The National Institutes of Health Dual Use Screening Program: A Proposed Quality Control Model

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Molly S. Stitt-Fischer, PhD, CPH
Fellow, National Biosafety and Biocontainment Training Program
Division of Occupational Health and Safety
OFFICE OF RESEARCH SERVICES
NATIONAL INSTITUTES OF HEALTH
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Research Oversight at NIH

Tier 1:

Dual Use Screening Questions Evaluated by PI During rDNA and Human Pathogen Registration

NIH IBC Evaluates Registrations

Tier 2:

NIH IBC Reviews any Amendments to rDNA and Human Pathogen Registration Documents

Research Registration Documents Reviewed by Safety Specialists During Annual Laboratory Surveys

NIH Pre-Publication Manuscript Review Process

Need for a Formalized QA/QC Process for Dual Use Screening Program

Tier 1:

Tier 2:

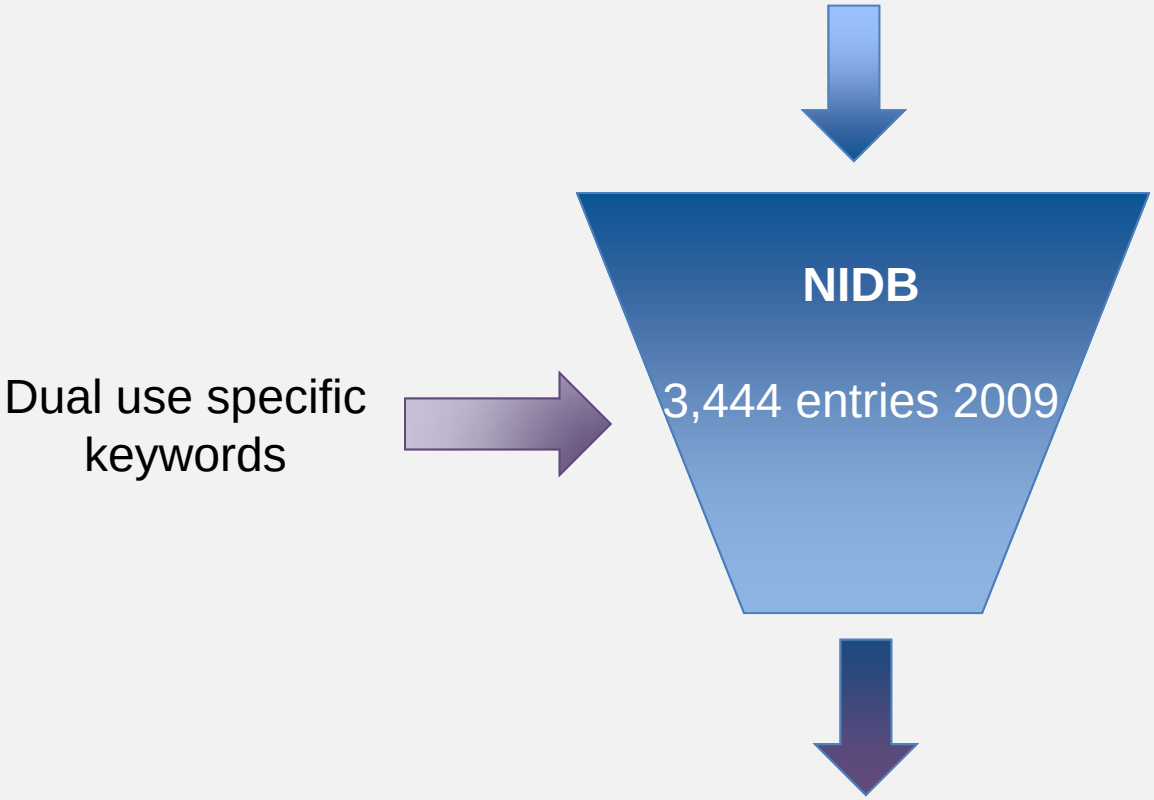
Registration Documents
ed by Safety Specialists
nnual Laboratory Surveys

Tier 3:

NIH Pre-Publication
Manuscript Review Process

NIH Intramural Database

Annual research progress summaries



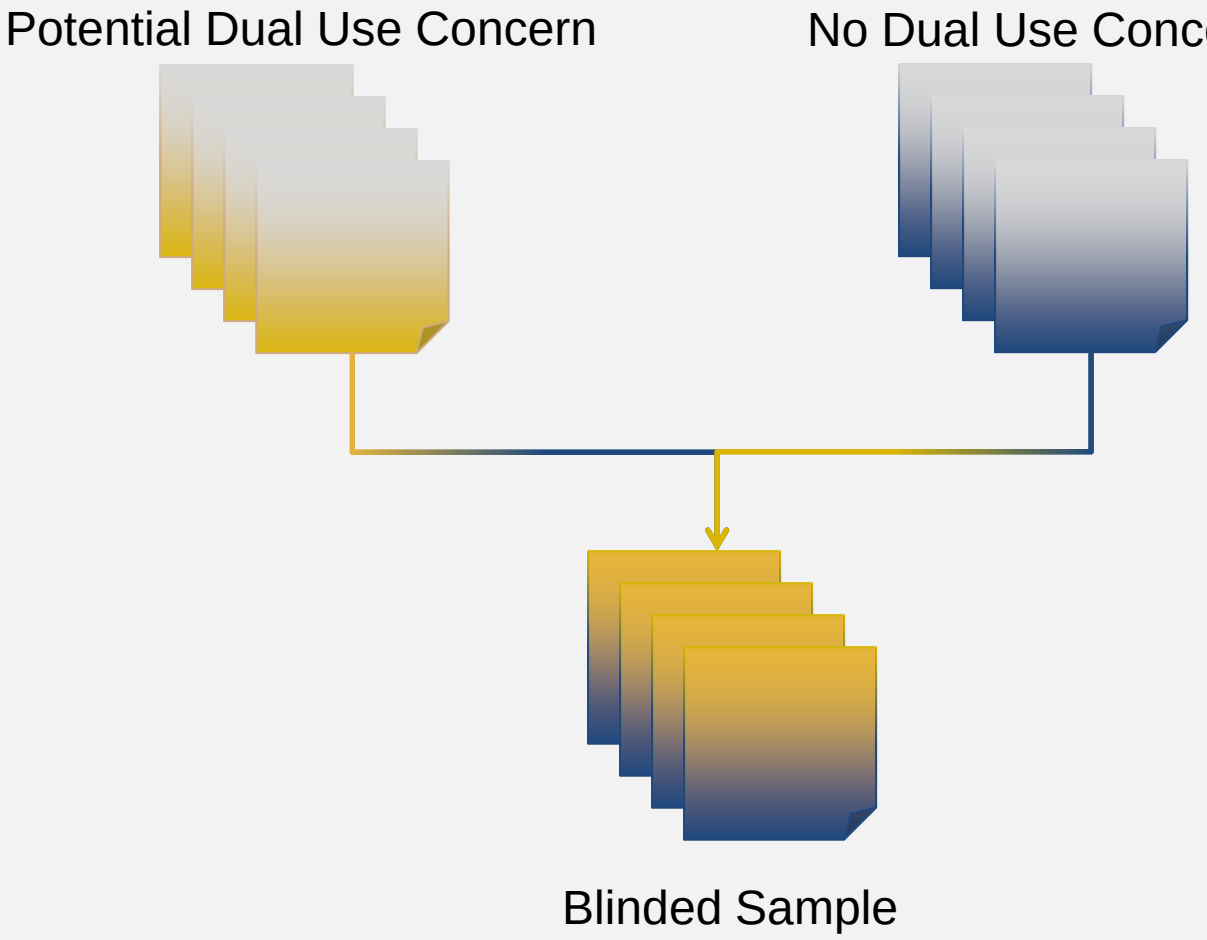
Identify research with potential dual use concern not captured by dual use screening questionnaire

Developing a set of dual use specific keywords: Where should we start?

- Terminology associated with dual use research of concern
  - Fink Report (Biotechnology Research in an Age of Bioterrorism, National Research Council)
  - National Science Advisory Board for Biosecurity
  - Review of dual use, biosafety, and biosecurity literature

Developing a set of dual use specific keywords: Where should we start?

rDNA Registrations Examined During 1st Tier Screening Retrospective Review:



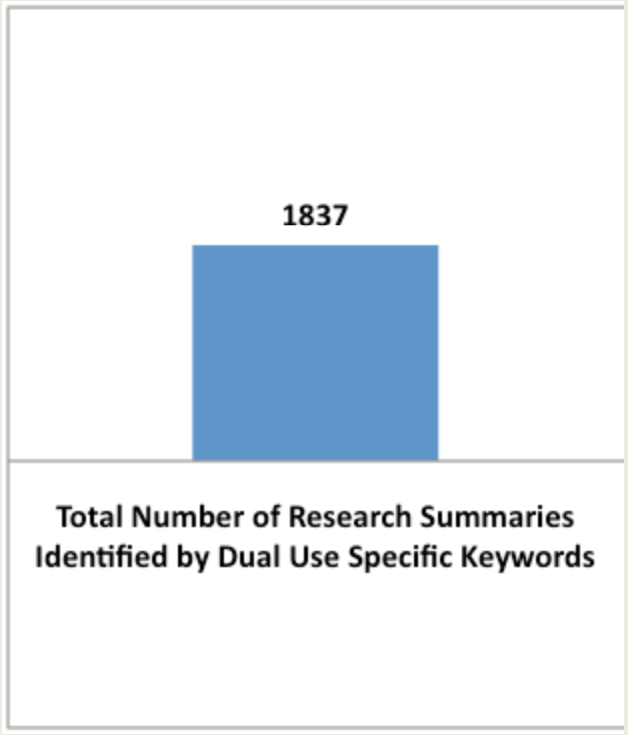
Defining the QC Process

Resources:

Fink Report
NSABB Report
Blinded Sample of rDNA Registration Documents

→ Develop Dual Use Specific Keywords and Query NIDB (3444 Total Research Summaries For 2009)

→ Specific Keywords Identified 1837 Research Summaries



Defining the QA/QC Process

Resources:

Fink Report
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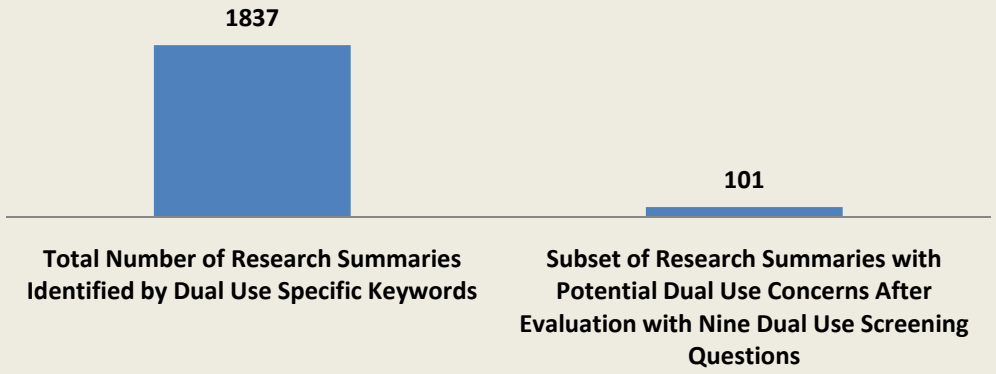
Develop Dual Use Specific Keywords and Query NIDB (3444 Total Research Summaries For 2009)

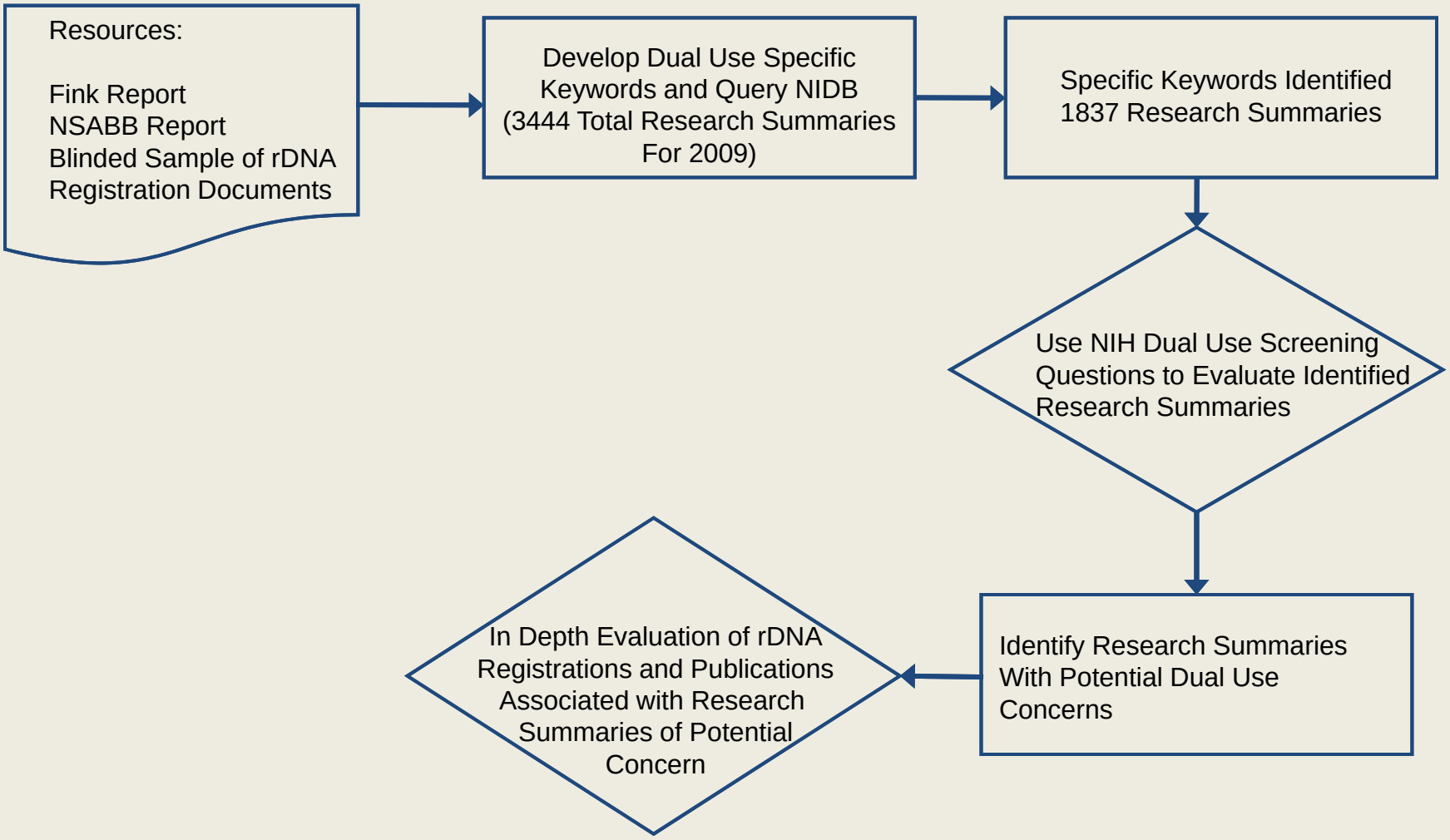
Specific Keywords Identified 1837 Research Summaries

Use NIH Dual Use Screening Questions to Evaluate Identified Research Summaries

Identify Research Summaries With Potential Dual Use Concerns



Defining the QA/QC Process

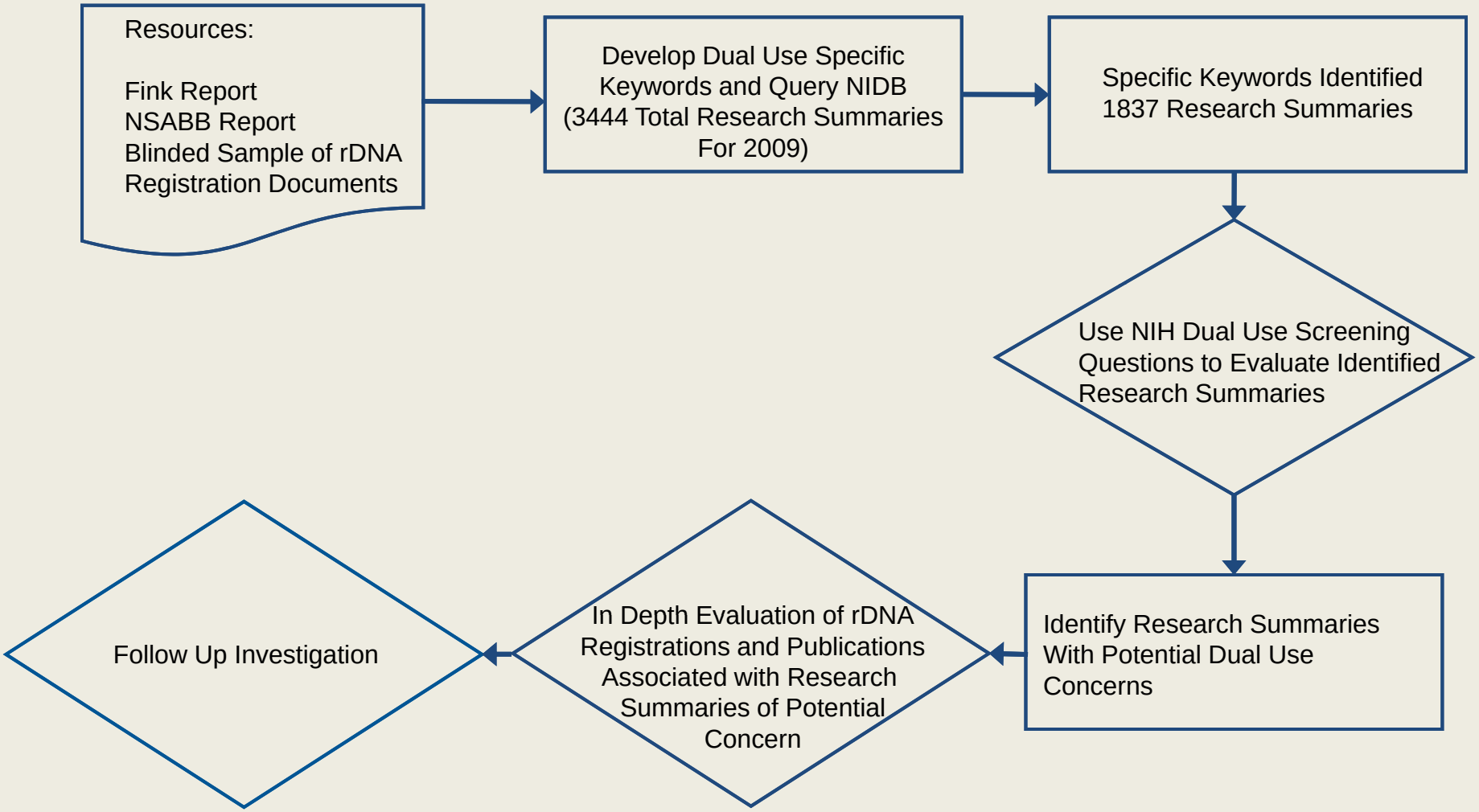


Defining the QA/QC Process

Two research summaries were determined to have potential dual use concerns

Dual Use Specific Keyword(s) that Identified Research Summary in NIDB	Summary of Research Project
Lethal infection Avian influenza H1N1 H5N1	De novo synthesis of influenza HA from cDNA sequences in the CDC/WHO pandemic influenza database
Bovine spongiform encephalopathy agent	Infectious prion proteins produced from expression of recombinant DNA in *E. coli*

Defining the QA/QC Process



Follow Up Investigation

- Neither of the two research projects had rDNA or human pathogen registration documents in the NIH electronic research registration and workflow system

- One researcher was located at another NIH campus
  - Paper rDNA registration
  - Campus rolled into electronic research registration system
  - rDNA registration now available electronically from any NIH campus

Follow Up Investigation

- One research project using synthetic genomic techniques to create expression vectors for recombinant protein purification

- Researcher contacted and rDNA registration document filed with NIH IBC

Lessons Learned

- **NIH has developed a robust screening program**
  - Both the dual use screening questionnaire and the quality control process identified research that was related to dual use "buzzwords"

Upon final examination none of the rDNA or human pathogen registration documents or annual research summaries were determined to involve research with potential dual use concerns.

Lessons Learned

- **No additional cost**
  - Leverage existing resources - IBC registration process and NIDB
  - Quality control process evaluations must be performed by personnel familiar with research techniques in the life sciences and dual use research concerns
  - Dual use specific keywords must be re-evaluated as life sciences research evolves

Lessons Learned

- **Screening program has no adverse effects on research progress**
  - PI checklist incorporated into existing registration process
  - Quality control process transparent to PIs
  - No effect on publication of research

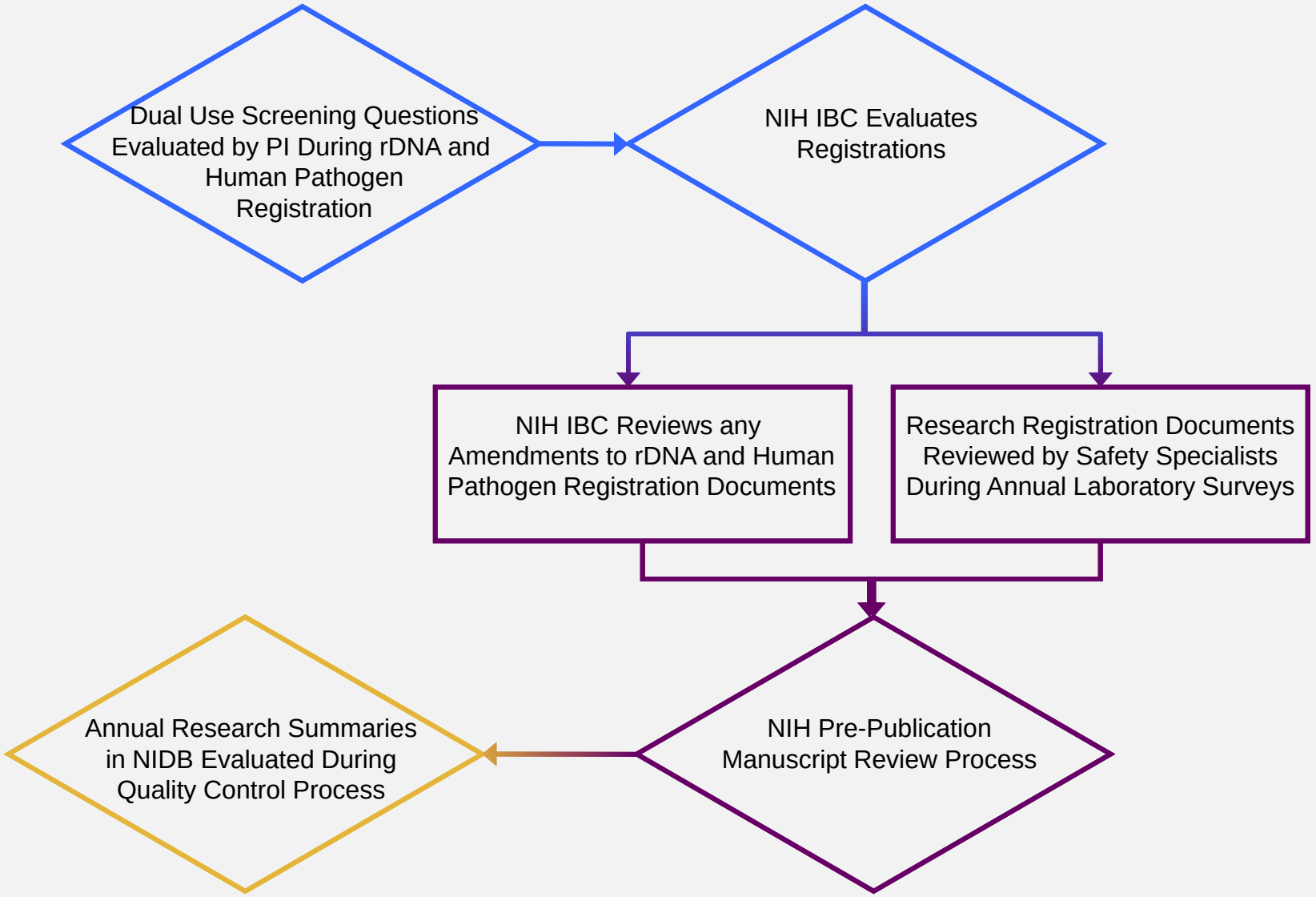
- **Need increased outreach efforts to foster awareness of dual use research concerns in the life sciences research community**
  - Particular focus on scientists in disciplines that are not traditionally part of the life sciences community
    - Biological engineers, chemists, physicists *etc.*

Lessons Learned

- **Model that can be adopted by a variety of institutions**

- **Are there existing processes that can be adapted to form the foundation of a dual use screening process at your institution?**
  - Annual progress reports required by grant agencies?
  - Progress reports as part of a yearly performance review?
  - Information linked to research budgets?

NIH Research Screening Process



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  - Deborah E. Wilson

Questions?

- National Biosafety and Biocontainment Training Program, National Institutes of Health
  - www.nbbtp.org
- Division of Occupational Health and Safety, National Institutes of Health
  - http://dohs.ors.od.nih.gov

20 Dual Use Specific Keywords Associated with Highest Number of Research Summaries Overall

Specific Keyword	Total Number of Research Summaries Identified in NIBD	Number of Identified Summaries that were of Potential Concern
Delivery	192	0
Vaccination	97	0
Toxin	74	1
Biodefense	56	2
Reverse genetics	50	6
M. tuberculosis	46	0
Stability increase	45	0
Lethal infection	39	6
Herpes B virus	36	0
Prion protein	31	0
Virulence factor	29	1
Potency increase	25	2
Ebola	21	2
Tropism	21	1
H1N1	20	3
Lethal challenge	20	2
Pandemic influenza	20	9
Infectious clones	19	0
BAC	18	1
Avian influenza	17	5
Total	876	41

20 Dual Use Specific Keywords Associated with Highest Number of Summaries of Potential Concern

Specific Keyword	Number of Research Summaries Identified that were of Potential Concern	Total Number of Research Summaries Identified in NIDB
Pandemic influenza	9	20
Immune response avian influenza	6	8
Lethal infection	6	39
Pandemic strains	6	10
Reverse genetics	6	50
Avian influenza	5	17
Francisella tularensis	5	5
Live vaccine strain	5	14
H5N1	4	14
Reassortant	4	11
Replication avian influenza	4	7
H1N1	3	20
Aerosol	2	9
Biodefense	2	56
Ebola	2	21
Known virulence determinant	2	2
Lethal challenge	2	20
Potency increase	2	25
Virulence motif	2	6
Avian parainfluenza virus	1	1
Total	78	355