Sponsored Clinical Trials: Processes to follow by Principal Investigators and Research Assistants

Contents

Initial Preparation

The sponsor will present the study proposal to the Principal Investigator (PI) to explore the interest and the feasibility of conducting the clinical trial at their institution. Once the PI shows interest, the sponsor will provide the PI with a confidentiality agreement to be signed before disclosing/elaborating on further study details. The PI will present the study to the concerned team and discuss the feasibility, appropriateness, and benefits of the proposed study.

Assessing feasibility

The sponsor provides the detailed feasibility checklist to the PI, who in turn will handle it to the RC (Research Coordinator) to be filled. The checklist includes, but is not limited to the following:

a. Recruitment expectations: assess if the estimated rate of subject recruitment according to the eligibility criteria meets in the protocol recruitment expectations in terms of number and timeframe.
b. Facility/space: ensure the availability of the appropriate facility/space, either in the Clinical Research Institute (CRI)'s Clinical Research Unit (CRU) or at another site (Clinics, hospital, unit, etc.). The RC will make sure the appropriate locations will be availability when needed (referring to the respective study protocol) and in coordination with the clinical team.
c. Staff: ensure the on-site study personnel-will-be available when needed according to the timeline of the study protocol. On-site study personnel includes but is not limited to physicians, research fellows, research coordinators, technicians, and nurses.
d. Pharmacy storage: contact the pharmacy personnel to assess if space is available for storage throughout the study duration and coordinate medication storage management accordingly.
e. Ability to do all required testing and examinations mentioned in the protocol: The RC will guide the trial sponsor representative to coordinate with the staff in charge of other departments/divisions/services. It is the responsibility of the Trial representative to coordinate and negotiate with all departments involved in the study to assess the budget and different tasks (Labs, psychology department, MRI...) while keeping the RC informed.

Review of schedule of event and setting the budget

American University of Beirut Medical
Clinical and Translational Research
Process for Clinical Trial Budgeting at AUB

Clinical Trial Initiation

- PI and funding agency finalize the initial proposal.
- Secure IRB approval.
- Prepare for clinical trial budgeting before signing the contract as per below

Adopt New Clinical Trial Charging Process

- Your Division or department will generate a list of common tasks/procedures/tests etc. that are used during clinical trials, i.e specialty assessment, administration of therapy, performing simple/moderate/complex questionnaire, charging for facility use, etc. in order to allocate cost and codes (kindly refer to the **below example** Appendix #1: Nehme and Therese Tohme Clinical Trial Charging sheet)
- Share the above list with the AUBMC comptroller in order to identify if any of these clinical trial tasks/procedures/tests has a previously allocated research cost at AUBMC. If so, and in order to secure consistency, better use same research cost applied while making sure that the AUBMC comptroller will create new codes for your division/department. If the task/procedure/test associated with your department has **no** previously allocated cost, the AUBMC comptroller will create a new code reference for your division/department
- Once the clinical trial charging code list is finalized, it shall be used as a expenditure reference when setting the clinical trial budget.
- Charging of regular AUBMC special procedures, lab tests, radiology tests, or any other test done outside your department/division will follow the usual charging process.
- Clinical Trial Budget might include other expeditures: personnel, miscelleneous (store items, stationary, patient meals, patient transportation, etc.)

Finalizing Clinical Trial Budgeting

- The finalized budget will be shared with the funding agency for approval.
- The approved budget will be used as reference by the OGC and AUB comptroller to identify account description while creating it on Oracle (i.e. PI fees, Patient costs, FTE costs, miscellenous etc)
- Sign the contract
- Secure an OGC transmittal form
- At initiation of the clinical trial, the funding agency needs to secure a start up fund that can minimum cover up the expenses of at least 3 subjects visits and RA salary for **# year** (to be placed in the contract)

Process for Clinical Trial Subject Charging at AUBMC

- The purpose of this process is to secure accurate charging of clinical trials (CT) costs and secure accurate collection of the charges
- This process and the charging sheet can be developed and adopted at either the departmental or divisional levels where clinical trials are taking place
- To proceed with this process, clinical trial charging sheet needs to be finalized

IRB submission

Once a verbal agreement is reached between the PI, the research team and the sponsor, the sponsor will draft an IRB application that will be shared with the PI for review and approval. Then the RC will forward it to the IRB office. The sponsor, represented by a CRA (Clinical Research Associate), will provide the site with the IRB approval support documents package (as indicated by IRB requirements) and secure signature as need be.

N.B: Research coordinators are encouraged to register for the good clinical research practice workshop that is being conducted on a regular basis and it tackles IRB submission, review and consent processes as well as a section on study management and logistics.

The package includes:

a. Submission letter: prepared by the sponsor, approved and signed by the PI.
b. In case the research is an interventional study, the application to be prepared is: Application to Conduct Research on Human Subjects, this application will be prepared by the RC with the help of the sponsor or provided by the sponsor then signed by the PI and the Chairperson. (PS: The Chairperson of the respective department signature is only required during the Initial submission. In subsequent submissions such as rebuttals, continuing reviews and amendments, the PI's signature is only required)
c. The approval of medical record review form targets chart review projects that are retrospective in nature. For studies intending to review charts in a prospective manner, the application to conduct research on human participant's application should be filled and submitted. The RC will prepare this application with the help of the sponsor, or it will be provided by the sponsor then signed by the PI.
d. Study Protocol
e. Informed consents: include all forms and translations of the consents respective to the study in question (English and Arabic versions, Consent forms for adults and parents, assent forms for adolescents (13-17 years of age) and children (7-12 years of age).
f. Investigator's brochures, available safety information, case report form, insurance certificates, and investigational new drug form
g. For research personnel (all research fellows, research assistants, clinical residents and staff involved in research) participating in clinical trials, the IRB specifically requires a

certificate of completion for the "Biomedical Basic refresher" CITI training course, GCRP or GRP training provided in house.

h. Additional documents (tests, checklists, patient diary, questionnaires, brochures, flyers, posters…).

Acknowledgment of receipt from the PI: The sponsor prepares a letter addressed to the PI regarding the package's receipt. The RA will secure the signature of the PI and send a scanned copy to the sponsor. The soft and hard copies of the scanned letter will be saved in the soft and hard files.

Acknowledgment of receipt from the IRB: The sponsor requires proof that the IRB has received the package in due time. Depending on the sponsor's request, the RC will secure one of the following steps:

- Sending an email to the sponsor including the submission letter signed by the PI and stamped by the IRB (Received + Date)
- IRB office signs the Acknowledgment of Receipt document (AoR) prepared by the sponsor.

Finally, RC will send the above package (excluding the PI Acknowledgement of Receipt (AoR)) as soft and hard copy files to the IRB (irb@aub.edu.lb).

Dear IRB officer,

On behalf of Dr. *John Doe*, kindly find attached the following documents related to the study entitled "*Example of Study Title*" Protocol ***XX.XX.00***:

- A letter from Dr. *Doe* regarding the submission.
- Informed consents
- CITI certificates of the newly added personnel
- Other documents

A binder containing the above-mentioned documents will be sent to the IRB today.

Best regards,

Sample Submission mail:

The IRB will send the RC an invoice of the IRB fees, who in turn will send it to the CRA to secure payments. Once paid, the CRA will send proof of payment to the RC who in turn will notify the IRB.

In case there is a need for modifications, IRB will issue an official letter containing initial review comments and requested "Modifications required to secure approval" and send it to PI who in turn will forward it to RC. RC will send the above letter to sponsor to secure correction in due time. Based on IRB review, sponsor will secure needed clarifications and corrections. Response should be within 3 months of IRB email/letter. If the sponsor exceeds the 3 months period, a new submission to the IRB will be required.

The IRB issues an approval package that includes the approved (and stamped) protocol, consents, fliers, data collection sheets and most importantly the Approval of Research letter. This approval contains two dates:

a. The Study expiry date
b. The deadline for continuing review submission

The RC will create an Excel sheet containing a list with expiration dates and deadlines for

Stydy name	Protocol Number	Type of Document	Expiry date	Submission Deadline	Comments
AAAA	AA.AAA.00	Continuing review	06-Jan-19	06-Nov-18	done
BBBB	BB2000_0000	Continuing Review	16-Jan-19	16-Nov-18	
CCCC	CC.AAA.01	Continuing review	17-Feb-19	17-Dec-18	
DDDD	AAA-2000-0000	Continuing review	17-Dec-19	17-Oct-19	done
EEEE	BA010101	Approval	Pending	Pending	

submission of the continuing reviews as per below example.

AUBMC research affairs section

If the study requires the usage of AUBMC owned or non AUBMC owned equipment (JCI requirement), medications (storage, dispensing, AUBMC services (Lab, radiology), staff (to secure EPIC access), RC will secure a form that includes different information related to the research study conduction at AUBMC. The form requires administrative approval of conducting the study at AUBMC. This will indirectly log the study on the EPIC AUBHealth research module to follow up on patient enrollment.

Secure Office of Grants and Contracts (OGC) Transmittal Form

While the above processes are taking place, the RC needs to secure the OGC transmittal form following the OGC regulations kindly refer to OGC link: http://website.aub.edu.lb/ogc/Pages/forms.aspx

To note that, the RC needs to send a hard copy of the filled and signed OGC transmittal form with the detailed budget and the initial proposal to the Office of OGC.

Negotiation of contract

Based on the feasibility assessment, and after obtaining IRB approval and after securing the transmittal form the PI will negotiate the proposal and budget with the sponsor to finalize the contract.

Signing the contract

Once the OGC reviews the contract and all parties approve its content, the OGC will secure signing the contract by the PI and the sponsor.

Shipments

The sponsor will provide the site with a document addressed to the Ministry of Public Health (MOPH) clarifying the shipment components of the clinical visits (for example, number of sample tubes). The RC will secure the signatures of the PI and Director of the department involved. Afterwards the sponsor will send signed letter to the Minister of Public health for a final signature and approval.

Secure Filing

The RC will prepare a soft and hard copy file of the Investigator Study File (ISF) for each clinical trial that includes at minimum:

a. IRB stamped documents (Approvals, Informed Consents (ICs), protocol…)
b. All communication with the IRB and the sponsor
c. The training log sheet provided by the sponsor
d. CITI certificates of the research team members

In addition, the RC will prepare the following documents for every participant:

a. Enrollment sheet: containing the case number of the participants enrolled with the date of enrollment (consent date).
b. Schedule of expected visits (can be prepared by the sponsor)
c. Excel sheet including deadlines for IRB submission for all site studies

Study Initiation

The sponsor will provide the site with a delegation of duties form. The RC will ensure that the sponsor is updating this form.

Whenever there are changes in research staff appointments, the RC will notify the IRB via email.

Sample Section of Delegation of Duties Form:

Name	Initials	Signature	Function	Study-related duties	Investigator's initials & delegation start date	Start of duties	End of duties	Investigator's initials & delegation stop date
XX			MRI Technologist					
YY			Sub-investigator					
ZZ			Sub-investigator					

Recruitment of participants

The protocol will identify how the participant will be approached by the research team. The RC will ensure every participant has read, understood and signed the informed consent (IC) in order to be considered enrolled in the study. The used informed consent has to be stamped by the IRB. Usually, the consent expires within one year from the date of the IRB stamp. The RC will always make sure to use the most recently stamped IC.

At AUBMC, the ICs are divided according to the patient's age:

1. Assents for children (7-12 years old)
2. Assent for adolescents (13-17 years old)
3. Parental/Legal guardian consent: for patients less than 18 years.
4. Adult consent (>18 years old)

The RC will save these consents in their respective study folder under lock per study protocol.

NB: once patient is enrolled, RC will enroll patient on EPIC.

Scheduling of participants

The RC will schedule appointments (infusion, MRI, psychology department …) preferably one month before the visit date.

Charging visits

The RC will charge the participant's visits following the prepared schedule of activities set in the budget.

Sample schedule of activities:

Visit	Screening	Period										
	1	2 (Baseline)	3	4	5	6	7	8	9	10	11	12
Week		1	2 (±2 days)	8 (±3 days)								
Informed consent												
Vital signs	X	X			X	X		X		X	X	X
PROs		X			X			X		X		
Brain MRI	X			X	X	X		X		X		X
Review inclusion & exclusion criteria												
Physical examination	X	X	X		X	X	X	X	X	X	X	X

For services done outside the clinical area or CRU (i.e. labs, radiology …), the RC will make sure concerned departments/divisions/services are charging and collecting their fees.

For each services to be charged, the RC needs to send an email to the AUBMC Senior Accountant requesting approval as per below:

1- Protocol number/study name
2- Patient's Case number (Patient's name is not to be mentioned for confidentiality)
3- Test codes to be charged
4- PTAO: this is an account number specific for each clinical trial

Dear X,

Please note that samples from #00000 will be undergoing X code: 0000 on 30th of August and #000000 on 4th of September 2018.

The corresponding charges are covered 100% by the study account (PI: Dr. X)

Kindly charge the below account to cover the fees:

P: 000000

T: 000000

A: 000000

O: 000000

Regards,

Sample Visit Charging mail:

To note once the charges are sent to the AUBMC Senior Accountant, statement of fees will be sent from AUBMC finance office to OGC office in order to create invoices and send them to the sponsor for collection.

Once the AUBMC senior accountant sends the financial coverage approval by email, the RC will print and present to the cashier to charge it on the system. The cashier/teller will provide the RC with the receipts that will be handled to the concerned departments/divisions.

The RC will make sure he/she are kept informed about all relevant invoices and transfers.

Continuing review

The continuing review is submitted on a yearly basis to IRB. The RC will secure the continuing review package preferably 2 months prior to study expiry including supportive documents as follows:

- Submission letter: prepared by the sponsor, and RC will secure PI signature. (Appendix 2)
- RC will fill the continuing review form provided by the IRB in coordination with the sponsor

- RC will secure IRB stamp on the previously stamped Informed consents that will be used instead of the previous outdated version.

Amendment

Throughout the study, many changes might take place, i.e. newly added tasks to the protocol, update in the informed consent, change in budget, etc. Consequently, the sponsor will prepare an amendment including all tracked changes and share with the RC, who in turn will communicate to the IRB.

Protocol deviation

During the study, deviations may occur, (for example, the patient can present to the clinic outside the window set in the protocol, and a task could not be completed) if the above occurs, the RC will send a protocol deviation report to the IRB, with the help of the sponsor.

Monitoring visits by the sponsor

Monitoring visits consist of on-site sponsor assessment of the research workflow including: proper completion of online/electronic/hardcopy case report forms, medication management and follow up on patient's compliance with prescribed medication protocol etc. When the sponsor is retrieving documents or study equipment, the RC must ask for an Acknowledgement of receipt. (Kindly refer to the AUBMC policy (HRP-MUL-004) on Visits and Audits for Clinical Research by External Entities)

Audit by IRB/JCI

JCI/IRB representative will conduct periodical audits to ensure that study management, consenting, documentation and adherence to inclusion-exclusion criteria are being accurately applied post IRB approval. Findings of deviations and potential non-compliance are communicated to IRB for review and decision.

DSUR and SASR submission to IRB

Different types of safety reports exist:

- DSUR (Development Safety Update Report) is an annual report.
- SASR (Semi-Annual Safety Report)

The RC will submit the safety report once received from the sponsor with a letter signed by the PI for:

"Any incident, experience or outcome that meets ALL 3 of the following criteria:

1. Is unexpected (regarding nature, specificity, severity, or frequency) given (a) the research procedures described in the protocol-related documents, such as the IRB-approved protocol and informed consent document and (b) the characteristics of the participant population being studied; AND
2. Is related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the procedures involved in the research may have caused the incident, experience, or outcome); AND
3. Suggests that the research places participants or others at greater risk of harm (including physical, psychological, economic, legal, or social harm) than what was previously known or recognized.

Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs) may be medical or non-medical, and include – but are not limited to – serious, unexpected, and related adverse events and unanticipated adverse device effects (see below). "Please note that adverse events are reportable to the Institutional Review Board (IRB) as UPIRSOs only if they meet all 3 criteria listed above."

For external adverse events (participants exhibiting serious adverse events outside AUBMC), there is no need to submit a report on these to the IRB unless some modifications to the protocol and/or consent forms are required due to the event.

For internal serious adverse events (participants exhibiting serious adverse events inside AUBMC), if the incident may require a temporary or permanent interruption of study activities by the PI or sponsor to avoid potential harm to subjects, these should be reported to the IRB via telephone or email immediately or as soon as feasible. Furthermore, a written report to the IRB using the UPIRSO Reporting Form should follow no more than 5 calendar days after the AUB PI becomes aware of the event.

Study Closure

The CRA will visit the site and review ISF (Investigator Study File) and will organize them with the help of RC. RC will inform OGC about the study closure who in turn will secure that all invoices are submitted as collected.

The RC will submit the following documents as hard and soft copies to the IRB:

1- Protocol closure report (available on the IRB website): the sponsor can support the RC to fill this form signed by PI.
2- Closeout letter from the sponsor
3- PI closure submission letter provided by the sponsor and signed by the PI.

Appendix #1

American University of Beirut Medical Center

Nehme and Therese Tohme Multiple Sclerosis Center

Clinical Trial Charging Sheet

Patient Name: Clinical Trial: ……..

Date of Visit: ……..

Please Charge the below-highlighted codes to: ……

Code	Test	Cost in $
00955	Informed Consent	……
00956	Documentation preparation/storage/archiving	
00953	Initial History/Physical exam/ Neurologic exam	
00954	Follow up Physical exam	
00952	Patient Questionnaire Simple	
00951	Patient Questionnaire Complex	
01320	EDSS	
01321	SDMT	
01322	9 Hole Peg test	
01323	8M Walk	
01324	12 leads ECG	
01325	Blood withdrawal	
00959	Sample handling/processing Simple	
01327	Sample handling/processing Complex	
01328	Urine pregnancy	
01329	Urine sampling	
01330	Vital Signs (BP,RR,SaO2,T,W,H)	
01331	Pharmacy (storage/preparation/administration)	
01332	OCT test	
01333	Nursing Assessment	
2045	Room and Board Charge	

Others:……

……..

Signature: ……

Appendix #2

To: Institutional Review Board Date: 00-XXX-0000

Protocol number: XX.XXX.00

Full Protocol Title: “Insert Title Here”

Subject: Continuing Review Form

Dear Sirs,

Kindly, we are enclosing the continuing review form for the study mentioned above, for your kind review and approval.

Please inform me if further information is required.

Thank you.

Yours sincerely,

“Insert Name and Signature of PI Here”