

Session II: Roles of the IBC within the *NIH Guidelines* Framework

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Better together.

Session II: Roles of the IBC within the *NIH Guidelines Framework*

- **Perspective from an IBC Chair at a Clinical Cancer Research Center (Fred Hutch and Seattle Cancer Care Alliance in Seattle) and a former RAC member**

What is the Seattle Cancer Care Alliance (SCCA)?

The SCCA brings together the outstanding adult and pediatric oncology patient care services of three world-renowned institutions:

- **Fred Hutch**
- **University of Washington**
- **Seattle Children's**

What is the Seattle Cancer Care Alliance (SCCA)?



**Fred
Hutch**



UW



**Seattle
Children's**

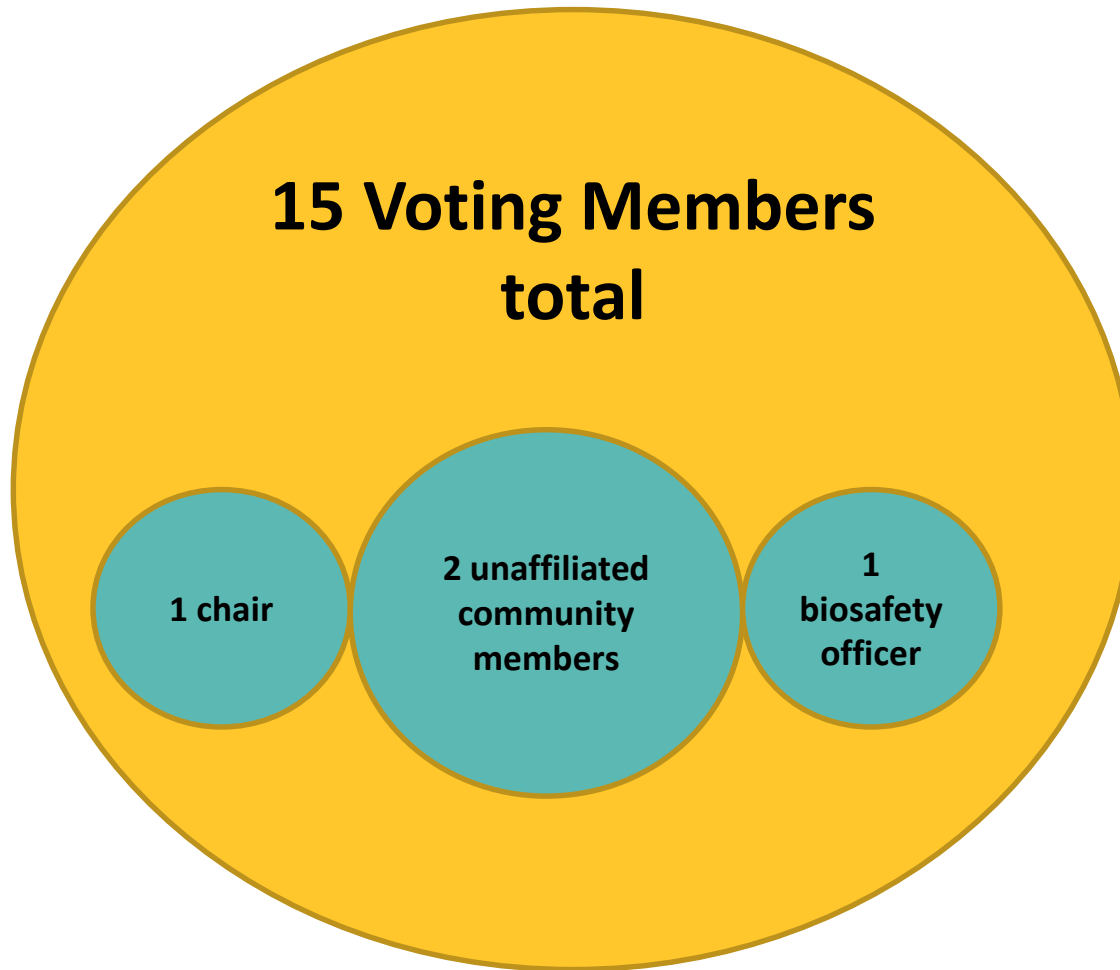


SCCA Overview



- **Founded in 1998**
- **376 physicians**
- **NCI-designated comprehensive cancer hospital in Pacific Northwest**
- **~ 500 stem cell transplants performed annually**
- **Immunotherapy and Gene Therapy**
- **Over 500 active clinical trials**

SCCA IBC Membership



SCCA IBC Overview

Purpose:

“To review new clinical trials involving potentially biohazardous lines of research occurring at the SCCA. Oversight includes a variety of experimentation including recombinant and synthetic DNA molecules, biological materials (e.g. infectious agents) and other potentially hazardous agents (e.g. carcinogens)”

- SCCA IBC Charter

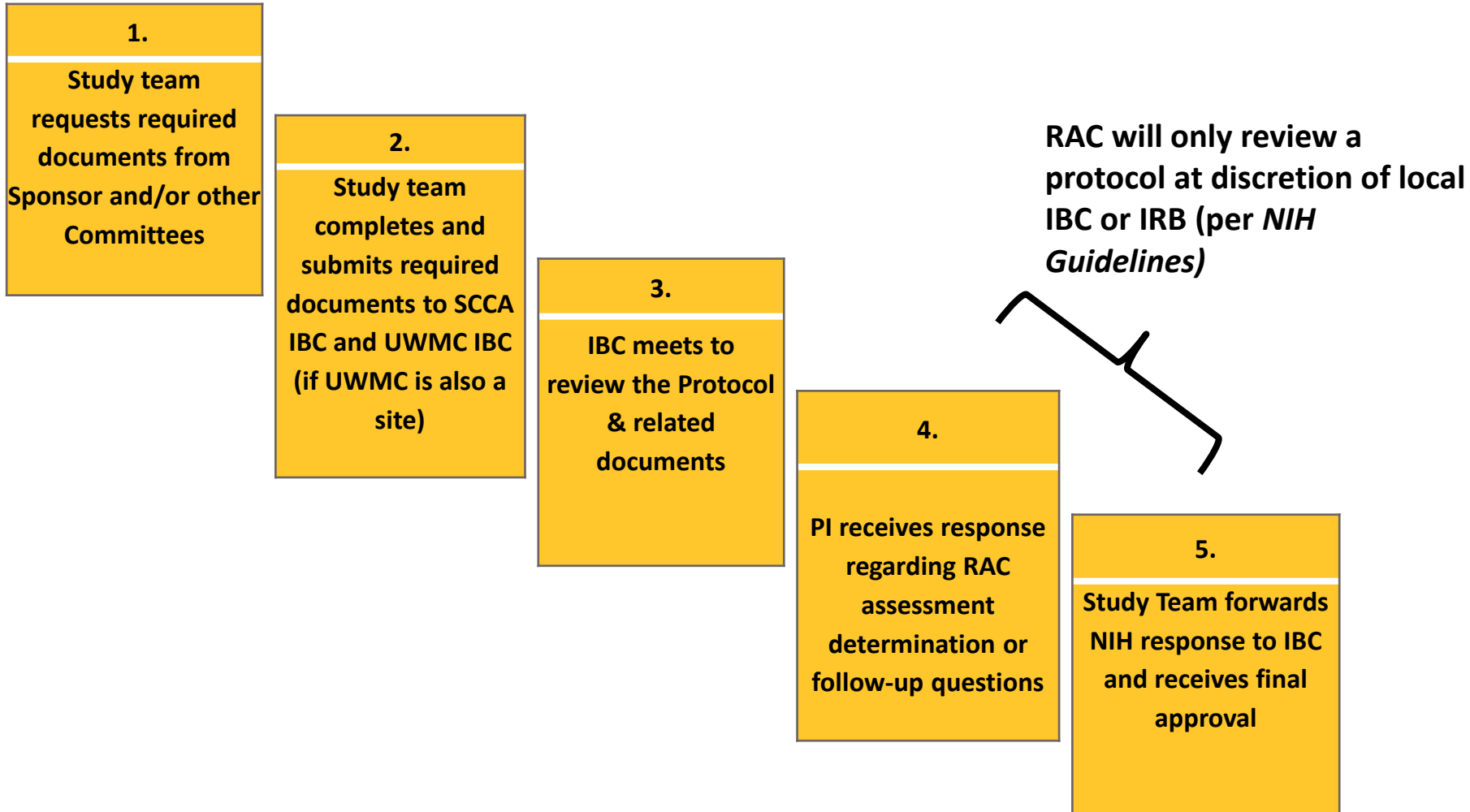
- **Founded in 2004**
- **> 40 protocols reviewed since inception**
- **32 protocols currently active**
- **Average of 4 to 5 protocols reviewed per year**
- **In total, SCCA opens on average 125 protocols per year**



How is your institutional biosafety oversight program system structured?



IBC Submission Process



Principal Investigator Responsibilities

- **Comply with specific protocols, practices and procedures described in NIH Guidelines and the FHCRC Hazard Awareness Management Manual**
- **Develop standard operating procedures to ensure the safe use of biohazardous and rDNA materials within your laboratories**
- **Ensure all laboratory staff have documented lab specific biosafety training (use the PI Training Script found on the EH&S website)**
- **Report incidents involving biological materials or rDNA to the Biosafety Officer**

Review NIH Guidelines Section IV-B-7 for the complete list of PI responsibilities

What is the scope of biosafety oversight at your institutions?

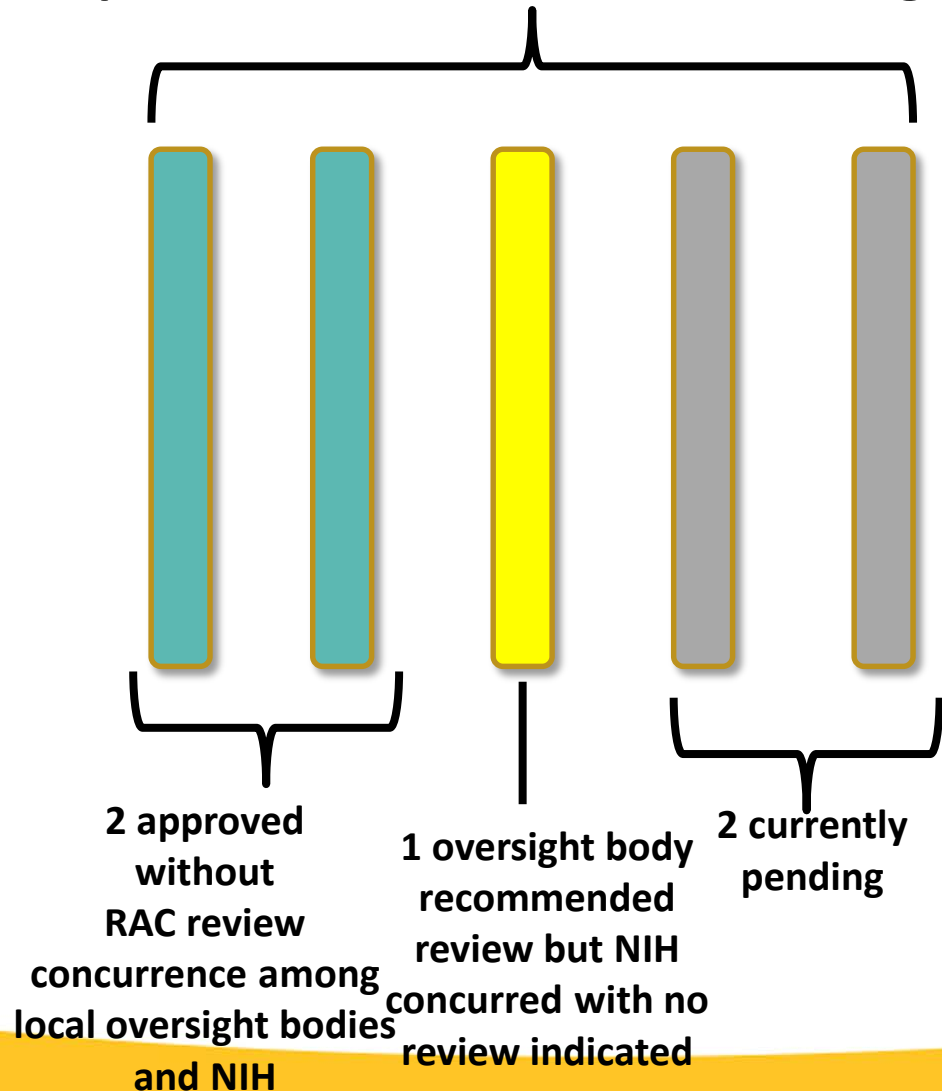
- **How widely do you use the principles in *NIH Guidelines* in terms of your approach to biosafety oversight and risk management at your institution**

With respect to the review of proposed recombinant DNA research our IBC follows the NIH Guidelines and the following points described in Section II and Section III of the NIH Guidelines need to be addressed:

- 1. Agent characteristics (e.g. virulence, pathogenicity, environmental stability)*
 - 2. Types of manipulations planned*
 - 3. Source(s) of the inserted DNA sequence (e.g., species)*
 - 4. Nature of the inserted DNA sequences (e.g. structural gene, oncogene)*
 - 5. Host(s) and vector(s) to be used*
 - 6. Whether an attempt will be made to obtain expression of a foreign gene, and if so, the protein that will be produced*
 - 7. Containment conditions to be implemented*
 - 8. Applicable section of the NIH Guidelines (e.g. Section III-D-1, Section III E-1, etc.)*
- **When reviewing the protocol and related materials provided the SCCA IBC Primary Reviewer addresses each item above which are adequately documented as fulfillment of the IBC review and oversight responsibilities described in Section IV-B-2 of the NIH Guidelines.**

Protocol Submission Stats since *NIH Guidelines RAC* review change

5 protocols reviewed since change



Benefits of having a biosafety oversight governance structure such as required by the NIH Guidelines – Challenges?

● Benefits of an IBC

- Conformity with NIH guidelines
- Public trust
- Safety of lab / clinic workers and the public
- Safety of patients
- Environmental risk assessment and protection
- Institutional Compliance

● Challenges

- Committee recruitment of members with appropriate expertise – given complex and emerging science
- Reciprocity among institutions when patients are being cared for at multiple sites

Interaction Between IBCs



At the moment, IBC's across institutions do not have reciprocity. Requirement that a clinical trial be reviewed and approved by each site where patients will receive treatment. What might be feasible at one sight may not be feasible at another

However, as a result of the recent changes to the RAC Guidelines there have been early discussions about the potential options for coordinating IBC reviews within the Cancer Consortium (SCCA, Seattle Children's, UW).

Impact of RAC Review Change in NIH Guidelines

SCCA IBC has seen no significant impact since change in *NIH guidelines*

- Increasing focus on local regulation has not led to higher volumes of protocol submissions (specifically for SCCA IBC)
- We have not seen a need to change timelines, workflow, or organizational structure following the change to RAC review rules

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Functions of the RAC

- **Major Actions and containment recommendations for research with Risk Group (RG) 4 agents such as Ebola, advice regarding amending the *NIH Guidelines* such as the addition of specific guidance for research with RG3 influenza viruses or modifying the scope to cover synthetic biology research**
- **Review of certain protocols selected by oversight bodies and NIH**
- **Forum for public discussion about scientific, safety, and ethical issues in life science research – educational meetings and workshops on gene editing, immunotherapy etc, ability for researchers to share important safety information prior to publications, eg how to best handle / treat Cytokine Release Syndrome (CRS)**

Major Actions involving specific research discussed by the RAC since 2000

NIH/RAC discussions	Nature of Major Action	Final Outcome
April to September 2007	Transfer of tetracycline resistance to Chlamydia	Approval given to transfer tetracycline resistance from <i>C. suis</i> (a swine pathogen) to <i>C. trachomatis</i> (a human pathogen). Containment and other conditions specified by the NIH Director.
June 2007 to April 2008	Transfer of chloramphenicol resistance to <i>Rickettsia typhi</i> and <i>R. conorii</i>	Approval given to transfer of chloramphenicol to <i>R. conorii</i> only. Containment and other conditions specified by the NIH Director.
December 2009 to March 2010	Transfer of tetracycline resistance to <i>Chlamydia trachomatis</i> serovar L2	Approval given with containment and other conditions specified by the NIH Director.
September 2015 to March 2016	Transfer of chloramphenicol resistance to <i>Rickettsia rickettsia</i> , <i>R. felis</i> , and <i>R. typhi</i>	Permission not given by the NIH Director for the transfer of chloramphenicol resistance to <i>R. rickettsia</i> , <i>R. felis</i> and <i>R. typhi</i> .

Biosafety Discussions at RAC Meetings

- **RAC Discussion on the biosafety of cloning RG4 *Mononegavirales* cDNA in non pathogenic *E. coli* K12. Chair: Federoff (2009)**
 - Conclusion of the RAC was that the cDNA cloning of Risk Group 4 single strand negative sense RG4 RNA viruses (eg Ebola and Marburg) could safely be performed at BL2 containment with appropriate biosafety and biosecurity measures
- **RAC Containment Reduction Discussions. Chairs: Zaia (2011); Fong (2013); Kiem (2015)**
 - Several discussions were held to discuss reduction in containment for defective negative strand RG4 viruses including defective Lassa virus, defective Ebola virus, and proposals for work involving defective positive strand hemorrhagic fever viruses
- **NHPs in BL4 Containment Settings: Primary Containment versus Open Caging. Chair: Don Kohn**
 - Discussion involving the risks and benefits of housing NHPs in open caging (without primary containment). These discussions led to changes in Appendix G for BL4 containment of NHPs.

Thank you

SCCA IBC Members:

Hans-Peter Kiem, MD, PhD (Chair)

Jennifer Adair, PhD

Shailender Bhatia, MD

Judy Campbell RN (Unaffiliated)

Lee Cranmer MD,

Terri Cunningham RN,

Shelly Heimfeld PhD,

Ronald Manger PhD,

Steve Pergam MD,

Seth Pollack MD,

Julia Piasecki (Unaffiliated)

Sarah Schwen RN,

Brian Till MD,

Cameron Turtle MD,

Don Wang (Biosafety)

Gina Roper – SCCA IBC Admin

Risk Levels Per NIH Guidelines

- NIH prescribes assigning risk groups as a basis for biohazardous agent classification:

Risk Group 1 (RG1)	Agents that are not associated with disease in healthy adult humans
Risk Group 2 (RG2)	Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are <i>often</i> available
Risk Group 3 (RG3)	Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions <i>may be</i> available (high individual risk but low community risk)
Risk Group 4 (RG4)	Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are <i>not usually</i> available (high individual risk and high community risk)

- An agent's risk group will then help determine the appropriate biosafety containment level (BSL)