Clinical Research
The “Dos” & the “Don’ts”

Version #1 – 8/2/12
Who’s Who in Clinical Research @ MSSM?

The Tisch Cancer Institute - Our Mission:

“Our mission is to build upon Mount Sinai Medical Center’s reputation for excellence in research and clinical care to find new ways to prevent, treat, and cure cancer. The Tisch Cancer Institute has access to levels of research expertise and patient care that few other cancer centers can offer”
Who’s Who in Clinical Research @ MSSM?

Cancer Clinical Trials Office Leadership

• Marshall Posner, MD – Medical Director
• Matthew Galsky, MD – Associate Medical Director
• Rosemarie Gagliardi, cEdD, MPH, CCRA – Senior Director

The Tisch Cancer Institute’s Cancer Clinical Trials Office (CCTO) provides the infrastructure and resources required to support patient-based cancer research for the Tisch Cancer Institute in the Mount Sinai School of Medicine
Protocol Approval Process

- IND Application (Up to 30-day review)
  - Hold
  - Exemption
    - Proceed
    - IRB / GCO Review
      - Address IRB Comments
        - Congratulations. You're approved!
        - Amended protocol
          - Can be concurrent
            - Internal approval
            - External approval

- Resource Allocation Evaluation*
  - Disease Focus Group
  - Protocol Review & Monitoring Committee

*Includes budget discussion with Bridget
When writing a protocol - Investigator-initiated trial (IIT)...

**DO**

- Use the IRB’s template for the protocol & consent form
- Remember to consult the online “Wizard” to see which committees your protocol will need to be reviewed at
- Write the consent form at a 6th grade reading level

**DON’T**

- Obtain an IND before getting PRMC approval for your study
- Forget to cite your sources – all references should be appropriately referred to in the text of the protocol

**HINT:**
If an HIV test is a required screening Procedure, you will be required to create an HIV consent form, as well. Use the IRB’s template as an example!
Protocol Development - Instructions & Explanations

**DO**

- Write clear descriptions in the protocol
- For processes that require extensive, detailed instructions (e.g. specimen handling/shipping procedures)
  - Prepare a separate document and attach it as an appendix.
  - Create an in-text reference to the appendix

**DON’T**

- Describe processes using vague language
- Incorporate procedures without providing a rationale

**HINT:**

*Failure to document and/or follow procedures is a frequent citation in FDA inspections*
Protocol Development - Version Control

**DO**

- Create a mechanism to control versions
- Consider using a cloud service so that reviewers in different locations have access to the same document
- Consider appointing a protocol champion who will make all changes to the document
- Use the document compare feature in Word to see changes as track changes aren’t always turned on
- Use a formal signature sign-off for final acceptance

**DON’T**

- Allow changes to be made to different versions of a protocol by separate reviewers
- Collaborate with multiple reviewers by sending drafts for review via email
- Consolidate multiple draft documents using Word’s combine function
Protocol Development - Study Calendar (X Diagram)

**DO**

- Verify the content provided in the tables and visit information against protocol text and informed consent form

- For lab tests that differ for certain visits, include a footnote explaining which tests are to be conducted

- Footnotes may include cross-references to protocol sections and appendices

**DON’T**

- Leave study procedures and assessments out of the study calendar

- Assume that all of the study activities are included in the calendar

- Forget to verify the information in the appendices against the protocol text and in-text references
Protocol Development - In-text References

**DO**

- Use the References toolbar in Word
  - Insert captions for tables, figures, etc
  - Use in-text cross-references to section headings, tables, figures, appendices, etc
  - Automate the Table of Contents

**DON’T**

- Repeat information if it’s already included in another section of the text.
- Reference another section, table, appendix without linking it in Word

**HINT:**
When a protocol is converted from Word to PDF section headings will convert to bookmarks and all cross-reference hyperlinks will apply to the PDF document.
This will greatly facilitate review of the protocol!
Protocol Development - Quality Assurance

**DO**

- Use a checklist to QA and finalize the protocol
- The QA process should include a check of the Abbreviations, Schema, Summary, Table of Contents, references, etc. against the protocol and appendices

**DON’T**

- Neglect implementing a quality system as errors in the protocol will create confusion among research personnel

**HINT:**

*Elements of an appropriate QA checklist include the following:*

- **Scientific QA:** scientific spell check, abbreviations, references, special symbols, and units of measure
- **Editorial QA:** spell check, grammar, punctuation, and in-text references
When holding an IND...

**DO**

- Contact the OCR office for assistance with completing initial IND applications
- Submit an annual progress report (within 60 calendar days of the anniversary of FDA approval)
- Maintain all FDA correspondence organized in a binder by serial submission number

**DON’T**

- Forget to submit any amendments to the protocol to the FDA for review
- Forget that the FDA has 30 days to review your initial IND application

**HINT:**
If you think that your trial may qualify for IND exemption, contact the OCR which will guide you through the application process
When submitting to the IRB...

**DO**

- Submit new applications, amendments, & continuing reviews to the IRB’s email address: irb@mssm.edu (mention the type of application, study title & GCO in the email). Also for documentation include a list of all the attachments.

- Remember to concurrently submit an application to the Grants and Contracts Office via InfoEd, as well as set-up the Financial Conflict of Interest forms in Sinai Central.

- Remember that anyone who will be involved in the design, conduct, or reporting of the research should be listed on the HRP 211 form & on the Delegation of Authority log.

**DON’T**

- Forget to use a HRP 224 “Reportable New Information” form for to submit updated Investigator Brochures, new risks or a safety issue, SAEs or protocol deviations.

- Walk over hard copies of the protocol submission to the IRB – they are now paperless!

- Forget to submit the package inserts for all approved drugs to the IRB with a new application & Investigator’s Brochures for all drugs not approved by the FDA.

- Submit new applications for a particular meeting; protocol submissions are accepted on an ongoing basis & are then assigned to a committee.
Medicare Coverage Analysis (MCA)

**DO**

- Determine if your trial is a Qualifying Clinical Trial (QCT)
- Include every possible visit and activity
- Specify if activities will be free to the patient, paid for by the sponsor, or billable to Medicare (Review the proposed CTA, Budget, ICF, and Protocol in tandem)
- Be keenly aware that anything not paid for by the sponsor that is also not billable to Medicare becomes an expense to the institution
- Ask for help (contact Bridget Hayes and/or Alex Morillo at BRANY) if you are unsure if something is billable to Medicare or not

**DON’T**

- Assume that research activities are automatically billable to Medicare
- Forget to document justification for billing to Medicare

**HINT:**
The MCA is one of the most beneficial tools for you to use in budget negotiations. Where possible, finalize the budget after reviewing the MCA

*Contact before negotiating with a company, submitting a grant, or submitting to the PRMC or IRB*
Budgeting Process

**DO**

- Review each scenario of the visit schedule to ensure that every research activity is being reimbursed.
- Use the appropriate fee schedules to negotiate an acceptable reimbursement rate for each qualifying research activity.
- Keep in mind that MSSM overhead is 35%. This is the minimum acceptable rate.
- Remember to negotiate for non-clinical activity that is research related (including monitoring visits, queries, patient travel, etc.).
- Contact Bridget Hayes* with budget-related questions.

**DON’T**

- Accept a budget that does not adequately cover the specific activities of the protocol or administering the trial.
- Accept any budget proposal without thorough review. (Many sponsors will attempt to convince you that “this is what we are paying everyone”). This should be a healthy financial decision for our institution.

**HINT:**

*Contact before negotiating with a company, submitting a grant, or submitting to the PRMC or IRB.*

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*Ask for what you really need to run the study. The Clinical Trials Office has helped negotiate budget increases upwards 40% of the original proposal.*
Contract Process

**DO**

• Make sure the language in the CTA is consistent with the Informed Consent Form, the Budget, and the Protocol

• Make sure that the terms of the payment schedule are clear

• Make sure that each section of the agreement is in compliance with MSSM policies

• Contact Christina Lin with contract-related questions

**DON’T**

• Sign the agreement until all questions and concerns have been sufficiently answered

**HINT:**
The contract is a legally binding document. It should not be signed before the final negotiations of the budget.
Regulatory Binders

**DO**

- Maintain accurate, up-to-date information in categorical and reverse chronological order
- Refer to the CCTO SOPs & guidelines on the CCTO website that describe what to maintain in a regulatory binder
- Maintain a log that lists the study documentation that is maintained in the binder, including all expiration dates on items such as licenses, etc
- If applicable, create a “note to file” to state that the following are located on the CCTO shared drive for the reg binder: updated CVs, licenses, lab values, IRB membership

**DON’T**

- Forget to keep signed copies of all signature pages (IRB paperwork, etc) in the binder

**HINT:**

Regulatory Binder items should be in reverse chronological order, with the most recent information on top!
EPIC

**DO**

- LINK RESEARCH ENCOUNTERS!
- Make sure orders are placed per protocol – research VS standard of care
- Only review the medical records of subjects or potential subjects
- Scan in a copy of the signed consent form into the subject’s medical record
- Contact 4-EPIC should you have any technical problems with the system

**DON’T**

- Forget for new studies, to request to have them added into EPIC as a dropdown choice
- Forget to check that your research orders have been placed & placed correctly – research VS standard of care

**HINT:**

Don’t let standing orders expire before the patient’s next visit – these should be reviewed
Informed Consent Process

DO

• Explain the schema, risks, cost, and side effects completely to the patient

• Use the current, IRB approved ICF/ICFs

• Ensure patients are aware that clinical trial participation is voluntary

• Be sure to follow the protocol’s guidelines for time constraints if you want to use the results from standard of care tests for research purposes

DON'T

• Print name, date, or print the time on the consent form for the patient

• Use an English consent form for a non-English speaking patient ~ have it translated into the patient’s language!

HINT:
The Informed Consent process should be an active process ~ give time for the patient to ask questions & feel comfortable with participating in a clinical trial
Eligibility Criteria

**DO**

- Use source documentation to support all items on the eligibility checklist
- Review the eligibility of potential research subjects with the research team before enrolling the patient into the study
- Ensure that for screening, if you want to use the results from standard of care tests done prior to the research, you should be sure to follow the protocol’s guidelines for time constraints

**DON’T**

- Forget to sign & date the eligibility checklist
- Forget to enter the values for all criteria on the eligibility checklist

**HINT:**

The MSSM IRB does not grant waivers for eligibility criteria for patients – they must meet all criteria required to participate in the study
CCTO Central Patient Registration

**DO**

- Submit informed consent(s), registration form, eligibility checklist, & sponsor approval (as applicable) to Central.Registration@mssm.edu
- Leave 1-2 hours for full approval
- Register screen failures through the Central Patient Registration system

**DON’T**

- Leave blank values for eligibility criteria
- Forget to sign-off on the eligibility checklist & registration form
- Send in submissions late on a Friday evening or over the weekend

**HINT:**

Always contact Central Patient Registration at least an hour before you plan to enroll a patient late in the day & keep them posted as to your progress
Pharmacy

**DO**

- Complete IDS forms for every drugs/biological product whose use is specified in the research protocol. The IDS form is available at [www.mountsinai.org/ids](http://www.mountsinai.org/ids)
- Contact the IDS regarding the use of controlled substances for research to discuss the required licensures
- Submit your project to the Program for the Protection of Human Subjects (PPHS) office while the IDS is reviewing your project. PPHS only requires IDS authorization prior to giving their final approval of the project

**DON’T**

- Forget to notify IDS when a study closes to discuss disposition of pharmacy records and return/destruction of remaining study materials
- Forget to include the principal investigator signature’s on the IDS form

**HINT:**

*Each drugs/biological product listed in IRB Form 211 Appendix B should have a corresponding IDS form completed*
Laboratory / Specimen Handling

**DO**

- Always wear gloves when handling specimens
- Verify that the specimen labeling & packaging information is in accordance with protocol requirements
- Follow the protocol instructions to determine where to ship specimens – note: central labs will have different requirements than local labs
- Be sure you are trained in Infection Control & Hazmat before you handle research specimens

**DON’T**

- Leave unlabeled specimens unattended
- Forget to ship specimens as per protocol – ex) on dry ice, ambient, etc
- Forget for research blood draws, drop off your tubes & instructions to the RTC lab in advance

**HINT:**
Your protocol and/or laboratory manual will guide you to determine the manner in which specimens need to be collected
SAEs & AEs

DO

- Use a MedWatch form FDA 3500a when reporting SAEs to the FDA. Report all deaths, expected or not, related or not
- Write the IND# on all MedWatch forms submitted to Industry and/or the FDA
- Review and sign AEs on the AE log in a timely manner and have investigator sign-off. Indicate if they are significant or non-significant
- Pay attention to the AE & SAE reporting requirements listed in the protocol
- Always ensure that an Investigator reviews & signs-off on the relationship (to study treatment) & the severity of the AE & if they are expected or unexpected

DON’T

- Report SAEs to the MSSM IRB unless they are in the opinion of the Investigator both unexpected and at least probably related to the research procedures
- Forget to use an AE log to track the subjects’ AEs throughout the course of the trial. The IRB requires a list of all AEs for the continuation submission

HINT:

AEs should be tracked if they are a new side effect, if the frequency has increased, and/or if the side effect has worsened in severity
Case Report Forms (CRFs)

**DO**

- Complete these in a timely manner – they should only lag a week behind the subject’s study visit
- Strike a line through errors, then initial & date next to the correction that is made
- Ensure that every data point is supported by source documentation
- Be sure to respond to all queries within the time frame specified by the protocol & sponsor

**DON’T**

- Ever use white out on paper CRFs!
- Forget to have the PI review & sign-off on CRFs in a timely manner
- Backdate CRFs or falsify any data!

**HINT:**

Remember…if it was not documented in the patient’s medical record, it was not done or never happened!
Who’s Who in Clinical Research @ MSSM?

Nancy Lowe – Associate Director (Regulatory Operations)

Richa Upadhyay, MD – Associate Director (Clinical Operations)

   Bridget Hayes - Finance Manager

   Christine Gultom – Financial Analyst

   Jen Cocco - Director, Research Administration Systems

   Julian Baez – Systems Data Analyst

Teena Kochukoshy - Central Patient Registration Coordinator

Robert Vaynberger – Administrative Secretary
Who’s Who in Clinical Research @ MSSM?

Tisch Cancer Clinical Trials Office

Benign Hematology: Dr. Aledort, Dr. Cromwell
Josella Aguilar (CRN)
Alok Shrestha (CRC)

BMT group: Dr. Isola, Dr. Malone, Dr. Grosskreutz, Dr. Scigliano, Dr. Osman, Dr. Nieto, Dr. Steinberg
Zachary Galitzeck (BMT Research Manager)
Helen Seedhom (CRN)
Angela Stangarone (CRC)
Christine Woo (CRN)
Who’s Who in Clinical Research @ MSSM?

**Breast group: Dr. Adelson, Dr. Raptis, Dr. Port**

Debby Lehrer, RN (CRN)

**GI group: Dr. Holcombe, Dr. Sung, Dr. Ohnuma**

Kiev Gimpel-Tetra (CRN)
Alok Shrestha (CRC)

**GU group: Dr. Galsky, Dr. Oh**

Diana Aristizabal (CRN)
Beth Inserra (CRC)
Who’s Who in Clinical Research @ MSSM?

**Head and Neck group: Dr. Posner, Dr. Sikora, Dr. Misiukiewicz, Dr. Bonomi**

Rachel Abbot (CRC)

Nadia Camille (CRC)

Patricia Strebel (CRN)

Lewis Winder (CRC)

**Malignant Hematology: Dr. Gabrilove, Dr. Brody**

Josella Aguilar (CRN)

Lisa Arabova (CRC)
Who’s Who in Clinical Research @ MSSM?

**MDS group: Dr. Silverman, Dr. Navada**

Lisa Arabova (CRC)

Erin Demakos (Administrative Director)

Rosalie Odchimar-Reissig (CRN)

**Melanoma group: Dr. Saenger, Dr. Friedlander**

Jean Hum (CRC)

Debby Lehrer (CRN)
Who’s Who in Clinical Research @ MSSM?

MPD group: Dr. Hoffman, Dr. Mascarenhas, Dr. Kremyanskaya

Jill Kleczko (MPD Research Manager)

Erin Demakos (Administrative Director, MPD-RC)

Jane Lew (CRC)

Carrie Newsom (CRN)

Lonette Sandy (Sr CRC)

Jimmy Siuty (Research Protocol Manager)
Who’s Who in Clinical Research @ MSSM?

Multiple Myeloma group: Dr. Jagannath, Dr. Chari, Dr. Cho

Lisa La (MM Research Manager)
Elaine Chan (CRC)
Katarzyna Garcia (CRC)
Danielle HyeMin Choi (CRN)
Kenneth Lau (CRC)
Who’s Who in Clinical Research @ MSSM?

Neuro-oncology: Dr. Germano
Kiev Gimpel-Tetra (CRN)
Jean Hum (CRC)

Sarcoma: Dr. Maki
Katrina Watson (Program Manager)
Who’s Who in Clinical Research @ MSSM?

**Regulatory Staff:**

- Suzan Aird
- Monika Anand
- Zachary Galitzeck
- Jude Gullie
- Aniceto Javaluyas
- Ethel Jiles
- Lena Nemelivsky
- Sanobar Parkar
- Pamela Manju Rajan
Thank you!