



Department for
Business, Energy
& Industrial Strategy



Genome Editing for Human Health

**Report of a roundtable to explore future
public engagement priorities**

Introduction

This report summarises a roundtable event held on the 22nd March 2018, which brought together policy makers, public engagement professionals and researchers working at the cutting edge of genome editing.

A short briefing paper was used to structure the conversations over the course of the roundtable, which is available separately.

The event addressed the following topics, through a mix of individual, table-based and plenary activities:

1. Discuss and agree a shared representation of the field of genome editing for human health (research and application)
2. Horizon scan key research and policy developments
3. Take stock of the public engagement that has been undertaken to date and the key lessons learned
4. Identify a strategic response to the preceding, agreeing how future public engagement activity might be better targeted and prioritised to address the opportunities and risks identified

This report uses the notes from the various discussions to identify the key conclusions and insights gleaned from the event. A draft report was shared with participants, and a number of helpful comments and suggestions were received which have been incorporated in this final version.

We would like to thank all the participants for their enthusiastic involvement in the event and for giving so generously of their time and expertise. The event has provided us with really valuable intelligence to inform future Sciencewise and NCCPE activity.

Executive summary

The roundtable confirmed that:

- The topic of genome editing for human health presents significant challenges and opportunities for public engagement and policy development
- The topic of genome editing for human health cannot easily be separated from genome editing in other organisms. Not only will human health be affected by genome editing in crops and farm animals, for example, but the public are also unlikely to fully distinguish between ethical debates about the technology's use in different organisms
- There is great value in bringing together people who are working in different areas of the field to build better coordination and mutual understanding
- The mix of scientists, policy makers and public engagement specialists at the roundtable was excellent; however, there were notable absences (for instance, representatives of the media; patient groups; other special interest groups)
- There are a number of challenges in drawing sensible boundaries around the topic. Developing a map of the field is at least a useful step in making this explicit and prompting precise questions about scope, but it does risk becoming redundant as science and application are moving very quickly; and it is likely to raise as many questions as it answers
- Sharing effective public engagement practice is essential. While there is much excellent work in train, there are still significant issues with the quality of the conversations going on between specialists and non-specialists. The role of front line healthcare workers was identified as one which requires careful attention
- A number of other actions crystallised at the event, which are recorded on page 19. No one 'big idea' surfaced; rather a number of suggestions for intelligent interventions to enhance the quality and robustness of intelligence gathering about public attitudes, which could be used to inform decision making and the design of future engagement activities.

1. Mapping the Genome Editing landscape

The workshop explored how the field of genome editing for human health might be described and explained to people with a stake and interest in the field, but not specialists in it. The event briefing paper contained a ‘straw man’ representation of the field which was discussed at some length during the workshop. The representation focused on four domains:

1. Genome editing technologies
2. Human genome editing technology applications
3. Human genome editing related research areas
4. Human genome editing research themes: areas where genome editing has transformational potential for human health

Participants were presented with a table which attempted to map some of the key areas. These were interrogated and working individually, on tables and in plenary, participants tested the categories that were described in the representation. The table that was discussed is shown below.

Domain	Focal points for investment and activity
1. Genome editing technologies	<ul style="list-style-type: none"> • Engineered nucleases <ul style="list-style-type: none"> ○ CRISPR/Cas9 (and derivatives) ○ ZFNs ○ TALENs • Recombinant adeno-associated virus (rAAV) • Homing endonucleases/ mega nucleases • Programmable base editing
2. Human genome editing technology applications	Basic research Genome-editing research conducted on human cells, tissues, embryos, and gametes in the laboratory. Clinical research Therapy by editing in somatic cells Therapy by editing in germline cells
3. Human genome editing related research areas	<ul style="list-style-type: none"> • Engineering cell-lines and organisms • Therapeutic genome editing • Screening (i.e. genome sequencing at/before birth) • Data analytics (i.e. large genome-size and population data) • Social and ethical issues pertaining to the technique / applications • Language, culture and communications • Practical and policy implications (i.e. for health service operations / system)
4. Human genome editing research themes: areas where genome editing has transformational potential for human health	<ul style="list-style-type: none"> • Treating human diseases (cancer, rare and common genetic diseases) • Preventing illnesses being passed from one generation to the next • Assisted reproduction • Preventing the spread of infectious diseases (e.g. zika and malaria) • Drug screening • Human ‘enhancement’

Participants suggested additions, identified areas requiring clarification and tested the logic and utility of such a representation of the field. While some participants agreed that a representation of this nature is useful to help define the territory, and for people to position themselves within it, there were a number of challenges identified:

- By focusing on techniques rather than outcomes or purposes, it risks quickly becoming out of date and fails to capture the dynamism of the field

- Who are the target audiences for the map? They could be (for instance) policy makers; healthcare professionals; media etc. Each will have different levels of knowledge to bring to bear, and different purposes for using such a map
- It's a hard field to draw boundaries around – there are lots of techniques on the margins that are relevant (for instance, stem cell techniques)
- The exclusive focus on human health is problematic, as much of the science interacts closely with developments in plant and animal biology (which will themselves often make a significant contribution to human health)
- The exclusive focus on genome editing is problematic, as many of the issues around trust and ethics can be more helpfully approached in the context of genetic science and technologies more broadly, including GM. A more productive framing might be to focusing on the problems to which genomic science more generally might contribute solutions

We have included more detailed feedback in Annex 1.

Next steps

There was measured enthusiasm for the utility of such a mapping of the field. We now feel confident that such a representation could serve a useful function to set boundaries and guide discussion, however it is neither sensible nor possible to create a fully comprehensive representation.

Two significant challenges will need to be addressed if this work is to be progressed.

Firstly, more work should be done to identify the **potential users** of such a representation, and to more clearly differentiate their information needs. This may well mean developing an overall map, but only presenting certain aspects of it to each of the potential user groups, or it may mean developing different maps to meet those different needs. We propose the following categories, building on suggestions made at the workshop:

- **Funders of genome editing research** keen to understand how their investment in research sits alongside others', to enable them to better understand their contribution; to identify gaps or duplication to inform future funding decisions
- **Policy makers** keen to grasp the nature of the field and what is being invested in, to provide background knowledge to inform policy choices
- **People working in engagement roles** (including teachers and journalists) keen to understand the current 'state of play', to provide them with a robust knowledge base to inform the design and delivery of engagement activities
- **People funding or coordinating engagement activities**, to identify where there are activities / resources, and where there are gaps, to prevent reinventing the wheel, while also highlighting opportunities and priorities
- **Patients / carers / health-curious citizens / patient charities** keen to understand the current frontiers of knowledge, to inform their own health choices and awareness
- **Wider civil society organisations** keen to understand the current frontiers of knowledge, to reflect on whether the technology might influence the context in which they work and their ability to achieve their objectives, and to inform their own choices and awareness
- **Professionals working in related areas** keen to be better informed so that they can improve their professional practice – e.g. to manage better-informed conversations with patients, or to improve crop viability. Examples might include innovation managers in hospitals, or farmers unions if the map was extended to include genome editing in plants and animals
- **Researchers** keen to understand how their areas of specialism sits within a wider landscape of research activity
- **Businesses** investing in developing applications, for example pharmaceutical companies investing in treatments, or companies investing in new seed varieties.

Secondly, more work needs to be done to work out the most useful way of providing a shared ‘scaffolding’ to support productive conversations about the area. The headings used in the draft representation (in the table above) are too technical and abstract. We suggest that a more pragmatic set of headings would be the following, which link more concretely to the application of the science to the ‘real world’:

<p>What is genome editing? How can the topic be explained to non-specialists so that they can have a well-informed grasp of the technical and societal / ethical underpinnings?</p>	<ul style="list-style-type: none"> • The underpinning science; the potential and actual applications; the philosophical / ethical and societal issues associated with it • Lessons learned about how to communicate about the science with non-specialists: common barriers to understanding; common ethical and attitudinal responses
<p>Current techniques and applications How is the science currently being applied to address human health? What are the key areas in which it is being applied?</p>	<ul style="list-style-type: none"> • What regulatory and engagement ‘journey’ have these followed to move from the lab into society? • What have we learned about public attitudes and concerns which can inform the development and regulation of future potential applications?
<p>New techniques and applications: which might realistically be achieved in the next 2 – 5 years What are the potential uses / applications for the science which are currently being developed and trialled and which might make it ‘to market’ in the next 2 – 5 years?</p>	<ul style="list-style-type: none"> • What could be the implications of these for human health and wellbeing? • What are the regulatory and ethical issues associated with these?
<p>Basic research What is the underpinning science / social science and what are the ‘big questions’ that are currently being addressed? What are the key ‘challenges’ / frontiers of new knowledge which are currently under investigation?</p>	<ul style="list-style-type: none"> • What could be the implications of these for human health and wellbeing? • What are the regulatory and ethical issues associated with these?

2. Horizon scanning research and policy developments

The workshop provided a useful opportunity to elicit from delegates (all of whom are working at the cutting edge of research, policy and engagement in the area) to identify what they perceived to be the most interesting and significant developments in research and policy in the next 3 to 5 years.

Horizon scanning - research

Headline developments in research that were identified included:

- In the immediate future, the focus will be on single gene conditions
- How to adapt CRISPR for delivery to its target – it’s currently a very large molecule
- The move towards genomic medicine and whole genome sequencing
- Gene drives (e.g. to eliminate mosquito populations or make them unable to transmit certain pathogens)
- Developing techniques that combine gene-editing with stem cell research (especially induced pluripotent stem cell research, which may raise fewer ethical issues).
- Clarifying ‘ex vivo’ and ‘in situ’ approaches to somatic genome editing
- Various issues about standards and in vitro/in vivo quality/regulation
- Evaluating safety, feasibility – current methods used to evaluate genome editing have had limitations

- DNA damage repair factors may be distinct in germ cells vs somatic cells with implications for feasibility and safety.
- Next 1-2 yrs, assessing outcomes of TALENS-type clinical trials and in 3-4 yrs of CRISPR-type, but for rare diseases in small numbers

A number of areas that would be likely to cause public concern were identified, including:

- Genome 2.0 – creating a stripped down genome or a synthetic human embryo; synthetic genomics: going beyond editing what is currently there to fundamentally re-engineering life, with enormous ethical issues
- In vitro derived gametes
- DIY Bio/ Citizen Science – the ability of others outwith science organisations to “meddle”. This is becoming easier and easier leading to increasing unofficial and unregulated activity, although there are many caveats around this area and how it might develop
- It was also noted that the 14-day rule may be increased in 3-5 years, and that this will be essential to broaden scope of embryo research

Horizon scanning – policy

Participants were invited to explore the various policy issues which are likely to arise in the near future. A number of topics were identified which have been summarised below. It was noted how difficult (and perhaps unhelpful) it is to try to clearly separate out the scientific research from the policy: there are so many areas, particularly where we are moving to application, where research blurs with policy.

It was also noted that many of these issues are not new, but they are new to a lot of people, which is why they need to be discussed and debated:

- **Biohacking:** how people will use (and abuse?) the technology outside the official research and regulatory system
- **Biosecurity** around unintentional misuse - e.g. accidental release/gain-of-function. This could happen in a regulated environment.
- **Regulation and trust in the system:** how can such a rapidly changing field be effectively regulated without slowing down innovation, but not losing public trust?
- **Global challenges (inc. regulation):** challenges in how research policy and clinical policy is being managed in different national contexts; differences between the global north and south with gene editing for an affluent world (worried about rare diseases, fertility, ethical food) and gene editing for poor citizens worried about food, basic healthcare etc
- **Managing the relationship between research / application / clinical use:** tensions in allowing research whether or not the technology/ application will be licenced for clinical use
- **Speed of change:** keeping pace with the rapid advances in the science and its application
- **Access to treatment / costs / equity:** who pays, and who decides who should benefit?
- **Human enhancement:** differentiating between treatment and enhancement.
- There are a variety of other **risk/benefit issues**, plus the issue of ‘**unintended consequences**’ (unknown unknowns) that may have profound policy connotations
- **Data:** appropriate handling of personal data; also digital sequence information - which may not be human (e.g. pathogen sequences). There is both the handling of the data/information; but also questions of IP/Patents and willingness to share for 'public good', and potentially a risk of publishing full sequence information of viruses/gain-of-function work.
- **Human / non-human interface:** the science spans both domains, but public attitudes can be very different
- **Germline and somatic clinical applications:** how significant is this distinction? How might public attitudes to this evolve over time?

- **The role of intermediaries in engaging with the public:** how do we support non-scientific professionals to understand the science, and more importantly how do we support them to give patients meaningful power and choice? What is the role of the media in supporting informed debate?
- **Safety and risk:** What are the long-term effects, particularly when germline is involved and changes are passed to future generations? What will be the societal consequences for those who choose / choose not to be treated (e.g. stigma)
- **Economics and business models:** securing appropriate investment and clarifying the role of government in this; ensuring that the benefits and risks are shared in an appropriate way
- **The role of government:** particularly, the challenge of keeping up with such a rapidly evolving field that is moving into application and clinical practice so quickly; the role of organisations like POST and HFEA. The relevance of the Science and Technology Committee's inquiry into [Genomics and Genome Editing in the NHS](#) was noted.

While this is a long list, it was also noted that it is not exhaustive, and that there would be value in trying to make it so through further desk research and expert knowledge elicitation. It would also be helpful to begin to cluster and contextualise the issues, drawing for example on work analysing the dynamics of the innovation landscape, such as the Innogen Institute's work on [foresighting business models and value chains for innovative technologies](#), and on [the proportionate and adaptive governance of innovative technologies](#).

Another suggestion was that the issues might be analysed through three lenses:

- The dimension of public concern about novel technologies about which a lot is known (natural vs unnatural; high personal benefit vs low personal benefit; high catastrophic potential vs low catastrophic potential etc etc)
- How they are similar or different to each other
- How they are similar or different to other technological 'controversies'.

These policy topics were returned to in the final part of the roundtable, with four areas prioritised by participants as being worthy of more in depth discussion. These were:

- **The role of government:** how can Government keep up with such a rapidly changing field, and provide appropriate oversight and regulation?
- **Engagement and expertise:** the role of intermediaries (e.g. healthcare professionals) in engaging the public
- **Developing a narrative:** framing productive conversations about genome editing
- **Concerns about human enhancement:** how can we minimise harms and maximise benefits in this contentious area?

These discussions are recorded in section 4 below.

3. Taking stock of public engagement

Taking stock of public engagement activity

Participants explored the public engagement that has been undertaken to date, through two lenses:

- **Helping the public to understand the science:** often framed as a conversation with the public, the primary goal is to help the public understand what can be a bewildering and potentially confusing topic
- **Public dialogue and deliberation:** structured dialogues which are intended to elicit public views and to directly influence policy decisions.

Drawing on the summary insights provided in the briefing paper, there was considerable discussion of the various challenges in supporting the public to develop an understanding of the science and of its social and ethical implications. Some of the key points are recorded below.

An overarching challenge was identified around developing the 'narrative' for genome editing. This was identified as a topic for deeper consideration in the final open space session. Participants' reflections also included the following topics:

Understanding and reaching different audiences

Participants noted that there were huge differences in different people's motivations and interests which needed to be taken account of:

- The need to cater for different needs and depths of understanding depending on the audience and their needs - curiosity or cure
- Public engagement should include presenting at events organised by charities which align themselves with support and managing hopes/understandings of affected patients
- Do we focus too much on building in depth understanding – which is unrealistic? Most people don't have the time or interest for this. Should we focus more on 'snapshot' understandings?
- Stratifying the conversation: what are the different channels we should be using and how should we go about it?
- We need more research into what the public think of genome editing and how naive or far from actuality it is, so 'correct understandings' can be fed in

Expectation management

- How do we avoid overhyping the tech and overpromising what it can do? If/when the science doesn't deliver, this will reduce trust. Many of the things that people are saying GE might do are unachievable – either because they are not controlled by one (or a few) genes, or because delivery mechanisms are a long way behind. It was also noted that there are strong vested interests - both commercial and academic – in promoting or discrediting different approaches and applications
- Managing expectations. We need to set realistic expectations – genome editing is potentially life changing but timelines can be very long. Many rare diseases are undiagnosed and researchers are still trying to understand the genetics
- Shattered expectations vs realistic expectations, in the context that many of diseases genome editing is being suggested for have no therapeutic options at the moment: the possibility of one is significant, particularly for ultra-rare disorders

Language issues

- Not having a common language across the genome editing field is a challenge for communications – for instance, different terms or analogies can be used to describe the same processes: *'I think there is a need to choose a few consistent terms for universal and continued use with the public'*

- Are we being overly pedantic using terms people don't understand or don't have time to understand: e.g. more people comprehend 'genetic' over 'genome'? 'If scientists are quibbling about concepts and definition, how on earth can you expect the public to work with these issues?'

What should we be talking about with the public?

- Some delegates argued that the public need to understand basic genomics, screening and diagnostics before they can understand genome editing. If screening raises issues and public concern, then genome editing will likely raise more
- It's not just about understanding the science. Understanding the business models, funding, choices, views of different groups, politics and power are equally important
- How have we got to this point, and where are we heading?
- You can't divorce gene editing from understanding molecular and cell biology. Some delegates argued that to understand genome editing you need to understand:
 - Cell: how many cells in the body, how many cell types?
 - Genome: how many genes?
 - Genes: how are genes regulated
 - What is relationship between gene and phenotypes throughout differentiation and development?
 - What happens when gene expression goes awry?
- Others felt it was less clear cut than this: depending on the discussion in question, the degree of information provided can differ. For example, the public don't need to know the statistics on the number of cells in their body ("lots" is sufficient to be able to understand genome editing).
- What are the topics for engaging the public – everything!
- We need to consult with the public to find out what they want from these technologies

Framing / narrative

- One delegate commented: *"Government framing is a disaster – it positions genome editing as a problem rather than an incredible opportunity."* Others noted that it was more a case of government being reticent to talk about the topic at all that was more of a concern.
- The role of the media is hugely significant – e.g. in amplifying particular areas of clinical research (e.g. designer babies) and influencing the wider public discourse and debate
- We need to foreground IP, ownership, access and the global race
- Is it true to claim that the public are rarely interested in the science, only in its applications? In outcomes rather than methods?
- The bio-ethical debate should be foregrounded
- Similarly, the importance of recognising it is a global issue, and that we have limited influence over the engagement/media in other countries. It is important to consider how global media stories are portrayed in the UK and the influence of this on both research and (future) implementation

The relationship between 'communication' and 'dialogue'

- A number of delegates agreed that there needed to more focus on clear, thoughtful communication – which is sometimes discredited as being 'one-way' and patronising, and the poor relation of 2-way dialogue: *'It seems to be politically incorrect to suggest that the public are in any way 'ignorant'... but they are. And so am I. And so are you. We do need to identify where there are misunderstandings and find ways to correct these. Having sufficient understanding is a key requisite for dialogue'*
- It was emphasised that the purpose for the engagement needs to be clear, both to those conducting the engagement and the participants. It must be clear whether the engagement is for information, or for feedback/shaping of policy etc.
- It was suggested that there would be value in establishing a list of trusted information sources and examples of some that are not trust-worthy

Several **practical suggestions** were made for how to take this discussion forward:

- The themes for engagement should be prioritised, on the basis of a clear rationale, so we have a logical approach to the topic rather than a scattergun one
- Establish multi-disciplinary working groups for specific areas of genome editing (rather than one overarching one which is far too broad) and use this to develop public engagement strategy
- Be more targeted: Not everyone needs to be included all the time for everything. For example, maybe it is just patients or prospective patients that are needed, or maybe engagement is specifically needed with those with religious beliefs who might form a significant corpus of the population with particular concerns that need to be elaborated
- PILOTING of material for understandability is critical for engagement, but is rarely done
- A national observatory on genome editing would have great value, capturing the information and narratives that are circulating so that we know what they know and can tailor engagement activities around that knowledge on genome editing. Two similar ideas have recently been suggested, by [Jasanoff and Hurlbut](#) and by [Burall](#).

4. Policy challenges: open space session

In the final 'open space' session, participants were invited to prioritise topics for more in depth discussion, with a view to informing future Sciencewise project activity. Four conversations took place:

- **The role of government:** how can Government keep up with such a rapidly changing field, and provide appropriate oversight and regulation?
- **Engagement and expertise:** the role of intermediaries (e.g. healthcare professionals) in engaging the public
- **Developing a narrative:** framing productive conversations about genome editing
- **Concerns about human enhancement:** how can we minimise harms and maximise benefits in this contentious area?

For each topic the groups were invited to consider:

- What's the policy choice / challenge?
- Why is it significant?
- What's the minimum level of public understanding needed to address it?
- What do we need to know about public attitudes and sensitivities to proceed with confidence?

Discussion group 1: Engagement and expertise: the role of intermediaries (e.g. healthcare professionals) in engaging the public

What's the policy choice/challenge? Why is it significant?

The group explored the critical role of professionals in mediating and supporting public understanding and decision making, in particular primary health care providers who work at the frontline. For example, if someone has had their genome sequenced and goes to their GP and their GP doesn't have info/ refer then what is the consequence? Heightened public concern? Self-medication? They identified two areas for further exploration:

- What model and resource should be applied to building professional understanding (and capacity) in Genome Editing, in order that risks are anticipated and opportunities gained? What needs to be done to build the capacity for people to respond and secure institutional readiness?
- Who are the people that are going to come into contact with GE from the public first? For example someone with concerns having a baby; someone who has had their genome sequenced; but also funders, home office inspectors, patient groups, other regulators.

What's the minimum level of understanding needed to address this?

- The group agreed that it would be useful to map different public and professional groups and their potential interactions with GE technology, and their information needs
- Some key basic understandings were identified, including: what the genome is, and how it works; the fact that it doesn't always work as expected; the difference between germline and somatic; causal vs association risk

What do we need to know about public attitudes/ sensitivities?

- The group agreed that public health professionals will become increasingly important, acting as key enablers of understanding across the whole system
- They briefly explored the role / responsibility of the healthcare professional in a genetic setting – is this to the person or to the family? (The dilemma expressed was if a father had a hereditary disease but asked for it not to be shared and the daughter had a baby that had the disease, who should the healthcare professional share with – respect the confidentiality of the father or let the daughter know?)

Other comments?

- The usefulness of social science work on genetic testing in practice was noted – it has a similar framing and explores similar issues and concerns.
- The media play a hugely significant role as intermediaries

Discussion group 2: Developing a narrative: framing productive conversations about genome editing

The group identified the following **headline points**

- The narrative and level of detail needed depends on the audience
- The political narrative needs to relate to economic growth / industrial strategy
- It needs to be honest and have authenticity (see * below)
- Narrative needs to work for ministers and government too
- Need to embrace the negatives as well.
- We mustn't try to simply educate the public: we need to find out what publics want too
- Context is key – what is the outcome, why is it better, who benefits?
- Don't overestimate what people know – and don't expect perfect recollection and understanding from people who've only heard or been told about it once.
- And don't overestimate what they WANT to know; often they are content to be told that everything is going to be OK by a sufficiently trusted person [they are too busy worrying about their more immediate everyday concerns...]

What do you need/ need to know?

- *Why you are initiating a conversation? You need a clear story to explain this to public participants
- Who you trust to deliver the message (which could describe an interlocutor who the public trusts; or someone the policy/science community trust to successfully engage with public audiences)
- How you frame the story
- Learning from past lessons
- Language consistency including simple vocabulary – for example, [Understanding Patient Data](#)

Questions/ challenges

- When is the right time to engage?
- What do you compare gene editing to? Metaphors and analogies are vital – but before we tweak the metaphors we have to know which ones are being used where, when, and by whom. See: <http://blogs.nottingham.ac.uk/makingsciencepublic/2017/11/17/genome-editing-metaphors-language-choices/>

Plenary discussion raised some additional points:

- It's not just about the science: we need to communicate structures, power and governance (i.e. the wider context for the science)
- The engagement needs to start from where the public are
- There are multiple publics and understandings (even within one person) so don't try to measure understanding, but instead look at types of understanding and map on to wider debate and policy etc.
- Take account of faith groups and personal faith
- A (single) 'narrative' is not enough. Stress 'realism', counter hype, including geno-hype: don't talk about designer babies unless you can explain what they are and aren't
- There are risks in the notion of narrative. The public (or representatives in NGOs etc) are liable to be wise to attempts to pre-frame a narrative and the backlash could be severe (loss of trust etc). This needs to be handled with care.

Discussion group 3: Concerns about human enhancement: how can we minimise harms and maximise benefits in this contentious area?

Policy challenge/choice

The group explored the intense ethical and political sensitivities and risks. These included: biohacking, and the possibility of these being people who are excluded from access to regulated treatments, and that the extent of biohacking will in part be a function of what happens at institutional level; the likelihood that someone (probably outside the UK) will just go ahead and create genome-edited baby outside regulatory frameworks (soon); the growing public excitement about the prospects of genomic medicine roll-out. Concern was also raised about the

current government framing of the genome editing – as a potential problem rather than an incredible opportunity. Against this background, the group explored:

- How do we develop a policy on genome editing that will enable us to minimise the harms and maximise the benefits? Can we generate a shared, useable understanding of the values, concerns, aspirations around germline editing that will be useful for policymakers?

Challenge area: what do the public need to understand about this area?

- germline / somatic distinction
- context - e.g., understanding PGD (preimplantation genetic diagnosis)
- known potential harms/benefits
- political history around the research/tech/application
- terminological clarity
- realism: it's not a "magic bullet", though it has enormous potential for human health
- what would access to the "quality" version of GE mean?
- allow publics to frame/develop their own understanding of GE - attend to analogies/sense-making process/how publics frame the risks and harms,

Policy challenge area – developing a narrative

- There was considerable discussion of germline/somatic distinction:
 - is germline editing as much of an issue amongst publics as it is perceived to be/is, amongst those in the field?
 - Really important to explain to publics (and regulators) the bioethical consequences of somatic and germline editing: some difference in view across the table as to whether this is as potentially difficult conversation as some think. One argument was that publics see health benefits of germline editing outweighing philosophical/ethical concerns
- The need to focus on precise definitions and meaning: "serious disease", "enhancement", "cosmetic"
- The need to address international policy questions too

Discussion group 4: The role of Government: how can Government keep up with such a rapidly changing field, and provide appropriate oversight and regulation?

The discussion did not result in consensus, but allowed a number of perspectives to be aired:

- Some agreed that good **regulatory architecture** is in place, but that there needs to be a more proactive strategy across government: an **anticipatory approach** is needed, which includes systematic foresight and pre-emptive and evolving dialogue to explore risks (without being unduly alarmist). This could involve mapping technological/scientific developments that are expected to happen, and then mapping what else needs to happen/be in place alongside this (e.g. regulations, engagement).
- For some, the risks of (for instance) off-target effects, bio-terrorism and other 'worst-case scenarios'; the prospect of synthetic human embryos; and the huge potential economic advantages of the UK remaining at the forefront of this field made such anticipatory and proactive engagement a strategic imperative. Such an approach could use mitochondrial replacement therapy as a model / case study: working back from the decision to approve MRT could help inform the process for taking genome editing forward. The risk of 'knee jerk reaction' was also identified, linked to Dolly the sheep and the Embryo Stem Cell line in 1997. It was also argued that this anticipatory work should be focused on what we are trying to achieve, rather than centring on the technology in isolation.
- Others queried whether we should be pre-empting policy decisions ahead of a 'policy moment'. 'Do we not have faith that we, in the UK, have a system that will be able to accommodate a shift when it happens?'
- The challenge of timescales came up several times. On the one hand, the field is fast moving and the pace of developments poses big challenges for current regulatory processes. On the other hand, lead in times from basic science to clinical application can take 15 – 20 years
- A specific challenge for government was identified in the current 14 day rule regarding embryo research. Any changes to this need to be carefully managed because the repercussions from any/no amendment to

the rule will have significant consequences for the UK's stance and outlook with human embryo research and germline genome editing

- The risk of current regulation unnecessarily inhibiting innovation was noted, and the importance of considering adapting our existing regulatory systems to take account of the needs of new biotechnologies. Is it appropriate for policy makers or regulators to make regulatory decisions about innovative technologies in a pre-emptive, precautionary way, before there is clear evidence of the need for regulation? Where possible we should think about using standards and guidelines to control the use of a technology, rather than legally based regulations that then are very difficult to adapt to future needs.

Cross cutting points included:

- As with many debates into novel technologies and public engagement, policy makers and practitioners often jump in without recognising that there is already existing research in the social science domain that might inform or answer some of the key questions e.g. factors that are liable to be of concern re novel technologies; case studies of governance or policy responses in other areas, and so on. There are many lessons that could be learnt from appropriate and targeted literature reviews
- The need for clarity of purpose in developing any engagement activity: expressed as a very clear question... whether about policy ('what is the best way to...?'), conducting engagement ('what is the best way to...?') or public attitudes ('what do the public think about...?').
- Social and natural science researchers need to work together so that accommodations can reasonably be made if and when necessary – each need to have some understanding of the other to assist government effectively.

What next for Sciencewise?

When we started this process we framed our interest as being in:

- the science of genome editing in humans
- the risks and benefits of this emerging science for human health, framed in terms of changes to human biology

As a result of the workshop and subsequent discussion, and in taking this work forward we think it is important to widen our frame of reference to include:

- the science of genome editing in humans, plants and other animals
- the risks and benefits of this emerging science for human health, framed in terms both of human biology and the wider societal impact of (for instance) modifying crops and farm animals

This re-framing is important, given the clear interdependencies of these different applications of the science, and in public understanding of the area.

Summary of proposed actions

In the light of the insight and feedback gathered at the event, and suggestions in the evaluation forms that were completed, we propose the following actions:

- Prepare short briefing documents which combine the event report and briefing paper content, targeting (a) researchers, (b) policy makers, and (c) public engagement specialists and media. These briefings will identify key insights relevant to each constituency. These briefing papers will include an updated version of the genome editing map, as a tool to help frame conversations between specialists and non-specialists
- The Sciencewise team will follow up the various suggestions for possible dialogue / intelligence gathering activities with key policy leads in relevant government departments and public bodies. Possible areas to explore further include:
 - The appetite for a mapping of anticipated scientific/technological advances in genome editing over time against what needs to be in place e.g. regulation, dialogue, foresight work
 - Specific topics for dialogue, e.g. genome sequencing (and related issues e.g. who can access the data) and genome medicine
- Feed the insights around developing a more robust 'information architecture' to support public understanding and insight into the Wellcome funded GEPES project, and the associated partner organisations who are supporting this project. These insights will inform the training resources being developed for this project by the Wellcome Genome Campus and NCCPE. Specifically, the challenge around better supporting frontline health professionals will be investigated further by the GEPES team.

Other suggested actions:

- Establishing an advisory or steering group to provide oversight and coordination of a comprehensive engagement programme on genome editing. This could be a precursor to developing further the 'observatory' concept outlined in Simon Burall's recent Nature article: [Rethink public engagement for gene editing](#)
- Develop a clearer articulation of the links between genome editing and the Industrial Strategy, to strengthen the economic case for investment in research and engagement, sensitive to the ethical and regulatory risks this might raise
- Support roundtable participants who wish to take aspects of the discussion forward
- Scope the development of a similar event to involve a wider group of interested parties, including media; patient groups; other special interest groups

- Explore how more value might be extracted from the existing academic literature, to address the various challenges identified through the workshop; identify gaps and the most appropriate mechanisms to address these (e.g. through new empirical research; commissioned dialogue exercises; expert knowledge elicitation (similar to this workshop) etc

Annex 1: workshop delegates

The following participants attended the roundtable

Policy and practice

- Katrina Nevin-Ridley - Director of Communications, Genomics England
- Mark Bale – Genomics Science and Emerging Technologies, SRE, Department of Health and Social Care
- Patrick Middleton - Associate Director of Communications and Engagement, BBSRC
- Brigid Feeny - Assistant Director, Place Team, Science, Research and Innovation, BEIS
- Amanda Hunn - Joint Head of Policy, Health Research Authority
- Jonny Hazel - Policy Advisor (Wellbeing), Royal Society
- Mark Robertson – Director, Science Policy Compass
- Sandy Starr – Communications Officer, Progress Educational Trust
- Sarah Norcross – Director, Progress Educational Trust
- Rachel Brown – Policy Officer, Academy of Medical Sciences
- Anna Wilkinson – Research Officer, Nuffield Council for Bioethics
- Sarah Rappaport – Policy Adviser, Wellcome
- Heather Browett - Policy Officer, Wellcome

Researchers

- Andrew Webster - Professor in the Sociology of Science and Technology, University of York
- Kathy Niakan - Human Embryo and Stem Cell Laboratory, The Francis Crick Institute
- Pleasantine Mill - Group leader, Institute for Genetics and Molecular Medicine, University of Edinburgh
- Helen Sang - Chair of Vertebrate Molecular Development, The Roslin Institute and R(D)SVS
- Waseem Qasim - NIHR Professor in Cell & Gene Therapy, Institute of Child Health & Great Ormond Street Hospital
- Doug Higgs – Director, Weatherall Institute of Molecular Medicine
- Bruce Whitelaw, Genus Personal Chair of Animal Biotechnology, Roslin Institute
- Amarpreet Kaur - PhD Candidate to the Sociology of Reproduction Research Group (ReproSoc) at the University of Cambridge
- Sarah Chan - Usher Institute of Population Health Sciences and Informatics, University of Edinburgh
- Julian Rayner - Director Wellcome Genome Campus Connecting Science, Group Leader Wellcome Sanger Institute
- Gene Rowe – Independent Research Consultant, GRE
- Robert Smith – Research Associate (Social Dimensions of Synthetic Biology), Department of Global Health & Social Medicine, King’s College London
- Gabby Samuel – Research Associate, Department of Global Health & Social Medicine, King’s College London
- Lydia Teboul – Head of Molecular and Cellular Biology, MRC Harwell Institute

Facilitators and hosts

- Paul Manners – Director, National Coordinating Centre for Public Engagement
- Simon Burall – Programme Director, Sciencewise
- Roland Jackson – Senior Consultant, Sciencewise
- Suzannah Lansdell – Dialogue and Engagement Specialist, Sciencewise
- Diane Beddoes – Senior Dialogue and Engagement Specialist, Sciencewise
- Hally Ingram – Programme Manager, Sciencewise
- Tony Whitney - Public Engagement in Science and STEM Inspiration, BEIS
- Alec Weir - Public Engagement in Science and STEM Inspiration, BEIS

Comments on the draft event write up were also received from:

- Brian Bigger, Group leader Stem Cell & Neurotherapies Laboratory, University of Manchester
- Brigitte Nerlich, Emeritus Professor of Science, Language and Society, Nottingham University
- Joyce Tait, Director, Innogen Institute

Annex 2: Gaps in the map, and other issues: more detail of the discussion

In considering the 'gaps' in the map, participants noted some generic areas which they felt were missing and should be represented. They also identified specific absences which are recorded in the table below. The generic issues identified included:

- **The link between genomics and genome editing is missing** e.g. genome sequencing. Genome sequencing and genome editing are very closely linked and it was noted that most people will have their genome sequenced well before editing enters the clinic. Engagement needs to be sensitive to both, as misunderstanding in one area can impact the other. However, there are also risks in linking the two. Linking genome editing with sequencing could raise unnecessary concern around current sequencing projects; or could try to paint with the same brush and not give adequate attention to the risks associated with genome editing.
- **There is a distinction between genome editing for human enhancement and for human health.** There is public support for using it to treat serious diseases, but they are less keen on enhancement. However, the line between enhancement and health is hard to define and maintain. As it stands, the map glosses over this very significant distinction. It was suggested that it could be helpful to distinguish two types of human enhancement:
 - 'cosmetic enhancement' e.g. tall or beautiful (whatever society currently perceives that to be)
 - 'preventing likely serious disease enhancement' e.g. an embryonic edit that protects ensuing human from common, and perhaps likely, future ailments such as atherosclerosis, Alzheimer's disease etcIt was also noted that discussion of human enhancement needs to be presented with lots of caveats about feasibility and should counter hyped-up claims about CRISPR babies/designer babies etc
- **The map says nothing about the economics of the field.** It was noted that company investment is driven by the notion that gene-editing is speedier and less cumbersome in regard to treatment of genetically based diseases. The impact on public sector health spend was also noted, considering the cost of treatment both to public budgets and via private payments and possible discrepancies this causes in access to treatment.
- **The accelerating pace of development,** fuelled by commercial interest, was identified as a key issue creating a host of issues, e.g. for regulation
- **The place of epigenome editing needs addressing** (which alters pattern of gene expression without altering DNA sequence). The editing of human RNA, TNAS does not involve editing of DNA. Should the definition of genome editing be loosened to include epigenome editing and RNA editing? It was noted that including this risks perpetuating misunderstanding of what a genome is, BUT these technologies are relevant to the field.
- **What is the relationship between genome editing and synthetic biology** and should Syn Bio be referenced in any way?
- There is nothing on the map about **regulation**, and the interaction between regulation, innovation and trust
- **The international dimension** of the science and policy landscape is missing
- It would be helpful to **separate technology from delivery techniques**
- **Safety** runs through all aspects but is not specifically identified in the current map
- **Is the framing too positive?** Themes talk of preventing, screening, enhancing, treating, but what of the negatives? Bioterrorism, biohacking, deliberate misuse of the tech?
- **The map talks about 'editing in'. What about editing 'out'?** Isn't that the point of genome editing?
- Does the map **risk raising peoples' expectations** unrealistically when some of the science isn't there yet?
- If the map is for 'genome editing for human health' – it might be worth considering a category of work that **relates to animals, but with implications for human health** (eg. gene drives in mosquitoes to reduce transmission of malaria)
- It was suggested (but not agreed) that the mapping could be reframed from 'genome editing for human health' to **'human genome editing'**. This would be a significant change – both narrowing the field (i.e. excluding all other organisms), but also widening it (e.g. enhancement).

A number of specific additions to the map were suggested by participants

Domain	Missing research activity?
<p>1. Genome editing technologies</p>	<ul style="list-style-type: none"> • The map should separate technology from delivery techniques – e.g. recombinant adeno-associated virus (rAAV) is delivery, not an editing tool • Remove rAAV or add in other vectors lentivirus, nanoparticle • Activity that goes beyond editing, e.g. synthesising genomes. • Gene additions e.g. via lentivirus. Pre-dates ‘editing’ and still experimental but increasing, with significant risks and issues attached • Research into new delivery mechanisms. These are different techniques from GE, but are integral to ensuring that diseases are treated. One example would be how to identify stem cells and then increase the number of them effectively, and then make the correction stick. • Differentiating somatic- into ‘in situ’ in the individual directly or ‘ex vivo’ in the individuals’ harvested cells and injecting them back in
<p>2. Human genome editing technology applications</p>	<p>It was noted that translational research is missing from this domain (between basic and clinical research)</p> <p>There were questions about the clarity of distinction between rows 2 & 3 and a general view that rows 2 and 3 need to be looked at again. Some suggestion that 3 needs to be “more granular”. Suggested additions included:</p> <ul style="list-style-type: none"> • In vitro derived gametes • How to move from in vitro research safely into in vivo, how to do it efficiently and what damage does it do? • Engineering cell lines and therapeutic bullets could go in box 2 • Stem cells not mentioned: clinical research revolves around models, cells lines • There is a hybrid type of genome editing that has emerged which uses the targeted precision of CRISPR to knock-in at a particular locus in the genome an engineered cassette to restore gene function- under the endogenous control of the gene of interest promoter- right time, right place and right levels. It is called HITI- homology independent transgene integration which appears to be operative in a wider proportion of cell types (due to cell cycle), particularly differentiated cell types that no longer divide like neurons or photoreceptors. It is a precisely controlled gene replacement- the therapeutic power of this may be huge, because you could target more patients with different mutations in the same gene with the same regulated reagents, so economic and regulatory benefits.
<p>3. Human genome editing related research areas</p>	<p>Various refinements were suggested, including:</p> <ul style="list-style-type: none"> • Animal models are necessary to accelerate bench to bedside progress • Differentiating between genome editing/research <u>in</u> humans and <u>for</u> humans - the latter encompasses a wider field (i.e., brings in environmental factors - animals/plants - the GM crops issue - e.g., GM crops for improved nutrition could impact on human health) • Large scale sequencing and pre-natal screening are not directly relevant to genome editing: they raise important questions but depends on why you’re doing them (and you do them for lots of other reasons) • Aren’t “therapy by editing in somatic cells”/”....germline cells” (row 2) the same as “therapeutic genome editing” (Row 3). Why the difference in phrasing across the two boxes?

	<p>Suggested additions included:</p> <ul style="list-style-type: none"> • Models of human disease and tissue engineering • Governance as a research area (perhaps under practical and policy implications) • Insurance issues (social / ethical) • Unknown unknowns – how to respond, legislation • Engineering nuclease – model validation, mutation • Antibiotics • Improving efficiency of homologous recombination by: 1) modified expression of components of the DNA repair mechanisms 2) tethering proteins (i.e. Biotin/streptavidin)
<p>4. Human genome editing research themes:</p>	<p>Suggested additions included:</p> <ul style="list-style-type: none"> • Xenotransplantation • Plants for vaccine development • SAFETY was noted as an important issue that isn't currently identified, for example <ul style="list-style-type: none"> ▪ On target and off target interventions – underappreciated complexity ▪ Some derivatives such as spf1 have unexpected off targets that are potentially dangerous (i.e. indiscriminately cutting RNA). Cpf1- is the enzyme in question. New variants are emerging- smaller size, diversified repertoire of sites in the genome we can target, possibly improved rates of HDR/repair because of the overhangs at the cut site. It can be assumed that new, improved variants and/or types of editors will emerge.