IRB 101 for BUMC Graduate Student IRB Submissions

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BUMC Clinical Research Resources Office (CRRO)

April 17, 2013

CRRO Clinical Research Resources Office

CRRO Clinical Research Resources Office

Supported by the BU CTSI and Office of Clinical Research (OCR)
Serving all BUMC Clinical Researchers

Regulatory Service and Education Program	Recruitment Services Program

• Consultation services
  • Study implementation
  • IRB application submission
• Tools and Resources *(web-site based)*
• Education programs for all levels of the research team
• Support for sponsor-investigators of FDA regulated research
• Quality Assurance Reviews
	• Consultation services
	  • Study implementation
	  • IRB application submission
	• ReSPECT Registry
	  • Community Outreach
	• StudyFinder
	• Resources
	  • Web-based templates, tools, plans, etc.

See our website: www.bumc.bu.edu/crro

Objectives

- Review of the Regulations guiding human subjects research
- Provide a few definitions to get started.
- Identify the role of the IRB and criteria for approval of a research project.
- List practical tips to aid in your IRB submissions.

My protocol!

The BEST Scientific Study EVER!!!!

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IRB

Protection of Human Subjects - Regs

United States Department of Health & Human Services

FDA

NATIONAL INSTITUTES OF HEALTH

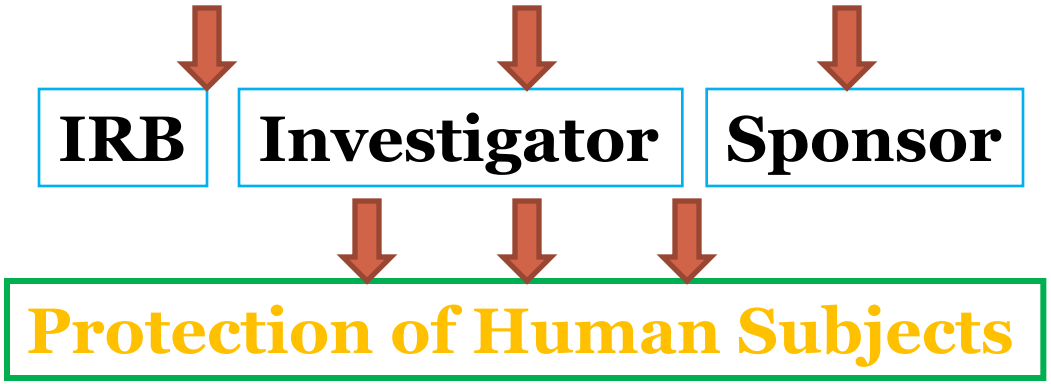
OHRP

U.S. Department of Health and Human Services
Office for Human Research Protections

Regulations
Guidance

Funding research
Policies
Guidance

Regulations
Guidance



Regulations Guiding Clinical Research

Subpart A: Protection of Human Subjects

45 CFR 46

OHRP

- Assurance
- Oversight
- Engagement

Informed Consent

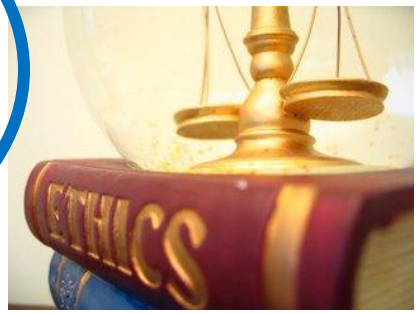
IRB Review/ Functions/ Operations

21 CFR 312, 812, 50, 54, 56

FDA

- Sponsor/investigator roles and conduct
- Drug/device dev't & testing process

- Subpart B: Pregnant women, Fetuses, neonates
- Subpart C: Prisoners
- Subpart D: Children
- Subpart E: IRB Registration



45 CFR 160, 162, 164

HIPAA (Health Insurance Portability and Accountability Act of 1996)

- Privacy and Security of protected health information

Common Rule

- 45 CFR part 46 (subpart A):
  Protection of Human Subjects
  - In 1991 45 CFR 46 adopted by 15 federal agencies: “Federal Policy for the Protection of Human Subjects”
  - Since then, added CIA and Dept. Homeland Security

Agriculture, Energy, Commerce, HUD, Justice, Defense, Education, Veterans Affairs, Transportation, HHS & Homeland Security. NSF, NASA, EPA, AID, Social Security Administration*, CIA, Consumer Product Safety Commission

Definitions

- Research (OHRP regs: 45 CFR 46.102 (d))
  - *"… a* systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge."

- Clinical Investigation (FDA regs: 21 CFR 312.3 (b))
  - "… any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice."

Definitions

- Interaction/Intervention (45 CFR 46.102 (f))
  - Both physical procedures by which data are gathered… and manipulations of the subject or the subject's environment that are performed for research purposes. Interaction includes communication or interpersonal contact between investigator and subject.

Definitions

- Private information (45 CFR 46.102 (f))
  - … info about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).
  - Private information must be individually identifiable i.e. the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects."

(**See OHRP guidance on coded data/specimens, 2008: http://www.hhs.gov/ohrp/policy/cdebiol.html)

More on Private Information (OHRP)

- In general, there are 3 ways by which the identities of subjects' data/specimens can be ascertained
  - **Direct identifiers:** name, medical record number, address, social security number, photographs
  - **Indirect identifiers:** data/specimens assigned a study ID that can be linked to identifiers via a mastercode or key
  - **Deductive Disclosure:** no direct or indirect identifiers but identity can be reasonably ascertained from the data itself (small population or specific data elements)

w/permission, excerpted from Mary Banks' Clinical Research Seminar Presentation 3/20/2013

More on Private Information (OHRP)

- **"Anonymous"**: (unofficial term) usually meaning that NO ONE is able to associate the data/specimens with individual subjects- not the holders of the data/specimens; not the recipients
  - The data/specimens don't contain direct identifiers
  - There are no indirect identifiers (linkage by mastercode)
  - There isn't a reasonable risk of deductive disclosure
- **Not Human Subjects** (NHS) – if data/samples are obtained from a repository (not directly from subjects) and the recipients of data/samples cannot reasonably ascertain the identities of the subjects, because
  - Data/samples are truly anonymous OR
  - Data /samples are coded and recipients never get access to mastercode/key and promise to never try to ascertain the identities of the subjects

w/permission, excerpted from Mary Banks' Clinical Research Seminar Presentation 3/20/2013

Exempt determination... 45 CFR 46.101 (b)*

1. **Normal educational practices** in established educational settings
2. Educational tests, **surveys, interviews**, or observation of public behavior -unless identified & sensitive**
3. Research on elected or appointed public officials or candidates for public office
4. Research using existing data, if publicly available or recorded without identifiers (existing = at time of submission to IRB)
5. Evaluation of public benefit service programs
6. Taste and food quality eval./consumer acceptance studies

*None of the categories apply to Prisoner research (Subpart C).

** does not apply to research with children except for research involving observation of public behavior when investigator(s) do not participate in the activities being observed.

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Determining when OHRP Regs Apply…

1) Does the activity involve Research? (46.102(c))

If yes, then…..

2) Does the research involve Human Subjects? (46.102(f))

If yes, then….

3) Does the human subjects research meet criteria for Exempt from 45 CFR 46? (46.101(b))

Decision Trees: http://www.hhs.gov/ohrp/policy/checklists/decisioncharts.html

IRB Submission for Exempt or NHSR?

- OHRP guidance on exempt determinations (Exempt Research Determination FAQs) notes that, b/c of potential for conflict of interest, investigators not be given the authority to make an independent determination that human subjects research is exempt.
- A variety of configurations of exemption authority are acceptable.
- BUMC policy: submission to the IRB of an exempt/NHSR application for determination.

http://answers.hhs.gov/ohrp/categories/1564

Don't forget HIPAA (45 CFR 160 & 164)

- Uses different terminology than OHRP
- HIPAA- looks at data in terms of 18 "safe harbor" identifiers
  - Name, address, SS#, MR#, **Dates (< year)**, ages >89, geographic information <state
- **De-identified** –stripped of **ALL 18** " safe harbor identifiers"
  - The master-code is not one of the identifiers unless it is derived from an identifier (like b-date or last 4 of SS#)
  - Data sets that contain dates (admission, discharge, surgery, birth, death, specimen collection, etc.) can't be called de-identified because dates are identifiers
- **Limited data set (LDS)**- is like a de-identified dataset as most identifiers must be stripped except dates, ages >89 and some geographic information

w/permission, from Mary Banks' Clinical Research Seminar Presentation 3/20/2013

HIPAA forms

- If accessing protected health information from a covered entity, include the applicable form(s) attached to your protocol
  - Authorization
  - Waiver
  - De-identified
  - Limited Data Set
  - Decedent
- Link to HIPAA forms on the IRB website
  - Under “Also see…”

Mutually exclusive terms re: Data

- Data cannot be
  - Anonymous and coded
  - De-identified and include dates
  - De-identified and a Limited Data Set (LDS)

w/permission, excerpted from Mary Banks' Clinical Research Seminar Presentation 3/20/2013

Informed Consent

- A cornerstone of ethical research is that prospective consent to participate in research be given by the subject or his/her legally authorized representative (LAR).

Elements of Consent

21 CFR 50.25 and 45 CFR 46.116 (a)

1) Study involves research, purpose, expected duration of the subject's participation, procedures, and identification experimental procedures;
2) Risks, discomforts
3) Benefits
4) Alternative procedures or courses of treatment
5) Confidentiality
6) Compensation for injury (for > minimal risk)
7) Contacts for questions and/or research-related injury
8) Voluntary participation…

Additional Elements of Consent

1) May involve risks to the subject (or to the embryo or fetus….) which are currently unforeseeable;
2) Termination without regard to consent;
3) Additional costs due to the research;
4) The consequences of a subject's decision to withdraw; procedures for orderly termination of participation;
5) A statement that significant new findings will be provided to the subject; and
6) The approximate number of subjects.

Use Consent Form Builder in INSPIR II

1) System allows you to build your consent form from a MS Word document that contains templated language for the required consent elements.
   - Build within the Informed Consent section of INSPIR in Study Management.

2) If you have a consent for an exempt study, it may be in the form of a letter that is attached to the application in Other Study Documents.

Waiving Informed Consent* (45 CFR 46.116 (d))

Must meet/justify all criteria:

1. Minimal Risk
2. Not practicable to conduct research without the waiver
3. Does not adversely affect subject rights and welfare
4. Provided w/additional pertinent information

* But in some cases of exempt research (such as survey research), you will still tell subjects the purpose of the research, what will be done with the data, who to contact with questions, etc. But the document and process can be more informal…..

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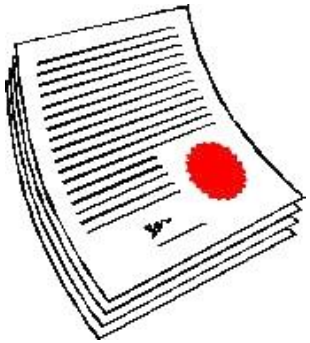
Waiving Informed Consent Documentation (45 CFR 46.117 (c))

- The consent document is the only document linking the subject with the research and main risk is breach of confidentiality



OR

- No more than minimal risk and no procedures for which written consent is normally obtained.

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The Institutional Review Board and the 111 Criteria

Institutional Review Board (IRB)

- Formally designated committee; at least 5 members
  - Function as an ethics committee; primary responsibility: protect rights and welfare of research subjects
- Review, approve, conduct periodic review (at least annually) of biomedical and behavioral research
  - Document that reviews take place in compliance with regs
- Empowered to approve, require modifications or disapprove research

Role of IRB

Keep in mind….

IRBs are rule ***enforcers*** <u>*not*</u> rule ***creators***

Leonard Glantz, JD

Associate Dean Emeritus, Academic Affairs

Professor, Health Law, Bioethics & Human Rights

Re-used with permission; Dr. Jim Feldman
Clinical Research Seminar presentation 4/17/13

Types of IRB Submission/Review

- Exempt/Non-Human Subjects Research (NHSR)
  - 6 categories of exemption
  - NHSR means that the project does not meet the human subjects research definition
- Expedited
  - 8 expedited categories
  - Minimal risk research
- Convened Meeting (Full Board)
  - Greater than minimal risk research

Projects that require IRB review

- Interventional Studies
- Observational Studies
- Medical Record Reviews
  - Retrospective
  - Prospective
- Use of human tissue/ samples and/or data
- Survey/Interview Studies
- QA/QI *("it depends"… is it "research?")*

* If the project meets a categorical exemption or is NHSR, can submit an abbreviated IRB application.

See OHRP's Exempt research FAQ:

http://answers.hhs.gov/ohrp/categories/1564

Your application will result in a determination by the IRB/other entity that the project does meet the exemption criteria per the regulations.

BUMC IRB Panels

- Blue: Sociobehavioral, public health, international, etc.
  - 2nd and 4th Thursdays, 12-2pm
- Green: Biomedical
  - 1st and 3rd Thursdays, 12-2pm
- Purple: Progress reports
  - 2nd and 4th Wednesdays, 9-11am
- Orange: Repositories and genetic research
  - 1st and 3rd Wednesdays, 12-2pm
- Red: expedited, exempt, NHSR
  - no meetings
- WIRB: multicenter industry-sponsored studies
  - Sponsor has to agree to specific language for the Compensation section of the Consent form

BUMC IRB Review Times

Review Time for Submissions that Reached Final Determination during March 2013

	Number	Days from submission until final determination*	Days in IRB office*	Days in investigator's office*
New Protocols				
Full-board	19	58 (10-162)	39 (6-74)	16 (1-89)
Expedited	13	15 (7-55)	12 (7-55)	0 (0-14)
Exempt	21	8 (0-158)	7 (0-94)	0 (0-142)
Amendments				
Full-board	19	16 (3-36)	16 (3-35)	0 (0-11)
Expedited/Exempt	70	14 (0-85)	12 (0-63)	0 (0-23)

* These columns show the median number of days (and range).

http://www.bumc.bu.edu/irb/bumcirb/irb-review-time/

The 111 Criteria:
Criteria for IRB Approval

"In order to approve research covered by these regulations the IRB shall determine that all of the following requirements are satisfied…"

21 CFR 56.111

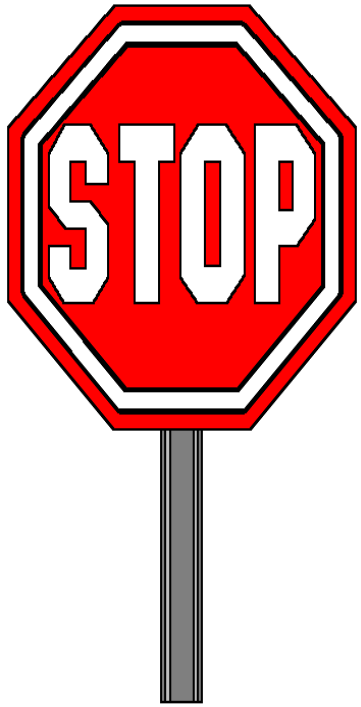
45 CFR 46.111

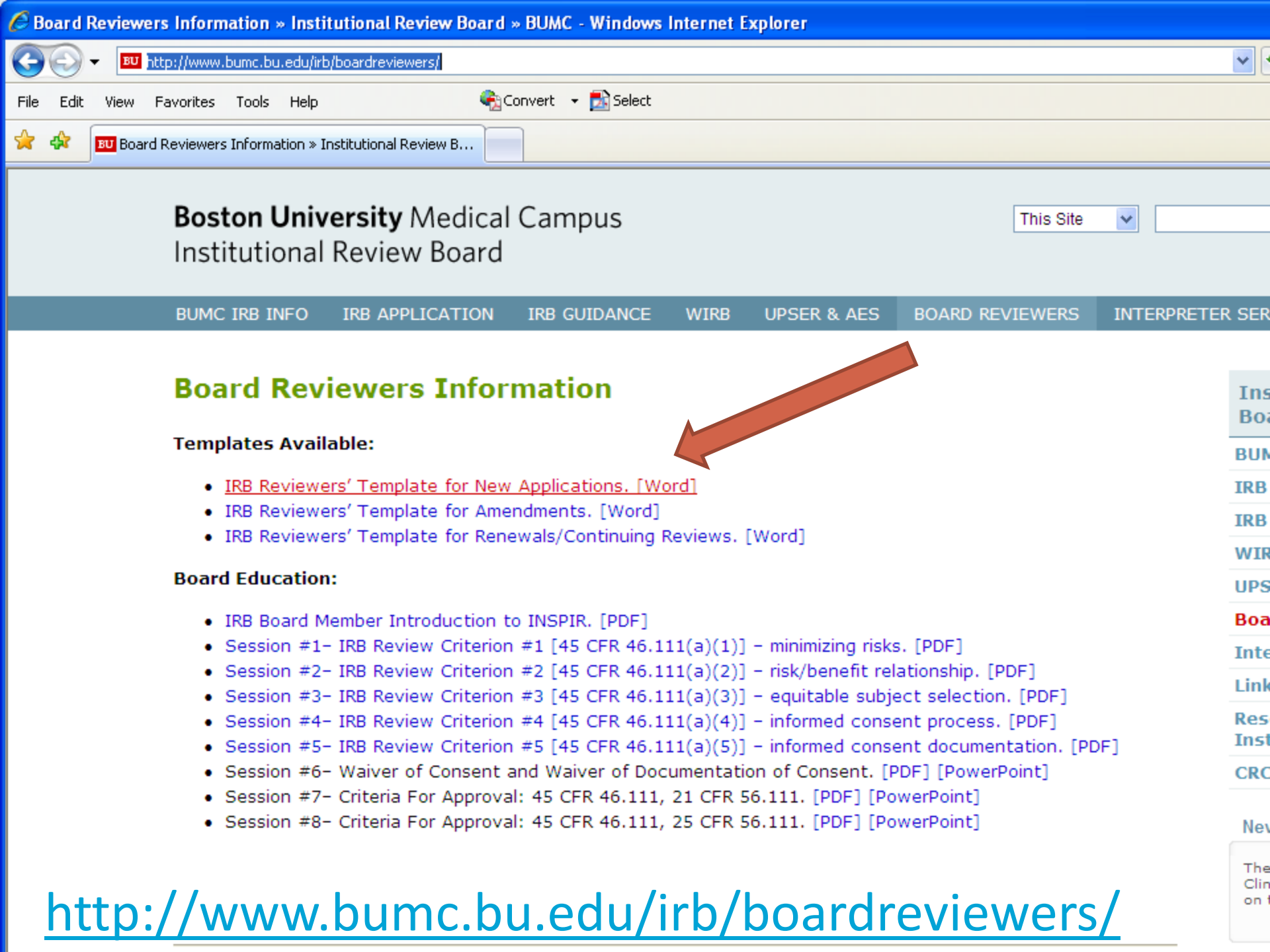
The 111 Criteria

1. Risks to subjects are minimized.
2. Risks to subjects reasonable in relation to benefits.
3. Selection of subjects is equitable.
4. Informed consent process.
5. Informed consent documentation.
6. Adequate provision for monitoring the data.
7. Provisions to protect privacy /maintain confidentiality.
8. Safeguards for vulnerable populations.

Deferral Decision

- Usually because insufficient information provided to the IRB for them to make a determination for one or more of the 111 criteria.
- If reviewed by the board, protocol will have to be revised and resubmitted and come back to the full board.





http://www.bumc.bu.edu/irb/boardreviewers/

New Application

Name of Investigator: IRB Study #:
Title of Protocol: Date of Meeting:
Primary Reviewers:

SECTION A: TITLE, INVESTIGATORS & GENERAL INFORMATION	YES	NO	N/A
1. Does the staffing and expertise appear sufficient to conduct this research?	☐	☐	☐
2. Have Conflict of Interest forms been submitted?	☐	☐	☐
3. Is there any conflict of interest for the PI or other study personnel?	☐	☐	☐
Comments:			

SECTION D: BACKGROUND/RATIONALE/PURPOSE	YES	NO	N/A
1. Is there suitable justification for a study involving humans?	☐	☐	☐
2. Is the research problem/hypothesis adequately stated?	☐	☐	☐
3. Are the specific aims of the research and how these will contribute to scientific/medical knowledge adequately described?	☐	☐	☐
Comments:			

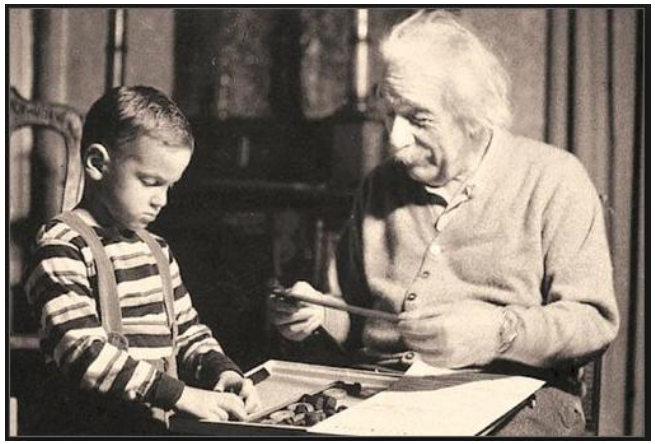
SECTION E: PROTOCOL RISKS/SUBJECTS	YES	NO	N/A
1. Is this research more than minimal risk? **Risk:** The probability of harm or injury (physical, psychological, social, or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Federal regulations define only "minimal risk." **Minimal Risk:** A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests [45 CFR 46.102(i)]. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of	☐	☐	☐

So … you have a research question!

- What you need to get started:
  - Get a faculty advisor experienced in clinical research
  - Decide what your role is…
    - Will you be working on somebody else's protocol as staff member?
    - Or, do you have a new research question?
  - NIH Human Subjects Protections Training on file
  - INSPIR II access
    - BU username and Kerberos password

Faculty Advisor

- Help you refine your idea and design the research
- May serve as co-investigator on your protocol, or is PI of a protocol that you are added to.
- Review/submit the IRB application (if a new research question/aim).
  - Must sign-off on your protocol if you are PI (list in INSPIR section 3.4)
- Help you carry out the data analysis and write your paper.

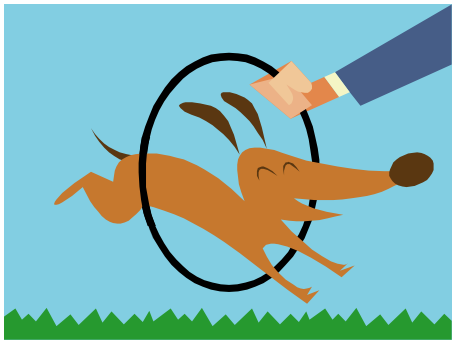


NIH Human Subjects Protections Training

- BU/BMC requires that researchers be “certified” in human subjects protection.

  http://www.bumc.bu.edu/ocr/certification/

- And don’t forget recertification via the Clinical Research Times if you plan to be here conducting research for > 2 years! http://www.bu.edu/crtimes



INSPIR (II)

- Integrated Network for Subject Protection In Research
  - BUMC's electronic, internet-based IRB system
  - https://inspir.bu.edu/iMedris/
- Need user name and kerberos password
  - bumchelp@bu.edu
  - x8-5914
- See CRTimes Feb. 2011
- Update your **personal profile** under "My Assistant," then "My Account."
  - You just have to do this once and you can only do it yourself.
  - Degree, Specialty, Primary number, Location, Affiliation, and Other Affiliation.

Tools to Help You: INSPIR Tutorials

www.bumc.bu.edu/irb

Boston University Medical Campus
Institutional Review Board

This Site | SEARCH

BUMC IRB INFO | INSPIR II | WIRB | UPSER, AES, DSMPS | IRB GUIDANCE | INTERPRETER SERVICES | LINKS

INSPIR II

INSPIR II stands for the **Integrated Network for Subject Protection In Research**. It is BUMC's electronic IRB system. The application runs on the internet so investigators can access it from any internet-connected computer around the world.

INSPIR II went LIVE! Click here (or on the image) to login.

A Farewell Song to INSPIR I

INSPIR II Overview and Announcements

On March 15, 2011, the BUMC IRB switched to a new IRB softwar[illegible] called INSPIR II (replacing INSPIR). All protocols from INSPIR I were migr[illegible]ver to the new system. Below are various resources for investigators to obtain information about INSPIR

- INSPIR II Instructions for Investigators
- Submit a INSPIR II Help Desk Request*
- Submit a Request to IS&T for a BU username and kerberos password
- Registration Form for Scheduling Department INSPIR II Training
- February 2011 CR Times Article
- INSPIR II Introductory Training Video
- INSPIR II Introductory Training PowerPoint

*INSPIR II Helpdesk Request – In order to efficiently route your questions to the most appropriate person in the IRB office, please submit an INSPIR II Helpdesk Request by going to this link.

INSPIR II FAQS

- User name/log-in/Personal Profile issues
- Migration Issues
- IRB Application Issues

Institutional Review Board

- BUMC IRB Info
- INSPIR II
  - INSPIR II Instructions for Investigators
  - Submit a INSPIR II Help Desk Request
  - Submit a Request to IS&T for a BU username and kerberos password
  - INSPIR II Super Users
- WIRB
- UPSER, AEs, DSMPs
- IRB Guidance
- Interpreter Services
- Links
- Research with Other Institutions
- Board Reviewers
- CRC IRB

News »

The February edition of the Clinical Research Times is on the newsstands!

Also See

Tools to Help You: INSPIR Tutorials

www.bumc.bu.edu/irb

Cheat Sheets

- INSPIR II Sections 1-10 (the mandatory sections)

How To

General

- How to log-in to INSPIR II
- How to update your Personal Profile (required for everyone listed on a study)
- How to update the department in your Personal Profile
- How to get the Study Assistant tab if you don't have it
- How to sign off on protocol as PI
- How to sign off on protocol by Department Chairs
- How to check the status of a submission
- How to add new internal investigators/resea
- How to send a study correspondence in INS
- How to view or print out the Approval Lette

New Study – Initial Reviews

- How to create a new protocol draft in INSPIR II
- How to find and open a draft in INSPIR II
- How to add a new Consent Form
- How to add a new Study Document
- How to setup Department Chair and Special Routing Sign Off
- How to sign off on protocol as PI
- How to sign off on protocol by Department Chairs
- How to respond to a Review Response for an Initial Review
- How to revise an existing Consent Form
- How to revise an existing Study Document

Tools to Help You

If you're serious about doing a good job, **these articles are MUST reads** and will save you a lot of time!!

- Working with Data:
  - CR Times Feature article:
    - "Privacy and Confidentiality Requirements in the Use and Disclosure of Information for Research," March, 2013
  - CR Times "From the CRRO" April 2012
    - "Going Retro?... Exempt Category 4 Submissions for Retrospective Chart reviews, and other studies using existing data/samples;" **see link in article to INSPIR app pdf w/comments**
  - Clinical Data Warehouse: Linda Rosen
    - http://www.bumc.bu.edu/ocr/clinical-research-clinical-warehouse-data-access/
    - Submit a data request form

Tools to Help You

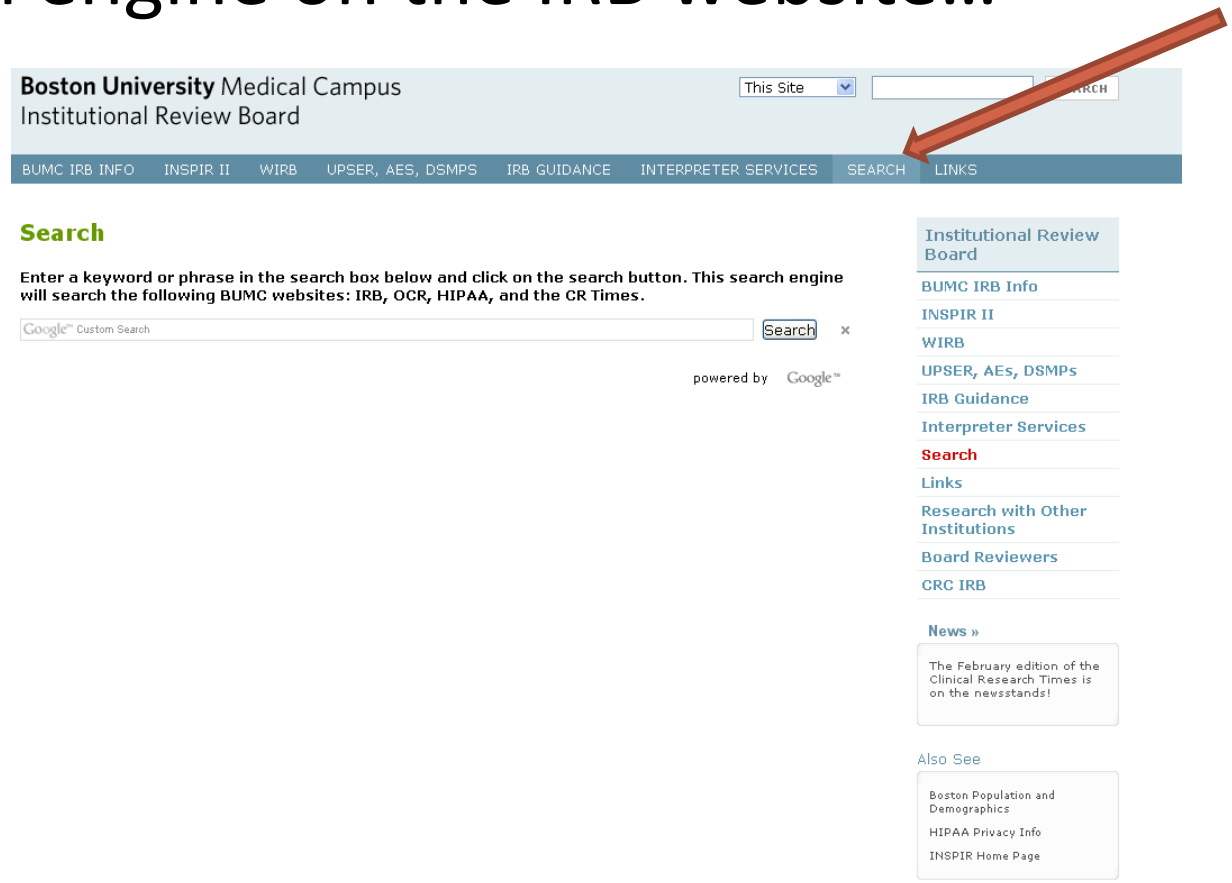
- CRTimes: www.bu.edu/crtimes
  - In particular, read the November 2011 feature article https://dcc2.bumc.bu.edu/ocr/ClinicalResearchNewsletter/article.aspx?article=369 (Improving IRB turn-around times)
- CTSI: http://ctsi.bu.edu/
  - Biomedical informatics, GCRU, statistical support, etc.
  - **REDCap** (Research Electronic Data Capture): secure web application for building and managing online surveys and databases.
  - **StudyTRAX:** electronic data capture system for clinical research
  - **Profiles**: web-based research networking tool
  - Much more!!!!
- Biospecimen Archive Research Core:
  - http://www.bu.edu/cores/cores/biospecimen-archive-research-core-barc/

Tools to Help You

- Clinical Research Resources Office (CRRO): www.bumc.bu.edu/crro
  - Regulatory and Recruitment support, consultation, services and tools.
  - ReSPECT Registry
    - Recruit participants from a Registry of individuals who sign up to hear about research studies taking place at BUMC.
  - StudyFinder
    - List your study to find participants or use it to look for someone with expertise and study interest you are looking for.

Tools to Help You

- Get an answer to your question with a simple search engine on the IRB website…



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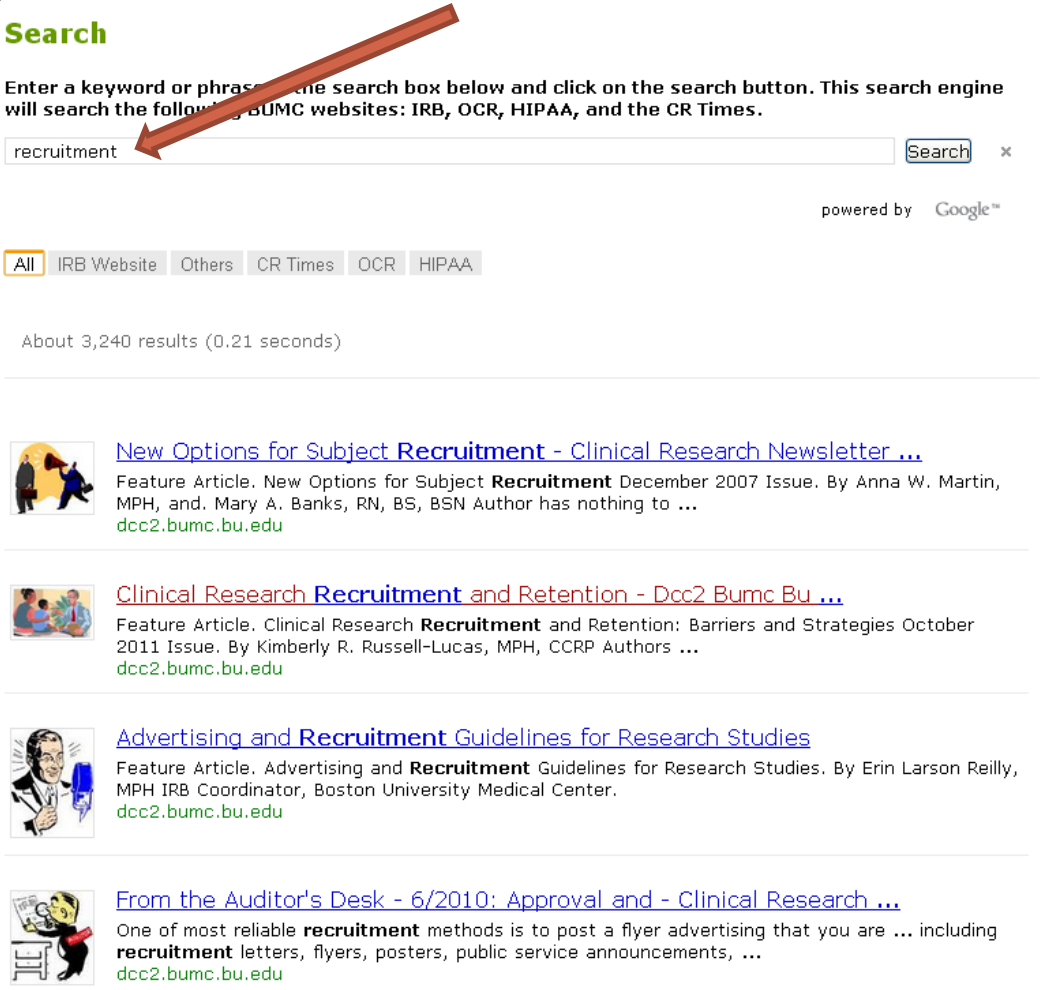
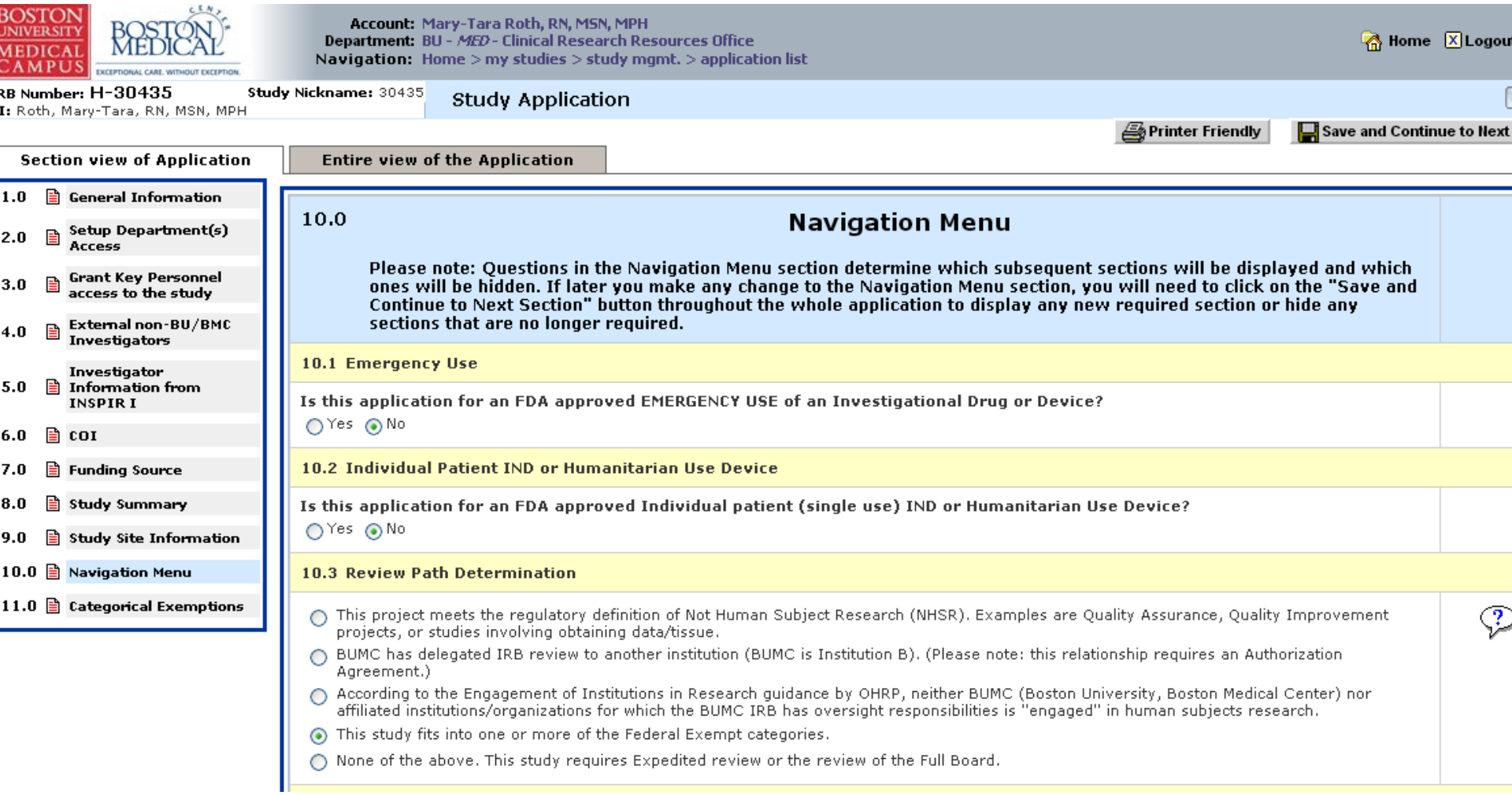


INSPIR example



Make sure your IRB submissions are complete and "ready for prime-time" BEFORE submission to the IRB…..
(and avoid common pitfalls!)

From many IRB letters……

"Administrative deferral:

This protocol has been administratively deferred because it is incomplete and not ready for IRB review."

Common Pitfalls to IRB Approval

What stands between you and a "smooth road" to IRB approval?

- Not seeking mentorship and guidance from faculty.
- Failure to answer the INSPIR II questions in full.
- The summary fails to describe the research in lay language.
- The Background does not justify why the study should be done.
  - There is no clear answer to the “So what?” question.
  - There is no supporting evidence or justification from the literature.
  - SOC procedures vs. research procedures are unclear.

- Informed Consent Form is too complicated or the justification for why informed consent should be waived is missing/incomplete.
- Inappropriate recruitment plans or recruitment plans that are just not well-described.
- Key documents are missing.
  - e.g. surveys; data collection forms; the grant, project prospectus or thesis proposal.
- Study data collection forms have direct identifiers on them, such as name or MRN.

- Failure to adequately address protection of vulnerable populations, such as children
- Inconsistent terminology
  - Anonymous, de-identified, coded
- Inappropriate/insufficient Data Safety Monitoring Plans (DSMPs)
- Insufficient routing of the application
  - (Biosafety, Pharmacy, GCRU, etc.)
- Wrong version of the application submitted!

And finally…..

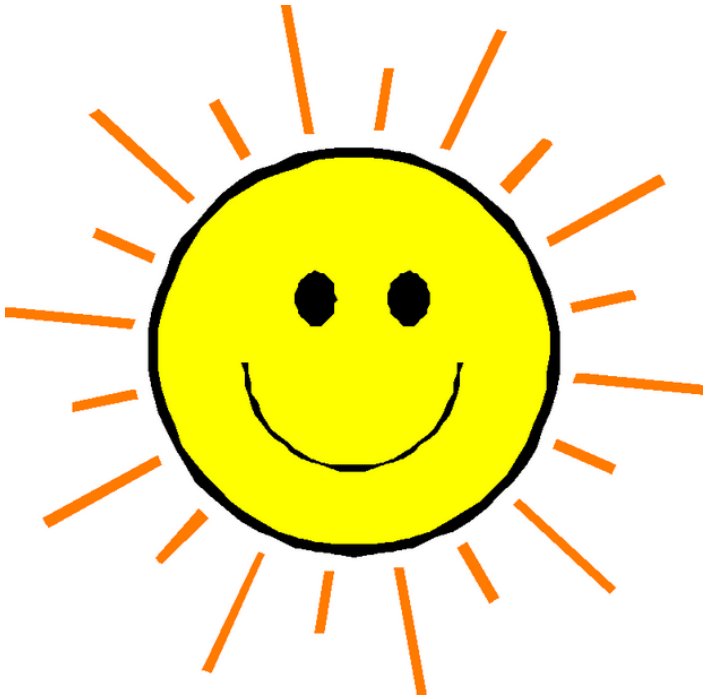
A few last words of Advice…..

Remember that conducting your research is a privilege, not a right

Perhaps more important, research participants themselves endow the investigator with the privilege of conducting research. Regardless of the risks of a particular research study, participants put their trust in the principal investigator and his/her staff. This trust must be protected, through the application of basic ethical principles, including respect for persons, beneficence, and justice (OPRR, 1979).

KISS Principle

Keep it Simple Sunshine!



Thank you!

Any questions?

Please complete and hand in the evaluation!