

Response 1

Option 4 (Regulate new techniques with different products to conventional breeding), but with a specific rider of only exempting processes that do not result in more than a codon change (3 consecutive nucleotides) to native sequence.

This option will be progressive and yet limit the risks to those currently accepted for chemical mutagenesis and radiation. Significantly, could allow using more precise, safer and humane tools for exactly the same outcomes as conventional breeding and chemical/radiation mutagenesis, without the regulatory burden.

Response 2

OTGR discussion paper: demote non-selective-advantage GM *Drosophila melanogaster* research to PC1

1.1 The proposed amendment

The amendment to the Gene Technology Regulations (2001) proposed here is that work with GM *Drosophila melanogaster*, when the modifications do not confer a selective advantage or produce an infectious agent, be downgraded to PC1 level containment.

1.2 The reclassification of GMO fly research is within the scope of the current review

The review calls for proposals for other amendments to the GT regulations, supported with rational and science-based arguments. In the past 15 years since the 2001 regulations were introduced, no incidents involving GM *Drosophila melanogaster* with adverse affects on human health or the environment have been reported. This is despite almost 4000 publications involving *D. melanogaster* annually (Pubmed), and despite other major countries at the forefront of scientific research (including the US and the UK) requiring only PC1-level containment for non-selective advantage *D. melanogaster*.

Importantly, Australia is now out of step with other countries with respect to containment regulations for this organism.

1.3 *Drosophila melanogaster* is a harmless species native to Australia

D. melanogaster is a common genetic model organism that has been used in scientific research for over 100 years. The species is harmless in terms of the environment, agriculture and human health, and is commonly found associated with human populations throughout the world, including in all Australian States and Territories. *D. melanogaster* is not a disease carrying vector, does not bite or sting and is not a crop pest. (Although *D. melanogaster* is commonly called a “fruit fly”, it is not a pest and is not responsible for crop destruction, as opposed to fruit flies of the family *Tephritidae* and the spotted-wing fruit fly *Drosophila suzukii*.)

The harmless nature of *D. melanogaster* was documented in a report by the Royal Society (UK) in 2001:

Methods for reproducibly creating stable, heritable GM insects were developed almost 20 years ago, using the well-known genetic model insect *Drosophila melanogaster*. **It is generally considered harmless as it is neither a significant agricultural pest nor a disease vector and no adverse consequences to human health or the environment of this large-scale genetic engineering have been reported.** Many thousands of different GM strains of *Drosophila* have subsequently been produced in laboratories around the world, and there are far more GM strains of *Drosophila* than there are of all other GM insects combined. It has become the paramount model organism for studying animal development and genetics.

– *Royal Society Report (May 2001)*, “The use of genetically modified animals”, paragraph 40, emphasis added.

1.4 GM *Drosophila melanogaster* that do not possess a selective advantage pose no risks to the environment

Genes present in the vast majority of GM *D. melanogaster* are from non-pathogenic species. These genes do not confer a selective advantage and are non-toxic and non-pathogenic. They are not able to cause genetic modification of non-GM flies that they might come into contact with (gene drive is excluded here).

GM *D. melanogaster* strains are domesticated and less fit than wild-type flies. Studies have shown that wild flies rapidly lose fitness when cultured in the laboratory (Hoffmann et al, *Evolution*, 55(2):436-438, 2001; Sgro and Partridge, *American Naturalist*, 158(6):657-658, 2001), losing the ability to tolerate environmental stresses found in the wild (such as temperature and humidity extremes). Typical laboratory strains of *D. melanogaster* have been cultured in laboratory conditions for over 70 years (>1000 generations), and as such would be unexpected to survive in the wild in the unlikely event that GM *D. melanogaster* escape containment.

1.5 The use of PC1 for non-selective-advantage GM *Drosophila melanogaster* is standard in other countries

Almost all GM *D. melanogaster* research conducted in the United States is considered Biosafety Level 1 (the least restrictive containment level) under NIH guidelines (*NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)*, 2016, Section III-D-4-a). Only when the nature of genetic modifications involve the production of an infectious agent or confer a selective advantage are higher levels of containment used (such as GM flies containing prion sequences or gene-drive constructs).

Similarly, in the UK a risk assessment in the form of an environmental impact statement is required when working with GM *D. melanogaster*. If that risk assessment concludes that the risk to the environment is minimal then Biosafety Level 2 containment is not required (*The Genetically Modified Organisms (Contained Use) Regulations 2014*).

The UK *SACGM Compendium of Guidance* further notes:

It is a regulatory requirement to thoroughly assess the risks posed by GM animals. However, in practice, activities with GM animals are unlikely to pose a risk to human health and the main consideration will be in regard to preventing the animal escaping into the environment. **Therefore, activities should be assessed in a way that is commensurate with the actual hazards posed. There is a need for an informed and pragmatic approach, rather than an overcomplicated assessment and unwarranted control measures.**

SACGM Compendium of Guidance, paragraph 25, emphasis added.

1.6 Only PC1 containment is required for other common genetic model organisms in Australia

The current Gene Technology Regulations allow work with GM mice, rats, rabbits, guinea pigs and the nematode worm *Caenorhabditis elegans* to be conducted in PC1 containment, when there is no selective advantage conferred by the modifications and the modifications do not result in the ability to secrete or produce an infectious agent. Downgrading non-selective-advantage GM *D. melanogaster* research to PC1 would be in line with the restrictions imposed on other common genetic model organisms in Australia.

1.7 Conclusions

The current requirement for PC2-level containment for GM *D. melanogaster*, when the modifications do not confer a selective advantage or produce an infectious agent, is not in line with the environmental risks posed by these flies. Further, the current legislation imposes a significantly greater level of containment than that required by other major scientific research countries such as the US and the UK.

It is recommended that research using GM *D. melanogaster*, when the modifications do not confer a selective advantage or produce an infectious agent, be downgraded to PC1-level containment, matching the current regulations for the containment of other common GM model organisms.