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

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

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

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.

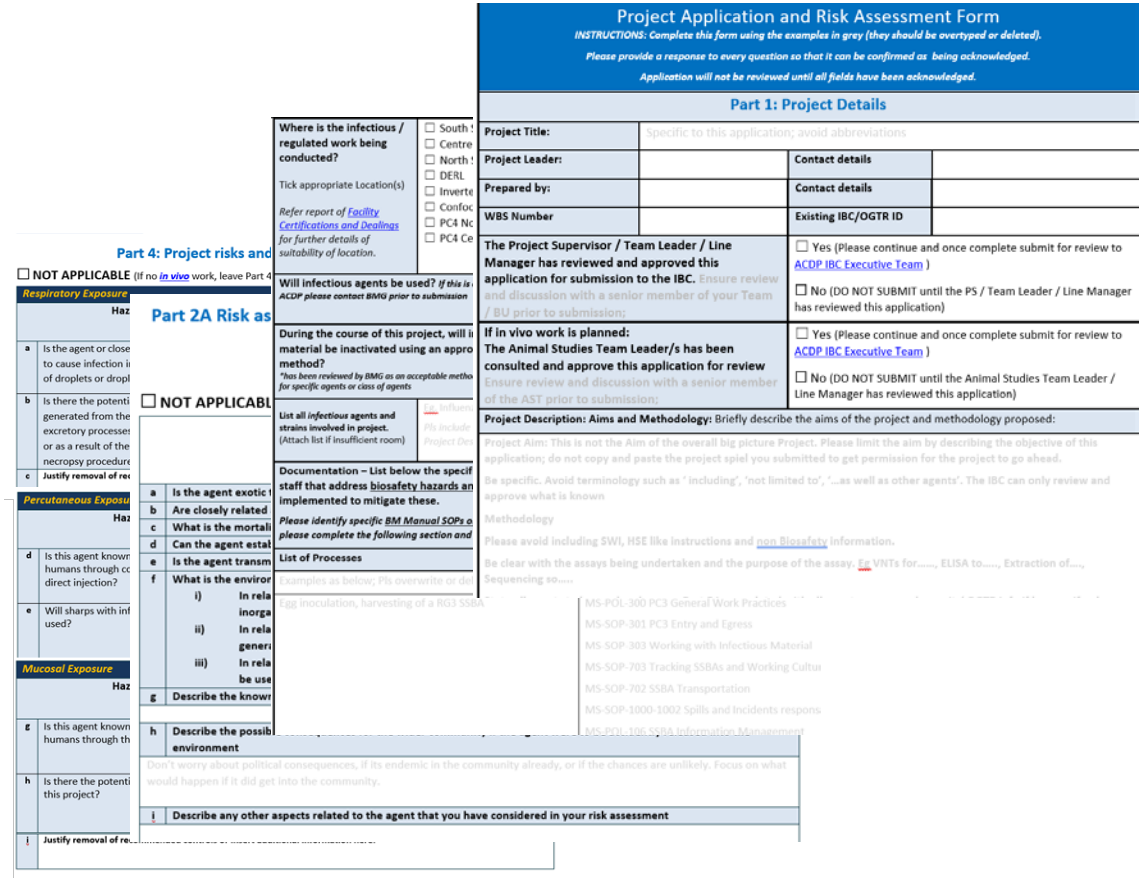
Leadership Awareness and Alignment
Committee is comprised of ACDP leadership from all scientific units on site and ensure alignment of projects with mission.

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

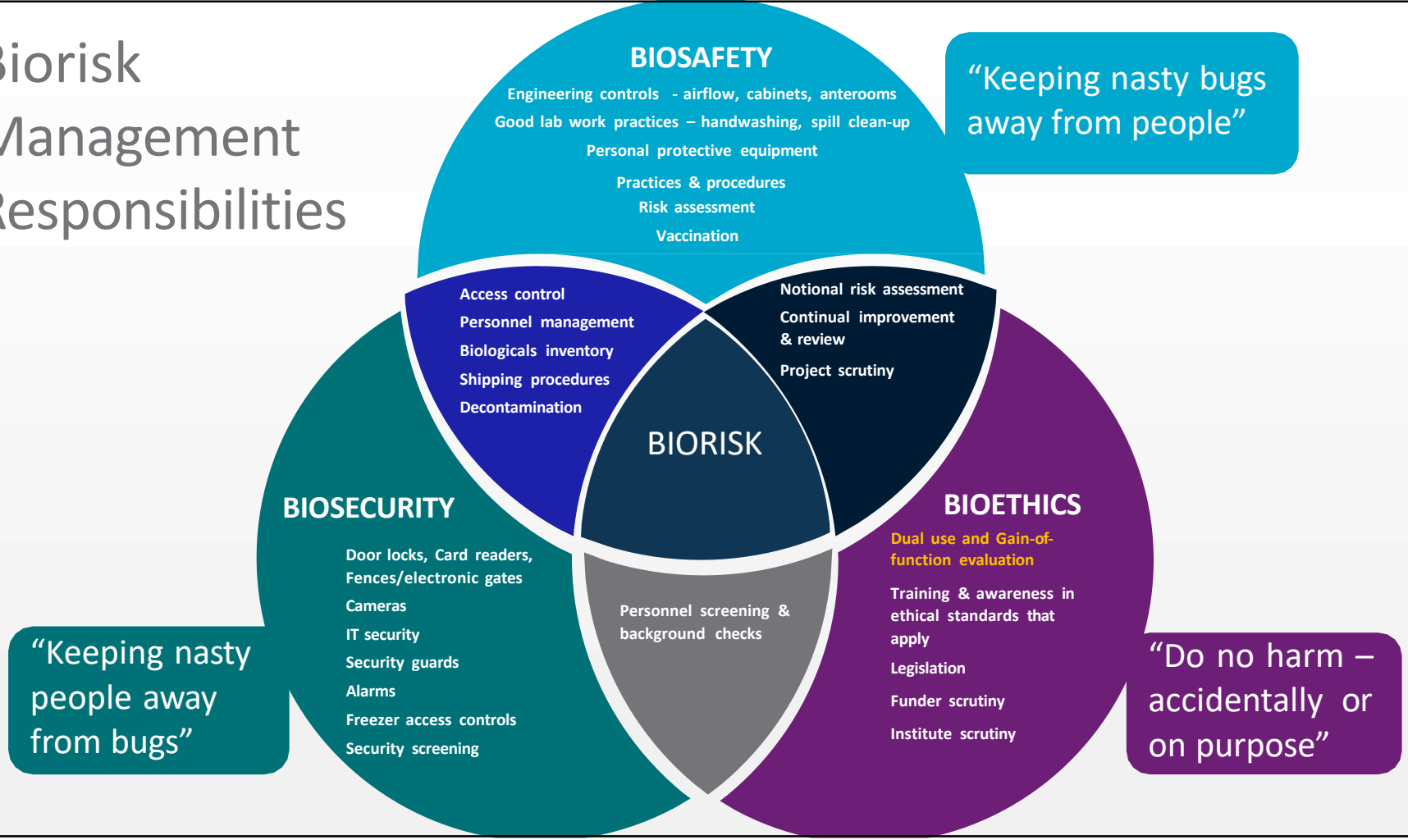
Part 1- What, where and how
Part 2A/B- Risk assessment for agent(s)
Part 3 and 4- Hazard controls
Part 5- Regulatory Compliance



What happens when the box is ticked?

Dual Use Research of Concern			
e	*Do you believe there are any Dual use implications that may be generated by this project?* *Please be advised that if Yes, approval from the DURC*	Y or N	*If yes, state below why you believe it is* and how the knowledge / information obtained could be misused:
		☑ YES ☐ NO	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

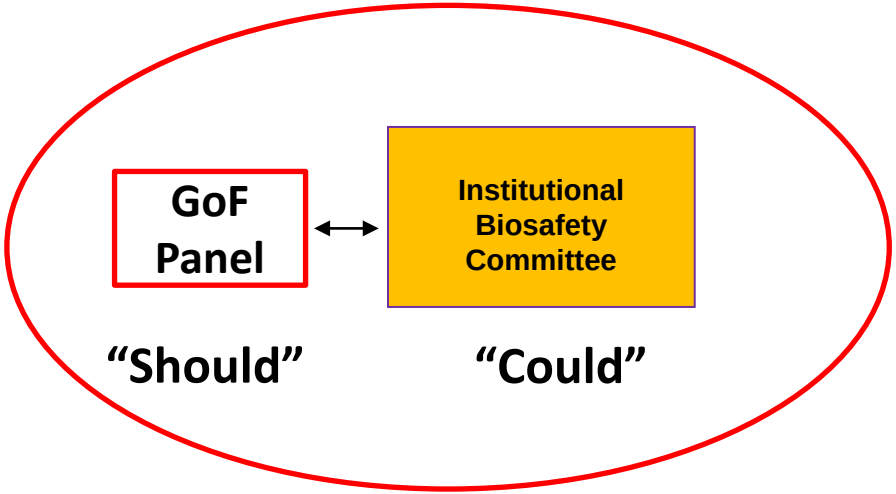
Biorisk Management Responsibilities



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:

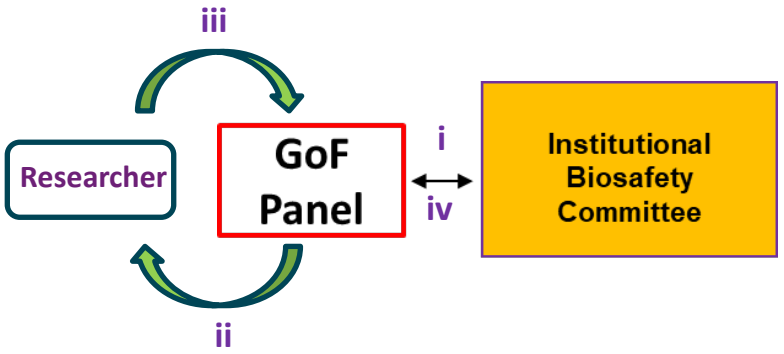
- ACDP Biorisk Manager (Chair)
- ACDP Director
- AAHL Science/Deputy Director
- H&B Science/Deputy Director
- Strategic Facility Operations Director

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

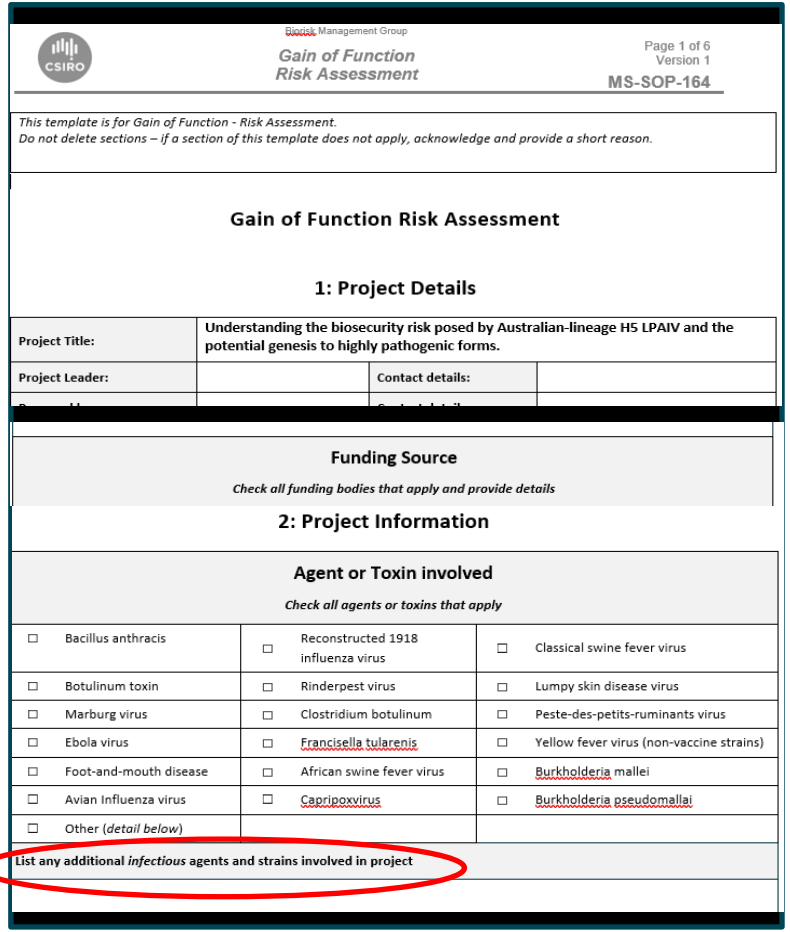
- Pandemic potential
- Funding Source
- Unaddressed safety concerns
- Unknown risk profiles and
- Benefits versus risks

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



Biorisk Management Group

Gain of Function Risk Assessment

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Version 1
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

☐ Bacillus anthracis	☐ Reconstructed 1918 influenza virus	☐ Classical swine fever virus
☐ Botulinum toxin	☐ Rinderpest virus	☐ Lumpy skin disease virus
☐ Marburg virus	☐ Clostridium botulinum	☐ Peste-des-petits-ruminants virus
☐ Ebola virus	☐ Francisella tularenis	☐ Yellow fever virus (non-vaccine strains)
☐ Foot-and-mouth disease	☐ African swine fever virus	☐ Burkholderia mallei
☐ Avian Influenza virus	☐ Capripoxvirus	☐ Burkholderia pseudomallai
☐ Other (*detail below*)		

List any additional *infectious* agents and strains involved in project

GoF Risk Assessment

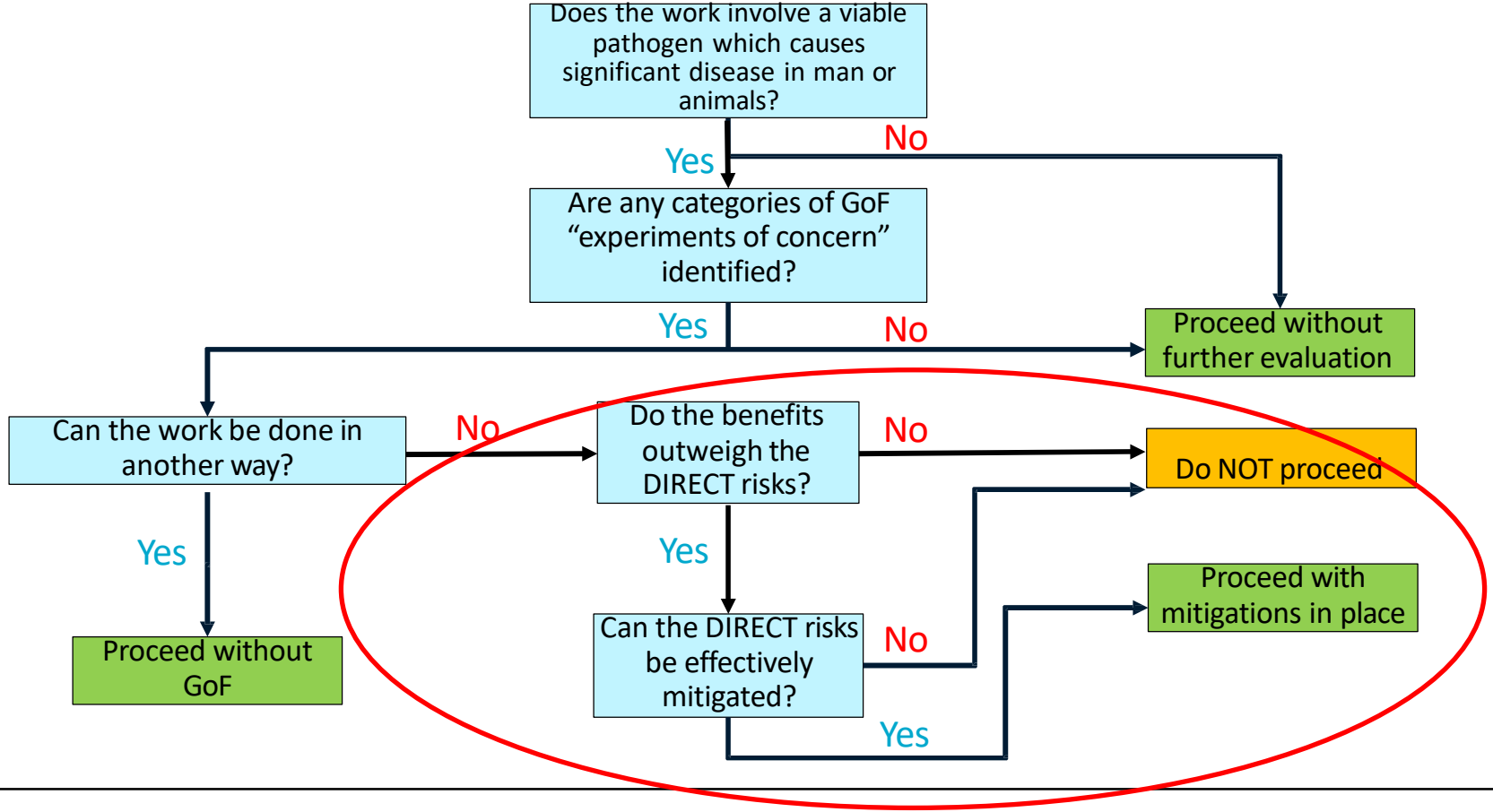
Key Areas Continued

- 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	
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.	
☐ Yes ☐ No	Enhances the harmful consequences of the agent or toxin
☐ Yes ☐ No	Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification
☐ Yes ☐ 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
☐ Yes ☐ No	Alters properties of the agent or toxin in a manner that would enhance its stability, transmissibility, or ability to be disseminated
☐ Yes ☐ No	Alters the host range or tropism of the agent or toxin
☐ Yes ☐ No	Enhances the susceptibility of a host population to the agent or toxin
☐ Yes ☐ 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	
Provide a justification of the experimental approach, clearly explaining why dual use/gain of function strategies are necessary	
Impact of Project/Research	
Describe the importance of the potential project/research outcomes for the wider community	

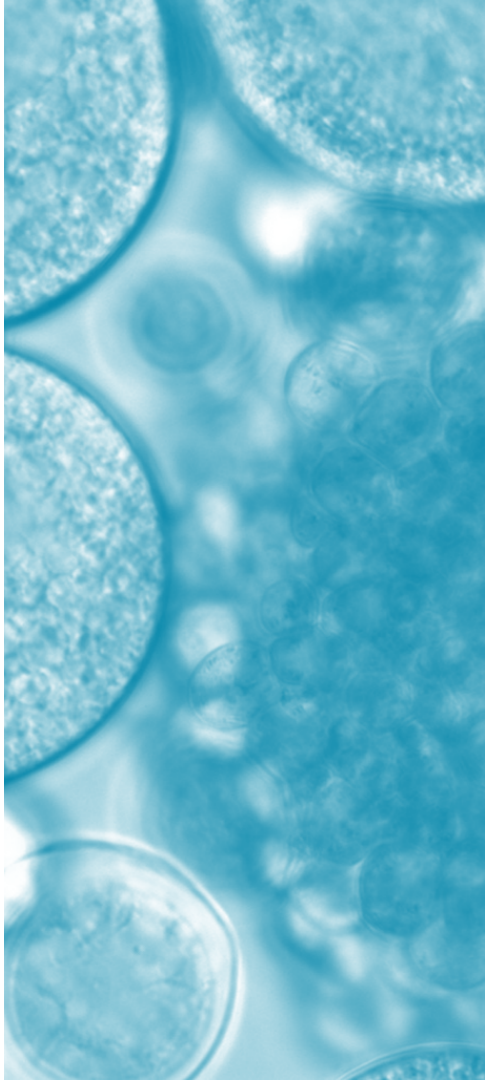
Steps in evaluation of projects for potential GoF at ACDP



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?

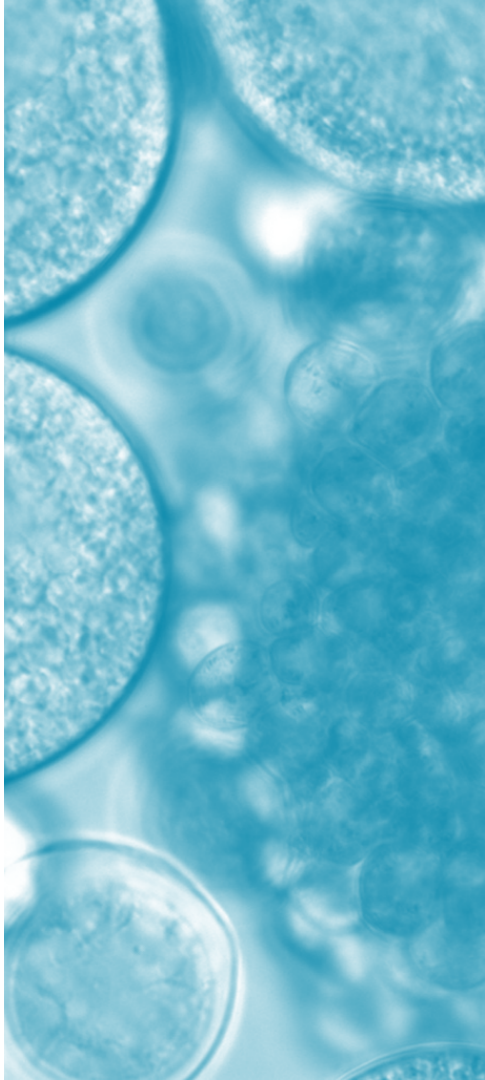
- **Facility is able to contain any strains arising from the study. Does that impact your decision?**
- **Results of the study could impact national policy and fuel new strategies to deal with disease surveillance and response on farms. How about now, are you convinced?**



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?

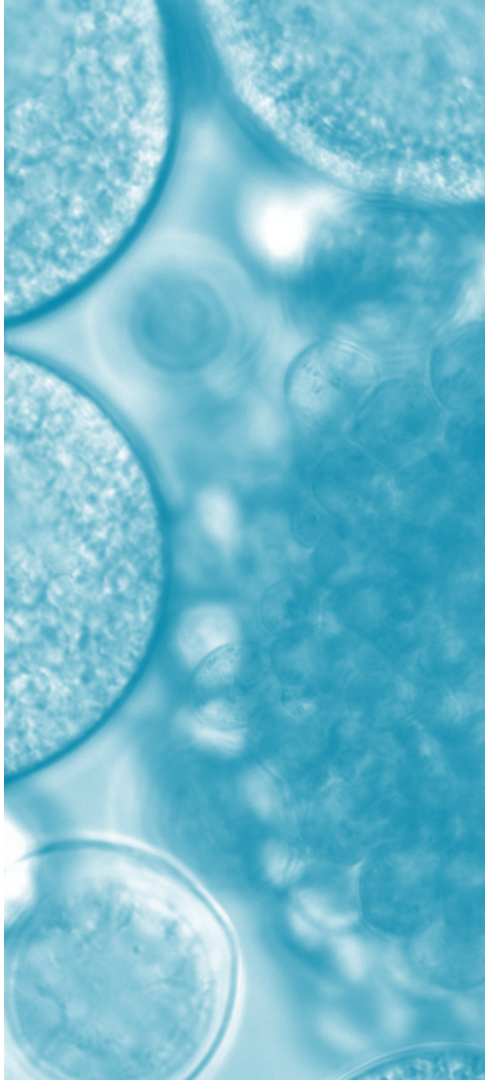
- **The research team feels that traditional loss of function methods be masked in the fully virulent strain. Does this change your mind?**
- **Creation of the clones and recombinant strains will take some time and the project is under a 3-year term. How about now, still approved/not approved?**



Render A Decision!

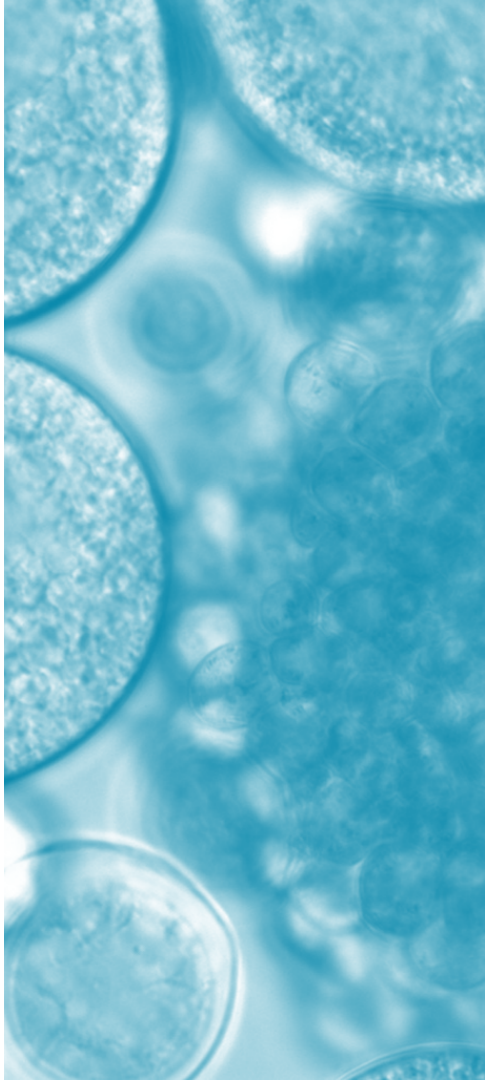
A researcher has proposed surface disinfectant testing on a high-consequence agricultural pathogen. As a precursor to this study the media conditions that promote the enhanced environmental stability will be determined and reported. Approved?

- **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 defendable 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