University of Cape Town
INSTITUTIONAL BIOSAFETY COMMITTEE (IBC)

POLICY ON REVIEW OF RESEARCH PROTOCOLS SUBMITTED TO THE IBC

The IBC is a Senate-level committee which provides review and oversight of research protocols and related activities conducted at the University of Cape Town involving recombinant or synthetic nucleic acid molecules, as well as potentially hazardous biological agents.

Background

The IBC is constituted to protect the interests of UCT-based activity, as well as the community and the environment, by ensuring that all activity involving recombinant or synthetic nucleic molecules, as well as other **potentially hazardous biological agents (**pHBAs), comply with national legislation and national and international guidelines on biosafety and environmental ethics.

Activities involving HBAs are subject to the Regulations on Hazardous Biological Agents of the Occupational Health and Safety Act 85 of 1993. Activities involving genetically modified organisms (GMOs) are subject to the Regulations under Section 20 of the GMO Act (*Genetically Modified Organisms Act* 15 of 1997) and the *Genetically Modified Organisms* Amendment Act 23 of 2006. Furthermore, UCT's Institutional Biosafety Committee (IBC) aims to comply with, and is not limited to, other relevant national and international acts, guidelines, and protocols such as the National Environment Management Act (Act no.107 of 1998), the Cartagena protocol on biosafety, the SA MRC Guidelines for Ethics in Medical Research: Use of Biohazards and Radiation, and the NIH Guidelines for research involving recombinant or synthetic nucleic acid molecules.

To ensure safety, ethics, and compliance, the IBC, as a Senate-level committee, will have oversight of Faculty-level Biosafety Committees (FBCs) to which it may delegate reviews of specific projects or project types (non-compliance, study closure reports).

The IBC will provide protocol-level review and monitoring support to UCT-based activities[1] when necessitated by funding requirements or other imperatives. The university requires that all activities using pHBAs are reviewed to the satisfaction of applicable regulatory and compliance requirements. If a project or protocol involves the use of animals and pHBAs, approval by the appropriate Animal Ethics Committee will also be required. Further approval may be required under Section 20 of the Animal Diseases Act (Act 35 of 1984). Human gene transfer projects will require Faculty Research Ethics Committee (REC) approval, which is contingent on approval by the IBC. The testing of any pHBAs in humans will require faculty REC approval, which is contingent on approval by IBC. Further approval for both human, plant and animal testing may be required under the GMO Act.

[1] "UCT-based activities" includes off-site studies, performed by UCT personnel

As a registered Institutional Biosafety Committee (IBC) with the US National Institutes of Health's (NIH) Office of Biotechnology Activities, the UCT IBC will provide review, monitoring and oversight of NIH-funded research in accordance with NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (2019) as well as the GMO Act for the review of research involving recombinant or synthetic nucleic acid molecules. The IBC will provide protocol-level review for all faculties doing work involving pHBAs, which will include issuing authorisation for specific projects. The initial review will be done by the relevant FBC and then by IBC or by an external biosafety committee with appropriate expertise (approved by the IBC, University of Cape Town) before the research activity may commence. The IBC will define which work on pHBAs is exempt from this process or will be managed by the FBC.

Different levels of Review Required for Different Types of Research

There are different levels of review required for different types of research at UCT that need to also be compliant with NIH guidelines. Refer to https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf. The terms of reference for the UCT IBC cover more than is covered by the NIH guidelines and so the UCT policy on review of these expanded pHBAs are included in table 2.

The basis of classification of different pHBAs by risk group is given in the table below.

Table 1: Basis for the Classification of Biohazardous Agents by Risk Group (RG)	
Risk Group 1 (RG1)	Agents that are not associated with disease in healthy adult humans
Risk Group 2 (RG2)	Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available
Risk Group 3 (RG3)	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available (high individual risk but low community risk)
Risk Group 4 (RG4)	Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available (high individual risk and high community risk)

A summary of the different levels of review for different types of experiments involving recombinant or synthetic nucleic acids is given in table 2 below followed by a more detailed description.

Guidelines for Proposals

Proposals will be submitted to the FBC following the instructions of the Faculty websites

Faculty of Health Sciences:http://www.health.uct.ac.za/fhs/research/faculty-biosafety-committee

Faculty of Science: http://www.researchsupport.uct.ac.za/biosafety

Proposals will be reviewed by FBC and then if necessary submitted to the IBC (refer to Table 2). Applicants are encouraged to submit "umbrella" projects where the organisms / experiments carry the same risks rather than a separate application for each experiment.

Table 2: SUMMARY OF UCT GUIDELINES FOR REVIEW OF RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACIDS

Level of Review	Example of types of research covered (Refer to NIH Guidelines for more detail)	Relevant section of the NIH guidelines or UCT guideline
IBC [1],	Experiments that compromise the control of disease agents in medicine through deliberate transfer of a drug resistance trait	NIH III-A
IBC approval and review for containment determinations [2]	Experiments involving the cloning of toxin molecules with LD50 of less than 100 nanograms per kilogram of body weight	NIH III-B
IBC and IRB approvaland review before research participant enrolment [3]	Experiments involving the deliberate transfer of recombinant or synthetic nucleic acid molecules into human research participants or gene editing of human embryos or participants.	NIH III-C
IBC approval before initiation	Creating stable germline alterations of an animal or plant germline or testing viable recombinant or synthetically modified microorganisms on whole animals or plants where BSL-2 containment or greater is necessary. This includes gene editing. GMO work involving biological agents of risk group 2 or above and/or requiring BSL-2 containment or above. GMO work involving culture volumes greater than 10L.	NIH III-D
IBC approval before initiation	Release into the environment of any potentially hazardous biological agents	UCT policy
IBC approval before initiation	Any research involving pHBAs at BSL3	UCT policy
FBC approval and recorded at IBC	Creating stable germline alterations of animals or plants by introduction of recombinant or synthetically modified nucleic acid molecules when these experiments require BSL-1 containment. This includes gene editing.	NIH III-E
FBC approval and recorded at IBC	Purchase or transfer of transgenic rodent. GMO work involving biological agents of risk group 1 where BSL-1 containment is sufficient.	NIH III-F
FBC approval and recorded at IBC	Research with any potentially hazardous biological agents not covered by the NIH guidelines such as unmodified pathogens.	UCT policy
Approval not required	Laboratory research involving clinical trials on pHBAs that do not involve GMOs or any BSL 3 laboratory component at UCT	UCT policy

1 If NIH funded then requires NIH Director review and approval
2 If NIH funded then requires NIH review for containment determinations
3 If NIH funded then requires NIH review before research participant enrolment

Exempt Experiments (Refer to Section III-F of NIH guidelines)

The following recombinant or synthetic nucleic acid molecules are exempt from the NIH Guidelines and registration with the Institutional Biosafety Committee is not required; however, other standards of biosafety may still apply to such research (for example, the Centers for Disease Control and Prevention (CDC)/NIH publication Biosafety in Microbiological and Biomedical Laboratories).

1. Those synthetic nucleic acids that: (1) can neither replicate nor generate nucleic acids that can replicate in any living cell (e.g., oligonucleotides or other synthetic nucleic acids that do not contain an origin of replication or contain elements known to interact with either DNA or RNA polymerase), and (2) are not designed to integrate into DNA, and (3) do not produce a toxin that is lethal for vertebrates at an LD50 of less than 100 nanograms per kilogram body weight. If a synthetic nucleic acid is deliberately transferred into one or more human research participants and meets the criteria of Section III-C, it is not exempt under this Section.

2. Those that are not in organisms, cells, or viruses and that have not been modified or manipulated (e.g., encapsulated into synthetic or natural vehicles) to render them capable of penetrating cellular membranes.

3. Those that consist solely of the exact recombinant or synthetic nucleic acid sequence from a single source that exists contemporaneously in nature.

4. Those that consist entirely of nucleic acids from a prokaryotic host, including its indigenous plasmids or viruses when propagated only in that host (or a closely related strain of the same species), or when transferred to another host by well-established physiological means.

5. Those that consist entirely of nucleic acids from a eukaryotic host including its chloroplasts, mitochondria, or plasmids (but excluding viruses) when propagated only in that host (or a closely related strain of the same species).

6. Those that consist entirely of DNA segments from different species that exchange DNA by known physiological processes, though one or more of the segments may be a synthetic equivalent. A list of such exchangers will be prepared and periodically revised by the NIH Director after appropriate notice and opportunity for public comment (see Section IV-C-1-b-(1)-(c), Major Actions). See Appendices A-I through A-VI, Exemptions under Section III-F-6--Sublists of Natural Exchangers, for a list of natural exchangers that are exempt from the NIH Guidelines.

7. Those genomic DNA molecules that have acquired a transposable element, provided the transposable element does not contain any recombinant and/or synthetic DNA.