RCR, Authentication of Key Resources, Biohazards

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Outline

- Responsible conduct of research
- Authentication of key resources
- Biohazards/Select Agent Research

Responsible conduct of research

- **NIH recognizes that instruction in responsible conduct of research occurs formally and informally in educational settings and that informal instruction occurs throughout the research training experience.**
- NOT-OD-10-019
- NOT-OD-22-055

Responsible conduct of research (definition)

NIH defines as the practice of scientific investigation with integrity.

It involves the awareness and application of established professional norms and ethical principles in the performance of all activities related to scientific research.

History of RCR requirements

1989- First notice, institutional training grants include activities related to RCR

1994- applications 1) **lacking a plan of RCR be returned without review**, 2) established review procedures, 3)established minimum requirements

2009- NIH requires all individual training, career development award, research education grant, and dissertation research grant must receive instruction in RCR.

2022- Instructional Component Recommendations

Relevant to..

- **Institutional training and institutional career development programs (T15, T32, T34, T90/R90, TL1, K12, or K30)**
- **Short-term training and research education programs (T35 and R25 programs lasting six or fewer months, short-term trainees supported on T15, T32 and T34 programs):**
  - duration should be considered in the design, implementation, and review of plans for instruction.
  - Duration should be appropriate for the total duration of the program.
  - On-line instruction could be appropriate.
- **Individual awards: F, K**
  - Fellows and scholars to tailor instruction in RCR to the needs of the individual.

Components of the RCR document

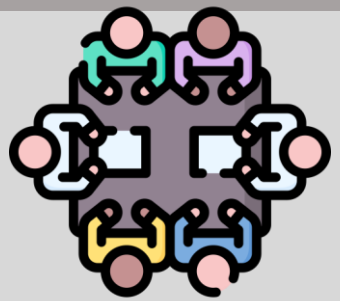
Components
Format
Subject matter
Faculty participation
Duration
Frequency

Components of RCR document
1. **Format of Instruction**

Face-to-face lectures

Coursework

Real-time discussion groups



- **Only on-line instruction is not acceptable.**
- Discussion-based instruction should **not exclusively employ video conferencing**
- Go beyond formal institutional courses, individual can develop their own scholarly understanding of the ethical issues.
- An individualized plan would also be appropriate where an institution does not have an established formal mechanism for such instruction.

Components of RCR document- 2. **Subject matter**

1. Conflict of interest– personal, professional, and financial – conflict of commitment, in allocating time, effort, research resources
2. Policies regarding human subjects, live vertebrate animal subjects in research, and safe laboratory practices
3. Mentor/mentee responsibilities and relationships
4. Safe research environments
5. Collaborative research
6. Peer review
7. Data acquisition and analysis; laboratory tools
8. Secure and ethical data use; data confidentiality, management, sharing, and ownership
9. Research misconduct and policies for handling misconduct
10. Responsible authorship and publication

Components of RCR document
3. **Faculty participation**

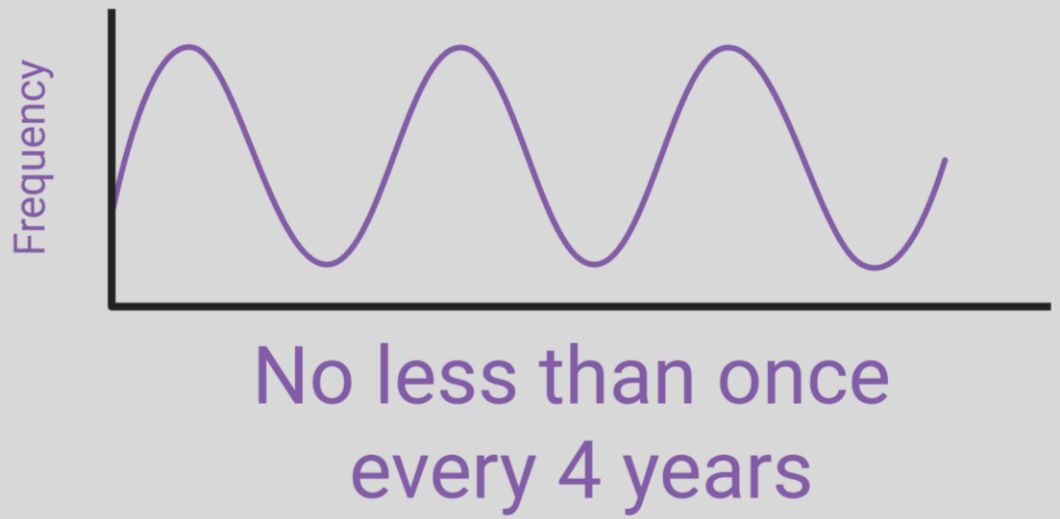
- Training faculty and sponsors/mentors are highly encouraged to contribute both to formal and informal instruction.
- Informal instruction occurs during laboratory interactions and in other informal situations throughout the year.

Components of RCR document
3. **Duration of instruction**

- Significant contact hours between the trainees and faculty.
- Acceptable programs generally involve at least eight contact hours.
- A semester-long series of seminars/programs may be more effective than a single seminar or one-day workshop.

Components of RCR document
4. **Frequency of Instruction**

- At least once during each career stage



Review criteria during peer review

**Comments are required on
Format
Subject matter
Faculty participation
Duration
Frequency

EXAMPLE OF A WELL WRITTEN RCR

I have completed formal instruction in the responsible conduct of research (RCR) and will complete additional RCR training appropriate for my career stage ….. This plan addresses NIH expectations for format, subject matter, faculty participation, duration, and frequency.

During my …., I completed graduate-level ethics and RCR coursework…... This instruction was delivered over a full academic term through lectures, case-based discussions, and written assignments. I also maintain CITI……,.
During this award, I will participate in ……. This faculty-led, small-group, discussion-based course is delivered over seven weeks, approximately four hours per week,. Topics include …….. I will also do RCR ….Certificate, …. Scholars seminars, ….Research Special Interest Group activities, and at least one formal CITI RCR refresher during the award period. These activities will strengthen my training in ……..

Faculty participation will be through …….. Ethical decision-making and RCR principles will be integrated into regular meetings with my co-primary mentors,……. At least twice annually, full mentorship-team meetings will include focused discussion of ethical issues arising in the award,.

Overall, my RCR plan includes ……

Authentication of key resources

No specific format

Authentication of key biological and/or chemical resources

Here, we describe methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies. We will only use standard laboratory reagents (i.e., buffers and other common biologicals or chemicals) that are provided with a certificate of authenticity and purity. Because these standard lab reagents are not expected to vary over time, we do not mention these below, as outlined in the PHS application instructions. Below, we describe the exceptions to this rule: antibodies for flow cytometry. We have used dkNET https://dknet.org/ of UCSD for validating some of the resources.

Cell cultures. … specific of cell lines

Antibodies. We will obtain antibodies from vendors with strong track records in the field. Prior to purchase, validation data for each antibody will be investigated through one or more of the various online resources devoted to this endeavor; these include but are not limited to antibodypedia.com and antibodyregistry.org. Most of the antibodies proposed are validated in the lab. These registries include trusted sources such as Abcam, Proteintech, Biolegend etc. Lot number for all antibodies will be logged as part of the experimental records. Specific antibodies that will be used that were generated using dkNET are shown in table.

*ELISA Immunoassays***.** All assays will be purchased in bulk from commercial vendors to ensure the same lot will be used for each assay when possible. Each assay will include internal controls including control plasma and a low, medium, and high protein spikes corresponding to values at 15, 50, and 85% of the standard curve concentrations to control for plate-to-plate variation and verify recovery from the matrix. Data will undergo quality control measures as specified by the manufacturers before entry into the database.

qPCR. Quantitative PCR (qPCR) will be performed on spheroids. All primers, probes, and standards have been designed using IDTDNA primer quest and oligo analyzer and tested for quality assurance by the manufacturer. We will use commercially available RNA isolation kits (Qiagen). qPCR for gene expression will use reverse transcription kits, SYBR master mixes and primers (Qiagen, and IDT).

Respirometry assays- All bioenergetic assays are purchased from Agilent (Seahorse XF Cell Mito Stress Test Kit).

We do not foresee any issues with reagent stability over the course of the funding period, as all proposed experiments utilize commercially available, validated reagents. Criteria for confirmation of acceptable standard curves, results from standards, and negative controls are included in our protocols.

Examples

Assay	Catalog Number, Company
Triglyceride content	Triglyceride-Glo™ Assay, J3160, Promega
ROS	Amplex Red A22188, ThermoFisher
ATP content	CellTiter-Glo® 3D Cell Viability Assay, Promega
VLDL secretion	Human ApoB ELISA (Genie)
MTTP activity	MTTP activity assay (Sigma)
Fatty acids	NEFA-HR kit (Wako Life Sciences)
Albumin	EHALB, ThermoFisher
Mitochondrial ROS	MitoSOX Red M36007, ThermoFisher
Mitochondrial membrane potential	MitoProbe™JC-1 Assay Kit M34152 (ThermoFisher)

Example

Chemical	Catalog Number, Company
William's E Medium	W1105-02, US Biologicals
Maintenance and Metabolism media supplement	HPRG720, ThermoFisher
GlutaMAX	35050061, ThermoFisher
Glucose	G8644, Sigma
Fructose	F3510, Sigma
IXA4	HY-139214, MedChem Express
HNF4α agonist	HY-176136, MedChem Express
^{13}C Algal Lipid Mixture,	487937 Sigma
WY-14643	C7081, Sigma
AICAR	A9978, Sigma
Plating and maintenance media	Invitrogro, BioIVT
Etomoxir	236020, Sigma

Example 3

Antibody	**Clone**	**RRID***
CD3	SP34-2	AB_2916375
CD4	L200	AB_2875372
CD8	BW135/80	AB_244335
CD28	CD28.2	AB_627002
CD38	HIT2	AB_10715033
CD45	H130	AB_419311
CD45RA	HI100	AB_627081
CD279	EH12.2H7	AB_2745541
CD14	M5E2	AB_2916417
Ki-67	Ki-67	AB_2739393
CD127	Clone HIL-7R-M21	AB_2296056
TIGIT		AB_2742064
TNFα	MAb11	AB_10893226
IL-1β	REA1172	AB_2801798
CD20	clone 2H7	AB_11153856
IL6		AB_3665391
IL10		AB_11207039
IL18	Clone #70625	
CD56	clone QA17A16	AB_2910523
CB1R	Clone # 368302 R&D Systems	

Biohazards and Select agent research

Biohazards- No specific format

In research strategy

Biohazards: Sample processing will be performed in laminar flow biosafety hoods, and cells cultured in dedicated BSL-2+ CO_2 incubators. Appropriate waste disposal and personal protective equipment will be used.

Select agent - no specific page limitation or format

1. Identify the select agent(s) to be used in the proposed research.
2. Provide the registration status of all entities where select agent(s) will be used.
3. Provide a description of all facilities where the select agent(s) will be used.

   a. Describe the procedures that will be used to monitor possession, use, and transfer of select agent(s).

   b. Describe plans for appropriate biosafety, biocontainment, and security of the select agent(s).

   c. Describe the biocontainment resources available at all performance sites.

- https://grants.nih.gov/policy-and-compliance/policy-topics/select-agent
- https://www.selectagents.gov/sat/index.htm
- https://osp.od.nih.gov/policies/biosafety-and-biosecurity-policy#tab2/

Thank you

https://www.ncbi.nlm.nih.gov/books/NBK236192/
https://grants.nih.gov/policy-and-compliance/policy-topics/research-integrity/rcr

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