

Technical review of the Gene Technology Regulations 2001:
Consultation - Options for regulating new technologies

1. Which option/s do you support, and why?

Option 3 as it focuses on the process (template guided repair) by which the organism is modified as a central consideration. This would be the most practical option as it would ensure the use of SDN2 and SDN3 in the CRISPR-Cas system to direct sequence changes is thoroughly examined while reducing unnecessary regulatory burden by excluding SDN1 as we agree that it is less likely for SDN1 to pose risks that are different to natural mutations, conventional breeding or chemical/radiation mutagenesis.

We do not support Option 4 as it does not provide a clear definition, and therefore it would be difficult to provide a precise distinction for the regulation of SDN2 and SDN3 for accredited organisations. This option is mainly focused on plant breeding applications where the outcomes can be distinguishable from the products of conventional breeding.

2. Are there other risks and benefits of each option that are not identified in this document?

There might be risk in attracting international research funding from countries such as the US who do not classify some applications of site-directed mutagenesis and oligo-directed mutagenesis products as genetically modified.

3. Is there any scientific evidence that any of options 2-4 would result in a level of regulation not commensurate with risks posed by gene technology?

Many of the modern techniques covered in Options 2-4 are more specific and targeted than mutagenesis techniques and so are much less prone to off-target effects; chemical and radiation mutagenesis result in many untargeted mutations throughout the genome, whereas genome editing techniques result in discrete, targeted changes.

4. How might options 2-4 change the regulatory burden on you from the gene technology regulatory scheme?

Option 2 would add to the regulatory burden on Institutional Biosafety Committees and Accredited Organisations to ensure compliance with this option. As the outcomes are not dissimilar from and naturally occurring mutants or products of techniques that are not gene technology, this seems unnecessary.

Option 4 would be the hard to regulate as a clear distinction between SDN-2 and is required. Also, we note that there is a likelihood that successive rounds of modifications using SDN-2 or ODM could result in substantial changes which are similar to the outcomes arising from SDN-3 changes, therefore it would be worth regulating SDN-2.

5. How do you use item 1 of Schedule 1, and would it impact you if this item was changed?

N/A.

6. Might contained laboratory research on GM gene drive organisms pose different risks to other contained research with GMOs, and how could these risks be managed? Supporting information and science-based arguments should be provided where possible.

Investigators dealing with GMOs are provided with training, and there are controls in place to minimise the risk of transmission. Researchers follow strict procedures and guidelines to manage the transport, storage and disposal of GMOs to reduce the risks to the health and safety of people involved in the dealing. It is unlikely that the generated GMOs will pose any significant risk to the environment as they are defective by nature and not currently known to cause any disease in humans or animals. In the unlikely event of an unintentional release of the GMO into the environment, we have a procedure for the decontamination of these GMOs.

Our organisation uses the CRISPR/Cas9 system to genetically modify cells using viral systems (AAV, Adenovirus, Lentivirus). Although the virus itself is replication incompetent and not currently known to cause any diseases to animals or humans, there is theoretically a very small chance that through a recombination even or retrotransposon insertion that it could acquire the correct packaging genes. The likelihood of such an event occurring is very low and we have taken extra precautions when handling all viral vectors to minimise the risk.

7. What RNA interference techniques are you using, and are there RNA interference techniques that you believe have unclear regulatory status? Please provide details of the techniques and science-based arguments for whether these techniques pose risks to human health or the environment.

Our organisation uses siRNA delivered by adenoviral or lentiviral vectors *in vitro* and *in vivo*. *In vitro*, cells are infected to evaluate changes to gene and/or protein expression. *In vivo*, RNAi is used to deliver genes to target organs to assess safety and efficacy of the technique. These techniques are of low risk to human health or the environment as the vectors used are replication defective. They may pose health and safety risks to staff are through aerosol and skin exposure, but precautions are undertaken to minimise these risks.

8. Do you have proposals for amendments to any other technical or scientific aspects of the GT Regulations? All proposals should be supported by a rationale and a science-based argument.

We would like end effects/outcome/products should be considered on a case-by-case basis.