

Transforming your Grant into a Protocol: Study Guide  
OCTRI Research Forum:  
February 2024  
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This study guide will expand upon the content of the presentation and provide references. The goal of this Research Forum is to provide best practices and guidance to transforming the research and human subjects sections of your grant into a study protocol that you can submit to the IRB for approval, implement with enough detail for your study to be successfully completed, and that can be shared with others as required (clinicaltrials.gov, journal editors, collaborators, etc.).

Learning Objectives (you can use the links to navigate this document):

- Understand [The differences between a grant, a protocol, and an operations manual](#)
- **Determine whether to revise an existing protocol or write a new protocol**
- Understand the **Required Protocol Elements**
- [Importance of Good Protocol Development](#)

## The differences between a grant, a protocol, and an operations manual

### Differences in the Goals of a Grant vs. a Protocol

#### Grant vs. Protocol Goals

- Grant/Proposal:
  - Written to convince reviewers
    - That your project is worthy
    - That you can complete the project



- Protocol
  - Written to explain who, what, where, when, why of your project
  - Must be clear and understandable
  - Detailed – without boxing you in when research meets real world



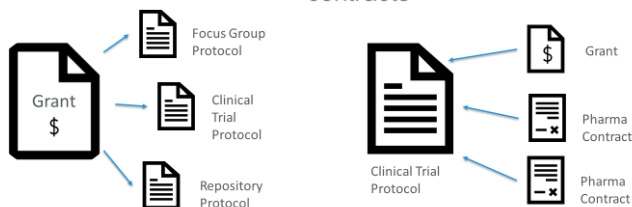
A grant or proposal is written to convince reviewers that your proposed project is scientifically sound and you have the expertise and resources to conduct the study.

A protocol is written to explain the who, what, where, when, why of your

project. A protocol must be clear, understandable, and detailed, without being so specific that you have protocol deviations when the conduct of the study meets the real world.

## Grants and Protocols

- A grant can include multiple protocols
- A protocol can be funded by multiple grants, foundations and/or pharma contracts



4

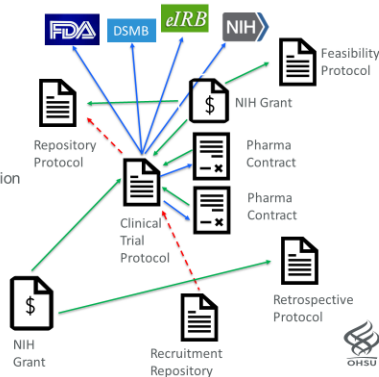


There isn't always a one to one relationship between the grant and the # of protocols.

Some grants describe multiple project phases/protocols that will be implemented over time. Some protocols are revised over and over again as new funding is obtained, new sub analysis is planned, or new ideas occur to the PI.

## If you want to Combine Grants/Protocols, You Need a Strategy

- Think carefully about:
  - Does it scientifically/operationally make sense
  - How/when you will **share/destroy** information
  - **Regulatory/reporting** obligations
  - **Funding/contractual** obligation
  - See study guide for more info



5

Matching multiple grant/protocol goals can get complicated if you don't have a strategy for regulatory compliance. Protocols that try to include too many objectives and study populations may no longer be understandable.

There can be frustrating consequences if you don't have a plan for compliance with

different funding requirements or future use of the study data.

## Determine whether to revise an existing protocol or write a new protocol

There will be times when you receive a new grant after you already have an IRB approved protocol. If the research is similar, you need to decide whether to revise the existing IRB approved protocol to add the new grant aims/activities, or write a new protocol to submit to the IRB. If the changes make the protocol confusing to the IRB, study team and/or study participants, it is best to write a new protocol. The following are some things to consider when making this decision.

## New Protocol or Revise Existing Protocol



- Consider writing a new protocol when:
  - New patient population
  - Unrelated aims
  - Risk of the new study is greater than the existing protocol
    - e.g. don't add an investigational drug to an observational study
  - Different study design
  - Different regulatory requirements
  - Different contractual requirements
- Consider revising an existing protocol when:
  - Aims of the study and design are the same/similar
  - Population, risks, design are the same
  - Minimal changes are needed
    - Extending the study duration
    - Increasing the number of participants
    - Add a new sub-analysis

Sometimes investigators already have an IRB approved protocol when they receive a new grant. There can be a temptation to revise an existing protocol instead of submitting a new protocol to decrease the study start-up time but this isn't always the best plan. For example, if

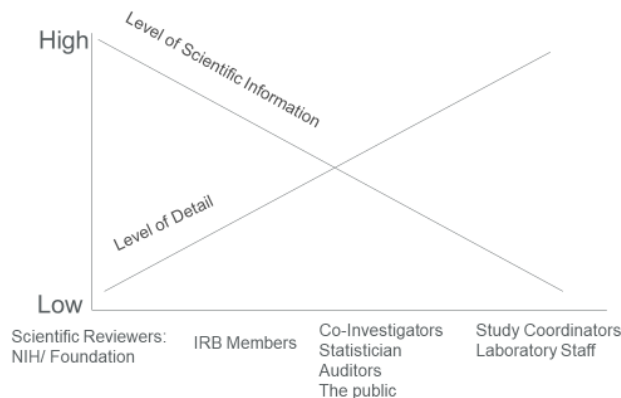
you have a minimal risk study that has expedited/exempt IRB review, it wouldn't make sense to add study aims and procedures that were greater than minimal risk because the study would then require full board review.



If you have multiple studies that you want to combine in one protocol, you should verify that requirements for data sharing/retention and contractual obligations/limitations align. For example, if a funder requires that they review/approve all protocol modifications before they are implemented, you might not want to add a new aim that includes Intellectual Property (IP) or other information you don't want to or cannot share.

Studies may have multiple documents that describe your research including: the grant, your protocol, operational manuals, instruction sheets, and other helpful documents you may draft to make your study run smoothly. These documents will have different information for different audiences but they must be consistent with one another.

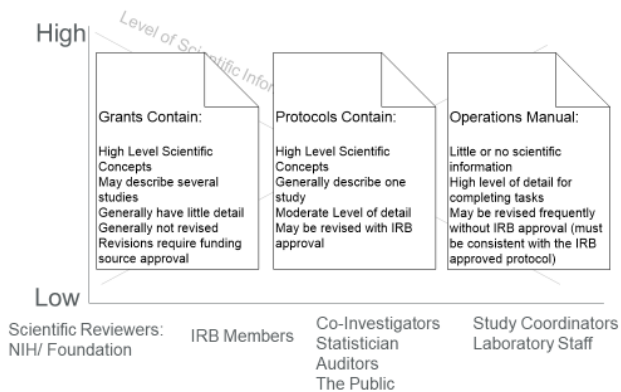
## Study Documents



Some documents have a high level of scientific information but a low level of detail on day-to-day study conduct and vice versa.

Not all reviewers/users of the study documents require the same level of information to perform their review/ study activities.

## Study Documents



The **grant** includes a high level of scientific information but not much information on the day to day study operations.

The **protocol** contains both scientific information and detailed information about the inclusion/exclusion criteria, statistical plan, and what will occur at each study visit.

**Operations manuals** include very detailed information on tasks that need to be completed in a specific way to

support the overall protocol. Operations Manuals may be called by other names (MOP- Manual of Procedures, MOO – Manual of Operations, work instructions, etc.) Studies may have several manuals or a large “handbook” style document. Examples include pharmacy manuals, lab processing/sample storage manuals, shipping instructions, etc. For example, lab staff will need to know how to process, label and store samples in great detail so you can rely on the data generated from the samples but won’t need to know the study inclusion exclusion criteria.

This training focuses primarily on taking the high level of information in the grant and developing the detailed study protocol.

Reviewer	Reason for Review
IRB	Subject protection, compliance with state/federal laws, institutional policies
FDA federal oversight (if applicable)	Protect public health
Study Coordinator/staff (e.g. statistician, nurses, lab, pharmacy, etc.)	Feasibility, operational implementation
Institutional Offices (CRBO, Radiation Safety, Knight CRRC, OCTRI, etc.)	Institutional Offices (CRBO, Radiation Safety, Knight CRRC, OCTRI, etc.) for compliance with state/federal law and institutional policies
The Public	Must upload protocols in clinicaltrials.gov for applicable clinical trials

Remember your audience(s) when you write your protocol. Not all reviewers will be experts in your area of research, have your level of scientific training or the clinical context. Plan to include crucial context and highlight details that are important for reviewers to understand how the study will be operationalized.

## Required Protocol Elements

NIH and FDA follow the ICH Good Clinical Practice Guidelines for protocol content. Some NIH institutes require you use their protocol template and provide [Toolkits and Educational Materials](#) for studies using existing data/specimens, observational studies, and interventional studies. FDA has guidelines for protocol content in 21 CFR 58.120 and has additional requirements for protocol content for studies that include automated

data collection. We won't go into detail on these requirements, other than to note you should understand what funding and regulatory requirements exist and include the required information in your protocols.

For this presentation we are going to use the structure of the OHSU protocol template to address the following protocol elements:

- Title
- Introduction, background, rational, literature review
- Aims/ Objective(s)
- Research Methods/ Study design
- Subjects (selection and exclusion), Setting, Study procedures, Interventions, Stopping Rules, Duration, Endpoints, Safety Assessments, etc.
- Risks/Benefits
- Statistical Analysis



## Writing the Protocol

- Start with a protocol template
  - OHSU IRB has a template with the required elements and instructions
    - You can use another template/format as long as the necessary content is included
  - If the study is cancer related, investigators must use Knight Cancer Institute Protocol Template



Scientific Ideals could include randomized, placebo controlled, double-blind studies. In the real world you have to balance these ideals with ethical considerations for placebo-controlled trials.

## Protocol Development

- Protocol Development is an **Art**
- Balance of scientific ideals and the real world
  - Balance of essential and trivial details
  - Balance of structure and flexibility



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Essential details could be how much blood to draw so you have enough for the tests you need, but who draws the blood (coordinator or lab staff) isn't required.

You need enough structure so that everyone involved collects usable data, while allowing for some clinic and patient differences.





## Title

- Give your study a descriptive/meaningful title that is specific, concise, and reflects the content of the study

### Example:

"A Study of Mindfulness"

What is wrong with this title?

How would you improve it?

Better title:

"The Effects of Mindfulness-Based Stress Reduction vs. Routine Care"

Best title:

"The Effects of Mindfulness-Based Stress Reduction in Patients with PTSD: A Randomized Controlled Multicenter Trial"



## Title –

Give your study a descriptive/meaningful title. The title should be specific, concise, and reflect the content of the study.

IRB, FDA, and other reviewers read hundreds of protocols a year. Make it easy for them!

The best title gives the reviewer a lot of information about the project before they start reading the protocol. This tells the reviewer the intervention, the patient population, and where (without specifics) it will happen.

## Introduction, Background, Rationale

Include a brief discussion of important research that provides background for the reviewers/study team members and the scientific justification for the study.

Include any relevant clinical, epidemiological, or public health background and/or context of the study.

The rationale for the study should plainly state the reason(s) for conducting the study. If applicable include information about the study population, disease, and limitations of existing knowledge.



## Introduction, Background, Rationale

- Include brief discussion of important background research and scientific justification.
- State the reason(s) for conducting the study, including relevant information about study population, disease, limitations of existing knowledge.
  - Shouldn't be a copy and paste from your grant.
- Explain why the procedures you propose will answer your research questions.



Include enough information to explain why the procedures you propose will answer your research questions.

It should be brief and shouldn't be a copy and paste from your grant. Protocols are intended to be informative not persuasive like grants.



## Aims/Objectives



### Aims/Objectives

- Make sure Aims/Objectives are measurable and align with the study duration.
- Write aims with a statement of purpose: "to assess" "to determine" "to compare" "to evaluate"
- Outcome measures should correspond with the study aims and hypotheses.
- Examples:
  - Too Vague – to learn about disease X
  - Better – to determine the risk factors for disease X
- Ensure that the aims in the grant match the aims in the protocol.



Ensure the objectives/aims in your grant match (or are easily mapped to) the objectives/aims of your protocol. The IRB/OPAM are required to do a concurrence review between the funding application and the protocol to ensure we are conducting the research that is funded under the grant. If you revise your study aims, population, or scope of your protocol after award, review the [NIH Policy Statement 8.1.2 Prior Approval Requirements](#) to determine if NIH prior approval of the changes is required.

## Research Methods/Study Design



### Research Methods/Study Design

- Describe the overall approach to the study (ex. prospective/retrospective, observational/interventional, blinded/open label, randomized).
- Describe the different groups, arms, and/or subject population.
  - You may need to describe certain protocol elements for each group/arm
- Study designs that meet the definition of a "clinical trial" may have additional requirements for [clinicaltrials.gov](https://clinicaltrials.gov) registration.
  - See study guide for more information.



The research methods section is typically the longest section of your protocol and includes the overall approach to the study, the participant groups, arms, population. It will also describe all of the study procedures. You can have a protocol with arms/groups with different study designs. For example: you could have a study with a retrospective arm and a prospective arm. You

may need to describe certain elements of the study for each group/arm (e.g. recruitment) if they are different.

Clinical trials have additional regulatory requirements ([clinicaltrials.gov](https://clinicaltrials.gov) registration, NIH prior approval) and can have an impact on budgeting (F&A).

## ClinicalTrials.gov –

Studies that prospectively assign people or a group of people to an intervention (drug/device/behavioral/educational) with or without a comparison group to study the relationship between a health-related intervention and a health outcome must be registered in clinicaltrials.gov to comply with FDAAA regulations, NIH and ICMJE policies. Some studies must also report study result as specified in 42 CFR part 11. See [“Am I required to submit results for my applicable clinical trial \(ACT\)?”](#)

If you are required to register your study, write your objectives with special care to ensure they will make it through the clinicaltrials.gov quality review and so you can post study results without unnecessary complications. Consider the following when writing your objectives:

- Clearly indicate which (if any) outcomes are for safety
- Avoid lumping outcomes – each outcome should have a discrete study result
- Clearly indicate which outcomes (if any) are secondary/exploratory – this will be important for reporting
- Outcome timeframes need to be specific (e.g. a study outcome of “at study completion” is too vague, it would be better to state at 1 year, if it can vary for participants specify something like “study completion, average 1 year”)
- Make the aims/objects understandable to the lay person since this is a public registry
- If applicable, describe scales and what they mean (high/low values)

You will need to post a copy of your protocol so make sure the protocol and your registration match throughout the duration of the trial.

We recommend taking a Three Little Bears approach to protocol development.

### Three Little Bears Approach to Protocol Development



- Not too little information
- Not too much
- Just right

Not so little information that study staff can't conduct study procedures consistently and/or the IRB doesn't know what you are doing.

Not so much information that you constantly have to revise your protocol to adapt to minor variations and/or report protocol deviations.



Just right – provides enough instruction for compliant study conduct while anticipating variation in practice and participant schedules/compliance.



## Study Population

### Study Population

- # of subjects – what details should you include?
  - # you plan to consent, # needed to complete the study
    - account for screen failures/subject withdrawals
- Inclusion/exclusion criteria - what details should you include?
  - Describe diagnosis and how individuals will be screened for eligibility
    - diagnostic measures used and timing, demographic information
- Inclusion of vulnerable populations (if applicable)
  - What populations and how will they be protected e.g. children, prisoners, decisionally impaired adults, limited English proficiency
- Subject withdrawal criteria – what details should you include?
  - Allowances for temporarily stopping drug/intervention
  - Non-compliance or Safety Issues



Include the # of subjects you plan to involve in the study. If applicable, distinguish between the # you plan to consent and the # needed to complete the research procedures, accounting for screen failures/subject withdrawals.

Describe the Inclusion/exclusion criteria used for selection of participants in the study. Include

criteria necessary for scientific rigor, but balance this the practicality of enrollment and the ability to generalize the data. If your inclusion criteria are too narrow, you may not be able to enroll enough participants in the study. If it is too broad you may not be able to answer your research question(s).

Describe how individuals will be screened for eligibility including the diagnostic measures used to determine if they qualify for the study. Describe demographic criteria and specify if you plan to include vulnerable populations (e.g. children, prisoners).



NIH has policies on participant inclusion and reporting in clinical trials.

[Inclusion Across the Lifespan](#) policy expands upon the [Inclusion of Children in Clinical Research](#) to include individuals of all ages so that the knowledge gained from NIH research is applicable to all those affected by the disease/condition.

[NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research](#)

include a requirement that recipients conducting applicable NIH defined Phase III clinical trials ensure results of valid analysis by sex/gender, race, and/or ethnicity are submitted to [clinicaltrials.gov](https://clinicaltrials.gov).

Consider these requirements when developing your inclusion/exclusion criteria, your recruitment plan, and your statistical plan.

## Example: Enrollment Criteria too Broad

Study: Blood samples collected to develop a new lab assay

- **Inclusion Criteria**

- Healthy Subjects

- **Exclusion Criteria**

- Evidence of infection
- On medication
- Medical conditions that may compromise the quality of cells
- Disorders that may cause problems for the subject

18



## Example: Enrollment Criteria Too Narrow

Study: Evaluating the relationship between hormone levels and PMS symptoms

- **Inclusion**

- Women between 18 and 30
- PMS symptoms every cycle for at least 1 year
- Normal pap smear within last year
- Regular Menstrual cycles >26 and <32 days

- **Exclusion**

- Hysterectomy
- Hormonal contraceptives in last 3 months
- History of smoking
- History psychiatric disorder
- History of alcohol/drug abuse
- Use of medications that could affect mood or sleeping
- Abnormal screening blood tests (TSH, LFT, HGB)
- Pregnancy within last year or plan to get pregnant during study
- Use of medications/ alternative treatments for PMS within the last 60 days
- History of insomnia
- History of Migraines

19



## Example: Enrollment Criteria Just Right

Study: Any Clinical Research Study

- **Inclusion Criteria**

- Characteristics that are relevant to the research question
- Demographic characteristics (e.g. age)
- Clinical characteristics (e.g. diagnosis)
- Geographic characteristics (e.g. Clinic Patients)
- Temporal characteristics (e.g. life expectancy greater than 6 months)
- Vulnerable Populations (if applicable)

- **Exclusion Criteria**

- Describe subset of population that won't be studied
- Characteristics that make it unethical to withhold treatment
- Subjects at high risk of side effects
- High likelihood of lost to follow-up
- Characteristics that might interfere with the quality of the data

20



## Recruitment Methods

### Recruitment Methods

- Describe when, where, and how potential participants will be identified and recruited
  - Describe advertising materials
  - Describe identifiable information you will need to use/collect prior to consent
    - (e.g. email addresses, phone #s, etc.)
  - Describe how you will identify potential participants
  - Describe how/when you will approach/recruit potential participants
- All recruitment materials require IRB approval prior to use
- We recommend you plan to use a variety of recruitment methods



Describe when, where and how potential participants will be identified and recruited. Explain whether you plan to approach people in the clinic, by phone, email, or other methods. If you plan to enroll participants from other sites (e.g. the VA) include that information too.



Describe any identifiable information you will need to use/collect prior to consent (e.g. email addresses, phone #s, etc.) and how will you identify the participants (Epic query, in clinics, referrals, [StudyPages](#))? Note: You must have IRB approval prior to accessing identifiable information.

All recruitment materials you plan to use (phone scripts, recruitment letters/emails, etc., etc.) require IRB approval

Clinical research recruitment information, presentations and tools can be found at <https://www.ohsu.edu/octri/find-and-recruit-participants-you-need>. OHSU has recruitment tools like StudyPages, [Cohort Discovery](#), and recruitment resources like the Recruitment Advisory Council and OCTRI services and consultation for Recruitment and Retention.

## Consent Process

### Consent Process

- Describe how you will obtain and document consent
  - Where, when and how you will consent
  - Using eConsent?
    - Include the platform and process you plan to use
  - Steps to minimize coercion/undue influence
  - How you will ensure participant understanding
- Special Considerations: Describe how you will consent participants with limited English proficiency, children/parents/ decisionally impaired adults, emergency research
  - See study guide for links to quick guides for these issues



The protocol should include a description of how you will plan to obtain and document consent. This should include where, when and how the consent process will take place. For example, will you consent in the clinic, over the phone, or via video conference. Include several options to allow some flexibility.



If you plan to use eConsent, include the platform and the process you plan to use (see. [OHSU Use of Electronic Consent Quick Guide](#)).

You should plan for and describe steps you will take to minimize coercion/undue influence of study participants and how you will verify they understand the study procedures, risks, benefits and other required elements of consent.

You should plan to include a patient population that is representative of the general population of participant with the disease. You should plan for and describe how you will consent participants with limited English Proficiency (see [OHSU IRB quick guide](#) for advice). If children are involved, you should describe your plan for child assent and parental involvement (see [Vulnerable Populations – Children Quick Guide](#)). If the patient population may need a legal authorized representative, describe how you will include them in the consent/assent process (see [OHSU Vulnerable Populations – Decisionally Impaired Adults Help Sheet](#)).

Spell out any requested modifications to the consent process (see OHSU [Consent – Waiver or Alterations Help Sheet](#)). For example, will you request a waiver of written documentation of consent.

## Setting

### Study Setting

- Sites/locations where your research team will conduct the study
  - Specify activities occurring at OHSU vs. other locations (ex. VA)
  - Specify where activities will occur and where data/samples originate
    - outside lab, samples from another institution, patient's home, telehealth
  - IRBs involved (Single IRB)
  - Multi-site studies have additional considerations
    - Clarify what activities are performed at OHSU or by OHSU personnel
    - Need to consider how each site will satisfy IRB review requirements
    - If OHSU is the coordinating center there is additional information required
- May want to move activities that may vary from site to site to an supplement (e.g. recruitment, consent, local data handling)



Describe all of the sites and locations where your research team will conduct the study. Specify activities occurring at OHSU and those occurring at other locations (e.g. VA, remote locations, over the phone, in the patient's home). Specify if there are other sites/IRBs involved in the study (e.g. are you using an outside lab, recruiting from a non-

OHSU clinic, receiving samples from another institution).



Clinical services (including clinical advice) that are conducted off campus or in a location not leased by OHSU, require [off campus authorization](#) from Risk management prior to starting procedure to ensure employees are covered by insurance.

The setting of study activities can impact additional reviews, approvals, and considerations for “engagement in research”. If you are planning a multicenter trial or a trial with remote data/sample collection or locations outside of OHSU visit the Clinical Research Collaboration Experts <https://www.ohsu.edu/octri/clinical-research-collaboration-experts-conducting-research-outside-ohsu> webpage to learn where to start, which offices to work with and other considerations. Consultations are available upon request.

Multicenter studies have additional considerations - will all sites conduct the same activities? will they all receive/collect identifiable data? If there are variations they should be included in the protocol or supplemental study documents. If OHSU is the coordinating center see the [OHSU Coordinating Center Activities Quick Guide](#).



For multicenter trials – the setting details may better be described in the local conduct supplement since it will differ at each site. This will help reduce confusion and allow for sites to conduct the study to best suit their clinic/institutional practices.

## Study procedures/interventions

### Procedures and Interventions

- Describe research procedures so they can be performed consistently
- Common medical procedures may not need a lot of detail
- State if any procedures are considered standard of care
- Measures and assessments
  - Procedures for physical exams, vital signs, handling samples
  - Procedures when intervention is temporarily stopped or a participant withdraws from the research study
- Data and Specimen banking (if applicable)
  - Indicate whether specimens may be used for future genetic research
- A schedule of events is often very helpful



Research procedures should be described in detail so they can be performed consistently by study team members (what, when, how). Common medical procedures may not need to have details to allow for appropriate variation among clinicians (if scientifically

acceptable). However, include important information about conducting common procedures if it is essential to the data collection. For example: Collecting information about the patient's medical history is a common study procedure but is it reported by patient? Collected from medical record? Or obtained in an interview with a licensed provider?

Measures and assessments - Include the study visits at which the biospecimens, images or other data will be collected and the specific laboratory tests to be performed. If lab results would trigger stopping the participants involvement or require reducing/increasing study medication state this.

Clearly indicate which (if any) procedures are considered standard of care. This helps the IRB determine the level of risk of the study. If you are collecting data from a greater than minimal risk procedure (e.g. CT Scan) but the patient would have had the CT scan whether they were in the study or not, the risk is then limited to data

collection/confidentiality. To be considered standard of care the procedures must happen at the same time, frequency, and extent as it would if the participant wasn't in the research study.

Include a description of the procedures that will be followed when a participant withdraws from the research study (e.g. return study drug, final safety labs, AE follow-up, collect diaries, etc.). Also include any individual subject withdrawal criteria. This includes when you will stop a participant's participation without their consent (Serious AEs, non-responsiveness to investigational treatment, non-compliance with the study drug/intervention). If you need to ensure compliance with the study intervention to be able to analyze the data, define a threshold for compliance and how you plan to measure it (drug diaries, surveys). Include any allowances for temporarily stopping or modifications to drug/intervention. For example, if a patient has side effects, can you allow them to taper the dose, reduce the dose, or stop and retry at a later time.

State whether you plan to share study results with participants (what results – e.g. overall study results or their personal lab results and when – e.g. after the study is unblinded)

Include a description of data and specimen banking (if applicable). If you plan to store data for future use, review the OHSU IRB's [Repository Protocol Checklist](#) (found under the Repository Forms accordion)

- Indicate whether specimens will be used for future genetic research
- How the data will be stored/shared – recommend you don't limit your future use by de-identifying data unless it is necessary

Finally, include the duration of the study for individual subjects and the study overall

## Schedule of Events

Procedure	Screening Visit	Visit 1 7 days +/- 2 days	Visit 2 30 days +/- 5 days
Consent	X		
Medical Hx	X		
Vital Signs <sup>1</sup>	X	X	X
Chest X-Ray <sup>2</sup>	X		
Randomization		X	

1 – BP, HR, Respiration taken after patient sits for 10 minutes

2 – Prior Chest X-Ray can be used if completed within 6 months of randomization

## Schedule of Events

In addition to a detailed text description of what will occur, a table of events provides a quick reference that is helpful for reviewers and individuals helping with the conduct of your study.



## Examples of Procedure Descriptions:

- Timing of procedures
  - Too specific: at 0800, day 7
  - Not specific enough: Subjects will return for a follow-up visit
  - Just right: day 7 +/- 3 days
- Include acceptable ranges
  - Lab values (LFT < 2x normal)
  - Blood volumes (up to 25 mls, approximately 25 mls)
- State when procedures are optional
  - Chest x-ray if not completed within last 6 months, or chest x-ray may be done at the investigators discretion

Build in flexibility where you can while preserving the scientific rigor of the project.

Specify when existing information from the medical records can replace study procedures (e.g. labs collected within the last month).

## Example: Procedure Detail

### Study evaluating a new pacemaker algorithm

- Too Little Detail:
  - Treadmill test
- Too Much Detail:
  - The treadmill will be calibrated before each treadmill test. Then the cardiac lab nurse (Nancy) will instruct the subject on the treadmill test, ask the subject if they have to go to the bathroom before they begin, carefully clean the skin with alcohol and possibly shave the skin before placing the electrodes (if subject sensitive to alcohol, water may be used)
  - This information would be better in the Operations Manual
- Just Right:
  - Subject will have a Bruce Protocol Stress Test

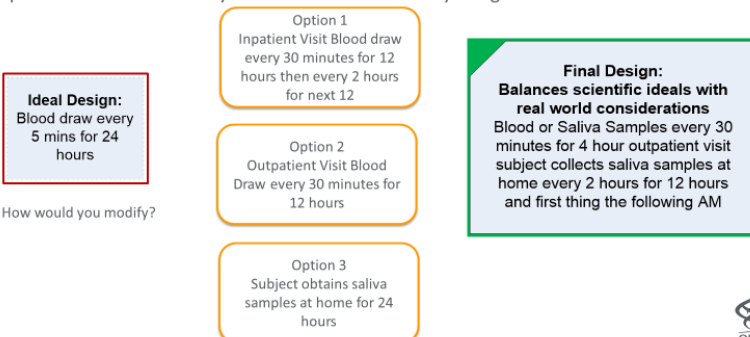


If the study involves standardized clinical procedures, you can simply list them by name.



## Example: Proposal states “Frequent blood draws”

A observational study of reproductive hormone patterns over 24 hours at different points in the menstrual cycle. What is an ideal study design?



Not all ideal study designs can be conducted in real life. For each procedure you should evaluate whether it can be completed with your staff, your equipment, and is a reasonable burden on the study participants.



## Risks and Benefits



### Risks and Benefits

- List reasonable foreseeable risks, discomforts, hazards, or inconveniences related to participation
  - Include probability, magnitude, duration and reversibility
- List risks for interventions and procedures
- List potential benefits to participants
  - Include probability, magnitude and duration
  - State if study won't have direct participant benefits
  - Participant compensation isn't considered a benefit

List the reasonably foreseeable risks, discomforts, hazards, or inconveniences to the participants related to their participation. List risks for interventions (drug, device, educational intervention) and procedures (blood draws, other medical procedures) and confidentiality.

You don't need to list all theoretical risks. Include the probability, magnitude and duration and reversibility of the reasonably foreseeable risks. Be consistent when determining the threshold for including risks (e.g. all risks that occur in >10% of patients in the investigator brochure or all common side effects listed on a label) and consider the patient population. If applicable, indicate if there are risks to embryo or fetus.

List potential benefits to participants, include probability, magnitude and duration. Your study may not have a direct benefit to participants but might benefit participants in the future. If this is the case, state this. Note: Compensation for study visits is not considered a study benefit. It should be included in the protocol in the recruitment section.

Explain the steps you plan to take to minimize study risks (e.g. regularly scheduled lab tests to detect a known risk, collecting minimum necessary participant data).

## Example: Risks

- Risks
  - Too Little Detail: No known risks
  - Too Much Detail: List every adverse event that a study subject encountered in previous studies without regard to relatedness or population
  - Just Right: Pick a cut-off for all study intervention and procedure related risks and be consistent

## Safety Assessments/Protection from risks

### Safety Assessments/Protection from Risks

- Safety Assessments/Protection from risks
  - Identify procedures conducted for safety
  - Determine how you will recognize, document, and report adverse events
- Stopping Rules/Criteria
  - Don't make them overly strict
  - Too Strict: If an Serious Adverse Event Occurs
  - Just right: Based on statistical and clinical context of your study

The protocol should clearly identify procedures conducted for safety, adverse event detection, documentation, and reporting requirements. Some details (coding, reporting methods/timelines) may be included in an operations manual instead.

Stopping Rules/Criteria – if your study has statistical or safety threshold stopping rules, include these in the protocol. For example, if you reach a statistically pre-defined criteria for safety (e.g. 3 subjects have a specific serious adverse event related to the study intervention you will stop the study until you can perform a complete interim analysis).

## Privacy, Confidentiality, and Data Security

### Privacy, Confidentiality and Data Security

- Describe steps taken to protect privacy during all phases of the study
  - Steps to secure data and specimens during storage use and transfer
- IRB has a [Security and Confidentiality Protocol checklist](#)

Common Error – stating data will be de-identified when it includes HIPAA identifiers (e.g. visit dates)

- Take the [Recognizing Coded and De-identified Data](#) short training

Describe the steps you plan to take to protect privacy during all phases of the study.

Include steps to secure data and specimens during storage use and transfer.

Use the IRB [Protocol](#)

[Checklist – Security and Confidentiality](#) (found under the “Protocol Templates” accordion on the IRB policies and Forms page).



All [18 HIPAA identifiers](#) have to be removed from data to be considered “de-identified” per 45 CFR 164.514(b)(2)(i). This includes dates of service/encounters. Most studies require dates for operations (participant visit tracking) and analysis. Good clinical practice guidelines require data be reproducible, so knowing the date of an encounter to verify data is important.

The IRB policies and forms page has links to additional information and OHSU policies.

If you need additional training on take the OCTRI [Recognizing Coded and De-identified Data](#) training

## Statistical Analysis Plan (SAP)



## Statistical Analysis Plan (SAP)

- A well defined SAP is essential for improving the validity and generalizability of clinical trials and other specific research.
- What does a good SAP include?
  - Endpoints (clearly indicate primary, secondary)
  - Method of analysis
  - Monitoring, interim/integrated analysis strategy
  - Comparisons and significance levels (predefined)
  - Exploratory data analyses
  - Get IRB approval for changes
  - Must be kept up to date (clinicaltrials.gov, publication) see study guide for more information



If you need assistance with your statistical analysis plan, contact the OHSU Biostatistics & Design Program by emailing [bdp@ohsu.edu](mailto:bdp@ohsu.edu).

## Importance of Good Protocol Development

### Conducting the Protocol for Compliance

- Once the study has IRB approval the study team is expected to adhere to the protocol without deviations (unless necessary for the safety of the subject)
- Make sure study staff read and understand the protocol
  - Have study staff acknowledge their roles in the study
  - Make sure study staff know how to identify and report deviations
  - Delegate study tasks to qualified individuals (e.g. physical exams delegated to MD, FNP, PA)
  - Supervise the conduct of delegated activities

### Protocol Modifications

## Protocol Modifications

- Submit a revised protocol to the IRB to address new information or address implementation/recruitment problems
- Strive to minimize modifications so that data remains “poolable”
  - Don’t want to compare apples and oranges
- Maintain consistency within and between the protocol, consent, and procedure manuals



A well-designed protocol that has been analyzed for feasibility and operational implementation shouldn’t require a lot of study modifications. Too many modifications to inclusion/exclusion criteria or study procedures may leave you with different study populations for analysis.

You can’t avoid all modifications, so when you do modify your protocol, maintain consistency within and between the protocol, consent, and procedure manuals to avoid protocol deviations.

## Protocol Best Practices

# Protocol Best Practices



- Write to your audience – if there is jargon define it
- Describe what you are going to do, not everything you might ever do
- Beware the “copy and paste” from other protocols
- Use boilerplate language when available
- Make it easy for reviewers, coordinators, auditors, others to understand
- Submitting a clearly written, consistent protocol will shorten your IRB review time
- Conduct a feasibility analysis

Conduct a feasibility analysis – make sure you can do what you propose. You should do a feasibility analysis when you write the grant but you may need to do another when you get the funding especially if a significant time has passed.

Bulleted lists and tables help reviewers and study team members understand and find information quickly. Grants have page limits but you can, and should, provide more detail in your protocol. This will make it easier for reviewers, coordinators, auditors and others

Use boilerplate language when available. For example, the REDCap Wiki has boilerplate language for REDCap, eConsent, Twilio and more.

Have your collaborators and study coordinator read it (especially if you are using their clinic/services) to make sure it is clear. Submitting a clearly written, consistent protocol will shorten your IRB review time

## Your Protocol may be Publicly Available

### Your Protocol may be Publicly Available

- Some major journals (e.g. Lancet, Annals of Internal Medicine) require submission of the protocol and post them with the trial manuscripts.
- All studies that are required to submit results to [clinicaltrials.gov](https://clinicaltrials.gov) must include a protocol/statistical analysis plan at time of results posting



Keep your protocol up to date and tidy.

Consider results reporting when deciding to revise or submit a new protocol to the IRB

Some major journals (e.g. Lancet, Annals of Internal Medicine) require submission of the protocol and post them with the trial manuscripts.

All studies that are required to submit results to [clinicaltrials.gov](https://clinicaltrials.gov) must include a protocol/statistical analysis plan at

time of results posting. Consider results reporting when deciding to revise or submit a new protocol to the IRB. Since the protocol maybe made public, give it your care and attention throughout the study so it looks professional and reflects the quality of your science.