Policy for Scientific Review of Clinical Protocols Utilizing the NIH Intramural Program's Clinical Center

Submission Requirements and Review Criteria

PURPOSE

The purpose of this policy is to describe the minimum requirements for NIH Institutes and Centers to integrate into their intramural scientific review policies related to clinical protocols.

DEFINITIONS AND SCOPE

"Clinical protocol" means the document outlining human subjects research that involves engagement with the subject and for this purpose requires IRB approval. Clinical protocols may include clinical trials[1], non-interventional natural history studies, screening protocols, and teaching and training protocols. Initially this policy pertains to all applicable clinical research carried out by intramural NIH staff at the Clinical Center. This policy may be revised to include all clinical protocols in the NIH intramural program.

Scientific review includes the initial concept and full protocol review, annual and quadrennial review of the ongoing protocol, and review of substantive amendments to the protocol that pose new scientific questions. Except for concept review, these reviews become a part of the official protocol record, are made available to the IRB, and NIH leadership.

The scientific review must include an assessment of the study's resource requirements for the Clinical Center and the Institute/Center (IC) sponsoring the protocol, as well as anticipated service needs provided by other ICs as applicable. If an IC wants to waive the scientific review, the reasons for the waiver should be submitted in lieu of the scientific review. IC leadership and the NIH Associate Director for Clinical Research/Chief Scientific Officer CC must sign off on the scientific review before protocols are sent for Institutional Review Board (IRB) review.

Full scientific review is not the purview of the NIH IRBs. However, should an IRB have concerns about the quality of the scientific review, or its absence, the Chair should speak with the IC Clinical Protocol Scientific Review Committee Chair (see below) to resolve these concerns prior to IRB review.

The Process of Concept Review

ICs may conduct the concept review in an initial discussion with the Clinical Director and/or the Scientific Director, by a central IC review committee, or within the lab/branch. The lab/branch will coordinate and schedule these reviews. The PI should provide the study background, objectives, design, eligibility, statistical section and references to the review entity. No minutes are required; the signature of the lab/branch chief or the chair of the central IC review committee indicates that the concept has been discussed and approved. This review should consider:

---

[1] The NIH definition of a clinical trial is "A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes." [http://osp.od.nih.gov/office-clinical-research-and-bioethics-policy/clinical-research-policy/clinical_trials#new_accordion_content__view-block_1-1]

- Feasibility of the study
- Fit of the study within the mission of the lab/branch and the IC's intramural division.
- Available lab/branch resources (and any additional resources that are needed outside the lab/branch)
  - Will the sponsoring IC provide adequate support to assure good study coordination, data management and statistics?
  - Should the study utilize a CRADA or clinical trials agreement (CTA) to provide resources (e.g. pharmaceutical off label use of drugs) to support the trial?

Required Materials for Initial Scientific Review

1. **Protocol Elements**

An NIH intramural clinical protocol must contain the following information to provide evidence that the investigator(s) has planned a feasible and scientifically excellent clinical study. To reduce duplication of data entry, it is envisioned that the research team will enter information into a protocol-authoring template when writing the protocol and the protocol-authoring template will allow relevant fields of the protocol to be readily available to scientific reviewers as described below. The NIH Clinical Trials Protocol Template https://osp.od.nih.gov/wp-content/uploads/2014/01/Protocol_Template_05Feb2016_508.pdf provides guidance about elements for a Clinical Trial protocol; templates for other types of protocols will be posted when available. General elements for all protocols include:

- Official protocol title
- Study Population: A description of the study population, including the sample size, gender, age, demographic group, required health status, and geographic location.
- Where study subjects will be seen if in addition to the Clinical Center.
- If a multi-site study:
  - What other clinical sites than the Clinical Center will be participating?
  - Is there evidence of the ability of the individual site or center to complete accrual?
  - Define the governance and indicate whether a coordinating center will be used.
- Recruitment and plans: A discussion of the availability of potential participants for the proposed study and the ability of participating sites to recruit and retain the proposed target number of participants. Approaches to be used for retention, cooperation and follow-up of those enrolled and to address any anticipated changes in the composition of the study population over the course of the study. Define milestones on recruitment over the duration of the study.
- For protocols with significant impact on the CC (e.g., ICU, cell processing, surgery) or on IC consult services, individuals from the CC departments and consult services should provide written confirmation of resource availability for consideration at scientific review. For all protocols being conducted at the CC the Protocol Resource Impact Assessment (PRIA) must be completed and reviewed by the CC, and provided for consideration at the time of scientific review.
- Statistical design and power: A statistical analysis plan must be included (see section 5 below "Statistical Analysis Plan").
- Study Duration: Estimated time (in months) from when the study opens to enrollment until: (a) completion of data collection and (b) final data analyses.
- If a multisite study is needed provide a justification for why the study cannot be conducted as a single center study at the NIH.

For Clinical trials:

- Define phase of the clinical trial (phase 0-IV).
- Description of the intervention to be tested: Interventions include drugs/small

molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

- If applicable, provide a description of the dose, frequency, and route of administration of the intervention(s).
- Group Assignment: Describe methods used to assign participants to study groups (treatment arms) and randomization.
- Description of the procedures to be followed in each arm of the trial.
- Provide the availability of Investigational Product (IP) and IND/IDE status, if applicable, and whether or not the investigators have had any interactions with the Food and Drug Administration (FDA).
- Specify primary and important secondary endpoints: In a Clinical Trial, the primary endpoint is the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.
- Describe preclinical data, if applicable, and confirm whether they have been replicated and whether appropriate attention to preclinical gender studies in animals or cells lines have been performed.

For Non-interventional natural history protocols:

- Define the hypothesis; if none, why is the study being done?

2. Clinical and Data Monitoring Plan

A clinical and data monitoring plan (e.g. https://www.nidcr.nih.gov/Research/toolkit) should be submitted. It should have two parts: 1) a Clinical Monitoring Plan for the quality assurance of the proposed clinical study through clinical monitoring activities; and, 2) a Data Monitoring Plan for the quality controls proposed through data monitoring activities. Proposals without these plans will not be reviewed.

The requirements for monitoring clinical trials as described below are in addition to the Data and Safety Monitoring Plan (DSMP).[2] The DSMP is a written description of the procedures for reviewing outcome data, reportable event data (including adverse reactions and unanticipated problems) and overall compliance with the protocol. It is intended to assure the safety and welfare of research subjects during the study and describes how patient safety in the trial will be monitored.

The purpose of the **Clinical Monitoring Plan** is to verify that the conduct and documentation of the clinical study comports with the Protocol, its Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable NIH human subjects research and federal regulatory requirement(s). Include the following descriptions in the Clinical Data Monitoring Plan:

- The persons/entity responsible for conducting the monitoring (e.g., Data Coordinating Center, Clinical Research Associate, study monitor from the Coordinating Center).
- The type and frequency of planned monitoring activities (e.g., Study Initiation, Interim Visits, Study Close Out), locations where monitoring will occur (e.g., participating clinical sites, data

[2]The NIH Intramural Policy for Data and Safety Monitoring is available at: SOP 17 (https://ohsr.od.nih.gov/public/SOP_17_v2_3-8-2016_508.pdf)

center, coordinating center) and data to be reviewed (e.g. % of subjects to be monitored).

- An overall description of the monitoring plan to ensure adherence to the protocol, adequate documentation of the consenting process, and the quality and consistency of the study intervention(s), including fidelity monitoring for behavioral interventions.
- The system to record and manage protocol deviations, unanticipated problems, SAEs and noncompliance.
- If applicable, the monitoring of facilities such as labs or pharmacies for adequate handling and storage of Investigational Products and specimens. Describe how Investigational Product(s) accountability and reconciliation are assured during and at the end of the trial per applicable regulatory requirements.
- Plans for handling any deficiencies that are uncovered and in cases of serious deficiencies the appropriate reporting to relevant authorities, including but not limited to the IRB, DSMB and/or FDA if applicable, institutional officials and the NIH.
- Plans for DSMB oversight.

The purpose of the **Data Monitoring Plan** is to ensure that validated systems and controls are in place to assure the integrity of the clinical research data being collected for the proposed study:

- Describe methods and systems for data collection (e.g., the research database being used and whether it is 21CFR11 compliant, Case Report Forms (CRFs)), data entry, data verification and data validation. Describe the data monitoring process and frequency and any planned mitigation strategies in the event of noncompliance.
- Describe methods and systems to ensure data confidentiality and subject privacy.
- Describe the process for locking the final data which refers to how data can be preserved by applying electronic security procedures such as 'locking' the data (see close out/Step 4 SOP #3 "Final Database Lock and Final Data Delivery" in http://prevention.cancer.gov/clinical-trials/clinical-trials-management/2003-dcp-consortia-early)

3. Data Access and Sharing Plan

The planned procedures on data access and sharing need to be defined and meet applicable data sharing and public/open access requirements. Consideration should include but are not limited to (a) the NIH intramural human data sharing policy, https://policymanual.nih.gov/3016, (b) ClinicalTrials.gov results reporting requirements, found at 42 CFR 11 and in the 2016 NIH Policy Dissemination of NIH-Funded Clinical Trial Information, https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-149.html, (c) the 2014 NIH Genomic Data Sharing (GDS) policy,https://gds.nih.gov/, and (d) journal, partner institution, and/or sponsor data sharing requirements, or other relevant agreement terms.

4. The Milestone Plan

Investigators should provide detailed project performance and timeline objectives, especially for interventional studies. For natural history studies this may include a description of accrual of different patient phenotypes. This section must include an overview of the anticipated project timeline for the following general milestones, as applicable:

- Registration of clinical trial in https: ClinicalTrials.gov (to be performed by Office of Protocol Services)
- Completion of regulatory approvals
- Enrollment of the first subject
- Enrollment and randomization, if applicable of 25%, 50%, 75% and 100% of the projected study population, including women, minorities and children (as appropriate).
- Define a plan of action if the study fails to meet its accrual milestones
- Completion of data collection time
- Completion of primary endpoint and secondary endpoint data analyses

- If applicable, completion of final study report
- Reporting of results in https://clinicaltrials.gov/ as required

These milestones may be negotiated with the IC Clinical/Scientific Director, as appropriate, and may need to be updated at subsequent annual and quadrennial scientific reviews described below.

5. Common Data Elements Applicability

NIH encourages the use of common data elements (CDEs) in clinical research, patient registries, and other human subject research to facilitate broader and more effective use of data and advance research across studies. CDEs are data elements that have been identified and defined for use in multiple data sets across different studies. Use of CDEs can facilitate data sharing and standardization to improve data quality and enable data integration from multiple studies and sources, including electronic health records. NIH ICs have identified CDEs for many clinical domains (e.g., neurological disease), types of studies (e.g. genome-wide association studies (GWAS)), types of outcomes (e.g., patient-reported outcomes), and patient registries (e.g., the Global Rare Diseases Patient Registry and Data Repository). NIH has established a "Common Data Element (CDE) Resource Portal" (http://cde.nih.gov/) to help investigators identify CDEs when developing protocols, case report forms, and other instruments for data collection. The Portal provides guidance about this CDE initiative and other tools and resources for the appropriate use of CDEs and data standards in NIH-funded research. Investigators should describe whether CDEs will be used in the proposed study; if CDEs are applicable but will not be utilized, applicants are expected to explain why.

6. Clinical Protocol Schedule of Events

A clinical protocol schedule of events should be submitted to provide a snapshot of the time it takes for protocol procedures to be completed by an individual participant during the trial see section 7.37 Schedule of Events Table in the NIH Clinical Trials Protocol Template (https://osp.od.nih.gov/wp-content/uploads/2014/01/Protocol_Template_05Feb2016_508.pdf)

For example:

a. Week 1 Screening/Baseline Visit (4 hours) - eligibility criteria, obtain informed consent, screening assessment(s), labs, etc.
b. Week 2, 4, 6, 8 Study Visits (3 hours) - intervention(s), assessment(s), labs, scan(s) etc.
c. Week 12 and 18 Follow-up Visits (3 hours) - assessment(s), labs, scan(s) etc.
d. Week 24 End of study visit (2 hours) - assessment(s), labs, scan(s) etc.
e. This document may be provided in a tabular or graphic format.

7. Statistical Analysis Plan

A detailed statistical analysis plan must be submitted (see Section 10, Statistical Considerations in the NIH Clinical Trials Protocol Template). (https://osp.od.nih.gov/wp-content/uploads/2014/01/Protocol_Template_05Feb2016_508.pdf)

Specify the number of subjects to enroll, the expected effect size, power and the statistical methods (per protocol, intent-to-treat) used to assess the primary outcome measure. A more detailed analysis plan, including a valid subgroup analysis, should be included for a phase III Clinical Trial.

8. Disease Community Engagement

- When appropriate specify the process for including disease community engagement (research subjects) in study design. For studies with clinical outcome endpoints, define whether research subject perspectives were included in defining clinical outcome measures (e.g. surveys distributed at patient conferences, direct meetings with patients and support group

representatives, patient representation on any study design group). When disease community engagement is used it is necessary to define the NIH process used for effectuating this engagement (e.g. use of NIH Conflict of Interest/Confidentiality short certification form https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/review_science/conflict_of_interest-bsc_reviews.pdf). If no process for disease community engagement used explain why.

- Describe the process for timely feedback to subject volunteers of study results and conclusions.

9. Investigator Qualifications

Include or reference a file containing the CV or relevant Biography of the Principal Investigator(s). Also include evidence to address the following considerations:

- Do the Principal Investigators (PIs), collaborators, and other researchers have well documented experience as investigators with appropriate training to participate in the project?
- If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)?
- If the project is collaborative, do the investigators have complementary and integrated expertise and is their leadership approach appropriate?

Scientific Review Process after Concept Review

Institutes and Centers (ICs) will conduct scientific review of complete protocols under the oversight of a central IC Clinical Protocol Scientific Review Committee within the office of the Clinical Director or Scientific Director. At an IC's discretion, this committee may include members from the protocol's originating laboratory/branch. Other reviewers, who will not be members of the laboratory/branch from which the protocol originates, will include the chair and co-chair, at least two additional IRP reviewers, and a statistician. The Review Committee Chair may appoint representatives from CC departments or consult services on the review committee. ICs are encouraged to use external subject matter experts to enhance the scientific review, possibly working with the IC's extramural Scientific Review Branch to obtain extramural reviewers from their lists of relevant experts who have been previously entered into the NIH system as reviewers; at an IC's discretion, the Scientific Review Committee could be comprised completely by external expert reviewers so long as the appropriate expertise is included. If ICs elect to use external reviewers, appropriate clearance of conflict of interest for participation must be obtained using a recommended short certification form (https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/review_science/conflict_of_interest-bsc_reviews.pdf).

The IC Scientific Review Committee should meet within two weeks of the submission of the protocol by the PI. A quorum for the review should include three medical/scientific reviewers with two outside the branch/laboratory where the work is to be conducted, and a statistician (if appropriate) plus the chair. Recommendations should be made by a majority vote. If a reviewer is unable to attend but has written comments to share they should be included but the vote should only be done by the quorum of reviewers present at the meeting. There should be an attempt to achieve consensus in all decisions. If the protocol is returned to the PI with stipulations, at the Chair's discretion, the PI response can receive expedited review by the Chair or the committee could be reconvened for further discussion.

ICs will provide a summary rating of the scientific review for each clinical protocol. 0=Poor, 10=Outstanding (see the Appendix Guidelines for Scientific Reviewer Comments for Initial Scientific Review of Protocol).

Initial Scientific Review

For each IC, the framework that reviewers use for scientific review of protocols should include responses to a series of questions presented in distinct categories presented in the **Appendix 1.** The goal is for the scientific review process to take no more than two weeks.

Prioritization of Protocols Using Scarce Resources at the NIH Clinical Center

NIH has developed a process to ensure that the scarce resources at the Clinical Center are utilized to support the best scientific opportunities. It is being piloted to establish best use of resources of the Cell Processing Section of the Department of Transfusion Medicine.

- The process will be overseen by a subcommittee of NIH IC Directors and chaired by the NIH Associate Director for Clinical Research/Chief Scientific Officer of the Clinical Center.
- Prioritization of protocols will be done after the initial Concept Review and Scientific Review is complete. Priority development will balance needs for new protocols with needs for on-going protocols.
- Clinical Directors whose Institutes/Centers utilize the scarce Clinical Center resource will make the initial prioritization within each IC of protocols that use the scarce resource using the prioritization tool in **Appendix** 2; it is anticipated that this tool will be adapted for prioritization of other scarce resources in the future.
- The Clinical Directors utilizing the scarce resource will then meet to harmonize priorities across ICs and establish a single prioritized list for use of the scarce resource.
- The Clinical Directors utilizing the scarce resource will then work with the Clinical Center's department chief and section chief responsible for the scarce resource to accommodate as many protocols as possible, paying particular attention to patient recruitment goals, recent and projected usage data and assuring that new user ICs and early career investigators get special consideration.
- Final priority for on-going studies will also ensure ethical issues are respected, particularly with regard to the potential termination of trials in which human subjects have already been enrolled.
- Protocols that receive a priority score below the resource capacity will be put in a queue for future review and ICs will be encouraged to use off-site resources to support these protocols.
- The IC Directors' subcommittee on protocol prioritization will adjudicate issues that may arise and make recommendations for funding mechanisms to expand (or decrease) as appropriate.

Evaluation of the prioritization process will be done by surveying the ICs after two years to assure highly meritorious protocols using scarce resources have been supported, tracking access to scarce resources by tenure track and other early carrier investigators, and tracking access by new user ICs.

Ongoing Scientific Reviews

Most clinical protocols remain active for more than a year and some for many years. To assure that protocols are on schedule to meet their milestones and the quality of science remains high as the environment of science evolves it is necessary to have ongoing reviews of protocols. Ongoing scientific reviews will be in the form of annual and quadrennial merit reviews. The ongoing reviews should be tailored to the nature of the protocol (e.g. clinical trial, natural history, training, etc.).

Annual Merit Review

Annual merit reviews evaluate protocol progress, identify problems, assure overseers that the project is on course, and if not, why not and what is being done to get it back on track. These reviews should assess resource commitment, and study progress (e.g. recruitment of subjects, toxicity, and continued importance) and be conducted in concert with the annual human subject's review when feasible. Annual

lab chief's protocol. Participation by members of the lab/branch and IC are encouraged to foster local engagement in the clinical research enterprise and to increase awareness of possible collaborations among intramural investigators. A written report signed by the Chair of the reviewing entity (who may be the Clinical Director), should summarize each review and become part of the protocol documentation.

Quadrennial Merit Review

Quadrennial merit reviews will be detailed, in-depth scientific reviews at least every four years, which consider the scientific justifications for continuation of the protocol. These scientific reviews are in addition to ongoing data monitoring and review of patient recruitment and are analogous to the extramural competitive scientific reviews of ongoing clinical trials and long-term observational studies that occur every 3-5 years. Quadrennial merit reviews are based on principles such as: Is this still the right study to do? Is this the right group to do it? Are the investigators using the best methods? Should it be continued? The quadrennial merit reviewers must include external subject matter experts, appropriately constituted with clinical investigators; clearance of conflict of interest of external consultants must be obtained using a recommended short certification form (https://oir.nih.gov/sites/default/files/uploads/sourcebook/documents/review_science/conflict_of_interest-bsc_reviews.pdf). A written report should summarize each review and be made available to the relevant Board of Scientific Counselors.

General Principles for Annual and Quadrennial reviews

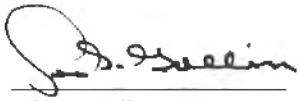
- Scientific timeliness and merit for continuation based on innovation, impact, significance and scientific approach.
- Determination of whether the study has reached its endpoints or shown futility.
- Is recruitment occurring and appropriate?
- Are the methods and approaches still appropriate?
- Is the project feasible, achievable and appropriate given the levels of IC and CC resource allocation?
- Is this project still aligned with the laboratory/branch, IC and NIH research goals?
- Have discoveries in the field significantly altered the direction or need for this protocol?
- For multi-center studies are the plans to add or drop enrollment centers, as needed, appropriate?

Routing of Scientific Reviews

Scientific reviews must be routed through the NIH electronic protocol management system and become part of the protocol package maintained by the NIH Office of Protocol Services. They are advisory to the IC leadership and the NIH Associate Director for Clinical Research.

Opportunity for Appeal of Scientific Review Outcome

Investigators may appeal the outcome of scientific review if they have information that would potentially alter the outcome or if they feel the process was not conducted appropriately. Appeals will be directed to the sponsoring IC's leadership (Clinical Director/Scientific Director). If after the initial appeal there are felt to be problems with how the review was conducted subsequent appeal can be made to the NIH Associate Director for Clinical Research.



5/24/17

John I. Gallin, MD Date
Associate Director for Clinical Research
Chief Scientific Officer, Clinical Center

5/25/17

Francis S. Collins, MD, Ph.D. Date
Director

Appendix 1– Guidelines for Scientific Reviewer Comments for Initial Scientific Review of Protocol

Protocol Title:_____
Principal Investigator:_____ **Reviewer**:_____

Type of Support:

- o Intramural
- o CRADA (specify)_____
- o Industry (specify)_____
- o Foundation (specify) _____
- o Bench to bedside award_____
- o U01 grant_____
- o Other_____

1. Scientific Merit/Background and Rationale. The protocol addresses an important problem or critical barrier to progress in the field.

- o Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____
_____

2.Objectives. Clearly stated specific aims aligned with well-defined endpoints and appropriate study design.

- o Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____
_____

3.Design. Clearly describes how study objectives will be achieved, methods to recruit patients, acquire data, and strategies to overcome anticipated barriers are defined. Addresses randomization, minimization of bias, patient follow up and masking/blinding (if applicable).

- o Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____
_____

4.Subject Eligibility Criteria. Specific inclusion/exclusion requirements and stratification factors (if applicable). Study populations (size, gender, age, and demographic group) are well defined and justified.

- o Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____

_____

5.Disease Community Engagement. Process for including disease community engagement (research subject) in study design and process for timely feedback to subject volunteers of study results and conclusions presented.

- Rating: _____ (0 Poor, 5 Outstanding)

Comment:_____
_____
_____

6.Outcome Characteristics and Endpoint Definitions. Clearly defined primary and secondary endpoints/outcomes. Note that for some natural history studies this element may not be appropriate.

- Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____
_____

7.Statistical Analysis and Sample Size. Appropriate and adequate study design statistical analysis plan. Prospective analysis plan, including sample size justification to achieve study objectives to minimize missing data. Note that for some natural history studies this element may not be appropriate.

- Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____
_____

8.Data monitoring. Practices and procedures to manage data analysis, quality, cleaning and storage well defined. Process for sharing data defined.

- Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____
_____

9.Muli-Center studies. Protocol describes capability of conducting study at the proposed sites with an appropriate organizational structure and, for studies with international sites, there is adequate description of the potential complexities for executing the clinical trial in these sites..

- Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____
_____

10.Principal Investigator Qualifications. Has the necessary skills, experience, time and resources to ensure that the study can be successfully completed, including identification of personnel to provide statistical computations and statistical expertise.

- Rating: _____ (0 Poor, 10 Outstanding)

Comment:_____
_____

_____

11. Plan to register protocol and report outcome data in clinicaltrials.gov.

- o Rating: _____ (0 Poor, 5 Outstanding)

Comment:_____
_____
_____

OVERALL ASSESSMENT RATING: _____(0 Poor, 10 Outstanding)

(Sum scores for all relevant elements and divide by the number of elements; if elements #5 and #11 are used they get half weight).

Comment:_____
_____
_____

RECOMMENDATION:

- o Return to PI with comments
- o Forward to IRB for consideration
- o Forward to IRB with comments

SUMMARY STATEMENT: Summarize below, at end of the committee discussion, what changes you request or questions you want conveyed to the PI.

Comment:_____
_____
_____

Appendix 2

Criteria for Prioritization of Cell Processing Protocols That Receive High Priority Scientific Review by ICs

Score each element as indicated: Scores will be added. Highest score indicates high ranking.

	Priority Score Range
Category I: Resource Requirements	
a. Whether protocol requires products that cannot be outsourced or would be cost-prohibitive to outsource. (10 = cannot be outsourced, 1 = easily outsourced)	1-10
b. Low level of complexity and resources required to meet cell processing, storage of cell products and other needs. (3 = low complexity, 1 = high complexity)	1-3
c. Relatively low number of patients to meet power analysis requirements (if number of patients required for study exceeds 100 a compelling reason for implementation needed given resource and time requirements). (10 = few patients, 1 high number of patients)	1-10
d. Duration to completion. (Brief=5, Indefinite=1)	1-5
Category II: Potential Impact of Proposed Research (ratings by ICs):	
a. High IC Scientific review scores from ICs (Outstanding=10; Excellent=5; Good=1)	1-10
b. Uniqueness of research (first in human or novel variants to existing approaches, not being studied elsewhere, not duplicative or confirmatory) (10 = first in human/NIH appropriate, 1 = "me too" project)	1-10
c. Address a critical public need/question (10 = critical/needed, 1 = not critical)	1-10
d. Optimally done at the CC; uses existing cohorts of CC patients and or special CC technologies. (5 = optimized for CC, 1 = not a great fit for CC)	1-5
e. Broad applicability – outcomes likely to develop a platform technique which impacts multiple diseases/organ systems spanning multiple ICs. (10 = broad applicability, 1 = narrow applicability)	1-10
f. If protocol successful, outcomes are likely to help move product closer toward FDA approval (i.e. provide evidence to help de-risk a new product for later commercialization). (3 = likely to lead to FDA approval, 1 = not likely)	1-3
Category III: Other factors including impact on CC research portfolio and intramural clinical research community as well as collaborators.	

a. *Principal Investigator*- Proposed research by newly recruited PI, tenure track or Asst.Clinical Investigators (10 = junior PI, 5 = mid-career, 1 = late career) 1-10

b. *Sponsor*- Sponsored by IC not yet using cell processing resources 1-5

c. *Leverage*- Leverages CRADA partners, including industry, which bring resources without skewing scope of facility (3 = outside resources, 1 = internal resources) 1-3

d. *Partners*- Partners with AMCs to bring intellectual/other resources 1-5

e. *Novelty value*. New capacity or resource added to CC 1-5