# Comments on NSABB Draft Report

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***Are there GOF studies that may be conducted but should require an additional level of review or oversight? ----- If so, what should that oversight entail? ---- Should that oversight occur at the federal or institutional level, or both?***

- Draft report adequately describes role and level of oversight review, recommendation and requirement of the BMBL, NIH guidelines, DURC and SATP as well as IBC and program review.
- Recent NIH review of ongoing programs in the GOF pause demonstrates commitment and ability to review in a manner to least hinder research progress.
- Current oversight mechanisms capture all areas of concern for influenza and CoVs

**Recommendations:**

- Clarification of GOF guidelines will allow for initial identification by PI, at institutional level, and facilitate any additional review of highly meritorious research ***DURING or IMMEDIATELY after*** scientific review process
- Don't add independent new mechanism for GOF
- Possibly harmonize / modify DURC + GOF to "Research of Concern" to allow one-stop guidance and review

## *How well does the NSABB's draft working paper identify the GOF studies of ~~(greatest)~~ concern?*

- Appropriately defines potential concern**: transmissibility + virulence + evasion of MCM.**
- Defines where GOF should ***NOT*** be invoked, including: mechanism of antivirals, vaccine escape, passage for increased replication of attenuated viruses.
- Recognizes that the **circumstances may change**: new pathogen, natural outbreak, vaccine, antiviral or mAb) that may change risk profile
- Organism / proscriptive approach to GOF may fail :
  - Over-represents fading and non-concerns and misses increasing or new concerns.
  - Discourages: High impact, innovative research on critical pathogens and discourages trainees from entering or pursuing research.

**Recommend:**

- Use of process approach for determination of relative risk throughout experimental design and iterative (e.g. at different experimental stages and outcomes)
- Wildtype viruses or natural strains should not be included in any GOF policy
- **Rationale for inclusion of CoVs has never been well demonstrated**. It should be reconsidered, possibly used as an example of RBA but not included in final Recs

## *Are there GOF studies that should not be conducted? If so, which studies and why?*

- **Possibly, but none should be listed in report**
  - Discourages thoughtful review of high impact science on most important problems
  - Distraction from opportunity to encourage biosafety, biosecurity, and training of new investigators.

**Recommendations:**

- General Principles + clear guidelines / questions about defined categories of potential concern will capture any clear ethical breach or gratuitous research.
- These should be defined (if any) on project and case basis, not as a goal of the report

***How well would the NSABB's draft principles and criteria permit the review GOF studies that have raised concerns and inform decisions about whether to fund such studies?***

**Recommendations:**

- Clear guidelines /questions for investigators and reviewers. **If you can't make it clear, leave it out.**
- Avoid absolutes in risk and benefit: stratify risk and benefit categories and apply on a project basis.

***How well would the NSABB's draft principles and criteria permit the review GOF studies that have raised concerns and inform decisions about whether to fund such studies?***

**Avoid the F-word (funding).**

- This should not be a threat that looms over research proposals.
- For NIH mechanisms (R, K, U), this should be post merit review for *highly meritorious peer-reviewed research,* that should **NOT affect funding, but should allow for modification of** aims, scope, approaches, mitigation, alternatives.
- Any combination of above under almost all circumstances should allow work to proceed.
- Encourage policy that allows funding and support to be used for this process of testing mitigation and alternatives.
- Don't incorporate up-regulation in security, safety or mechanism (EG BSL4, classification).

# Proposed Conceptual Approach for *Funding* Potential GOF Studies of Concern

**Identify proposals anticipated to involve GOF studies of concern, as described by the following attributes:**

i. Highly transmissible

ii. Increased virulence, and

iii. Resistant to control measures.

**Review proposal to determine whether they meet the following criteria:**

i. Reviewed and scientifically meritorious

ii. Potential risks compared to the potential benefits are justified.

iii. No feasible, equally efficacious alternative approaches to same scientific question with less risk

iv. Capacity to carry out research safely and securely.

***Proposals not meeting these criteria should not be funded.***

**3. Fund, do not fund, or fund with required additional risk mitigation measures or stipulations.**

**4. Conduct the research in accordance with applicable oversight policies.**

i. Research should be reviewed regularly at the institutional level

ii. Research should be reviewed regularly by the Federal funding agency

## Proposed Conceptual Approach for *Review*

**Identify proposals anticipated to involve GOF studies of concern, as described by the following attributes:**

i. Highly transmissible

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i. Reviewed and scientifically meritorious

ii. Potential risks compared to the potential benefits are justified.

iii. No feasible, equally efficacious alternative approaches to same scientific question with less risk

iv. Capacity to carry out research safely and securely.

***Proposals not meeting these criteria would be considered on a case basis for possible modification, risk mitigation, alternatives, or alteration in scope***

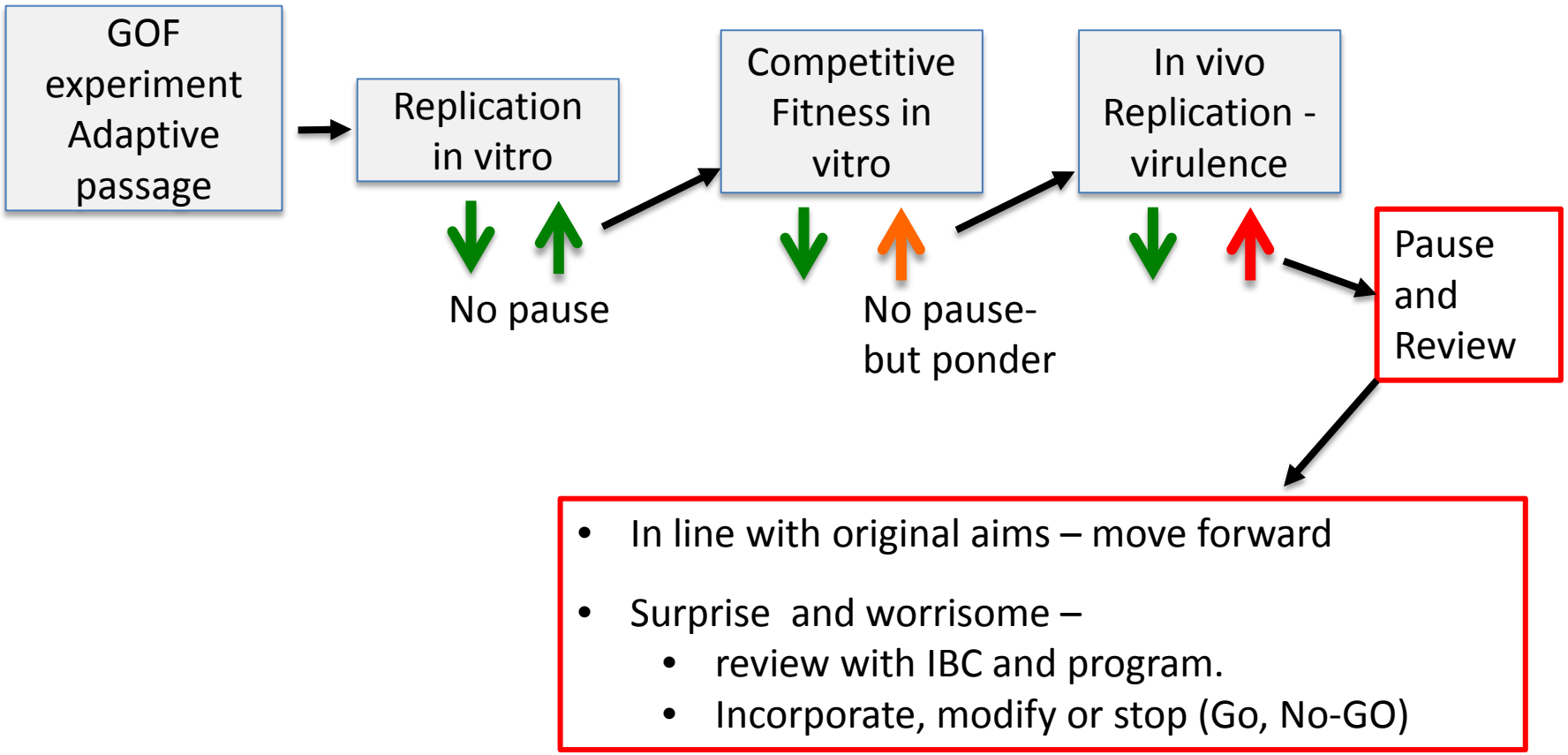
**4. Conduct the research in accordance with applicable oversight policies.**

i. Research should be reviewed regularly at the institutional level

ii. Research should be reviewed regularly by the Federal funding agency

# Design and Process Model for GOF management

Design – Initiate -- Milestones and Review Criteria -- Pause and Review – Go / No Go



# *Any other comments comments about the report?*

- Additional risks not incorporated in report
  - Current approach encourages distrust of scientists and their motivations – by other scientists and the public
  - Broad statement to young investigators that these fields are dangerous -- to pursue as careers
  - Institutions may stop supporting emerging pathogen research
  - Significant potential for loss of research trajectory, investigators, complete research programs,
  - Potential loss of fields of research
- Outcomes and implications feel mostly proscriptive and punitive
  - Encourage open recognition and reporting of possible risk
  - Reward novel approaches and best practices to use new methodologies, approaches, and biosafety practices to achieve research goals.

## *Any other comments comments about the report?*

- **Land the Plane -** View from 40,000 feet seems clear, but provides no guidance or ability to test / model implications of recommendations
- One practical example is worth a thousand theoretical discussions
- Use a Case Based Approach and incorporate these in your final recommendations. Consider these in followup NAS meeting