Working Draft of the Criteria for Identifying Dual Use Research of Concern

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Dual Use Research

- In broad terms, dual use life sciences research is legitimate research that could be misused to threaten public health or national security
- The argument could be made that *most if not all* life sciences research *could* be considered "dual use"
- The Working Group recognizes that there needs to be some added benefit toward protecting society by identifying certain research as "dual use"

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Purpose of the Criteria

- The Working Group wanted to focus these criteria to identify specific life sciences research that could be of greatest concern for misuse
- Therefore, the purpose of the criteria is to identify the particular life sciences research that should be considered "dual use research of concern"

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IMPORTANT

A designation of research as "dual use research of concern" simply means that it *may* warrant special consideration regarding conduct and oversight

It does *not* mean, a priori, that the work should not be performed or that the results should not be published

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Key Concepts

- The primary goal of identifying dual use research of concern is to minimize the potential for misuse of biotechnology *without hindering the progress of science and the important benefits that it yields*
- Any biosecurity concerns pertain to the misapplication of information or technologies resulting from the research, not the conduct of the research itself
  - Biosecurity versus biosafety

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Key Concepts

- **Ensure the relevance of the criteria**
  - Life science research is an extraordinarily dynamic field that encompasses many diverse disciplines
  - In the face of new advances and technologies, the criteria will require periodic review and modification
- **Specificity of Scope**
  - There is a compelling need for the criteria to be sufficiently specific to ensure that they capture only that research which is dual use of concern

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Key Concepts

- **Principal Investigator and the Research Institution**
  - **The Principal Investigator is in the best position to make the initial evaluation of his or her work for its dual use potential**
  - **Both share primary responsibilities for the identification, evaluation, and oversight of dual use research**

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Working Draft of the Criteria

It is likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel. Of particular concern is research that is likely to (any of the following):

a) Render an immunization ineffective or disrupt immunity
b) Confer to a pathogenic agent or toxin, resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin
c) Enhance the pathologic consequences of an agent or toxin
d) Increase the transmissibility of a pathogenic agent
e) Increase the capability of a pathogenic agent or toxin to be disseminated
f) Alter the host range or tropism of a pathogenic agent or toxin
g) Enhance the susceptibility of a host population
h) Generate a novel pathogenic agent or toxin or reconstitute an eradicated pathogenic agent

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Threshold

It is likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel

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Circumscribing the Research Areas of Concern

Considerations:

- **Identify areas of research that may capture the range of areas where dual use potential *may* exist**
- **Examine existing criteria used for identifying agents/experiments of concern, e.g.**
  - **Criteria utilized in generating the Select Agent List**
  - **The NRC "Experiments of Concern"**
- **Terminologies were carefully chosen to focus on research that might be considered as "dual use of concern" without casting too broad a net**

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Research Areas of Concern

a. Render an immunization ineffective or disrupt immunity

- Could allow a host population to become susceptible to disease that it would/could have otherwise been protected against
- Immunization refers to the active or passive induction of immunity through inoculation or infection
  - This includes antitoxins and toxoids
- Immunity encompasses all aspects of host immunity, e.g. adaptive, innate, etc.

Research Areas of Concern

b. Confer to a pathogenic agent or toxin, resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin

- The inability to effectively prevent or treat various disease caused by certain pathogenic agents or toxins, can result in heavy economic and logistical burdens to the public health infrastructure, compromise the food supply, etc.
- "Pathogenic agents" are agents, including infectious vectors, that are capable of causing a pathologic change in the host
- Clinically and/or agriculturally useful prophylaxes or therapeutics include first or second line treatment measures or alternative treatment measures for special populations
  - e.g. pregnant women or the immunologically compromised

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Research Areas of Concern

c. Enhance the pathologic consequences of an agent or toxin

- The ability to prevent or treat disease may be compromised since prophylaxes or therapeutics may no longer be effective
- "Pathogenic consequences" encompasses properties such as virulence, infectivity, toxicity, and route of exposure of a toxin

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Research Areas of Concern

d. Increase the transmissibility of a pathogenic agent

- Increasing the rate at which an agent can spread could impede attempts to contain disease outbreak
- "Transmissibility" encompasses
  - The ease with which an agent spreads from host to host
  - Contagiousness
  - Infectivity
- This includes transmission between hosts of the same species or between hosts of differing species

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Research Areas of Concern

e. Increase the capability of a pathogenic agent or toxin to be disseminated

- Effective dissemination of a pathogenic agent or toxin could result in large scale exposure and the inability to prevent or treat ensuing disease and/or damage
- "Dissemination" is the ability to effectively spread an agent or toxin throughout or among, a host population, the environment, or materiel, ensuring significant exposure
- This includes the environmental stability of the agent or toxin

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Research Areas of Concern

f. Alter the host range or tropism of a pathogenic agent or toxin

- Altering the host range could endanger populations that normally would not have been susceptible and for which prophylaxes and therapies may be absent
- "Host range" is the number of different species that can become infected by the pathogen, causing disease in the host or allowing it to become a carrier

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Research Areas of Concern

g. Alter the susceptibility of a host population

- Rendering host populations vulnerable to pathogenic consequences of an agent or toxin could result in disease of epidemic proportions
- This area of concern is *not* intended to include research affecting an individual host or research cohort
- Host population implies that information yielded by such research could be misapplied for large scale effects

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Research Areas of Concern

h. Generate a novel pathogenic agent or toxin, or reconstitute an eradicated pathogenic agent

- Applies to agents and toxins for which there is no known or widely available prophylaxes or therapeutics, that could evade diagnostics, or those for which there is little known immunity
- A novel agent or toxin is one that is not known to have previously existed in nature and is considered unique based on biological or other properties
- Eradicated agents include those that are thought to no longer exist and those that are thought not to be in circulation

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Additional Considerations

- Some of the other elements considered but not included in the criteria
  - "Weaponization"
  - Diagnostic and Detection Modalities
  - Equipment
- These elements, as well as others, could always be reconsidered for inclusion in the criteria

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Evaluation and Oversight Issues

- This Working Group was not charged with developing guidelines for the oversight of dual use research
  - That will be the focus of a working group in the near future
- However, various evaluation and oversight issues arose during development of the draft criteria
- It was important to keep these questions in mind while developing the criteria to provide context
  - In addition, compiling these issues could aid the follow-on working group

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Evaluation and Oversight Process

What it might entail

- Initial Assessment
- Institutional Review
- Institutional Guidance and Oversight
- Federal Guidance and Oversight

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Initial Assessment

- Purpose
  - Determine if the research should be considered dual use research of concern
- Responsibility
  - Principal Investigator
- Potential Tool
  - Based on the Criteria for Identifying Dual Use Research of Concern
  - Worksheet for Dual Use Potential
    - Which could also be used to perform periodic re-evaluations

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Worksheet for Dual Use Potential

1. Is it likely that the research could enable the:
   a) Rendering of an immunization ineffective or disruption of immunity?
   b) Confirmation to a pathogenic agent or toxin, resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin?
   c) Enhancement of the pathologic consequences of an agent or toxin?
   d) Increase in transmissibility of a pathogenic agent?
   e) Increase in the capability of a pathogenic agent or toxin to be disseminated?
   f) Alteration of the host range or tropism of an agent or toxin?
   g) Enhancement of the susceptibility of a host population?
   h) Generation of a novel pathogenic agent or toxin, or the reconstitution of an eradicated pathogenic agent?

2. Criteria for identifying Dual Use Research of Concern: Including consideration of Question 1a-h above, is it likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel?

3. Does the research involve a select agent or an agent that requires BSL-4 containment?

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Initial Assessment

- If the answer to any subpart of Question 1 is YES, that aspect of the research must be carefully reconsidered by a *designated knowledgeable institutional official* for its dual use potential
- If the answer to Question 2 is YES, the research is dual use research of concern and must undergo an *institutional biosecurity review* to determine if any additional oversight is necessary
- If the answer to Question 3 is YES, the research must undergo an *institutional biosecurity review*, using the above criteria, to determine if it is dual use research of concern will be made
- If the answer to ALL Questions is NO, the research is not dual use research of concern, however the determination must be certified by a *designated knowledgeable institutional official*
- All research should be periodically reevaluated for dual use potential as work progresses

To Be Determined

- Designated knowledgeable institutional official
  - Second set of eyes to (rapidly) evaluate and verify the initial assessment
  - A certain amount of institutional discretion as to who qualifies
    - e.g.: Department Chair, Section Chief, BSO, RO
- Institutional biosecurity review
  - The review process and the reviewing body attributes will be the subject of future discussions
    - e.g.: BSO, RO, IBC, some other entity?

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Evaluation and Oversight Process

- Initial Assessment
- Institutional Review
  - Verify the Investigator's Assessment
  - If dual use of concern, determine if oversight in addition to that already in place is warranted
- Institutional Guidance and Oversight
  - Ensure institutional responsibilities are being met
    - e.g. reviews and assessments
  - Coordinate and monitor oversight
- Federal Guidance and Oversight
  - Ensure compliance
  - Periodic re-evaluation and update of the criteria

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Evaluation and Oversight Issues

- When would an initial assessment/re-assessment be performed, who would perform it and to whom would it be submitted to?
- Will there be required training for investigators and institutional officials regarding the evaluation and oversight of dual use research?
- Should certain communications resulting from designated dual use research of concern be reviewed prior to release?
- What institutional entity will be responsible for dual use research oversight and compliance issues?
  - What attributes and expertise should this entity possess?
  - What authority would this entity need?

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Research Scenarios

- The Working Group "tested" the Worksheet for Dual Use Potential using research scenarios; a process that proved to be valuable
- The next few slides will provide some examples of how an initial assessment for dual use research of concern might proceed

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Research Scenario 1

An investigator wishes to produce a phage display library of small peptides to screen for sequences with antimicrobial properties against *Yersinia enterocolitica*

***Yersinia enterocolitica* low-pathogenic strain Y-108C biogroup 4, serotype O:3**

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Research Scenario 1 Initial Assessment

1. Is it likely that the research could enable the:

a)	Rendering of an immunization ineffective or disruption of immunity?	NO
b)	Confirmation to a pathogenic agent or toxin, resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin?	NO
c)	Enhancement of the pathologic consequences of an agent or toxin?	No
d)	Increase in transmissibility of a pathogenic agent?	NO
e)	Increase in the capability of a pathogenic agent or toxin to be disseminated?	NO
f)	Alteration of the host range or tropism of an agent or toxin?	NO
g)	Alteration of the susceptibility of a host population?	NO
h)	Generation of a novel pathogenic agent or toxin, or the reconstitution of an eradicated pathogenic agent?	NO

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Research Scenario 1
Initial Assessment

2. Criteria for identifying Dual Use Research of concern: Including consideration of Question 1a-h above, is it likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel? **NO**

3. Does the research involve a select agent or an agent that requires BSL-4 containment? **NO**

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Research Scenario 2

An investigator wishes to express the YadA protein from *Yersinia pseudotuberculosis* in *Yersinia enterocolitica* to assess mechanisms of bacterial uptake in human cells.

***Yersinia enterocolitica* YadA does not promote efficient uptake**

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Research Scenario 2 Initial Assessment

1. Is it likely that the research could enable the:

a)	Rendering of an immunization ineffective or disruption of immunity?	NO
b)	Confirmation to a pathogenic agent or toxin, resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin?	NO
c)	Enhancement of the pathologic consequences of an agent or toxin?	No
d)	Increase in transmissibility of a pathogenic agent?	YES
e)	Increase in the capability of a pathogenic agent or toxin to be disseminated?	NO
f)	Alteration of the host range or tropism of an agent or toxin?	NO
g)	Alteration of the susceptibility of a host population?	NO
h)	Generation of a novel pathogenic agent or toxin, or the reconstitution of an eradicated pathogenic agent?	NO

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Research Scenario 2 Initial Assessment

2. Criteria for identifying Dual Use Research of concern: Including consideration of Question 1a-h above, is it likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel? NO

3. Does the research involve a select agent or an agent that requires BSL-4 containment? NO

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Research Scenario 3

An investigator wishes to express the pIP1202 and the pIP1203 plasmids from *Yersinia pestis* strains 16/05 and 17/95 in *Yersinia pseudotuberculosis* in to assess mechanisms of antibiotic resistance.

***Yersinia pestis* 17/95 and 16/95 were isolated from human cases of bubonic plague; pIP1202 and pIP1203 conferred different antibiotic resistances to those strains**

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Research Scenario 3 Initial Assessment

1. Is it likely that the research could enable the:

a)	Rendering of an immunization ineffective or disruption of immunity?	NO
b)	Confirmation to a pathogenic agent or toxin, resistance to clinically and/or agriculturally useful prophylaxes or therapeutics against that agent or toxin?	YES
c)	Enhancement of the pathologic consequences of an agent or toxin?	No
d)	Increase in transmissibility of a pathogenic agent?	NO
e)	Increase in the capability of a pathogenic agent or toxin to be disseminated?	NO
f)	Alteration of the host range or tropism of an agent or toxin?	NO
g)	Alteration of the susceptibility of a host population?	NO
h)	Generation of a novel pathogenic agent or toxin, or the reconstitution of an eradicated pathogenic agent?	NO

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Research Scenario 3
Initial Assessment

2. Criteria for identifying Dual Use Research of concern: Including consideration of Question 1a-h above, is it likely that the knowledge, products, or technologies derived from this research could be inadvertently or deliberately misapplied by others to pose a threat to public health, agriculture, plants, animals, the environment, or materiel? **YES**

3. Does the research involve a select agent or an agent that requires BSL-4 containment? **NO**

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Next Steps

- **Feedback**
  - This working draft of the criteria was composed through a detailed process of Working Group deliberations
  - The Working Group is interested in any comments NSABB may have
  - With approval from the NSABB, the Working Group would like to solicit broad public feedback and input
- **Guidelines for Oversight**
  - The Working Group would like to transition its focus to developing guidelines for the oversight of dual use research of concern
  - NSABB could then consider *both* the criteria and the guidelines together when developing a formal recommendation