LIBR
Laureate Institute for Brain Research

THE UNIVERSITY of TULSA

K Club, Week 9

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Today's Topics




- Protection of Human Subjects from Research Risk
- Inclusion of Women and Minorities
- Inclusion of Individuals Across the Lifespan
- Revisit Inclusion Enrollment Report
- Action Items

K Application Sections

Research

- **Specific Aims** (1 page)
- **Research Strategy** (6 pages: **Significance, Innovation, Approach**)
- **Training in Responsible Conduct of Research** (1 page)
- **Project Summary / Abstract** (30 lines of text)
- **Project Narrative** (3 sentences)
- **Protection of Human Subjects from Research Risk**
- **Inclusion of Women and Minorities**
- **Inclusion of Individuals Across the Lifespan**
- **Inclusion Enrollment Report**
- **Budget + Budget Justification**
- **Bibliography + References Cited**

Career

- **Candidate Information and Goals for Career Development** (6 pages: **Candidate Background, Career Goals/Objectives, Career Development/Training Plan**)
- **Plans and Statements of Mentor and Co-Mentors** (6 pages)
- **NIH Biosketches** for you, Mentor, Co-Mentors (max 5 pages each)
- **Three Letters of Reference**
- **Letters of Support from Collaborators, Contributors and Consultants** (6 pages max)
- **Cover Letter**

Setting

- **Facilities and Other Resources**
- **Equipment**
- **Environment and Institutional Commitment to Candidate**
- **Resource Sharing Plan**

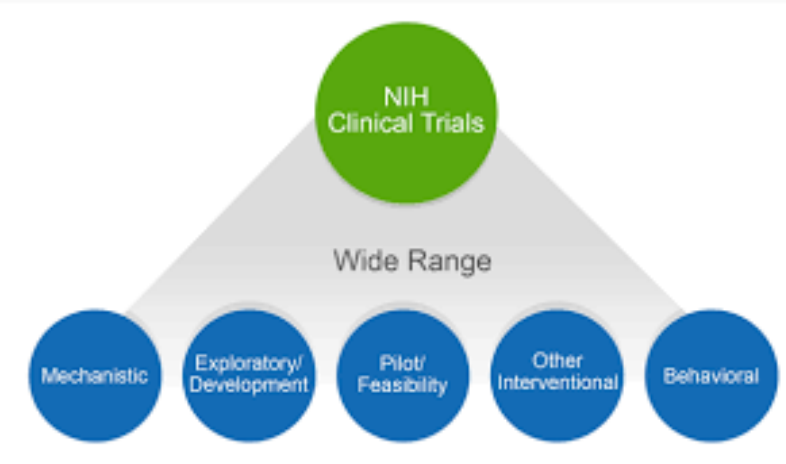
Definition of a Human Subject

- A living individual about whom an investigator is conducting research:
  - 1. Obtains information or biospecimens through intervention or interaction with the individual OR uses, studies, or analyzes the info from biospecimens
  - 2. Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens

- NOTE: If you are doing secondary data analysis ONLY and have NO access to subjects' identifiable private information, talk to your **Primary Mentor** ASAP about whether your de-identified data qualifies as non-human subjects research
  - If your Mentor agrees that it is, you have to submit a document explaining how, if the project involves human specimens or data, the project meets with criteria of non-human subjects research
- If you are doing any new data collection with individuals, you definitely are doing human subjects research (not exempt)

Definition of a Clinical Trial

- Does your study involve human participants?
- Are the participants prospectively assigned to an intervention?
- Is the study designed to evaluate the effect of an intervention on participants?
- Is the effect being evaluated a health related biomedical or behavioral outcome?
- If YES, then you have to fill out more paperwork than non-clinical trials
- https://grants.nih.gov/ct-decision/index.htm



Protection of Human Subjects from Research Risk

3 Basic Ethical Principles

- Respect for Persons
  - Voluntary Consent
  - Privacy/Extra Protection
- Beneficence
  - Risk
  - Confidentiality
  - Monitor Data for Safety
- Justice
  - Subject Selection Equality, Vulnerable Populations, Populations of Convenience

Protection of Human Subjects from Research Risk (no page limit)

- NIH Podcast: Am I doing Human Subjects Research?
  - https://nexus.od.nih.gov/all/2020/09/01/new-all-about-grants-podcast-am-i-doing-human-subjects-research/

- Applications that propose to involve human subjects must address:
  - 1. Risks to human subjects
  - 2. The adequacy of protections against risk
  - 3. Potential benefits of the research to subjects and others
  - 4. The importance of the knowledge to be gained
  - 5. A data and safety monitoring plan

1. Risks to Human Subjects

- Describe the following:
  - Description and justification for the proposed involvement of human subjects
  - Characteristics of subject population (number, age range, and health status)
  - Inclusion/exclusion criteria
  - Rationale for involvement of vulnerable populations (e.g. fetuses, pregnant women, children, prisoners, institutionalized individuals, or others)
  - Role of collaborating sites where research will be performed
  - Description and justification of research procedures (including dosage, frequency, etc. of intervention)
  - Description of what research material, data, and information will be collected
  - Access to personally identifiable information collected and retained
  - Management and protection of materials and information
  - All potential risks to subjects (physical, psychological, financial, legal, or other) including likelihood and seriousness
  - Any alternative treatments or procedures

2. Adequacy of Protection Against Risks

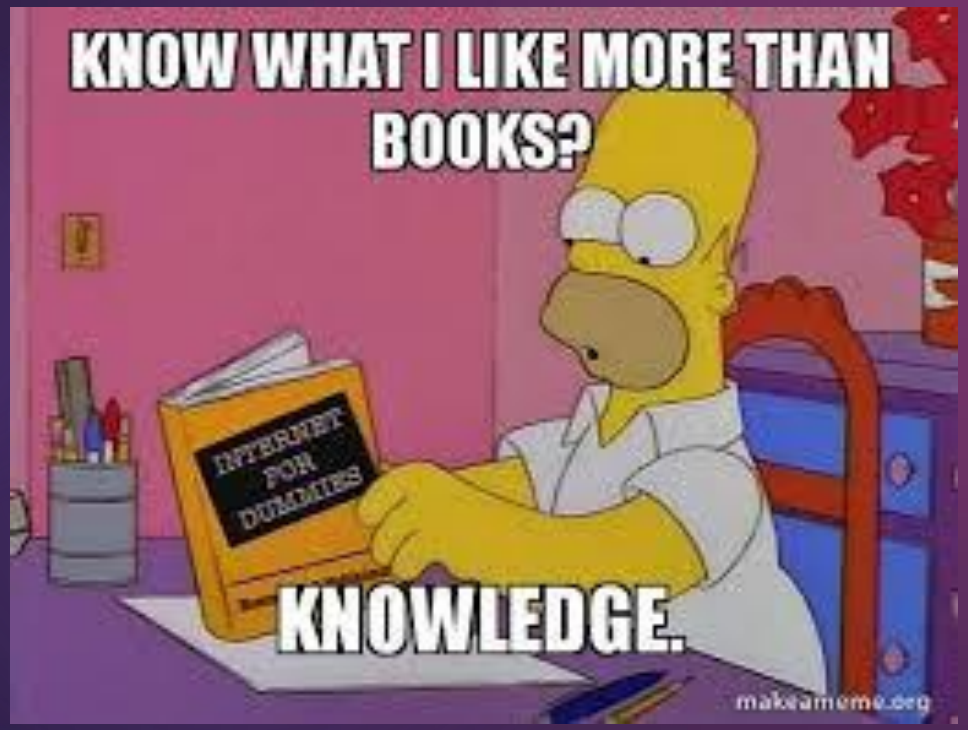
- Explain the following:
  - How subjects will be recruited
  - Description of INFORMED CONSENT
  - Waiver for any elements of consent
  - How risks described previously, including PRIVACY and CONFIDENTIALITY, will be minimized
  - Additional protections for vulnerable populations
  - Ensuring necessary medical/professional intervention for adverse events

3. Potential Benefits of the Research to Subjects and Others

- Describe how *potential risks* to subjects appear *reasonable* in relation to *anticipated benefits*

4. Importance of the Knowledge to be Gained

- Describe how *potential risks* to subjects appear *reasonable* in relation to the importance of the *knowledge* that may result from the study



5. Data and Safety Monitoring Plan

- Description of a *monitoring plan*: who will be responsible for monitoring and the process by which *adverse events* and *unanticipated problems* will be reported to all relevant regulatory bodies
- For clinical trials, you need to have a detailed plan set up
- For non-clinical trials you *still* need to have this section

Protection of Human Subjects from Research Risk

- This document will be the basis of your Human Subjects proposal that you submit to your University's Institutional Review Board (IRB) after you get Reviewer feedback on your K application

- Even though this section may take awhile to draft now (it can be 10-20 pages long), it will come in handy when you're getting ready to submit your study proposal to the IRB!

Inclusion of Women and Minorities (1 page)

- In this section, you are explaining your reasoning for including/excluding:
  - Biological sex / gender: Males and females
  - Ethnic categories
    - Hispanic
    - Non-Hispanic
  - Racial categories
    - American Indian / Alaska Native
    - Asian
    - Native Hawaiian or Other Pacific Islander
    - Black or African American
    - White
    - More than one race

Inclusion of Women and Minorities (1 page)

Here is the content you need to include:

- **1. Inclusion on the Basis of Sex/Gender and Race/Ethnicity**
  - Planned Distribution of Subjects
  - Description and Rationale of Subject Selection
  - Rationale for Exclusion
  - Description of Outreach Programs for Recruitment
- **2. Additional Requirements for Clinical Trials**

1. Inclusion on the Basis of Sex/Gender and Race/Ethnicity

Planned Distribution of Subjects

- If you are collecting NEW data, provide a description of your plans for including individuals in your study on the basis of:
  - Sex / Gender
  - Race / Ethnicity
- If you are using PRE-EXISTING data:
  - Is there a description of the planned distribution of subjects regarding Sex/Gender and Race/Ethnicity?
  - Is there an explanation if the Sex/Gender and/or Racial/Ethnic composition is unknown?
  - Is there a description of the Sex/Gender and Racial/Ethnic composition for the population base of the existing dataset, if known?

1. Inclusion on the Basis of Sex/Gender and Race/Ethnicity

Description and Rationale of Subject Selection

- Describe subject selection criteria and your rationale for selection considering the:
  - Population at risk for the disease/condition under study
  - The scientific objectives and proposed study design

1. Inclusion on the Basis of Sex/Gender and Race/Ethnicity

Rationale for Exclusion

- If the proposed sample specifically excludes a group at risk for the disease/condition under study, you need to provide justification (citations) for your rationale
  - You could provide citations on the lack of differences on the basis of sex/gender, race/ethnicity
  - You could explain the need to fill a particular research gap
  - You could explain that you are using pre-existing data or samples when more representative data/samples are not available for secondary data analysis

1. Inclusion on the Basis of Sex/Gender and Race/Ethnicity

Description of Outreach Programs for Recruitment

- Describe recruitment and outreach plans or other methods for enrolling the individuals proposed as part of the sample

2. Additional Requirements for Clinical Trials

(if this isn't applicable to your grant, you can put N/A for this section)

- Valid analyses may be described as stratified analyses that explore how well the intervention works among sex/gender and racial/ethnic groups
- Depending on current knowledge of the disease/condition under study, the analyses may need to be adequately powered to detect differences in individual subgroups
- Applicants should address whether they plan to test or not test for differences in effects among sex/gender, racial, and/or ethnic groups and why that is or is not appropriate
- This may include supporting evidence and/or data derived from animal studies, clinical observations, metabolic studies, genetic studies, and pharmacology studies as well as observational, natural history, epidemiology and/or other relevant studies
- Additional factors may include planned primary and secondary outcomes and whether there are previous studies that support or negate the likelihood of differences between groups

2. Additional Requirements for Clinical Trials

Does the applicant address their plans in the context of one of the following?

___ **When prior studies strongly support significant differences**: Plans to conduct adequately powered valid analyses to detect significant differences in intervention effect among sex/gender, racial, and/or ethnic subgroups for each primary outcome.

___ **When prior studies strongly support no significant differences**: Plans to include and analyze intervention effect in sex/gender, racial, and/or ethnic subgroups. (Representation of sex/gender, racial, and ethnic groups is not required as subject selection criteria, but inclusion is encouraged).

___ **When prior studies neither support nor negate significant differences**: Plans to conduct valid analyses of intervention effect in sex/gender, racial and/or ethnic subgroups (without requiring high statistical power for each subgroup) for each primary outcome.

2. Additional Requirements for Clinical Trials

- Applicants should address the following issues for ensuring valid analyses:
  - inclusive eligibility criteria – in general, the cost of recruiting certain groups and/or geographic location alone are not acceptable reasons for exclusion of particular groups;
  - allocation of study participants of both sexes/genders (males and females) and from different racial and/or ethnic groups to the intervention and control groups by an unbiased process such as randomization;
  - unbiased evaluation of the outcome(s) of study participants; and
  - use of unbiased statistical analyses and proper methods of inference to estimate and compare the intervention effects by sex/gender, race, and/or ethnicity, particularly if prior evidence strongly suggests that differences exist. Stratification or other methods may be utilized.

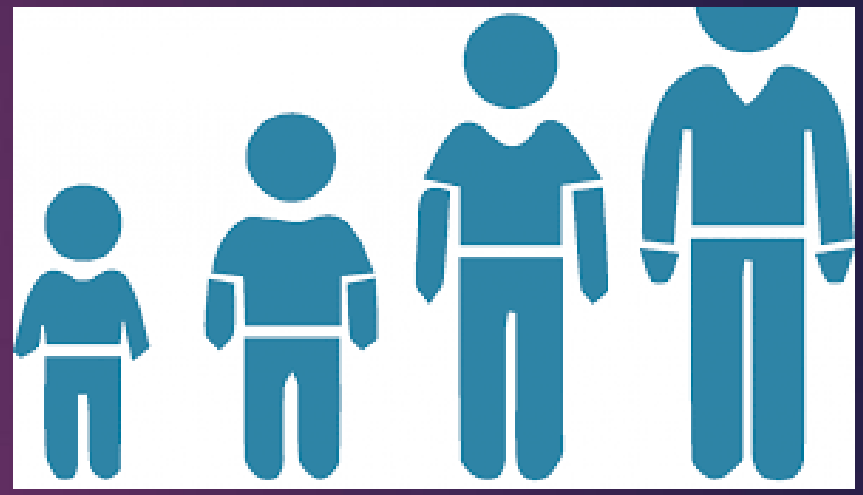
Inclusion of Individuals Across the Lifespan (1 page)

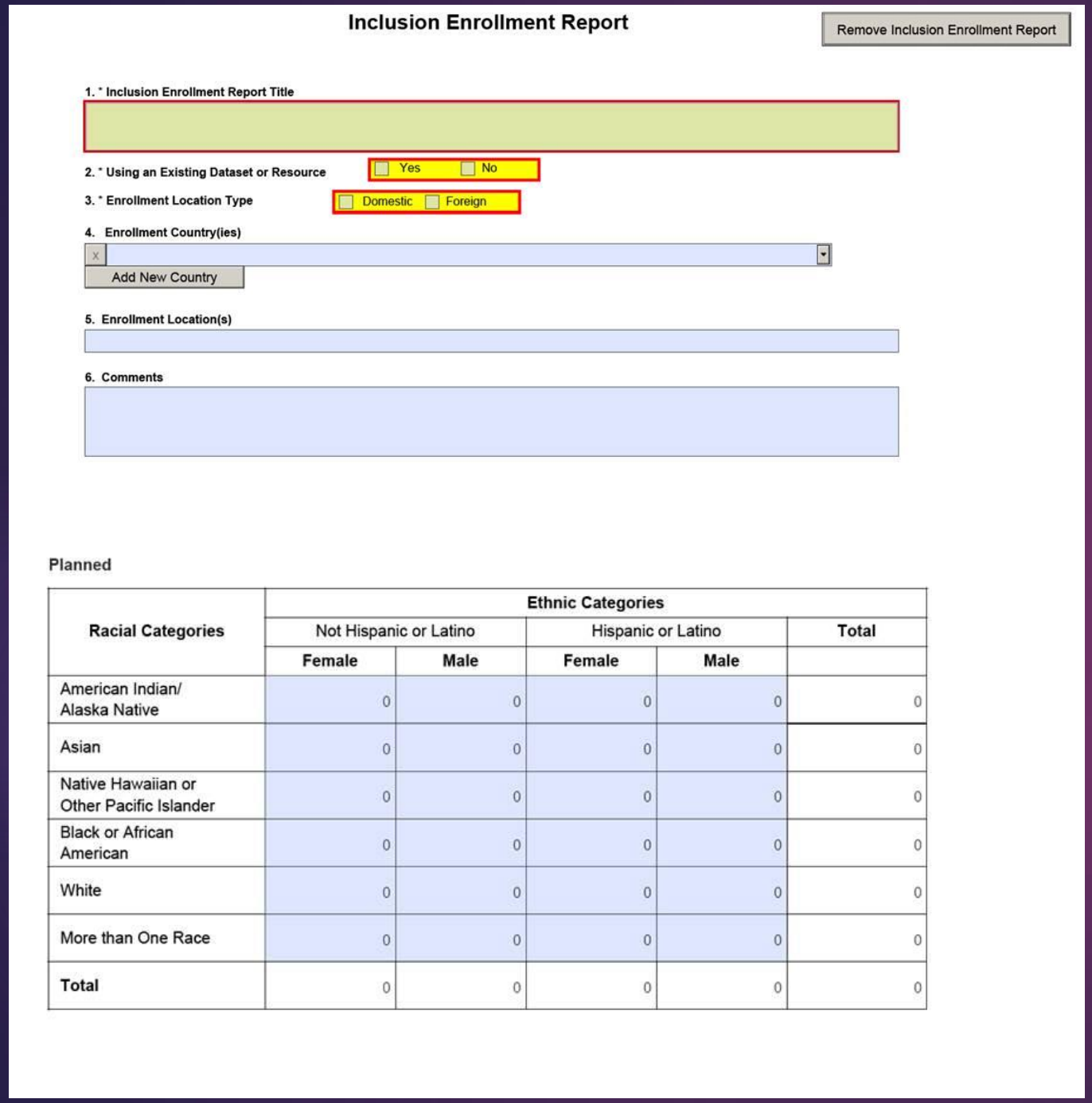
- Describe and give a rationale of the age ranges of individuals expected to be recruited

- Describe and justify the exclusion of individuals based on age – below are VALID reasons for exclusion:
  - **The disease or condition does not occur in the excluded age group, or the research topic is not relevant to the excluded age group.**
  - *Example: A study of Alzheimer's disease proposes to exclude children.*
  - **The knowledge being sought in the research is already available for the excluded age group or will be obtained from another ongoing study, and an additional study will be redundant.**
  - *Example: A drug studied and approved for use in children will now be studied only in adults.*
  - **A separate, age-specific study in the excluded age group is warranted and preferable. While this situation may represent a justification for excluding individuals based on age, consideration should be given to taking age differences into account in the study design, whenever feasible.**
  - *Example: A clinical trial designed to promote self-monitoring of blood glucose levels in adolescents with Type 1 diabetes proposes to include only adolescents.*
  - **The study will collect or analyze data on pre-enrolled study participants (e.g., longitudinal follow-up studies that did not include data on children, or analysis of an existing dataset) and data inclusive of individuals across the lifespan are not available to address the scientific question.**
  - *Example: A study which began prior to implementation of the NIH Policy and Guidelines on the Inclusion of Children proposes follow-up to examine long-term outcomes of individuals with the condition. The original study excluded children, and similar data are not available from a cohort that includes children.*
  - **There are laws or regulations barring the inclusion of individuals in a specific age group in research.**
  - Example: Regulations for protection of human subjects allow consenting adults to accept a higher level of risk than are permitted for children.
  - **The study poses an unacceptable risk to the excluded group, such that their participation would not be considered ethical by the local IRB, peer review and/or NIH staff.**
  - *Example: Children are excluded from a Phase I study for a treatment that includes significant risk, including death. Evidence suggests the potential benefits to children do not outweigh the risks.*

Inclusion of Individuals Across the Lifespan

- Describe the expertise of the investigative team for working with individuals of the included age groups
- Describe the facilities available to accommodate children and older adults, if applicable
- Inclusion of an appropriate distribution of children and older adults to contribute to a meaningful analysis relative to the purpose of the study, if applicable





Inclusion Enrollment Report

Remove Inclusion Enrollment Report

1. * Inclusion Enrollment Report Title

2. * Using an Existing Dataset or Resource ☐ Yes ☐ No

3. * Enrollment Location Type ☐ Domestic ☐ Foreign

4. Enrollment Country(ies)

Add New Country

5. Enrollment Location(s)

6. Comments

Planned

Racial Categories	Ethnic Categories				
	Not Hispanic or Latino		Hispanic or Latino		Total
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	0	0	0	0	0
White	0	0	0	0	0
More than One Race	0	0	0	0	0
Total	0	0	0	0	0

Revisit the Inclusion Enrollment Report

and fill in all of the cells!

- Do an NIH search to find the most recent version of this form (e.g., SF424 Forms if that is where your FOA tells you to look)
- Make sure the #s and %s in each group matches what you wrote in the **Inclusion of Women, Minorities and Children** section
- Make sure that your total # of subjects matches what you say you will recruit in other places in your application

Action Items

- Complete drafts of the following and send to your **Primary Mentor**:
  - **Protection of Human Subjects from Research Risk**
  - **Inclusion of Women and Minorities**
  - **Inclusion of Individuals across the Lifespan**
  - **Inclusion Enrollment Report**

- Revisit what outstanding sections still need feedback from your **Co-Mentors and/or Consultants, Collaborators, or Contributors**