Ethical issues in genome editing
Submission to Nuffield Council of Bioethics

Perspectives on genome editing

- The use of CRISPR/Cas9 is being adopted in the scientific community at a revolutionary pace. This revolution is comparable to the introduction of PCR in the second half of the 1980ies. The impact of the current revolution cannot be underestimated.
- Genome editing is more than the editing of genomes by means of nucleases that cut the DNA. Also ODM is a technique of genome editing.
- Genome editing is also more than just altering one or a few base pairs. Also the replacement of complete alleles should probably be seen as genome editing. This is editing in the sense that it is a deliberate and precise 'surgical' replacement of one existing gene by another. The result often is that one introduces multiple mutations in one gene at the same time.
- Genome editing is not only about introducing 'new' edits; it is also very much about introducing existing mutations or alterations into specific strains that do not possess that particular mutation or alteration. Simply because the CC9 is the most efficient and fastest way to introduce these mutations. So in many cases, especially in micro-organisms, there is nothing new about the organisms created.
- Genome editing is very much about creating additional genetic variation within existing strains or species. In particular in plant and animal breeding. It has nothing to do with the introduction of 'foreign' genetic material or the crossing of species boundaries. Of course the genes that code for the nucleases may be present at certain stages, but this is mostly temporarily, and they will not be present in the final product. Also, already technology is evolving to avoid the introduction of genes coding for the nucleases. The use of (pre-assembled) protein complexes may suffice in many instances in the future.
- If the edits that are achieved by genome editing can also occur in nature as a result of natural phenomena (as a result of faults in gene copying, or of natural radiation (sunlight), or exposure to certain chemicals), to what extend should the edited organisms then be regarded as 'novel'? And what does this mean from an ethical point of view?
- As knowledge and technology evolve 'off-target' effects seem to become more and more manageable and avoidable.
- It is well possible that regulatory approaches towards genome edited organisms will differ in different parts of the world. This may lead to thresholds for the application of genome editing that may be higher in certain parts of the world and less opportunities for those parts to benefit from this technological development. There is a great need for international harmonization in the area of genome editing, not only in terms of what type of regulatory oversight is deemed necessary (safety legislation), but also in terms of what type of applications we find desirable, ethical and responsible.

Genome editing in plant science

- The alterations achieved by gene editing are comparable to what one can achieve through conventional mutation breeding, which also can generate point mutations, frameshift mutations, small deletions and insertions, genome rearrangements, etc. The main difference is that classical mutation breeding, especially when using radiation or chemical mutagens, is a shotgun approach leading to hundreds or thousands of 'blind' mutations, where genome editing starts from molecular knowledge and is targeted and precise.
- Genome editing will greatly enhance our possibilities to create novel varieties in crops that are very difficult to breed, because they are either sterile or can only be propagated in a vegetative form.
- Europe has a very well developed plant breeding industry, among which a lot of SMEs. If genome editing in plants would be heavily regulated, this would translate into high thresholds for SMEs to take advantage of genome editing. There is a strong opposition to globalization and the role and power of multinationals. We should avoid pushing genome editing in the hands of only those that have pockets deep enough to afford high regulatory costs, while on the other hand guarantee safe and responsible use.
- We have a duty of care and should develop and use genome editing and genome edited organisms in a safe and responsible manner. The question in this particular case is whether or not the familiarity that we have with the development of crops in which mutations and other small genetic alterations have been introduced in a blind manner, also applies for genome edited plants. Can we use that familiarity with the effects of classical mutagenesis? And does the way that conventional plant breeding sector develops, selects, evaluates, tests and registers new varieties also warrant enough safety for genome edited crops? Probably yes, because otherwise we would end up in situations where the same mutation has to go through a special legally binding registration process that requires a lot of testing when the mutation has been produced by genome editing, and none of this when the mutation has been achieved by conventional mutagenesis, or natural random mutagenesis (i.e. sunlight). This would be disproportionate and discriminatory.

Genome editing in animals

- Genome editing is widely adopted for the development of new animal models in fundamental and biomedical research. It is very likely that this will have a beneficial impact on our abilities to develop new drugs, vaccines and therapies. It is likely to serve as an accelerator.
- In terms of ethics there are considerable differences between how animals are being regarded and this will have consequences for what type of genome editing in animals will take place and where. Already now it appears likely that Asia, and in particular China, will apply genome editing in a wide variety of animals and for a wide variety of purposes. How do we deal in Europe with such international developments?

Genome editing in micro-organisms

- Micro-organisms have a greater genomic plasticity than higher organisms, which means that small genetic alterations are far more likely to occur, and often also already do occur.
- It is especially in micro-organisms that genome editing will be applied to bring into strains already existing mutations.
- It should not be underestimated how many applications of genome editing in micro-organisms can be foreseen. And these will have a wide variety of applications in (veterinary) medicine, food and feed and industrial applications (the bio-based economy).

Biomedical research and human applications

- Genome editing makes it easier to achieve small mutations and gene repair in human cells compared to current technology. This puts pressure on the debate about deliberately introducing genetic alterations in the human context, which in the past has led to the 'somatic versus germline' debate. In general the same ethical arguments still apply for applications in the germline. Especially the autonomy argument to be able to decide for yourself, and the right of future generations to decide for themselves, still applies. But perhaps at the moment that genome editing is estimated to be 100% safe, and safer than current approaches, this pressure may become higher.

Military and security considerations

- There is already a debate on the use of so-called 'gene drives', which are genetic constructs based on CRISPR that allow an edit to be pushed into a population, even when the edit itself would have a fitness disadvantage. Can such a technology be misused when it would fall into the wrong hands? In principle almost any technology can be misused. In the case of gene drives it is perhaps difficult to imagine that persons that would want to do harm with a gene drive could do so and avoid harm to themselves or to their own surroundings. But for sure it will be important to prevent that a gene drive that potentially has negative consequences for human health or the environment, would fall into the wrong hands. But as such this does not present a new challenge when compared to existing biosecurity threats.