications.parliament.uk/pa/ld201516/ldselect/ldsctech/68/6802.htm

**c. human health, with regard to treating disease, avoiding genetic disease and human enhancement**

Genome editing

3. Recent technological developments such as CRISPR-Cas9 have cast a spotlight on the potential clinical applications of gene-editing, as the technique is efficient, quick and inexpensive. It holds significant potential for improving human health (Case Study 1: Second generation CFTR gene repair) but these uses need to be justified by sufficient evidence of safety and efficacy.

4. Research to date has focused primarily on editing in somatic cells (non-reproductive cells in the body) with the aim of repairing or eradicating mutations in the DNA that could cause disease, or to engineer beneficial changes for cell therapy (Case Study 1). Editing of germline cells (sperm or egg cells) raises greater ethical issues as changes made can be passed onto future generations. The technology is not yet developed enough to be suitable for therapeutic and clinical use. We strongly support the use of genome editing technologies as a research tool, and research to further develop potential clinical applications of this in both somatic and germline cells.

**Case Study 1: Second generation CFTR gene repair**

Cystic fibrosis is a life-limiting inherited condition caused by tiny, yet crucial 'typing' errors in the CFTR gene. The Cystic Fibrosis Trust is funding a study which aims to restore normal CFTR gene function by correcting these 'typos'. Using CRISPR/Cas9 technology, the study team are looking at cutting out a stretch of DNA where the six most common CF-causing mutations (and more than 80% of the rarer ones) are located, and replacing this region with the normal sequence. If successful, this study will allow permanent correction of more than 80% of cystic fibrosis mutations in cultured lung cells.

Genomics

5. Genomic medicine has huge potential for identifying genetic predispositions to disease (Case Study 2: TREM2 genetic discovery). For example, knowing that a patient has a genetic predisposition to a certain type of cancer, justifies more regular screening to spot cancer early if it develops, or enables a decision to offer elective treatment such as mastectomy to ensure a cancer does not develop. Patients can also be given an early opportunity to make changes to their lifestyle if their predisposition is related to an environmental factor.

6. Genomic technology facilitates sophisticated diagnoses and tailoring of medical treatments to the individual characteristics of each patient. Through precision medicine we have the ability to classify individuals into subpopulations that differ in the biology that will have implications for their prognosis, or in their expected response to a specific treatment. Interventions can then be concentrated on those who will benefit, sparing side effects for those who will not (Case Study 3: Precision Medicine). There is also an economic benefit to the NHS through preventing wastage of therapies that are unlikely to work. Specific characteristics of disease progression can also be identified by looking for genomic markers which can indicate whether a patient is responding to a treatment and inform their next steps.

**Case Study 2: TREM2 genetic discovery**

An Alzheimer's Research UK funded Fellowship made a landmark genetic discovery which threw a spotlight on the role of the immune system in Alzheimer's. This found that rare variations in the DNA code of an immune gene called TREM2 could triple a person's risk of Alzheimer's. The discovery sparked a new wave of research across the globe, providing strong evidence that the body's natural defence mechanism may be driving the progression of the disease.

**Case Study 3: Precision Medicine**

Cancer Research UK, working in partnership with pharmaceutical companies, is leading precision medicine research with the National Lung Cancer Matrix trial. As part of the Experimental Cancer Medicines Centres network, researchers are using the genetics of lung tumours to identify small groups of patients who because of the specific genetic changes causing their cancer, are more likely to benefit from a certain drug. This allows several drugs to be assessed within a single trial. Trials like this hopefully speed up the development of new, tailored treatments for patients. It is vital that such trials are supported by the NHS, and are able to recruit patients from a multiple sites.

**2. Whether current regulations in particular areas of genomics and genome-editing are consistent, and whether they are adequate to meet the requirements of different 'product' and 'process' based approval processes;**

7. As genomic technologies progress, a pragmatic regulatory framework will need to keep pace with the science to maximise the potential benefits to health.

Genome editing

8. The different applications of genome editing in human biology - research, somatic cell therapy, and germline therapy - are at different stages of development and associated with different risks and implications. It is therefore important that these different applications are regulated appropriately and proportionately. The UK has a strong track record in robust, risk proportionate regulatory processes that adapt to developments in technology.

9. We believe that the UK currently strikes a good balance with the regulation of genomic and genome editing technologies. The Human Fertilisation and Embryology Authority licenses genome editing in embryos for research on a case by case basis, but the legislation does not permit germline editing. At present there is no clear case for adjusting this legislation. If in the future there are significant potential benefits for the clinical use of germline editing then a roadmap to allow the clinical use of germline editing will need to be carefully mapped out while addressing social and ethical concerns. Mitochondrial donation is one example of how this can be done effectively (Case Study 4: Mitochondrial donation).

10. The application of genome technologies in plants, animals and microbes is covered by EU legislation on genetically modified organisms (GMOs). The European Commission is yet to clarify their position on whether organisms produced by genome editing are covered by existing GMO legislation. Clarity here would help reduce uncertainty, and improve regulatory approval times.

11. Regulatory changes for new technologies need to be underpinned by comprehensive public engagement to ensure the change is acceptable and sustainable for the communities affected by these developments, for example where Genetically Modified Insects (GMI), crops and animals are to be released for vector control.

**Case study 4: Mitochondrial donation - lessons from other technologies**
Mitochondrial donation is a clear example of successful public debate and engagement on a controversial scientific issue that had social, ethical and legal aspects and connected research, regulation and the public. The Human Fertilisation and Embryology (Mitochondrial Donations) Regulations provided a framework for the use of new techniques for the prevention of mitochondrial disorders and were passed by the UK Parliament in 2015. These were the culmination of seven years of dialogue and scrutiny, including independent ethical reviews, three separate reviews of the scientific evidence on the techniques' safety by an independent panel of experts [1], and an independently validated public consultation [2], which revealed broad public support.

[1] http://www.hfea.gov.uk/6372.html
[2] http://www.hfea.gov.uk/docs/Mitochondria_evaluation_FINAL_2013.pdf

Genomics

12. One area in which regulations are not proportionate is for innovations in diagnostic tests involving genomic technologies. Regulation needs to be pragmatic and not adopt a 'one-size-fits-all' approach throughout the development pathway. Case study 5 is just such an example of when an inflexible approach to application of the EU In Vitro Diagnostics regulation could hamper innovation in this field.

**Case Study 5: In Vitro Diagnostics regulation**
CE Marking on a product is a manufacturer's declaration that a product complies with the essential requirements of the relevant European legislation and indicates that the product may be legally placed on the market in an EU member state. When initial research is being conducted to identify whether there is any relationship between a drug and a genetic mutation (clinical utility), it would be disproportionate to require diagnostic tools to meet the standard of CE marking. Many academic trials that allocate patients to different treatments depending on their genetic mutation are run in laboratories that adhere to Good Laboratory Practice (GLP). They have UK Accreditation Service (UKAS) accreditation, robust validation processes, and participate in the National External Quality Assurance Scheme (NEQAS) in addition to regular sample swaps between testing labs. These standards allow locally-developed tests to be of high quality and robustness, and should be sufficient at this early stage of the diagnostic development pathway without the need for CE marking.

### 3. The ethical, social and safety concerns from genomics/genome-editing in the treatment of disease and its impact on the environment;

Genome editing

13. The use of genome editing raises numerous important ethical questions, particularly in germline genome editing. Active early engagement with the widest range of stakeholders must be undertaken prior to any exploration of potential clinical applications.

14. The differences between somatic and germline research, and the differences between research and clinical applications, need to be carefully distinguished in ethical discourse about the benefits and risks of genome editing technologies.

15. It is important to ensure that as new genome editing technologies rapidly develop, the science and innovation do not move too far ahead of public understanding and policies. Significant anxieties and distrust can result if there is insufficient engagement and objective exploration of the risks, benefits, potential harms and uncertainties surrounding the introduction of complex new technologies[2]. The introduction of mitochondrial donation regulations is a good illustration of how this can be done well and generate significant public support for a crucial new technology (Case study 4).

16. It is important that when complex ethical issues arise as a result of the development of genomic technologies, scientists and ethicists can be convened at an early stage to debate and discuss these. Groups such as The Hinxton Group and the Nuffield Council on Bioethics are well established to bring global experts together in this way to address these issues and concerns as they emerge.

17. Public concerns about the introduction of GM crops provide a lesson about the dangers of not engaging the public effectively in this discourse. Companies and academics proposing release of GMIs, GM crops and GM animals need to engage regulatory authorities, citizen groups and the Government from an early stage, ensuring dialogue with all groups in the community. We strongly believe that people need to understand both the risks and the benefits of these GM technologies so that they can come to an independent and well-informed view.

Genomics

18. If the scale of genomic testing is increased, it is vital that patients are made aware of how their genomic data could be used, both for their own individual care and the potential for other uses to improve health, care and services through research and planning. This will ensure that fair processing requirements under data protection legislation are met and will ensure that there is ongoing trust and support for research that relies on the use of genomic data.

[2] Nuffield Council on Bioethics 'Genome editing: an ethical review' http://nuffieldbioethics.org/project/genome-editing/ethical-review-published-september-2016/

19. Linking genomic and clinical data provides a wealth of opportunities for research, specifically for optimising treatments and developing robust prognostic markers at the population level. For cancer treatment, the most value would be derived from linkage of genomic data with the cancer registry.

20. Patients are generally incredibly supportive of their cancer data being used: 94% of people with cancer supported their cancer data being used for research; 89% supported their data being used for direct care. However, patients would like to be told about this: 83% believed it is important that people with cancer are informed about the cancer registry[3].

21. To ensure that use of genomic data is supported, communication must be planned and information delivered effectively and accessibly to patients, health professionals and the public. For example, work to ensure awareness of the cancer registry is currently being undertaken by Public Health England[4] following recommendations made by Cancer Research UK and Macmillan Cancer Support[5].

### 4. Genomics England's 100,000 sequenced genomes initiative, including its progress and safeguards (including data consent and security);

22. The 100,000 genomes project is an ambitious initiative and the ability to link genomic data to medical records has great potential. Providers must be supported and effectively resourced to undertake this approach, so that genomic diagnosis can be implemented as a standard of care within the NHS.

23. From the outset of the initiative, Genomics England established an Ethics Advisory Group to help steer its consent processes and ensure a rigorous ethical framework for how genomic data was collected, managed and used. We consider the inclusion of ethics advice early on in the process important to the progress and success of the 100,000 genomes project. Genomics England have also worked hard to improve sample acquisition pathways and their aim to have an additional sample taken for research at diagnosis would revolutionise pathology-based approaches to cancer treatment.

24. Genomics England is laying strong foundations for genomic medicine already and the resulting infrastructure, including the Genomic Medicine Centres could be used to drive the adoption of genomic medicine in the healthcare system more generally. The NHS should be fully equipped for genomic medicine across the UK and allow genomics to become as mainstream as other testing.

### 5. The adequacy of investment in infrastructure and skills/training in the NHS to take forward genome medicine;

25. To ensure that the NHS benefits from new technologies it is essential that healthcare professionals have appropriate education, training and resources to use them. New technologies, such as genomics, must be adopted into generalist and specialist curricula in a timely fashion to facilitate the uptake of innovation across the NHS.  This includes increased resource and expertise in the precision medicine support workforce, including: molecular pathologists, bioinformaticians, statisticians, clinical geneticists, genetic counsellors. The UK currently has major skills gaps for these roles[6.]

26. It is critical that genomics research is funded across all parts of the innovation chain, from basic research through to clinical products. The focus on treatment outputs as a key indicator of success should not lead to a funding shift towards later-stage research, particularly as incomplete knowledge of the basic biology is one of the primary barriers in the field.

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[3] Ipsos MORI, 2016: 'Perceptions of the cancer registry: attitudes towards and awareness of cancer data collection', Cancer Research UK and Macmillan Cancer Support. http://bit.ly/2hQQQmh

[4] National Cancer Registration and Analysis Service, Public Health England: http://www.ncras.nhs.uk/

[5] Cancer Research UK and Macmillan Cancer Support, 2016: 'Review of Informed Choice for Cancer Registration' http://bit.ly/2iPvqrC

[6] ABPI 'Bridging the skills gap in the biopharmaceutical industry': http://www.abpi.org.uk/our-work/library/industry/Documents/Skills_Gap_Industry.pdf

27. Lessons must be learned about how best to approach this type of challenge from evaluating the implementation and development of Genomics England, including the importance of effective communication across the NHS.

28. The Government and the NHS need to ensure that the IT infrastructure and workforce are capable of supporting genomic medicine, which involves huge amounts of data. The health service should move towards a panel testing approach for molecular diagnostics, which produces significantly less data than whole genome and whole exome approaches. Panel testing would support access to existing approved medicines, avoid side-effects in those patients for whom certain treatments would not work, and lead the development of new precision drugs by identifying patients suitable for clinical trials. Government should also seek to develop a policy on access to molecular diagnostic tests within the NHS, which help to detect the genetic mutations that allow us to separate patients into groups.

29. Targeted diagnostics should be used for example in situations in which sample tissue is limited or for confirmation of the presence of a known mutation. In 2015 the Department of Health announced that an additional £300m per year will be provided for cancer diagnostics by 2020, including 25,000 more molecular diagnostic tests per year[7]. While this is a positive development, this funding is unlikely to cover the full range of tests performed, for cancer or for other genetic conditions.

**6. The extent to which genomics should be part of the Industrial Strategy initiative**

30. Government has made it clear that science will be at the heart of its Industrial Strategy. We welcome Government's intention to strengthen the global standing of UK research and its commitment to increase the science budget by £2 billion a year by 2020.

31. Genomics can play a key part in a future industrial strategy. The UK has the existing expertise, is already one of the world leading places to do genetic research, and has a strong record in handling complex ethical issues associated with new technologies. Additional Government support and investment can further enhance the UK's genomics capability across academia and industry.

32. A good example of this additional investment to strengthen an existing structure is the UK Biobank's genotyping project. Using the world's leading cohort of 500,000 participants, funders and government investment has allowed large scale genetic analysis which will improve understanding of hundreds of conditions and support the life sciences industry to develop improved diagnosis and treatments. Additionally, the National Institute for Health and Biomedical Informatics Research funded by the MRC could bring together academic, industry and health service to support digital innovation in life sciences.

33. The UK is not only a world leader in the life sciences but has the unique benefit of the NHS. This makes the UK the best place in the world to initiate the practical use of genomics for patient benefit.

34. Government's investment in research supports the UK economy in a number of ways. It attracts private investment from overseas, builds a skilled workforce and contributes towards the generation of income from commercialised products. The industrial strategy is an opportunity for the UK to put science at the heart of its plan for growth.

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[7] Department for Health 'From 2020, people with suspected cancer will be diagnosed faster' https://www.gov.uk/government/news/from-2020-people-with-suspected-cancer-will-be-diagnosed-faster