



BRIDGING POLICY AND ACTION: GAIN-OF-FUNCTION RESEARCH AT THE AUSTRALIAN CENTRE FOR DISEASE PREPAREDNESS

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ACDP – AUSTRALIA'S NATIONAL BIOCONTAINMENT FACILITY
www.csiro.au





The Australian Centre for Disease Preparedness respectfully acknowledges the Wadawurrung people of the Kulin Nation, the Traditional Owners of the land on which ACDP sits. We pay our respects to their Elders past and present.

ACDP's Reference Laboratory Role

ACDP helps protect Australia's multi-billion agriculture industries, and the nation, from emerging infectious and emergency animal disease threats.

WOAH

WOAH Collaborating Centres

- Laboratory Capacity Building
- New and Emerging Diseases
- Diagnostic Test Validation Science in the Asia-Pacific Region

WOAH Reference Laboratory

- Bluetongue
- Hendra and Nipah virus diseases
- Highly pathogenic & low pathogenic avian influenza
- Newcastle disease
- African swine fever
- Classical swine fever
- Abalone herpesvirus
- Ranavirus
- Yellow head disease
- Epizootic haematopoietic necrosis virus



UN/FAO

- FAO Reference Centre for Animal Influenza & Newcastle Disease
- FAO Reference Centre for Biorisk Management
- UNSGM Designated Laboratory for Biological Weapons

WHO

- Representation on WHO SARS-CoV-2 Expert Group
- Global Outbreak & Response Network (GOARN) partner

National Reference Laboratory

Terrestrial animals

- 27 diseases of multiple species
- 2 cattle diseases
- 5 sheep & goat diseases
- 11 equine diseases
- 16 swine diseases
- 10 avian diseases
- 4 diseases of other species

Aquatic species

- 24 fish diseases
- 13 mollusc diseases
- 15 crustacean diseases
- 3 amphibian diseases

Innocuity testing



ACDP Project Approval Overview

**Project Application
and Risk Assessment**



**Project
Submission**

**Institutional
Biosafety
Committee**

Access To ACDP

Project Safety and Compliance

All projects that deal in infectious, GM or biosecurity (imported) material are required to submit a PARA to the IBC for review.

Leadership Awareness and Alignment

Committee is comprised of ACDP leadership from all scientific units on site and ensure alignment of projects with mission.



The PARA

Project Application and Risk Assessment (PARA) reviewed as a function of the IBC

Designed to address if the proposed work can be done at ACDP

- Part 1- What, where and how
- Part 2A/B- Risk assessment for agent(s)
- Part 3 and 4- Hazard controls
- Part 5- Regulatory Compliance

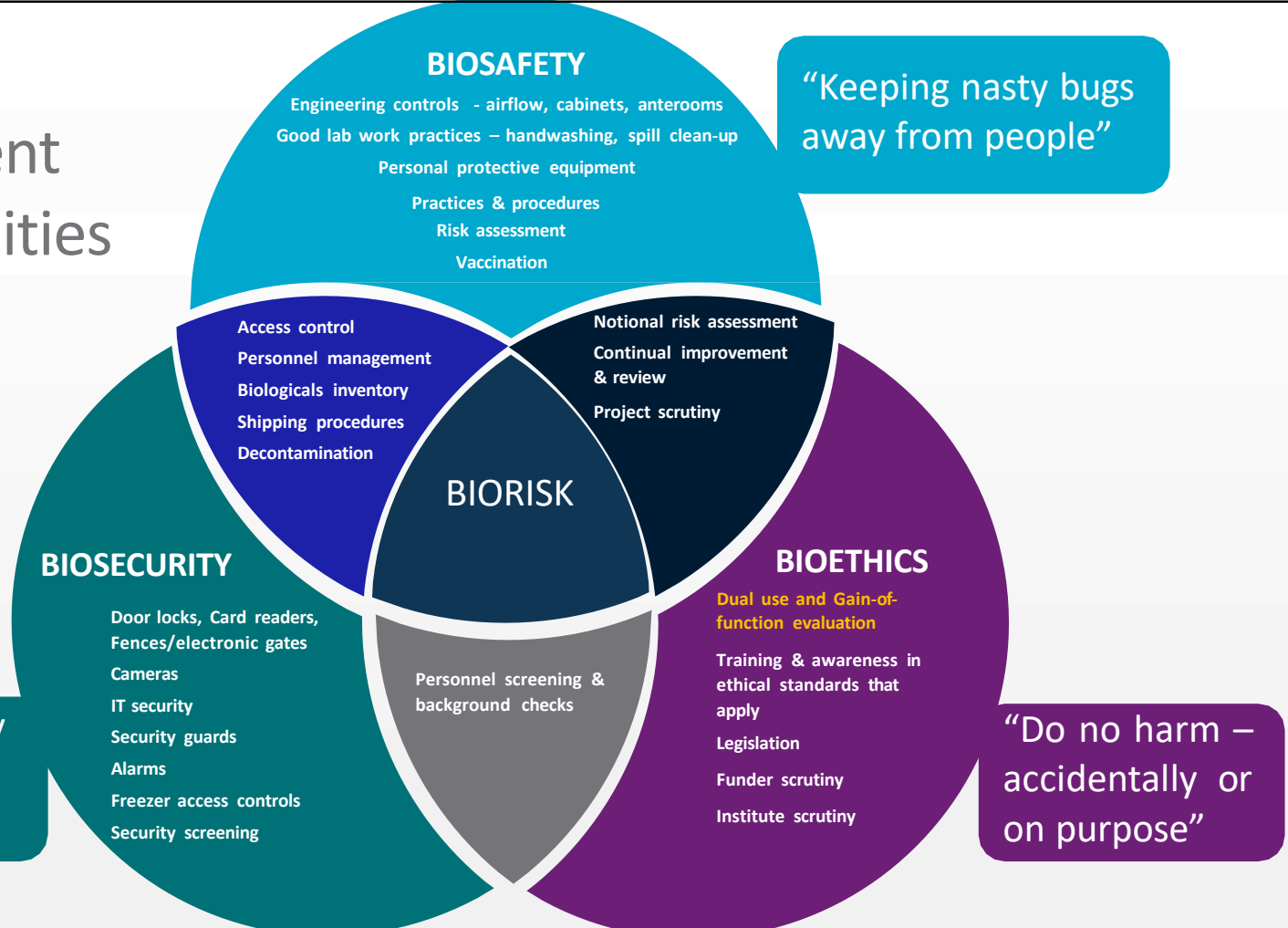
Project Application and Risk Assessment Form	
INSTRUCTIONS: Complete this form using the examples in grey (they should be overtyped or deleted). Please provide a response to every question so that it can be confirmed as being acknowledged. Application will not be reviewed until all fields have been acknowledged.	
Part 1: Project Details	
Project Title:	Specific to this application, avoid abbreviations
Project Leader:	Contact details
Prepared by:	Contact details
WBS Number	Existing IBC/OGTR ID
The Project Supervisor / Team Leader / Line Manager has reviewed and approved this application for submission to the IBC. Ensure review and discussion with a senior member of your Team / BU prior to submission.	
<input type="checkbox"/> Yes (Please continue and once complete submit for review to ACDP IBC Executive Team) <input type="checkbox"/> No (DO NOT SUBMIT until the PS / Team Leader / Line Manager has reviewed this application)	
If in vivo work is planned: The Animal Studies Team Leader/s has been consulted and approve this application for review Ensure review and discussion with a senior member of the AST prior to submission.	
<input type="checkbox"/> Yes (Please continue and once complete submit for review to ACDP IBC Executive Team) <input type="checkbox"/> No (DO NOT SUBMIT until the Animal Studies Team Leader / Line Manager has reviewed this application)	
Project Description: Aims and Methodology: Briefly describe the aims of the project and methodology proposed: Project Aim: This is not the Aim of the overall big picture Project. Please limit the aim by describing the objective of this application; do not copy and paste the project spiel you submitted to get permission for the project to go ahead. Be specific. Avoid terminology such as 'including', 'not limited to', 'as well as other agents'. The IBC can only review and approve what is known. Methodology Please avoid including SWI, HSE like instructions and non Biosafety information. Be clear with the assays being undertaken and the purpose of the assay. E.g. VNTs for..., ELISA to..., Extraction of..., Sequencing so...	
MS-POL-300 PC3 General Work Practices MS-SOP-301 PC3 Entry and Egress MS-SOP-303 Working with Infectious Material MS-SOP-703 Tracking SSBA's and Working Culture MS-SOP-702 SSBA Transportation MS-SOP-1000-1002 Spills and Incidents response MS-POL-106 SSBA Information Management	
Part 4: Project risks and <input type="checkbox"/> NOT APPLICABLE (if no in vivo work, leave Part 4)	
Part 2A Risk as <input type="checkbox"/> NOT APPLICABLE	
Where is the infectious / regulated work being conducted? Tick appropriate Location(s) Refer report of Facility Certifications and Dealings for further details of suitability of location.	<input type="checkbox"/> South <input type="checkbox"/> Centre <input type="checkbox"/> North <input type="checkbox"/> DERL <input type="checkbox"/> Inverte <input type="checkbox"/> Confoc <input type="checkbox"/> PC4 Nc <input type="checkbox"/> PC4 Ce
Will infectious agents be used? If this is: ACDP please contact BMG prior to submission	<input type="checkbox"/> Yes <input type="checkbox"/> No
During the course of this project, will material be inactivated using an approved method? *has been reviewed by BMG as an acceptable method for specific agents or class of agents	<input type="checkbox"/> Yes <input type="checkbox"/> No
List all infectious agents and strains involved in project. (Attach list if insufficient room)	<input type="checkbox"/> Yes <input type="checkbox"/> No
Documentation – List below the specific staff that address biosafety hazards as implemented to mitigate these. Please identify specific BM Manual SOPs or please complete the following section and	
List of Processes Examples as below; PIs overwrite or delete Egg inoculation, harvesting of a R03 Strain	
a Is the agent exotic? b Are closely related c What is the mortality d Can the agent establish e Is the agent transmissible f What is the environment? i) In relation to the agent ii) In relation to the agent iii) In relation to the agent	g Describe the known h Describe the possible environment i Describe any other aspects related to the agent that you have considered in your risk assessment
Respiratory Exposure Haz a Is the agent or close to cause infection if of droplets or dropl b Is there the potential generated from the excretory process or as a result of the necropsy procedure c Justify removal of re	
Percutaneous Exposure Haz d Is this agent known humans through cc direct injection? e Will sharps with inf used?	
Mucosal Exposure Haz g Is this agent known humans through th h Is there the potential this project? i Justify removal of re	



What happens when the box is ticked?

Dual Use Research of Concern			
e	<p>Do you believe there are any Dual use implications that may be generated by this project?</p> <p>Please be advised that if Yes, approval from the DURC</p>	<p>Y or N</p> <div><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</div>	<p>If yes, state below why you believe it is and how the knowledge / information obtained could be misused:</p> <p>State reasons here: This project aims to compare the molecular determinates of pathogenicity between attenuated and highly pathogenic filoviruses. Switching of genes may result in some attenuated viruses increasing in virulence. It is not expected that any generated virus would be more pathogenic than the wild-type Ebola virus</p>

Biorisk Management Responsibilities

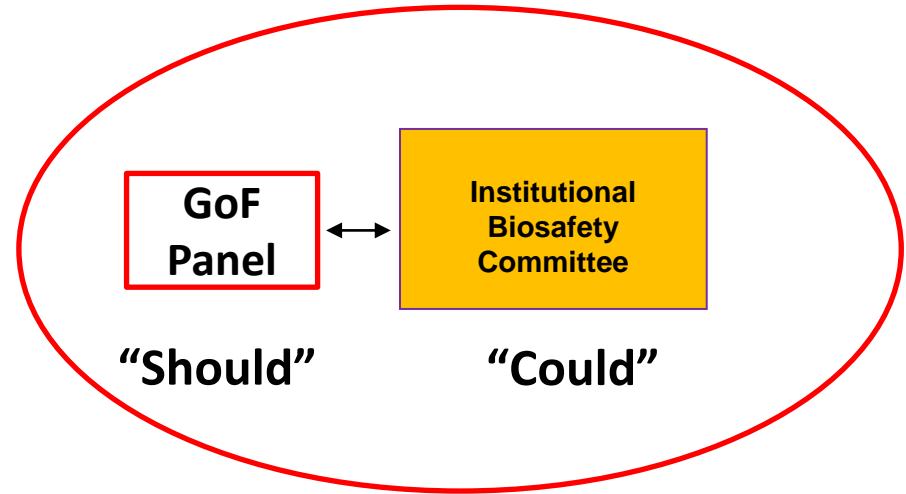




Establishment of the GoF Review Panel

Important Considerations for the establishment of the GoF Review Panel

1. Leverage existing review pathways
2. Decision making capability
3. Minimise added time for project review and approval
4. Include scientists and ACDP leaders to make well-rounded decisions
5. Primary consideration for **“should”** the work be done at ACDP. IBC focus on whether the work **“could”** be done.





Decision Makers

GoF Membership Composition:

- ACDP Biorisk Manager (Chair)
- ACDP Director
- AAHL Science/Deputy Director
- H&B Science/Deputy Director
- Strategic Facility Operations Director

Observers

- IBC member nominated by the IBC chair
- CSIRO communications



GoF Panel Review Process

(i) GoF Risk Assessment Document Provided to the Researcher

(i) Project description

(ii) Key questions

(iii) Justification for experimental design

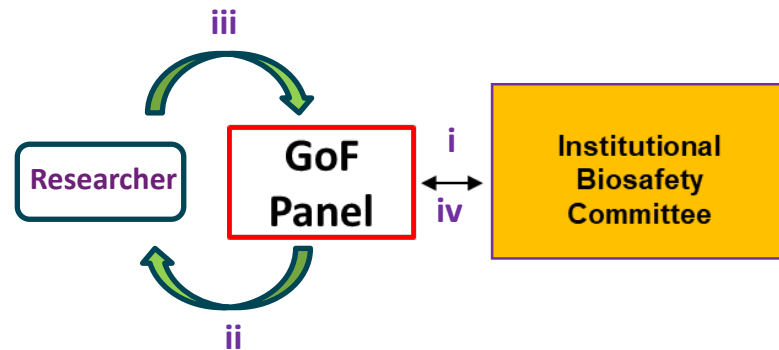
(iv) Project impact statement

(ii) Panel convenes when a project is identified

(iii) Meeting includes the researcher and supervisor

(iv) Panel makes a determination which is communicated back to the IBC and researcher through a decision memo

(i) Decision memo captures key discussion elements and approved/not approved statement with applicable conditions



Focus of the review: GoF Panel Terms of Reference

Primary Considerations

- Enhanced production
- Morbidity/mortality
- Transmissibility,
- evasion of immunity and
- resistance to drugs or evasion of medical countermeasures

Additional Considerations

- Pandemic potential
- Funding Source
- Unaddressed safety concerns
- Unknown risk profiles and
- Benefits versus risks



GoF Risk Assessment

Modified from the U.S. NIH Document
to meet Australian/ACDP Needs

Key Areas

- Project Details
- Funding Source
- Agent(s) Involved
 - Adapted to focus on Australian SSBA but not exclusive to these agents

CSIRO		Bioscience Management Group		Page 1 of 6 Version 1
CSIRO		Gain of Function Risk Assessment		MS-SOP-164
This template is for Gain of Function - Risk Assessment. Do not delete sections – if a section of this template does not apply, acknowledge and provide a short reason.				
Gain of Function Risk Assessment				
1: Project Details				
Project Title:	Understanding the biosecurity risk posed by Australian-lineage H5 LPAIV and the potential genesis to highly pathogenic forms.			
Project Leader:		Contact details:		
Funding Source Check all funding bodies that apply and provide details				
2: Project Information				
Agent or Toxin involved Check all agents or toxins that apply				
<input type="checkbox"/> Bacillus anthracis	<input type="checkbox"/> Reconstructed 1918 influenza virus	<input type="checkbox"/> Classical swine fever virus		
<input type="checkbox"/> Botulinum toxin	<input type="checkbox"/> Rinderpest virus	<input type="checkbox"/> Lumpy skin disease virus		
<input type="checkbox"/> Marburg virus	<input type="checkbox"/> Clostridium botulinum	<input type="checkbox"/> Peste-des-petits-ruminants virus		
<input type="checkbox"/> Ebola virus	<input type="checkbox"/> Francisella tularensis	<input type="checkbox"/> Yellow fever virus (non-vaccine strains)		
<input type="checkbox"/> Foot-and-mouth disease	<input type="checkbox"/> African swine fever virus	<input type="checkbox"/> Burkholderia mallei		
<input type="checkbox"/> Avian Influenza virus	<input type="checkbox"/> Capripoxvirus	<input type="checkbox"/> Burkholderia pseudomallei		
<input type="checkbox"/> Other (detail below)				
List any additional infectious agents and strains involved in project				



GoF Risk Assessment

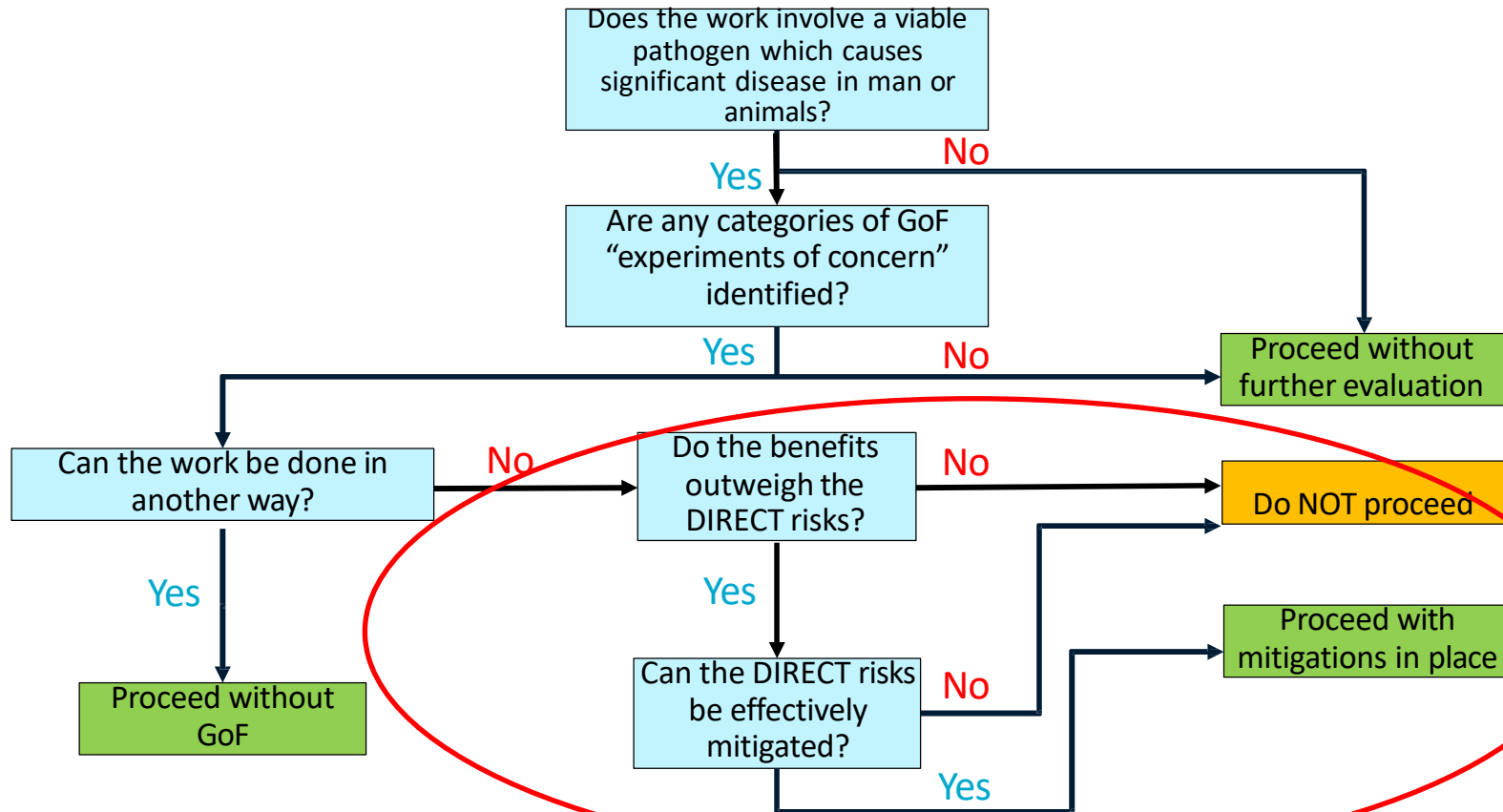
Key Areas Continued

- Experimental Effects
 - Why should the panel be involved
- Justification for experimental approach
- Impacts of the predicted outcomes
 - Experimental justification versus impacts has been the major discussion point in the panel meetings thus far

3: Project assessment

Assessment of Experimental Effects	
<i>Assess whether research aims to produce, or is reasonably anticipated to produce one or more of the experimental effects. If YES, provide additional information to explain the associated risks and how the concern is addressed.</i>	
<input type="checkbox"/> Yes <input type="checkbox"/> No	Enhances the harmful consequences of the agent or toxin
<input type="checkbox"/> Yes <input type="checkbox"/> No	Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification
<input type="checkbox"/> Yes <input type="checkbox"/> No	Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates its ability to evade detection methodologies
<input type="checkbox"/> Yes <input type="checkbox"/> No	Alters properties of the agent or toxin in a manner that would enhance its stability, transmissibility, or ability to be disseminated
<input type="checkbox"/> Yes <input type="checkbox"/> No	Alters the host range or tropism of the agent or toxin
<input type="checkbox"/> Yes <input type="checkbox"/> No	Enhances the susceptibility of a host population to the agent or toxin
<input type="checkbox"/> Yes <input type="checkbox"/> No	Generates or reconstitutes an eradicated or extinct agent or toxin or will synthetic biology techniques be used to construct a pathogen, toxin, or potentially harmful product
Justification of Experimental Approach	
<i>Provide a justification of the experimental approach, clearly explaining why dual use/gain of function strategies are necessary</i>	
Impact of Project/Research	
<i>Describe the importance of the potential project/research outcomes for the wider community</i>	

Steps in evaluation of projects for potential GoF at ACDP

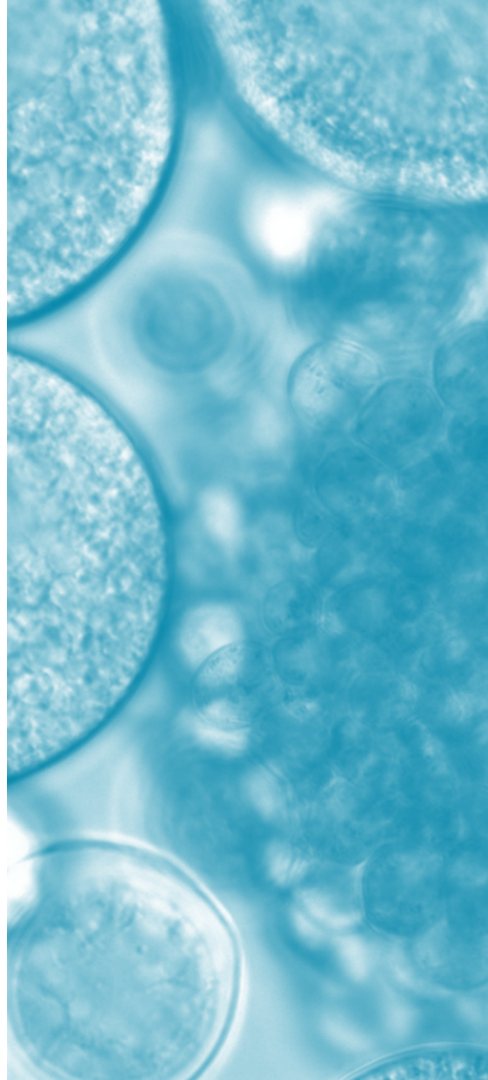




Render A Decision!

A researcher has requested to modify known virulence determinants from an Australian RG3 pathogen that exists in a low pathogenesis state in Australia to reflect exotic strains of the same type that are for some reason highly pathogenic. The aim is to determine if the Australian agent is capable of becoming highly pathogenic. Approved?

- **Facility is able to contain any strains arising from the study. Does that impact your decision?**
- **Results of the study could impact national policy and fuel new strategies to deal with disease surveillance and response on farms. How about now, are you convinced?**

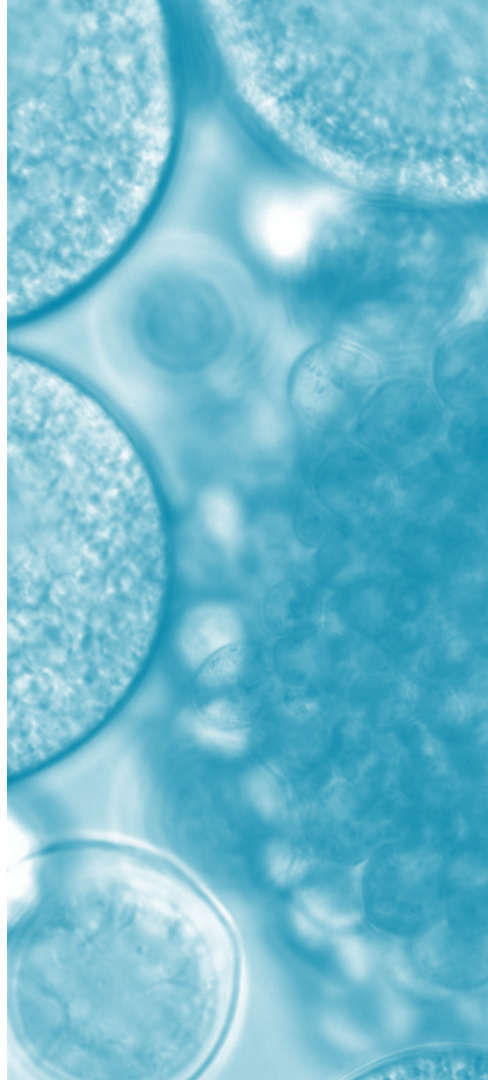




Render A Decision!

A researcher has requested to engineer proteins from a fully virulent RG4 pathogen into an avirulent strain of the same RG4 pathogen to assess the function of these proteins and their impact on pathogenesis. Approved?

- **The research team feels that traditional loss of function methods be masked in the fully virulent strain. Does this change your mind?**
- **Creation of the clones and recombinant strains will take some time and the project is under a 3-year term. How about now, still approved/not approved?**

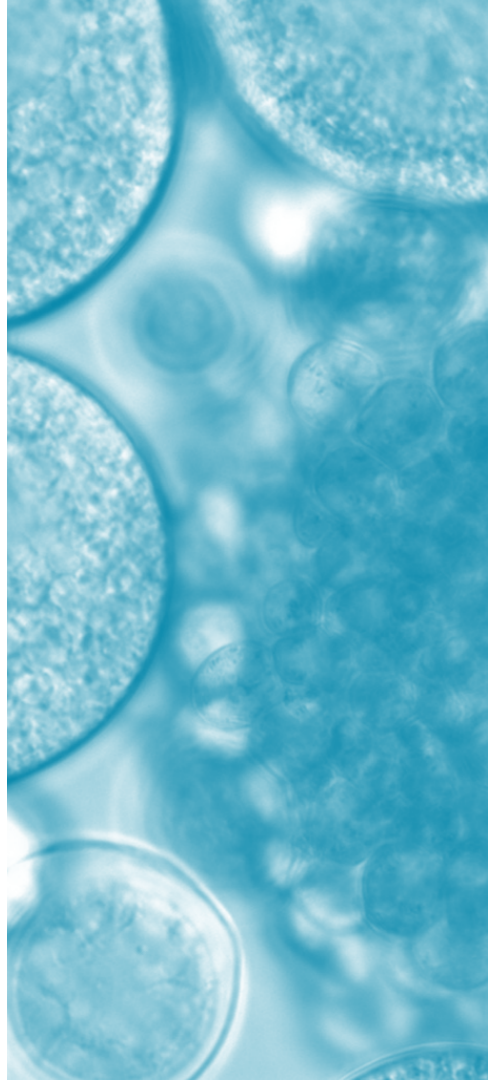




Render A Decision!

A researcher has proposed surface disinfectant testing on a high-consequence agricultural pathogen. As a precursor to this study the media conditions that promote the enhanced environmental stability will be determined and reported. Approved?

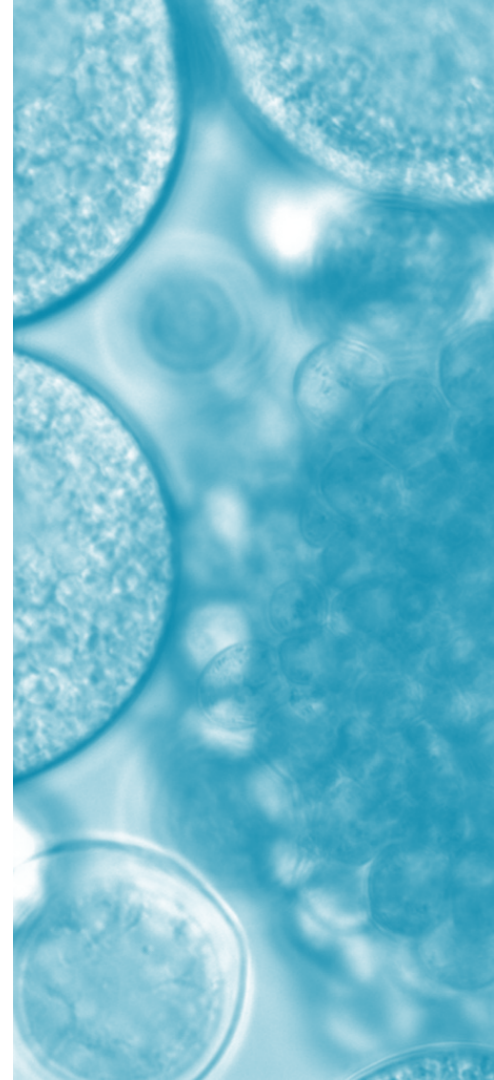
- **The pathogen is non-infectious to humans and doesn't match the review panels criteria. Should this project even be considered by the panel?**
- **The pathogen is exotic to Australia and an agri-terrorism event would disrupt a multi-billion dollar livestock sector. Should public interest weigh into your decision?**





Lessons Learned (so far)

- **Decisions are difficult and likely can't be characterised as "right" or "wrong"**
- **The goal is to render defensible decisions based off organisational alignment**
- **Large amount of variability between organisations**
- **Use available guidance and resources to create a framework that best fits your risk profile.**



Thank you

