Purpose

These guidelines issued by the University of Adelaide Institutional Biosafety Committee (IBC) are to ensure:
- University personnel (staff and students) whose research involves genome editing technology are informed of the regulatory compliance required by the IBC.
- The IBC has records of any modified organism that have been made, developed, produced or manufactured using genome editing technology.

Scope

The IBC recognises the importance that the introduction of genetic change is a fundamental methodology in biomedical, biological research and a key method for crop and animal improvement through the addition or removal of particular features.

Recent technological advances for the modification of DNA sequences, commonly referred to as genome editing, allow specific changes to be induced at defined locations in plant and animal genomes.

The most important new technology is referred to as CRISPR/Cas, which allows targeted genome modification through an RNA-based mechanism. TALEN and ZFN technologies also exist and operate in a similar manner by generating double-stranded breaks in DNA in a site-specific manner. However, these technologies are mostly now superseded by the CRISPR/Cas systems.

The scope of these guidelines is for research involving genome editing technology with reference to the widely used CRISPR/Cas system.

Definitions

IBC: The University of Adelaide Institutional Biosafety Committee (IBC) administers gene technology regulatory compliance at the University according to the Gene Technology Act 2000 (Act) and the Gene Technology Regulations 2001 (Regulations) and corresponding State legislation. The IBC acts as an interface with the Australian Government Office of the Gene Regulator (OGTR) for the University.

OGTR: The OGTR provides administrative support to the Gene Technology Regulator who is responsible for administering the national regulatory system for gene technology as set out in the Act.

Gene technology as defined by the Act means any technique for the modification of genes or other genetic material, but does not include:
(a) sexual reproduction; or
(b) homologous recombination; or
(c) any other technique specified in the Regulations (Schedule1A-Techniques that are not gene technology).

Genetically Modified Organism (GMO) as defined by the Act means:
(a) an organism that has been modified by gene technology; or
(b) an organism that has inherited particular traits from an organism (the initial organism), being traits that occurred in the initial organism because of gene technology; or
(c) anything declared by the Regulations to be a genetically modified organism, or that belongs to a class of things declared by the Regulations to be genetically modified organisms;

Organisms that are not genetically modified organisms as described in the Regulations (Schedule1):
a mutant organism in which the mutational event did not involve the introduction of any foreign nucleic acid (that is, non-homologous DNA, usually from another species).
For example, mutant organisms generated using mutagenesis (i.e. radiation (electromagnetic, particle), chemicals and/or transposons) are not considered to be GMOs.
Genome Editing Technology CRISPR/Cas

CRISPR/Cas allows targeted genome modification through an RNA-based mechanism. The double-stranded DNA breaks caused by the CRISPR/Cas and other systems are repaired by non-homologous end-joining (NHEJ). This causes mutations in the targeted sequences that are unpredictable and, therefore, indistinguishable from naturally-occurring mutational events (e.g. as caused by ionising radiation).

However, it is possible to direct the repair of the double-stranded breaks by addition of a repair template that must be comprised of DNA and that operates by the process of homology directed repair (HDR). The process of HDR is not completely precise and can potentially produce changes in a genome that are not as desired e.g. inclusion of template sequences together with random sequence changes as produced by NHEJ or even insertion of the template sequence at other positions in the genome.

IBC Requirements

Dealing Authorisation

The IBC recommends that University personnel (staff and students) review the classifications (listed below) for research involving genome editing technology prior to commencement of work. The research classifications provided by the IBC will indicate whether a Dealing authorisation is required or a Notification of Intent (NOI) should be forwarded to the IBC Secretary.

The IBC consider the classifications are consistent with the definitions of gene technology and genetically modified organism under the current Act and Regulations:

- Genome editing technologies that do not involve introduction of DNA into cells or introduction of technology components into cells that operate through a DNA-intermediate (e.g. reverse transcription systems) and that cause changes that are indistinguishable from naturally occurring mutation events do not produce genetically modified organisms as defined by the current Act.
  
  Example:
  deletion mutations generated by injection of CAS9 mRNA and gRNA into mouse zygotes to create “knock-out” mice
  
  o This research requires a NOI prior to commencing the work.
  o This research does not require a Dealing authorisation from the IBC prior to commencing the work.

- If DNA is introduced into cells (e.g. during genome editing of plants) or HDR is attempted then genetically modified organisms can be produced as defined by the current Act.
  
  Example:
  editing of a precisely defined mutation into the mouse genome by injection into mouse zygotes of CAS9 mRNA, gRNA and an oligonucleotide bearing the mutation sequence.
  
  o This research requires a Dealing authorisation from the IBC (Exempt registration or Notifiable Low Risk Dealing) and where necessary the Office of the Gene Technology Regulator (OGTR) prior to commencing the work.

* Notification of Intent (NOI) form is attached.
This **NOI** must be completed by University personnel, whose research involves genome editing technology, such as the CRISPR/Cas based system, but the research **does not** require a Dealing authorisation from the IBC.

*ie DNA is not introduced into cells (this covers deletion of genes and repair by non-homologous end-joining (NHEJ))*

NOI to be submitted to IBC Secretary at:

[ibc@adelaide.edu.au](mailto:ibc@adelaide.edu.au)

**1**  
**Researcher Details**

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**2**  
**Genome Editing Technology Details**

<table>
<thead>
<tr>
<th>CRISPR/Cas</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td><strong>Other</strong> (please specify)</td>
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Scientific name of modified organism(s) (this includes cell lines that are modified by genome editing)

Modified trait(s) and gene(s) responsible