WRAIR
Scientific Review Committee (SRC) Overview

6 April 2022

WRAIR
Walter Reed Army Institute of Research

Areas of Focus

I. **Scientific Approval of Human Subjects Research Protocols**

II. **Process Overview**

III. **Scientific Review Committee Membership and Key Stakeholder Responsibilities**

Focus Area 1

I. **Scientific Approval of Human Subjects Research Protocols**

II. **Process Overview**

III. **Scientific Review Committee Membership and Key Stakeholder Responsibilities**

Why Scientific Review?

AR 70-25, 3-2.c(3) Use of Volunteers as Subjects in Research & DoDI 3216.02

"The protocol or test plan is submitted to a scientific review committee composed of individuals qualified by training and experience, and appointed by the commander of the unit to evaluate the validity of the protocol. The purpose of this peer review is to assure that the protocol design will yield scientifically useful data which meets the objective(s) of the study. The committee recommendations and actions taken by the investigator in response to the recommendations are submitted with the protocol to the HUC [Human Use Committee]."

WRAIR SOP UWZ-002, Version .03, 18 May 2020
WRAIR Policy 63, Scientific Review Committee, 27 Jan 2022

When is Review by SRC Required?

Scientific Review <u>Required</u>

- Human subjects research studies, whether minimal risk or greater than minimal risk

Scientific Review <u>Not Required</u>

- Exempt research
- Program evaluation
- Public health activities, e.g. surveillance studies under the direction of a public health authority
- Research not involving human subjects

Scientific review is critical, beyond just complying with regulations and SOPs. It is necessary to ensure the scientific integrity of the study.

*Please note that activities that are not required to undergo SRC review may have their own vetting processes by other agencies or review bodies

Who are the Main Participants?

WRAIR Components Involved in Review and Scientific Approval Process:

- Human Subjects Protection Branch (HSPB)
- Chief Science Office (CSO)
- Scientific Review Committee (SRC)
- Center Directors /OCONUS Directors
- Branch Chiefs

Other Proponents:

- Principal Investigators (PIs)

**AFRIMS has its own SRC, and therefore AFRIMS studies typically do not undergo SRC review at WRAIR.*

How May Approval be Granted?

Three Ways to Grant Scientific Approval of Human Subjects Research

1. **Scientific Review Committee**

   Approval by the WRAIR SRC

2. **Outside Scientific Review**

   Approval by a non-WRAIR SRC

3. **Exempt Human Subjects Research**

   Approval by the Center Director / OCONUS Director

Outside Scientific Review

a. In some instances, WRAIR has a standing general practice with other institutions' SRCs. In these cases, the institution will supply a formal memo indicating approval and no SRC review is required. Examples include NIAID/DAIDS CSRC, PSRC, and Operation Warp Speed/Countermeasures Acceleration Group protocols.

b. In other instances, protocols with external scientific review and approval may be considered by the CSO on a case-by-case basis.

c. A signed approval document and evidence of the conduct of a scientific review process are important determinants for CSO acceptance. If the review is not accepted, the CSO forwards the protocol to the SRC Chair for SRC review.

   Note: The WRAIR and NMRC IRBs accept each other's approvals under an institutional agreement.

Exempt Human Subjects Research

Conditional Approval by the Branch Chief, Center Director, or OCONUS Director

a. Principal investigators must submit all protocols through their Branch Chief, Center Director, or OCONUS Director

b. The Director/Chief must establish and certify, by signature, that the protocol has scientific merit, is feasible and is militarily relevant

c. The protocol is scientifically approved via this mechanism only on the condition that the Human Subjects Protection Branch (HSPB), through the WRAIR Institutional Review Board, determines that the protocol constitutes exempt subjects research

WRAIR Scientific Review Committee

New Protocol Submissions - The SRC Chair receives new protocols from the HSPB if not previously reviewed or if the CSO determines an external review is not accepted.

Amendments –

a. The SRC Chair receives amendments for review if the changes may affect the scientific methods of the protocol. (Amendments that involve only administrative changes do not require review and are not sent to the SRC Chair).

b. If the amendments involve minor changes, the Chair may first need to verify whether scientific review is needed. If the Chair determines that SRC review is not needed, they will document this by email. Criteria for making the determination of when amendments require SRC review are outlined in SOP.

c. For amendments that require review, depending on how significant the changes are, the Chair may choose to use a full review process or review the changes him/herself.

Selecting SRC reviewers

- The Chair selects the members of the SRC who will review the protocol based on the type of study, the methodology, research topic, and disciplines involved in the research, and by the collective expertise required to make a determination of scientific acceptability.

Identifying SRC Reviewers: points to consider

Study protocol – categorized by:

- ***Study Methodology:*** (e.g., clinical trial, observational study)
- ***Discipline(s)*** relevant to the protocol: (e.g., pharmacology, neuroscience)
- ***Study Intervention***: (e.g., drug, vaccine, behavioral, device)
- ***Study Population***: (e.g., US military, international, pediatrics)

SRC members – expertise and experience characterized by:

- ***Types of studies they have led as a PI*** (methodology)
- ***Discipline(s)***
- ***Research questions/interventions*** they typically study
- ***Study Populations*** they have worked with directly (e.g. not just acquired samples through clinical studies conducted by others)

Identifying reviewers—example:

- Protocol for a Phase 2a randomized clinical trial of a new, investigational vaccine for Dengue. Protocol endpoints are immunogenicity, primary protection against Dengue fever, safety. Study sites are in Thailand and the Philippines.

Reviewer criteria to look for (not all necessarily in one reviewer):

- RCT experience
- Vaccine development/ immunology
- Statistical expertise
- International research experience

A sample of reviewers

Reviewer 1	*Reviewer 2*	*Reviewer 3*
•***Main studies: clinical trials in HIV treatment, other infectious diseases*** •Disciplines: internal medicine, epidemiology • Research topics: optimizing HIV treatment, quality of care, opportunistic infections •***Study populations: sub-Saharan Africa, US***	•Main studies: AI and mathematical modeling in infectious disease research •Disciplines: microbiology, bioinformatics, biophysics, ***statistics*** •Research topics: antibody/ antigen interactions, immunologic profiles in infectious disease •Study populations: N/A	•Main studies: multidrug resistant organism (MDR) surveillance, diagnostics, and nosocomial infections •Disciplines: microbiology, molecular biology •Research topics: emerging MDR organisms, threats to human health •Study populations: international and domestic

Reviewer 4	*Reviewer 5*	*Reviewer 6*
•***Main studies: early phase vaccine clinical trials,*** controlled human infection models (CHIM) •Disciplines: internal medicine, infectious disease •***Research topics: vaccine development, malaria, Hanta, Dengue, Ebola*** •Study populations: US	•Main studies: vaccine development and preclinical assessment vaccines for enteric pathogens •Disciplines: microbiology, immunology •Research topics: vaccine development, Shigella; animal challenge models •Study populations: N/A	•Main studies: survey research on PTSD, acute stress responses, behavioral/cognitive psych studies of effects of sleep on behavior and performance •Disciplines: Psychology •Research topics: self-control, resilience, sleep •Study populations: US military

Identifying Reviewers – Additional Considerations

- All clinical trials should have a statistician as a reviewer
  - Member should have appropriate background (e.g. Masters or PhD in statistics) to provide substantive review
- Study Methodology is the most important category…at least one reviewer should have experience leading similar type of study
- Assign mix of reviewers so that all (or most) categories have a match--not all reviewers match on each category
- If there is lack of relevant expertise among non-conflicted reviewers, Chair should identify outside reviewers
  - HSPB Director, RIO, and/or CSO may assist in identifying appropriate reviewers

Focus Area 2

I. Scientific Approval of Human Subjects Research Protocols

II. Process Overview

III. Scientific Review Committee Membership and Key Stakeholder Responsibilities

Document Flow

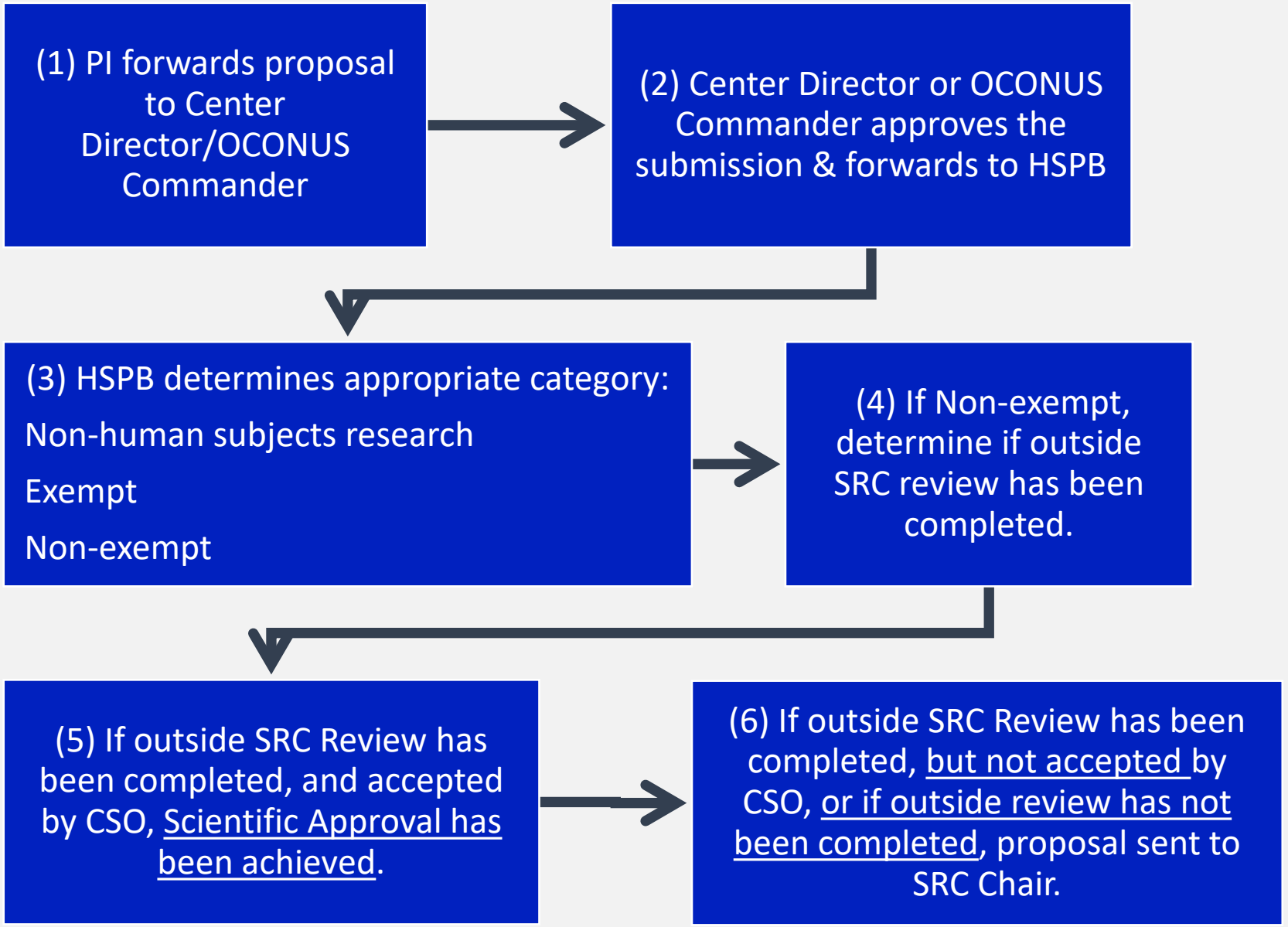
1. PI / Center submits protocol to HSPB
2. If not previously reviewed and/or approved, HSPB forwards the protocol to the SRC Chair.
   - If previously approved by external scientific review body, HSPB forwards the protocol and the review to the CSO for concurrence. *(within 3 business days of receipt)*
   - If the CSO concurs with previous approval, the protocol is scientifically approved. If the CSO does not concur, the protocol is forwarded to the SRC Chair.
3. Chair selects 3 SRC members and forwards entire packet (protocol and supporting documents) to reviewers via pathway on V drive or email. *(within 3 business days of receipt from HSPB)*
4. SRC reviewers each review the protocol and forward their comments to SRC Chair via email *(within 10 business days of receiving protocol)*
5. Chair compiles comments and forwards to PI. *(no more than 3 business days from receiving comments from reviewers)*

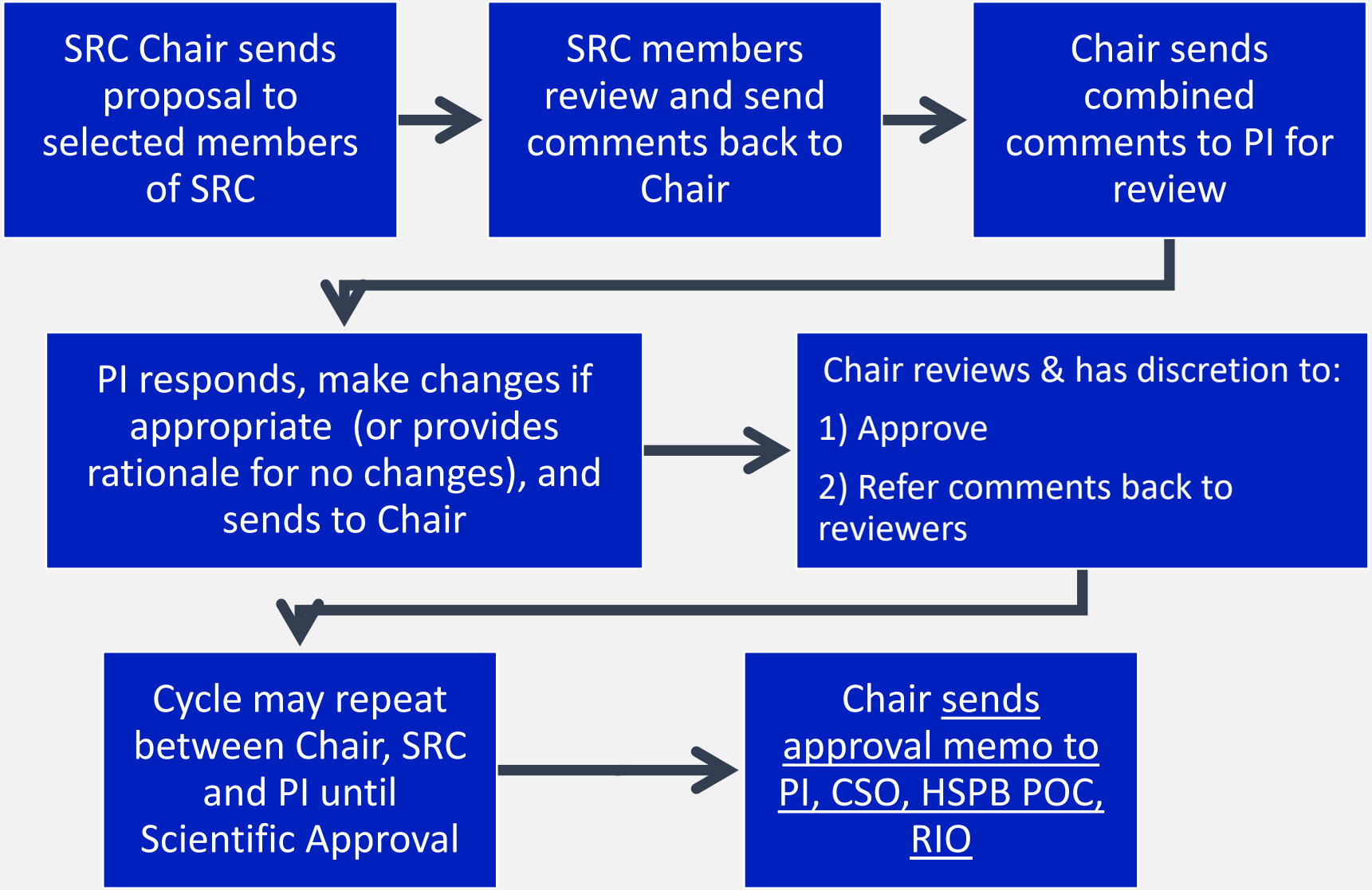
Document Flow - 2

6. PI responds to the SRC comments and prepares revised protocol and response memo and sends these to SRC Chair. *(within 10 business days of receipt of review unless an extension is requested)*
7. SRC Chair consults with the SRC reviewers regarding the PI's response to determine if the response is adequate. The Chair has the discretion to decide on their own if the response is satisfactory in cases where they do not need input from the SRC reviewers.
8. If response is deemed satisfactory, the Chair approves the protocol. SRC Chair sends approval memo to the PI. If not satisfactory, SRC responds to PI with further requested changes—cycle repeats.

The following 4 individuals should be CC'd on all emails:

- ***CSO***
- ***HSPB Director***
- ***Research Integrity Officer***
- ***HSPB POC***


(1) PI forwards proposal to Center Director/OCONUS Commander
(2) Center Director or OCONUS Commander approves the submission & forwards to HSPB
(3) HSPB determines appropriate category:
Non-human subjects research
Exempt
Non-exempt
(4) If Non-exempt, determine if outside SRC review has been completed.
(5) If outside SRC Review has been completed, and accepted by CSO, Scientific Approval has been achieved.
(6) If outside SRC Review has been completed, but not accepted by CSO, or if outside review has not been completed, proposal sent to SRC Chair.


SRC Chair sends proposal to selected members of SRC
SRC members review and send comments back to Chair
Chair sends combined comments to PI for review
PI responds, make changes if appropriate (or provides rationale for no changes), and sends to Chair
Chair reviews & has discretion to:
1) Approve
2) Refer comments back to reviewers
Cycle may repeat between Chair, SRC and PI until Scientific Approval
Chair sends approval memo to PI, CSO, HSPB POC, RIO

Focus Area 3

I. Scientific Approval of Human Subjects Research Protocols

II. Process Overview

III. Scientific Review Committee Membership and Key Stakeholder Responsibilities

Membership

Positions:

Chair, Vice Chair, General members

Selection:

Scientific staff (*MIL, CIV, CTR*) are appointed by the Commander or his/her designee, based upon recommendations of the Center Directors. The Chair must be an experienced military or civilian investigator. The SRC will reflect diverse scientific expertise, appropriate to adequately review the research portfolio. Service on the SRC shall be reflected on performance reviews.

Criteria:

1. Has served as PI on at least one protocol
2. Has expertise relevant to the portfolio of studies reviewed by the SRC
3. Recommended by Branch Chief or Center Director

Duration:

Chair/Vice Chair: 1-year minimum

General members: 2-year minimum, staggered rotation

Roles and Responsibilities of SRC Chair

- Assigns reviewers for each protocol to be reviewed
- Carries out the review process via email or via convened meeting, as appropriate
- Reconciles disparate opinions among SRC members
- Interacts with the PI regarding responses
- Serves as point of contact for receipt of documents and communications from the HSPB or CSO, and timely distribution of SRC communications
- Assists the CSO in managing conflict of interest issues
- Adheres to WRAIR Policy 63, which defines the SRC's establishment, SOP UWZ-002, which delineates the process, in accordance with Policy 25, which outlines the process for determining what constitutes human subjects research

Roles and Responsibilities of Committee Members

- Accepts assignments from SRC Chair, provided protocol aligns with their expertise and experience
    - Informs the SRC Chair if the protocol falls outside of their area of expertise
- Receive protocol materials from the SRC Chair
- Notify the SRC Chair of any conflict of interests
- Review protocols/protocol packets in accordance with SOP UWZ-002
- Provide comments to SRC Chair within 10 business days
- Attend meetings, as appropriate
- Review protocol revisions made in response to SRC input, as appropriate, in coordination with the SRC Chair

Roles and Responsibilities of Other Offices

- **Principal Investigators**
  - ✓ Submit the protocol in accordance with Policy 25.
  - ✓ Respond to the Chair for clarifications and minor issue resolution.
  - ✓ Make changes to the protocol as required by the SRC OR provide written justification and rationale for not making changes
  - ✓ Manage strict version control.
  - ✓ Submit the scientifically approved protocol & supporting documents to the HSPB.
- **Branch Chiefs/ Center Directors/OCONUS Directors**
  - ✓ Evaluate and approve all protocols for submission to HSPB/SRC to ensure that they are:
    - ✓ Scientifically sound
    - ✓ Feasible
    - ✓ Militarily relevant
- **Center Directors**
  - ✓ Evaluate and approve all protocols when Branch Chief is member of protocol team
  - ✓ Recommend to the CSO appropriate researchers to serve on SRC

Roles and Responsibilities of Other Offices - 2

- **Human Subjects Protection Branch (HSPB)**
  - ✓ Assess whether amendments have scientific impact or are only administrative
  - ✓ Follow guidance of SOP to determine if SRC review is needed
  - ✓ Forward protocols to SRC Chair for review, as appropriate
  - ✓ Maintain all records and documents related to the protocol, including those accrued in the scientific review process.
  - ✓ Include SRC review comments and responses as well as final SRC approval memo in the IRB packets for review, whether by full board or expedited reviewer (IRB Chair or Chair Designee).

Roles and Responsibilities of Other Offices - 3

- **Chief Science Officer (CSO)**
  - ✓ Determine if outside scientific reviews are acceptable in situations where there is no general practice to accept the external review
    - ✓ Determine on a case-by-case basis if WRAIR will defer to the outside scientific review.
  - ✓ Coordinate with SRC Chair to choose outside reviewers when specialized expertise is needed
  - ✓ With SRC Chair, mediate disagreements between investigators and SRC if impasse has been reached
  - ✓ With SRC Chair, mediate any unresolved concerns about conflict of interest in the case of any specific review, and when needed, determine COI management plan
  - ✓ Select SRC members and Chair/Co-chair with input from Center Directors; submit appointment memos for signature by Commander

Roles and Responsibilities of Other Offices - 4

- **Research Integrity Officer (RIO)**

  - ✓ Provide support for SRC Chair to choose outside reviewers when specialized expertise is needed
  - ✓ Support SRC orientation process and training
  - ✓ Provide input to CSO regarding selection of new SRC members
  - ✓ Coordinate periodic updates to SRC Policy and SOP
  - ✓ Conduct evaluation of SRC processes, as needed, to inform CSO of any needed updates/changes

Back Up Slides

Glossary of Acronyms

SRC – Scientific Review Committee

IRB – Institutional Review Board

HSPB – Human Subjects Protection Branch

CSO – Chief Science Office/Officer

RIO – Research Integrity Officer