



House of Commons Science and Technology Committee Genomics and Genome editing Inquiry:

Written evidence jointly submitted by the Society for Applied Microbiology (SfAM) and the Microbiology Society (GEN0057)

Summary

1. This joint response from the Society for Applied Microbiology (SfAM) and the Microbiology Society (Appendix 1) emphasises the importance of considering genomics and genome editing in relation to fundamental and applied microbiology science involving bacteria, viruses, fungi and other microorganisms. Our response highlights:
 - 1.1. Techniques for sequencing and modifying genomes have been an integral part of fundamental and applied microbiology since genomics studies began. Consequently, genome sequencing and engineered microbes contribute greatly to the significant impacts being seen within microbiological research. These innovations span many areas, including health, agri-food, environmental science and industrial biotechnology.
 - 1.2. Fundamental microbiology underpins the discovery and development of many transformative, widely-used tools for genomics such as CRISPR/Cas.
 - 1.3. Improved techniques for genome sequencing, ever-increasing repositories of microbial DNA sequence data and advanced gene editing technologies are making microbial genomics easier and more cost-effective. These advances are driving new research across different areas of microbiology, for example, the discovery of microbial diversity, investigating the evolution and spread of infectious diseases and antimicrobial resistance, and microbial biotechnology for biomedical and industrial applications. UK scientists are at the forefront of much of this research.
 - 1.4. Some microbiology-relevant issues relating to skills and infrastructure, regulation, and social and ethical considerations.
2. We note that the breadth of 'genomics and genome editing' means that our response is by no means comprehensive. We highlight some examples of where genomics and genome editing is impacting on microbiology and its applications, and some related issues raised by our members. Our response is complementary to the written evidence submitted by the Royal Society of Biology (RSB); both SfAM and the Microbiology Society are Member Organisations of the RSB.

Impacts of microbial genomics and genome editing

Microbiology is a driver of genomics and gene editing technologies and these technologies have significantly advanced the study of microbiology.

3. Fundamental microbiology research has driven, and continues to drive, the discovery and development of transformational and universal tools and techniques for all genomics and genome editing research. Advances in these technologies and their application to microorganisms are revolutionising microbiology and its applications across many areas, including human and animal health, agri-food, environmental science and industrial biotechnology.

Gene editing and genome engineering:

4. Techniques for modifying and engineering genomes are mainly derived from fundamental blue skies research on the genetics of bacteria, viruses and other microorganisms, from the discovery of restriction enzymes, through development of gene cloning technology, to CRISPR/Cas genome editing.
5. Editing and engineering of microbial genomes is not novel, in contrast to human genomes. However, CRISPR/Cas and other new targeted gene editing methods are more accurate and efficient than many existing technologies. Longstanding use of technologies for gene editing and genome engineering by microbiologists for fundamental and applied science provides a wealth of experience and valuable knowledge to the research community.
6. The examples below highlight existing widespread use of engineered bacteria and viruses in research and biotechnology across health, agri-food and bio industry. Research efforts have also pushed the boundaries of new possibilities, including the construction of entire microbial genomes (e.g. poliovirus) from chemical precursors and the development of bacteria with newly-designed DNA bases not seen in nature.¹ However, the beneficial impacts of these synthetic genomes have yet to be realised.
7. We also note that knowledge of genome sequences is important for the application of genome editing technologies such as CRISPR/Cas, which require accurate knowledge of an intended DNA sequence target. Consequently, access to easily available microbial DNA sequence data and low cost synthetic DNA has been vital to revolutionising the application of gene editing.

Genome sequencing:

8. Microbial genomics has played a key role in the progression of genome sequencing capabilities, which now allow us to readily sequence the genomes of more complex organisms. For example, beginning in the 1970s the first genomes sequenced were those of viruses of increasing size and complexity; the first prokaryote genome was sequenced in 1995 (the bacterium *Haemophilus influenza*); and the first unicellular eukaryote genome was sequenced in 1996 (*Saccharomyces cerevisiae*, Baker's yeast). Modern sequencing techniques, such as next-generation sequencing (NGS), whole genome sequencing (WGS) and metagenomics, and cheaper and faster sequencing,

¹ <https://www.theguardian.com/science/2017/jan/23/organisms-created-with-synthetic-dna-pave-way-for-new-entirely-new-life-forms> accessed 30-01-17

have accelerated progress, led to new discoveries across microbiology research, and provided new areas of study.

9. WGS allows the complete DNA sequence of an organism's genome to be determined in one procedure. Genome data are then used to identify and compare different microbial strains accurately, detecting subtle differences in DNA makeup, facilitating disease surveillance, environmental monitoring and food chain surveillance. WGS is also rapidly becoming cheaper, faster and more accessible through development of new technologies such as the portable MinION kit.² The Society for Applied Microbiology's position statement on WGS highlights that, if supported by sufficient training and infrastructure, WGS techniques complement the existing toolbox of traditional molecular and culture-based techniques used in the clinical setting.³
10. Metagenomics, which involves sequencing the collective DNA of all microbes from an environmental or host sample, and high-throughput sequencing of single genes (e.g. 16S rRNA genes, aka metataxonomics) that can be used to distinguish different microbes, have also been important enabling techniques for microbiology research and discovery. Advances in these approaches and other 'omic techniques have been important drivers of the rapidly growing area of microbiome research, in which data on microbial genomes, proteins and metabolites are used to investigate the diversity and activities of microbial communities associated with different hosts (e.g. humans, animals, plants) and environments (e.g. marine, soils, built environment). Microbiome research stands to improve our understanding of health, disease, and environmental and industrial bioprocesses, in addition to revealing novel microbial genes, enzymes, drugs and other natural products of potential use. Use of these 'omic approaches has resulted in the discovery of much new microbial biodiversity and novel roles, which were previously undetectable, showing that we currently have only a rudimentary understanding of microbial biodiversity and microbiome function, with the potential for many new discoveries.
11. Although much microbiome research remains early stage, national and international consortia and projects are seeking to develop this area of science and associated skills, technologies and infrastructures. For example, the US Federal Government announced a National Microbiome Initiative in 2016, including Federal agency investment of \$121m over two years, in addition to substantial external investment.⁴ UK microbiologists are involved in a wide range of EU- and UK-funded microbiome research projects. The Microbiology Society has established a Microbiome Expert Working Group to explore the challenges and opportunities associated with this rapidly growing area of research across health, agri-food, environmental science and industrial biotechnology.⁵

Impacts of microbial genomics and genome editing for food security, safety and production

Food safety and security:

12. Microbes impact significantly on the entire food supply chain. Some of these are harmful, reducing productivity by killing crops and livestock, causing food spoilage and ultimately

² <https://nanoporetech.com/> accessed 19-01-17

³ SfAM position statement on whole genome sequencing, <http://www.sfam.org.uk/en/about/policy/position-statements.cfm>

⁴ <https://obamawhitehouse.archives.gov/the-press-office/2016/05/12/fact-sheet-announcing-national-microbiome-initiative>

⁵ <http://www.microbiologysociety.org/policy/microbiome-policy-project.cfm>

resulting in human disease through food contamination. The 2011 *E. coli* outbreak in Germany provides a vivid example, the deadliest in recent history, and highlights one of the first cases where WGS was used to both identify the rare O104:H4 strain responsible and trace the source of foodborne illness.⁶ Genome sequencing has become a key tool for food microbiologists and epidemiologists, allowing new capabilities. For example:

- 12.1. In 2014, whole genome sequencing data from Public Health England was used to trace a European-wide outbreak of *Salmonella* infection to a single European egg producer. This example was used by the Food and Agriculture Organisation of the United Nations (FAO) in 2016 to demonstrate that WGS may contribute to "*greater consumer protection, trade facilitation, and food/nutrition security*".⁷
- 12.2. Analysis of microbial genomes throughout the entire food chain is also being investigated. For example, IBM and Mars Inc. have established a large-scale project which will utilise genomics alongside big data technology to establish a "*microbial baseline*", essentially a "*benchmark representing normal microbe communities, which food and health officials can use to understand what triggers contamination and the spread of disease*".⁸
- 12.3. Antimicrobial resistance (AMR) poses a threat to the health of humans and livestock generally, as well as posing a significant global food security risk.⁹ Genome sequencing is used to identify newly-emerging AMR genes in bacteria, such as was the case in 2015 with the detection of the *mcr1* gene in bacteria from food animals, meat and people - encoding resistance to a last-resort antibiotic colistin. Microbiologists at the Animal and Plant Health Agency also detected the presence of the *mcr1* gene in British pig farms in 2016 and it has since been reported from many other countries.¹⁰ This evidence contributed to a European Medicines Agency recommendation that the use of colistin in animals be minimised, based upon opinion from the Antimicrobial Advice Ad Hoc Expert Group (AMEG).¹¹
- 12.4. Microbiologists have manipulated the genomes of viruses to develop extensively used vaccines that protect livestock and companion animals from a wide range of infectious diseases.¹² New genome editing techniques have the potential to grant quicker and easier production of such vaccines, as exemplified by the recent use of CRISPR/Cas9 for the development of a poultry vaccine against Marek's disease virus.¹³

Genomics and food production:

13. UK researchers are using high-throughput sequencing approaches such as metagenomics to investigate plant and soil microbiomes and pathogens associated with

⁶ European Food Safety Authority (2011). Shiga toxin-producing *E. coli* (STEC) O104:H4 2011 outbreaks in Europe: Taking Stock. *EFSA Journal* 2011; 9(10):2390

⁷ FAO (2016). *Applications of Whole Genome Sequencing in food safety management*. <http://www.fao.org/3/a-i5619e.pdf>

⁸ <http://www.research.ibm.com/client-programs/foodsafety/index.shtml> accessed 10-01-16

⁹ <http://www.fao.org/news/story/en/item/382636/icode/> accessed 20-01-17

¹⁰ <https://aphascience.blog.gov.uk/2016/11/18/colistin-an-antibiotic-of-last-resort/> accessed 20-01-17

¹¹ http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000639.jsp

¹² Lauer, K.B, Borrow, R. and Blanchard, T.J. (2016). Multivalent and Multipathogen Viral Vector Vaccines. *Clin. Vaccine Immunol.*, 24, 1, e00298-16; Li, Y. et al. (2011). Recombinant herpesvirus of turkeys as a vector-based vaccine against highly pathogenic H7N1 avian influenza and Marek's disease. *Vaccine*, 29(46), 8257-8266

¹³ <http://www.poultryworld.net/Health/Articles/2016/12/Is-GM-technology-the-future-of-poultry-vaccines-74867E/> accessed 30-01-17

crop systems.^{14,15} Such research could help inform agricultural methods to promote beneficial crop-microbe associations that reduce losses to disease, reduce fertiliser use, or enhance crop growth, and help identify novel biopesticides and biofertilisers.

14. Genomics is also being applied to study the microorganisms used in the production of fermented foods. For instance, metagenomic data of cheese-related organisms can be used to improve our understanding of how these microbes function and interact. This research could potentially identify new starter cultures and inform novel processes to improve food quality and consistency.¹⁶
15. UK microbiologists are also employing high-throughput sequencing and metagenomic techniques for research on the gastrointestinal microbiomes of chickens, cows and other livestock in relation to disease, health and nutrition, and improving the welfare, efficiency and sustainability of livestock production, and product quality.¹⁷

Impacts of microbial genomics and genome editing on health

Human microbiome research

16. There has been a rapidly growing interest in research on the human microbiome, the communities of microbes found in and on the body (e.g. mouth, skin, gut). Metagenomic and other 'omics' approaches are key enabling tools for this research and researchers are investigating potential links between the composition and genetic diversity of the human microbiome and health and disease, and the impact of factors such as diet and antibiotic use.

Genomics and infectious disease

17. Genomics has revolutionised fundamental and translational research on infectious diseases in humans and animals. Developments in whole genome and metagenomic sequencing are presenting new opportunities to improve detection and surveillance of infectious diseases. The value of genomic sequencing technologies has been reported extensively by the PHG foundation,¹⁸ Public Health England¹⁹ and in the POSTnote *Surveillance of infectious disease*.²⁰ In addition, we wish to highlight some key areas of current research raised by our members:

- 17.1. Epidemiology and surveillance:** Genomics informs effective public health responses through its application in monitoring the threat, origin and transmission of infectious disease outbreaks. For instance, in 2011 whole genome sequencing was utilised to investigate an outbreak of methicillin-resistant *S. aureus* (MRSA) in a neonatal unit in Cambridge, revealing a staff member as the likely source of disease spread.²¹ Genomics is also important for understanding virus evolution and spread, for example in the surveillance of current influenza strains. This technology

¹⁴ <http://www.microbiologysociety.org/policy/briefings.cfm/publication/food-security-from-the-soil-microbiome>

¹⁵ http://link.springer.com/protocol/10.1007/978-1-4939-6691-2_7

¹⁶ Bora, N. and Ward, A.C. (2014). *Analyzing the Metagenome of Smear Cheese Flora Using Next Generation Sequencing Tools. In Diversity Dynamics and Functional Role of Actinomycetes on European Smear Ripened Cheeses*, pp 137-153. Editors: Bora, N., Dodd, C. and Desmasures, N.

¹⁷ <http://www.ruminomics.eu/> accessed 08-01-17

¹⁸ <http://www.phgfoundation.org/project/id/> accessed 30-01-17

¹⁹ <https://www.gov.uk/government/news/whole-genome-sequencing-to-revolutionise-investigation-of-outbreaks-of-infectious-disease> accessed 30-01-17

²⁰ [Parliamentary Office of Science and Technology \(2014\). Surveillance of infectious disease. POSTnote 462](#)

²¹ <http://www.the-scientist.com/?articles.view/articleNo/33771/title/Real-time-Outbreak-Sequencing/> accessed 27-01-17

proved important in monitoring the 2014 Ebola outbreak²² and, importantly, in trying to understand why some people exposed to the virus did not contract the disease.

- 17.2. Microbiologists are taking advantage of whole genome sequencing technologies to support international efforts in tracking disease. The Global Microbial Identifier (GMI) is a key initiative that aims to provide an internationally-accessible store of genomic information and epidemiological data, to facilitate the tracking of infectious and foodborne disease.²³ UK-based experts remain a key contributor to the GMI, representing 10% (23 out of 228) of members. The *Microreact* project, supported by the Microbiology Society's peer-review journal *Microbial Genomics*, is another such initiative, providing a free data visualisation and sharing platform that allows scientists and health professionals worldwide to better understand disease outbreaks.²⁴ Genome sequencing approaches are also important for the development of automated surveillance systems, which will be designed to detect the spread of closely related microbial genomes. A clear advantage of such systems is the high potential for rapid identification of possible disease outbreaks and antimicrobial resistance.
- 17.3. **Diagnostics:** Developments in microbial genomics offer potential solutions for more accurate and rapid sequencing-based diagnostic tests for bacterial and viral infections, which has been identified as a crucial factor in reducing inappropriate prescription of antibiotics. For example, invited speakers at the Society for Applied Microbiology Antimicrobial Resistance meeting in 2016 highlighted genome sequencing as a method with high diagnostic potential, allowing microbes to be identified, by certain signature genes, from patient blood, urine and sputum.²⁵ Advantages include reduced sample preparation times and the potential to observe small populations of microbes that would otherwise be undetectable by conventional diagnostic methods.
- 17.4. Additionally, a member highlighted that the UK is at the forefront of new technologies such as Oxford Nanopore Sequencing and 'big data' centres that have the potential to transform microbiology, medicine and biomedicine yet further. Initiatives aimed at integrating genomic technologies into the NHS and devolved Public Health authorities will make our health services world-leading in the use of genomics to tackle infectious disease.
- 17.5. **Antimicrobial resistance:** Monitoring and predicting the risk of pathogen resistance to antimicrobial drugs from their genome sequences will likely enable more informed prescription of antimicrobials and promote antibiotic stewardship.
- 17.6. Metagenomics and WGS approaches are also enabling research to track the evolution and spread of antimicrobial resistant microbes and resistance genes between humans, animals and agricultural, urban and natural environments, which

²² Quick, J. et al. (2016). Real-time, portable genome sequencing for Ebola surveillance. *Nature*, 530, 228-232. See also <http://nextstrain.org/ebola/>, which tracks evolution of the Ebola virus in real-time.

²³ <http://www.globalmicrobialidentifier.org/about-gmi> accessed 19-12-16

²⁴ <https://microreact.org/> accessed 20-01-17

²⁵ Jeanes, C. and O'Grady, J. (2016). Diagnosing tuberculosis in the 21st century – Dawn of a genomics revolution? *International Journal of Mycobacteriology*, 5, 384-391; Schmidt, K. et al. (2017). Identification of bacterial pathogens and antimicrobial resistance directly from clinical urines by nanopore-based metagenomic sequencing. *Journal of Antimicrobial Chemotherapy*, 72, 104-114.

will, for example, enable quantification of the impact of antibiotic usage on the environment, an important area which to date has been relatively unexplored.

17.7. A Microbiology Society member also highlighted that Public Health England and microbiologists at the University of Oxford are involved in a global collaboration called *CRyPTIC*, which plans to sequence tens to hundreds of thousands of tuberculosis genomes from clinical samples collected around the world to find undiscovered drug resistance mechanisms and speed up diagnosis of the disease.²⁶

17.8. **Understanding host-pathogen interactions:** Genomics is also important for understanding interactions between hosts and pathogens. For example, next-generation genomic sequencing applied to transcriptomics (RNA-Seq) has been particularly powerful in understanding host responses to microbial infections, particularly the responses of cells infected with intracellular pathogens, such as viruses and bacteria like *Listeria* spp. and *Salmonella* spp.

17.9. **Infectious diseases of plants and animals:** Genomic sequencing is also increasingly important for infectious disease research, surveillance and epidemiology in both plants and animals (livestock, companion animals, wildlife). Genomic research on some animal pathogens is not only important for agriculture and animal health; a large proportion of emerging human infectious diseases are zoonotic, originating in animals (e.g. Ebola, H5N1 Avian Influenza, and foodborne diseases including *Campylobacter* spp. and *Salmonella* spp).²⁷

Discovery and development of vaccines and medicines:

18. **Drug discovery:** Recognising the microbial origin of many important drugs (e.g. penicillin), researchers have focused on 'bioprospecting' microbiomes at the genomic level for novel medicines – so called 'genome mining'. Microbiologists are collaborating with medicinal chemists and bioinformaticians to search the genomes of microorganisms for genes and entire biosynthetic pathways that may reveal new therapeutics.²⁸ Other approaches being explored include bioprospecting soil metagenomes for antibiotics.²⁹

19. Genome editing technologies are also helping researchers to develop new drugs for widespread diseases, for example malaria.³⁰ Modern techniques such as CRISPR/Cas9 are being used to manipulate the genes of pathogenic microorganisms, in the hope of identifying potential drug targets. This technology has proved to be important for malaria research, since genetic engineering through previously available techniques has been difficult and time consuming.

20. **Vaccine development:** Genome engineering and genome sequencing techniques are important for the development of vaccines against infectious diseases, such as Ebola, Zika, pandemic influenza and polio. Genome engineered viruses are already widely used in the creation of seasonal and pre-pandemic influenza virus vaccines. The impact of

²⁶ <http://modmedmicro.nsms.ox.ac.uk/global-team-aim-for-faster-tb-diagnosis/> accessed 27-01-17

²⁷ <http://www.microbiologysociety.org/policy/briefings.cfm/publication/emerging-zoonotic-diseases>

²⁸ Ziemert, N et al. (2016). The evolution of genome mining in microbes – a review. *Nat. Prod. Rep.*, 33, 988-1005

²⁹ Borsetto, C. and Wellington, E.M.H (2016). Bioprospecting Soil Metagenomes for Antibiotics. *Topics in Biodiversity and Conservation*, 16, 113-136

³⁰ Ghorbal, M. et al. (2014). Genome editing in the human malaria parasite *Plasmodium falciparum* using the CRISPR-Cas9 system. *Nature Biotechnology*, 32, 819-821.

genomics and genome editing is likely to grow rapidly in coming years, for example, as genomic sequencing strategies are being used by virologists to evolve new and more sophisticated virus strains that may result in more stable vaccines (e.g. for polio).

21. **Gene therapies and immunotherapies:** Genome engineered viruses (especially lentiviruses and adeno-associated viruses) are also being used in most approaches for gene therapy,³¹ and are playing an increasingly important role, for example, in developing potential therapeutic cancer vaccines.³²

Impact of microbial genomics and genome editing on industrial biotechnology

22. Industrial biotechnology (IB) refers to the exploitation of biological resources to produce and process desirable materials, chemicals and energy. The potential for growth of the IB sector within the UK is enormous, with an estimated increase in turnover from £2.9bn to £8.6bn over 20 years (2014-2035).³³ Many processes in industrial biotechnology use microbes directly, such as bacterial, mould and yeast cultures, or utilise resources derived from these organisms, such as enzymes. Advances in genomics and genome editing have the potential to revolutionise IB, accelerating the discovery of new and increasingly efficient bioprocesses. Genomics and genome engineering technologies also offer insights and potential in relation to other industrial applications, such as bioremediation and metal extraction.^{34,35}
23. A Microbiology Society member noted that the manufacturing industry will continue to use and improve older, well established methods of genome editing in the development of new and existing microbial processes. Newer technologies are proprietary, with ownership often undecided, and licensing involves adding cost to businesses which may be marginally profitable in direct competition with chemistry based alternatives.

Bulk and high-value products

24. Microbes are integral to the generation of many chemical products, ranging from raw materials for the chemical industry,³⁶ to natural vanilla flavouring from genetically engineered yeast.³⁷ The creation of engineered microbes through “synthetic biology” (SynBio) can offer faster and more sustainable access to important chemicals for the pharmaceutical, home and personal care, agricultural, food and beverage sectors.³⁸ Precise genome editing techniques, alongside an improved understanding of microbial metabolism and physiology, are crucial for the advancement of SynBio approaches. UK industry has generated genetically modified microorganisms for contained use for almost 40 years.³⁹ Advancing technology has made this process increasingly precise and well defined as well as faster and cheaper.

³¹ Skipper, K.A. and Mikkelsen, J.G. (2015). Delivering the goods for genome engineering and editing. *Hum. Gene Ther.*, 26, 8, 486-497

³² Larocca, C and Schlom, J (2011). Viral vector-based therapeutic cancer vaccines. *Cancer J.*, 17, 5, 359-371

³³ Capital Economics (2015). *Biotech Britain. An Assessment of the impact on industrial biotechnology and bioenergy on the United Kingdom Economy*

³⁴ Prakash, D. et al. (2013). Bioremediation: a genuine technology to remediate radionucleotides from the environment. *Microbial biotechnology*, 6, 4, 349-360.

³⁵ Dunbar, W.S. (2017). *Biotechnology and the mine of tomorrow*. *Trends Biotechnol.*, 35, 1, 79-89.

³⁶ http://www.rh-fs.com/Markets/Health/Articles/BiotechnologyBook/Health03_Microorganisms.pdf accessed 23-01-17

³⁷ <http://www.evolva.com/vanillin/> accessed 18-12-16

³⁸ <http://rosset.bio.ed.ac.uk/engineering-microbial-systems> accessed 18-01-17

³⁹ Windass, J.D. et al. (1980). Improved conversion of methanol to single-cell protein by *Methylophilus methylotrophus*. *Nature*, 287, 396-401

25. Engineered microbes are increasingly used in the industrial production of sorely-needed vaccines and medicines, potentially improving access to healthcare whilst being more environmentally sustainable, by superseding more resource-intensive processes. Recent examples include the use of genetically modified yeasts for the production of artemisinin, an important antimalarial drug,⁴⁰ and vital components of human papillomavirus (HPV) vaccines.⁴¹ Genetically modified microbes also offer the potential to improve the production of antibody-based therapies, which currently rely on cells derived from mammals.⁴²

Prospects for the energy sector

26. Microbes are also being applied to provide unique solutions to the global demand for increased energy security. Microbiologists are using metagenomic analysis to understand how microorganisms process organic matter into biofuel (for example in anaerobic digestion reactors), or even directly into electricity (in microbial fuel cells).⁴³ This research has enormous potential: tangible benefits include the sustainable generation of energy from wastewater,⁴⁴ agricultural by-products and industrial pollutants.⁴⁵
27. Genome engineering is set to improve the prospects of biofuel as a viable alternative to fossil fuels. Microbiologists are editing the genomes of bacteria and yeast in the hope of generating biofuels from renewable sources, such as plant matter, to be used in many applications from heating to jet propulsion.⁴⁶

Genomics and the industrial strategy, skills and infrastructure

Importance of microbial genomics for industrial strategy

28. As demonstrated throughout this submission, microbial genomics and gene editing contribute significantly to the UK research and innovation landscape, including the bioeconomy. If the UK government industrial strategy is to recognise the benefits of a strong bioeconomy, then support for enabling technologies and research, including microbial genomics, is important. However, to be forward-thinking, continued support of fundamental microbiology research is vital to see a healthy pipeline of new scientific discoveries, such as CRISPR/Cas. Strategic and blue skies research are both crucial to facilitate and realise real innovation.

Infrastructure and skills requirements

29. Building fundamental and applied microbiology skills, capacity and infrastructure is important to progress the scientific, societal and economic impacts of genomics. We emphasise that other skills and techniques in microbiology such as isolating and

⁴⁰ <http://www.path.org/news/press-room/422/> accessed 04-01-17

⁴¹ Path (2000). HPV Vaccines: Promise and challenges

⁴² Spadiut, O *et al.* (2014). Microbials for the production of monoclonal antibodies and antibody fragments. *Trends Biotechnol.* 32(1), 54–60

⁴³ Rittmann, B. E *et al.* (2008). Pre-genomic, genomic and postgenomic study of microbial communities involved in bioenergy. *Nature Reviews Microbiology*, 6, 604–612; Ramos, J-L *et al.* (2016). Benefits and perspectives on the use of biofuels. *Microbial Biotechnology*, 9(4), 436–440

⁴⁴ Northumbrian Water. Developing the clean fuel of the future. https://www.nwl.co.uk/_assets/documents/Hydrogen.pdf

⁴⁵ <http://rosser.bio.ed.ac.uk/engineering-bacteria-electricity-production> accessed 18-01-17

⁴⁶ http://www3.imperial.ac.uk/newsandeventspggrp/imperialcollege/newssummary/news_2-9-2014-16-0-8 accessed 23-01-17; <http://newscenter.lbl.gov/2016/05/10/one-pot-recipe-for-jet-fuel/> accessed 23-01-17.

culturing microbes, microbial physiology and modelling complement cutting-edge genomic and genome editing techniques, and are not superseded by them. Our joint response⁴⁷ to the 2014 *BBSRC and MRC review of vulnerable skills and capabilities* highlighted several relevant vulnerable UK skills and capabilities including: bioinformatics expertise to interrogate genomic data; industrial biotechnology and bioenergy, including skills in synthetic biology; and microbial physiology. Participants who attended a recent series of Microbiome Research Stakeholder Workshops organised by the Microbiology Society also highlighted skills and training needs in bioinformatics and microbiology, and the need for better integration of skills, expertise and knowledge across genomics, bioinformatics, microbiology and other disciplines. Participants also highlighted the need to further develop tools, infrastructure and standards for collecting, analysing, storing and sharing microbial genomic data. Positive initiatives were noted, including the MRC-funded Cloud Infrastructure for Microbial Bioinformatics⁴⁸ and ELIXIR, the European infrastructure for life science information.⁴⁹

Regulatory, ethical, social and safety issues

30. We note and endorse the Royal Society of Biology's written response to this inquiry, which discusses some regulatory, ethical, social and safety issues concerning genomics and genome editing. We highlight some additional microbiology-relevant issues below that were raised by our members.

Regulation

31. At present there is uncertainty surrounding the regulation of gene editing techniques in relation to the status of an organism as 'genetically modified'.⁵⁰ Responses from some of our members indicated their support for regulation that is based on the characteristics of an organism, rather than the method used to manipulate its genome. This preference is mirrored throughout much of the scientific community, and forms the basis of the BBSRC's position on the genetic improvement of crops.⁵¹
32. A Microbiology Society member, involved in a current EASAC assessment of genome editing, also suggested that because new genome editing techniques simplify technology rather than (with the possible exception of some parasites) fundamentally alter our capabilities for genome alteration in microbes, current regulatory frameworks in the UK that apply to GMOs may be able to deal satisfactorily with the area of genome editing in microorganisms from the perspective of process-based regulation.
33. Microbiologists have long worked with the Health & Safety Executive (HSE) on the risk assessment and controlled use of engineered, often pathogenic, microorganisms. The HSE maintains a mandatory public register of GMOs, including microbes that are used in contained settings (e.g. an academic lab or industrial site).⁵² The register already contains instances of the use of CRISPR/Cas9 for the genetic manipulation of

⁴⁷ <http://www.microbiologysociety.org/download.cfm/docid/252C082B-E192-4A6A-B346DCE4C622B05A>

⁴⁸ <http://www.climb.ac.uk/> accessed 30-01-17

⁴⁹ <http://www.elixir-uk.org/> accessed 30-01-17

⁵⁰ [http://www.europarl.europa.eu/RegData/etudes/BRIE/2016/582018/EPRS_BRI\(2016\)582018_EN.pdf](http://www.europarl.europa.eu/RegData/etudes/BRIE/2016/582018/EPRS_BRI(2016)582018_EN.pdf)

⁵¹ <http://www.bbsrc.ac.uk/documents/genetic-crop-improvement-position-statement-pdf/>

⁵² <http://www.hse.gov.uk/biosafety/gmo/notifications/publicregister.htm> accessed 04-01-17

microorganisms, so is likely to be sufficient in monitoring the future contained use of genome edited microbes.

Gene drives:

34. The Nuffield Council on Bioethics report on genome editing comprehensively covers the concerns and potential impacts of gene drives in the environment.⁵³ Microbiologists are investigating ways to mitigate the risks of gene drive release. For example, researchers working on yeast laid the groundwork for the development of “*molecular safeguards*” that could minimise the risk of unwanted genome editing or even overwrite the changes introduced by an earlier gene drive.⁵⁴ Recent efforts have also identified proteins from viruses, which can specifically block the CRISPR/Cas9 system.⁵⁵ Such safeguards have the potential to inform the responsible design of gene drives in more complex organisms, such as insects, or to even directly combat accidental or purposeful gene drive release.

Biosecurity and dual-use of research

35. Despite the considerable benefits of genomics and gene editing, these technologies and some microbiology research utilising them raise potential ethical and biosecurity concerns, for example, risks of dual-use to create bioweapons. Discussion of dual-use microbiology predates new gene editing techniques such as CRISPR/Cas, but accessibility and efficiency of new technologies could potentially facilitate easier development of bioweapons, such as viruses or bacteria that are engineered to target specific populations, or the plants/animals on which societies rely on for food, necessitating ongoing dialogue to evaluate risks and benefits associated with technological advances. The Microbiology Society’s 2014 *Position Statement on Biosecurity and the Dual-Use of Research* opposes indiscriminate restrictions to scientific research, but recognises the need for any research undertaken and/or published to balance risks of misuse against any potential benefits. Any research needs to be conducted safely and ethically, taking into account relevant regulations, and the need for open dialogue between the scientific community, policy-makers, the wider public and other stakeholders.

Informing and engaging the public

36. The potential for genome edited microbes to be increasingly used in an expanding range of commercial applications may cause concern to the public if sufficient engagement efforts are not made. For example, research commissioned by the Food Standards Agency into public attitudes on GM-free labelling indicated that consumers wish to be informed of GM content, but that public knowledge of the science behind GM is lacking and can lead to negative perspectives.⁵⁶ That said, the public may be more responsive to veterinary and biomedical applications of GM technologies such as GM vaccines,⁵⁷ highlighting that more research into societal views may be required.
37. The potential impacts of microbial genomics and genome editing, as well as potential ethical issues and risks, mean that it is important to engage and appropriately inform the wider public. Citizen science projects may also be used to collect data to inform research.

⁵³ Nuffield Council on Bioethics (2016). Genome editing: an ethical review, p79.

⁵⁴ DiCarlo, J. E. et al. (2015). Safeguarding CRISPR-Cas9 gene drives in yeast. *Nat. Biotechnol.*, 33, 1250-1255.

⁵⁵ Rauch, B. J. et al. (2017). Inhibition of CRISPR-Cas9 with Bacteriophage Proteins. *Cell*, 168, 150-158.

⁵⁶ https://www.food.gov.uk/sites/default/files/792-1-1401_1893_FSA_GM_Labelling_Report_Webversion.pdf

⁵⁷ <http://www.vetvacnet.ac.uk/sites/vetnet/files/user-files/research-paper/pdf/08-16/GM%20vaccines%20Vet%20Rec.pdf>

For example, the Microbiology Society recently published public video describing CRISPR-Cas.⁵⁸ Another example highlighted to us was the *Good Germs, Bad Germs* project; this collaboration between scientists, social scientists and the FSA aims to enable members of the public to participate in metagenomic analysis of the bacterial communities found in their kitchens.⁵⁹ There also exist citizen science projects enabling members of the public to have their microbiome analysed using sequencing methods.⁶⁰

Appendix 1 – About the Society for Applied Microbiology and the Microbiology Society

38. The **Society for Applied Microbiology (SfAM)** is the oldest microbiology society in the UK, serving microbiologists around the world. As the voice of applied microbiology, SfAM works to advance, for the benefit of the public, the science of microbiology in its application to the environment, human and animal health, agriculture, and industry. It works in collaboration with other organisations to ensure evidence-based policymaking and, in partnership with Wiley-Blackwell, publishes five internationally acclaimed journals. Value for money and a modern, innovative and progressive outlook are the Society's core principles. A friendly society, SfAM values integrity, honesty and respect, and seeks to promote excellence and professionalism and to inspire the next generation of microbiologists.
39. The **Microbiology Society** is a membership organisation for scientists who work in all areas of microbiology. It is the largest learned microbiological society in Europe, and has a worldwide membership based in universities, industry, hospitals, research institutes and schools. The Society publishes six key academic journals in microbiology and virology, organises international scientific conferences and provides an international forum for communication among microbiologists and supports their professional development. The Society promotes the understanding of microbiology to a diverse range of stakeholders, including policy-makers, students, teachers, journalists and the wider public, through a comprehensive framework of communication activities and resources.

⁵⁸ <https://www.youtube.com/watch?v=52jOEPzhpzc>

⁵⁹ <https://www.goodgerms.org/> accessed 30-01-17

⁶⁰ <http://britishgut.org/> accessed 30-01-17