

**University of California, San Francisco
Helen Diller Family Comprehensive Cancer Center**

PRMS Site Committee Selection Policy

PRMS Procedure for Identifying Appropriate Site
Committee(s) for Review

Purpose

Per NCI guidance for Comprehensive Cancer Centers, it is particularly important for Centers involved in clinical research to establish a mechanism for assuring adequate internal oversight of the conduct of all cancer clinical trials in the institution or institutions that formally comprise the Center. The focus of the Protocol Review and Monitoring System (PRMS) is on *scientific merit, priorities and progress* of the clinical research in the Center. The PRMS has the authority to open protocols that meet the scientific merit and scientific priorities of the center and to close protocols that do not demonstrate adequate scientific progress.

PRMS responsibilities at this institution are carried out on two separate levels to ensure optimal oversight of progress and performance. There is initial review by the applicable Site Committee or Committees followed by independent review by the Protocol Review Committee (PRC). The purpose of this policy is to document the process whereby appropriate Site Committee authority and oversight of a trial is determined.

Procedures

Every protocol must have one Site Committee designated as the responsible site committee. In some cases, input from other Site Committees may be required, as outlined in this policy. **The PRC has the authority to request additional Site Committee reviews other than those outlined below.** However, the designated Site Committee always holds review and monitoring authority over the protocol and is responsible for the conduct of all procedures outlined in the PRMS Site Committee Review Policy, as well as any additional responsibilities outlined below. The designated Site Committee is responsible for protocol development, review, monitoring, and conduct [i.e., Protocol Project Manager (PPM) and Clinical Research Coordinator (CRC) support is the responsibility of the designated site committee]. Disagreement as to the appropriate assignment of a protocol to a specific site committee, or requests for exceptions to these rules by a Principal Investigator (PI) or site committee will be adjudicated by the Cancer Center Clinical Research Oversight Committee (CCCROC).

1. Disease-Specific Protocols

Interventional protocols focused on only one disease type are the purview of the relevant disease-specific Site Committee wherever one exists, unless they meet the criteria for one of the modality-specific Site Committees below. E.g., a phase 3 melanoma treatment protocol which is not using immunotherapy, radiation, radionuclides or imaging is the responsibility of the Cutaneous Oncology Site Committee. In some situations, an organ-specific site committee may have purview over more than one organ site in the relevant system. For example, a protocol designed to treat patients with both gastric and colorectal cancer would be the responsibility of the Gastrointestinal Site Committee, and a protocol designed to treat subjects with both kidney and bladder cancer is the responsibility of the Genitourinary Site Committee.

Any trial reviewed and managed by a disease-specific Site Committee which includes therapeutic non-radiopharmaceutical radiation must also adhere to the Radiation Oncology Site Committee review criteria outlined in Section D below.

2. Modality-Specific Protocols

Modality-specific protocols refer to studies conducted by one of the modality-specific Site Committees (see below), and may involve a single disease, or may be **disease agnostic**, i.e., enroll subjects from two or more disease types *not* overseen by the same Site Committee. The modality-specific Site Committees are:

- Cancer Immunotherapy Program (CIP) Site Committee
- Experimental Therapeutics Program (ETP) Site Committee
- Supportive Care Site Committee
- Radiation Oncology Site Committee
- Molecular Imaging and Radionuclide Therapy Site Committee

A. Cancer Immunotherapy Trials

Cancer Immunotherapy protocols are defined as those protocols with interventions either comprised of, or designed to target, immune cells; and/or whose major mechanistic component entails the study of an intervention's effect on the immune system.

Some cancer immunotherapy trials will be overseen by the CIP Site Committee, others by a disease-specific Site Committee, or by the ETP Site Committee as outlined below. The site committee with primary responsibility for the trial must review the trial according to requirements laid out in the PRMS Site Committee Review Policy.

Any trial reviewed and managed by the CIP Site Committee which includes therapeutic non-radiopharmaceutical radiation must also adhere to the Radiation Oncology Site Committee review criteria outlined in Section D below.

i. Disease Agnostic Immunotherapy Trials

All immunotherapy trials that are disease agnostic (i.e., target enrollment of 2 or more cancer types) and that meet one of the following criteria will be overseen by the CIP

- Immunotherapy treatment-intensive* trials (e.g., adoptive transfer of immune cells, study leukaphereses, Chimeric Antigen Receptor [CAR] trials)
- Immunotherapy immune monitoring-intensive* trials (e.g., serial biopsies, neoadjuvant studies)
- First in human and Phase 1 immunotherapy trials

* The identification of a protocol as “immune monitoring-intensive” or “treatment-intensive” will be made at the time of protocol review in the CIP Site Committee, with involvement of the study PI and representatives of the relevant disease-specific Site Committee(s). If agreement cannot be reached as to whether the study is or is not “intensive”, the matter will be referred to the CCCROC for adjudication.

Review process:

- Formal Full Committee review, approval and prioritization by the CIP Site Committee
- AND**
- Input from a member of each relevant disease-specific Site Committee regarding feasibility for enrollment (e.g., competing trials, patient availability) and agreement to participate in the study. The member may be that Site Committee’s chair, co-chair, or a representative who sits on the CIP Site Committee. That member’s verbal or written agreement *must* be obtained by the CIP Site Committee Chair or Co-Chair and documented on the Chair or Co-Chair Summary of Review form.
 - Formal scientific review of these protocols at each relevant Site Committee is not required, but can be undertaken at the discretion of the relevant Site Committee Chair.
 - In trials with multiple disease cohorts, every effort should be made to open as many of these cohorts as possible. However, if any individual Site Committee chooses to not participate in such a trial because of competing trials or concerns about feasibility, the study may still be opened by the CIP, provided other relevant Site Committee(s) have agreed to support it, and the PRC Chair feels that accrual and scientific goals are not impacted.
 - The CIP will have responsibility for the conduct of these trials.
 - Any trial which includes therapeutic non-radiopharmaceutical radiation must also adhere to the Radiation Oncology Site Committee review criteria outlined in Section D below.

ii. Single-Disease Immunotherapy Trials

In general, these trials will be under the purview of the disease-specific Site Committee, EXCEPT when any one of the following three criteria are met, in which case the CIP will have oversight of the trial:

- First in human and Phase 1 immunotherapy trials
- Immunotherapy treatment-intensive* trials (e.g., adoptive transfer of immune cells, study leukaphereses, Chimeric Antigen Receptor [CAR] trials)
- Immunotherapy immune monitoring-intensive* trials (e.g., serial biopsies, neoadjuvant studies)
- The CIP Site Committee can choose to decline a single disease immunotherapy trial that otherwise meets criteria for review by CIP, if it determines that the study is more appropriately conducted by the relevant disease-specific site committee, e.g., for safety reasons. This process requires a written notification by the CIP Site Committee Chair or co-Chair to the PRC, and written approval by PRC Chair or co-Chair.

* The identification of a protocol as “immune monitoring-intensive” or “treatment-intensive” will be made at the time of protocol review in the CIP Site Committee, with involvement of the study PI and/or representatives of the relevant disease-specific Site Committee(s). If agreement cannot be reached as to whether the study is or is not “intensive”, the matter will be referred to the CCCROC for adjudication.

Review process for trials under the purview of CIP:

- Formal Full Committee review, approval and prioritization by the CIP Site Committee.
- AND**
- Formal prioritization and Expedited review and approval by the relevant disease-specific Site Committee, as per the PRMS Site Committee Review Policy (i.e., one Expedited review form and one Chair/Co-Chair Summary of Review form). The principle goal of this review is to assess the study for feasibility (patient availability), and prioritization within the research portfolio of the disease-specific Site Committee.
 - All remaining responsibilities of the designated Site Committee as outlined in the PRMS Site Committee Review Policy (e.g., protocol amendment reviews, accrual and safety reviews) apply *only* to the CIP Site Committee.
 - The PI (or designee), and a CIP Site Committee CRC will attend the relevant disease-specific Site Committee meetings to provide updates for as long as patients remain on study.
 - Any trial which includes therapeutic non-radiopharmaceutical radiation must also adhere to the Radiation Oncology Site Committee review criteria outlined in Section D below.

B. Experimental Therapeutics Trials

Three working groups housed *within* the ETP Site Committee will review relevant trials: 1) Phase I trials; 2) Genetic Syndrome (inherited disease) trials (e.g., BRCA); and 3) Phase II and higher “basket trials”, i.e., any disease agnostic trials that do *not* require the expertise of the Genetic Syndrome working group and do *not* fall under the oversight of the CIP.

i. Disease Agnostic Experimental Therapeutics Program Trials

These trials include:

- Disease agnostic non-immunotherapy trials (all phases)
- Protocols that involve use of an immunotherapeutic agent with published phase 2 or higher safety data, together with a non-immunotherapeutic investigational agent will be reviewed in the ETP Site Committee, with input provided as needed by the CIP Site Committee

Review process:

- Formal Full Committee review, approval and prioritization by the ETP Site Committee
- AND**
- Input from a member of *each* relevant disease-specific Site Committee regarding feasibility for enrollment (e.g., competing trials, patient availability) and agreement to participate in the study. The member may be that Site Committee’s chair, co-chair, or a representative who sits on the ETP Site Committee. That member’s verbal or written agreement *must* be obtained by the CIP Site Committee Chair or Co-Chair and documented on the Chair or Co-Chair Summary of Review form.
 - Formal scientific review of these protocols at each relevant Site Committee is not required, but can be undertaken at the discretion of the relevant Site Committee Chair.
 - In trials with multiple disease cohorts, every effort should be made to open all or as many of these cohorts as possible. However, if any individual Site Committee chooses to not participate in such a trial because of competing trials or concerns about feasibility, the study may still be opened by the ETP, provided other relevant Site Committee(s) have agreed to support it, and the PRC Chair feels that accrual and scientific goals are not impacted.
 - The ETP will have responsibility for the conduct of these trials.
 - Any trial which includes therapeutic non-radiopharmaceutical radiation must also adhere to the Radiation Oncology Site Committee review criteria outlined in Section D below.

ii. Single-Disease Experimental Therapeutics Program Trials

In general, these trials will be under the purview of the disease-specific Site Committee, EXCEPT when one of the following criteria are met, in which case the ETP Site Committee will have oversight over the trial:

- First in human non-immunotherapy trials
- Phase I trials with non-immunotherapeutic investigational agents (alone or in combination) that do not have safety data from prior trials,
- Non-immunotherapeutic Phase I trials requiring intensive PK/PD monitoring (defined as PK/PD analyses requiring greater than [$>$] 2 consecutive days or greater than [$>$] 4 samples at any one visit)
- Protocols that involve use of an immunotherapeutic agent with published phase 2 or higher safety data, together with a non-immunotherapeutic investigational agent will be reviewed in the ETP Site Committee, with input provided as needed by the CIP Site Committee
- The ETP Site Committee can choose to decline a single disease ETP trial that otherwise meets criteria for review by ETP, if it determines that the study is more appropriately conducted by the relevant disease-specific site committee, e.g., for safety reasons. This process requires a written notification by the ETP Site Committee Chair or co-Chair to the PRC, and written approval by PRC Chair or co-Chair.

Review process for trials under the purview of ETP:

- Formal Full Committee review, approval and prioritization by the ETP Site Committee.
- AND**
- Formal prioritization and Expedited review and approval by the relevant disease-specific Site Committee, as per the PRMS Site Committee Review Policy (i.e., one Expedited review form and one Chair/Co-Chair Summary of Review form). The principle goal of this review is to assess the study for feasibility (patient availability), and prioritization within the research portfolio of the disease-specific Site Committee.
 - All remaining responsibilities of the designated Site Committee as outlined in the PRMS Site Committee Review Policy (e.g., protocol amendment reviews, accrual and safety reviews) apply *only* to the ETP Site Committee.

- If the trial is under the purview of the ETP, the Principal Investigator (or designee), and a ETP Site Committee CRC will attend the relevant disease-specific Site Committee meetings to provide updates for as long as patients remain on study.
- Any trial which includes therapeutic non-radiopharmaceutical radiation must also adhere to the Radiation Oncology Site Committee review criteria outlined in Section D below.

C. Supportive Care Trials

Protocols designed to maximize comfort, minimize side effects, or mitigate against a decline in the participant's health or function (i.e., not intended to cure a disease), such as symptom management, palliative care and/or survivorship, are the purview of the Supportive Care Site Committee.

i. Disease Agnostic Supportive Care Trials Review Process

- Formal Full Committee review, approval and prioritization by the Supportive Care Site Committee
- AND**
- Input from a member of *each* relevant disease-specific Site Committee regarding feasibility for enrollment (e.g., competing trials, patient availability) and agreement to participate in the study. The member may be that Site Committee's chair, co-chair, or a representative who sits on the Supportive Care Site Committee. That member's agreement *must* be obtained by the Supportive Care Site Committee and documented on the Chair or Co-Chair Summary of Review form.
 - Formal scientific review of these protocols at each relevant Site Committee is not required, but can be undertaken at the discretion of the relevant Site Committee Chair.
 - In trials with multiple disease cohorts, every effort should be made to open all or as many of these cohorts as possible. However, if any individual Site Committee chooses to not participate in such a trial because of competing trials or concerns about feasibility, the study may still be opened by the Supportive Care Site Committee, provided other relevant Site Committee(s) have agreed to support it, and the PRC Chair feels that accrual and scientific goals are not impacted.
 - The Supportive Care Site Committee will have responsibility for the conduct of these trials.

ii. Single-Disease Supportive Care Trials Review Process

These trials will be under the purview of the disease specific site committee. The disease specific site committee will be responsible for the review, approval,

prioritization, and conduct of these trials. Input from the Supportive Care Site Committee is recommended but not required.

D. Radiation Oncology Trials

Radiation oncology protocols are defined as those protocols with interventions involving any form of non-radiopharmaceutical radiation intended to have therapeutic or palliative properties against cancer, either alone or in combination with systemic therapy (either approved therapies such as hormonal manipulations, chemotherapy, or immunotherapy, **or** investigational therapies where the investigational pharmacy is used and/or IND safety reporting is required).

Some radiation oncology trials will be overseen by the Radiation Oncology (RO) Site Committee, while other trials will be under the purview of a disease-specific or modality-specific Site Committee, as outlined below. The site committee with primary responsibility for the trial must review the trial according to *all* requirements laid out in the PRMS Site Committee Review Policy.

i. Standard of Care Radiation Therapy Trials Combined with Experimental Systemic Therapies

All standard of care radiation trials combined with any form of experimental systemic agents (including chemotherapy) and having no radiation-therapy endpoints will be overseen by either the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee if it meets any applicable criteria (see 2.A. and 2.B. above), **or** the relevant disease-specific Site Committee if it does not meet CIP or ETP criteria.

The review process for these trials is outlined below:

- Formal Full Committee review, approval and prioritization by the disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee.
- AND**
- A Supplemental Site Committee Review form completed by the Radiation Oncology (RO) Site Committee.
 - The disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee will have responsibility for research management of these trials.

ii. Experimental Radiation Therapy Trials Combined with Experimental Systemic Therapies

All experimental radiation trials combined with any form of experimental systemic agents (including chemotherapy) will be overseen by either the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee if

it meets any applicable criteria (see 2.A. and 2.B. above), **or** the relevant disease-specific Site Committee if it does not meet CIP or ETP criteria.

The review process for these trials is outlined below:

- Formal Full Committee review, approval and prioritization by the disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee.
- AND**
- Formal Full Committee review, approval and prioritization by the Radiation Oncology (RO) Site Committee.
 - The disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee will have responsibility for research management of these trials.

iii. Experimental Radiation Therapy Trials Alone or Combined with Standard of Care Systemic Therapies

All experimental radiation trials with no accompanying systemic agents, and those combined with any form of standard of care systemic agents (including chemotherapy), will be overseen by the Radiation Oncology (RO) Site Committee.

The review process for these trials is outlined below:

- Formal Full Committee review, approval and prioritization by the Radiation Oncology (RO) Site Committee.
- AND**
- Input from a member of each relevant disease-specific Site Committee regarding feasibility for enrollment (e.g., competing trials, patient availability) and agreement to participate in the study. The member may be that Site Committee's chair, co-chair, or a representative who sits on the Radiation Oncology (RO) Site Committee. That member's agreement *must* be obtained by the Radiation Oncology (RO) Site Committee and documented on the Chair or Co-Chair Summary of Review form.
 - Formal scientific review of these protocols at each relevant Site Committee is not required, but can be undertaken at the discretion of the relevant Site Committee Chair.
 - In trials with multiple disease cohorts, every effort should be made to open as many of these cohorts as possible. However, if any individual Site Committee chooses to not participate in such a trial because of competing trials or concerns about feasibility, the study may still be opened by the Radiation Oncology (RO) Site Committee, provided other relevant Site Committee(s) have agreed to support it, and the PRC Chair feels that accrual and scientific goals are not impacted.

- The Radiation Oncology Site Committee will have responsibility for conduct of these trials.

E. Molecular Imaging and Radionuclide Therapy Trials

Imaging protocols are those using diagnostic imaging or one or more radioactive agents for diagnostic purposes only, with no therapeutic intent. Radionuclide therapy protocols are defined as protocols using one or more radioactive agents to either treat a malignancy, or to determine a specific treatment as defined within the protocol.

Some molecular imaging and radionuclide therapy trials will be overseen by the Molecular Imaging & Radionuclide Therapy Site Committee, while other trials will be under the purview of a disease-specific or modality-specific Site Committee, as outlined below. The site committee with primary responsibility for the trial must review the trial according to *all* requirements laid out in the PRMS Site Committee Review Policy.

i. Molecular Imaging and Radionuclide Therapy Trials with Therapeutic Intent with or without Experimental Systemic Therapies

All trials using an imaging or radiopharmaceutical (radionuclide) agent(s) with therapeutic intent, regardless of whether or not it is combined with any form of experimental systemic agents (including chemotherapy), will be overseen by either the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee if it meets any applicable criteria (see 2.A. and 2.B. above), **or** the relevant disease-specific Site Committee if it does not meet CIP or ETP criteria. Therapeutic intent includes both trials where the radiopharmaceutical is used to directly treat the cancer as in radioligand therapy, and also refers to trials where a molecular imaging agent is used to determine a specific treatment as defined within the protocol.

The review process for these trials is outlined below:

- Formal Full Committee review, approval and prioritization by the disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee.
- AND**
- A Supplemental Site Committee Review form completed by the Molecular Imaging and Radionuclide Therapy Site Committee.
 - The disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee will have responsibility for research management of these trials.

ii. Imaging Trials with no Therapeutic Intent Alone or Combined with Standard of Care Systemic Therapies

All trials using molecular imaging with no therapeutic intent and with no accompanying systemic agents, and those combined with any form of standard of care systemic agents

(including chemotherapy), will be overseen by the Molecular Imaging and Radionuclide Therapy Site Committee.

The review process for these trials is outlined below:

- Formal Full Committee review (or Expedited, as applicable), approval and prioritization by the Molecular Imaging and Radionuclide Therapy Site Committee.
AND
- Input from a member of *each* relevant disease-specific Site Committee regarding feasibility for enrollment (e.g., competing trials, patient availability) and agreement to participate in the study. The member may be that Site Committee's chair, co-chair, or a representative who sits on the Molecular Imaging and Radionuclide Therapy Site Committee. That member's agreement *must* be obtained by the Molecular Imaging and Radionuclide Therapy Site Committee and documented on the Chair or Co-Chair Summary of Review form.
- The Molecular Imaging and Radionuclide Therapy Site Committee will have responsibility for research management of these trials.

iii. Imaging Trials with no Therapeutic Intent Combined with Experimental Systemic Therapies

All trials using molecular imaging with no therapeutic intent but combined with any form of experimental systemic agents (including chemotherapy) will be overseen by either the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee if it meets any applicable criteria (see 2.A. and 2.B. above), **or** the relevant disease-specific Site Committee if it does not meet CIP or ETP criteria.

The review process for these trials is outlined below:

- Formal Full Committee review, approval and prioritization by the disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee.
AND
- A Supplemental Site Committee Review form completed by the Molecular Imaging and Therapy Site Committee.
- The disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee **or** the Experimental Therapeutics Program (ETP) Site Committee will have responsibility for research management of these trials.

Adjudication

The CCCROC will adjudicate any disputes regarding responsibility.

Other Cross-Cutting Site Committees

The Pediatric Oncology/Pediatric Leukemia Site Committee will be the “default” responsible Site Committee for all protocols involving minors. Any other criteria in this policy will not apply if minors are involved – unless the Pediatric Oncology/Pediatric Leukemia Site Committee declines responsibility. If they do, that should be documented and provided to the PRC.

Any other cross-cutting or disease-type agnostic protocols not covered by the above Site Committees will be brought to the CCCROC for assignment to a Site Committee. Should the need arise for future establishment of new disease agnostic Site Committees, similar principles to those above will be utilized. New Site Committee establishment is overseen by the CCCROC as noted in the PRMS Site Committee Membership Policy.

Alternate Procedure

None.


Policy Approval

This policy document was approved by the following personnel on the following dates:



Eric Small, MD
Deputy Director,
Helen Diller Family Comprehensive Cancer Center

10.10.19
Date



Alan Ashworth, PhD
President,
Helen Diller Family Comprehensive Cancer Center

22nd Oct 2019
Date

**University of California, San Francisco
Helen Diller Family Comprehensive Cancer Center**

Policy Revision Summary of Changes

Policy Title: PRMS Site Committee Selection Policy
Version Date: September 12, 2019
Version Number: Revision 3

Notes: Page number corresponds to page number in updated version (Revision 3).
New text in modified paragraphs is shown as ***bold italics*** and deleted text is shown as ~~strikethrough~~.

Page No.: All pages		Section: Footer
Original Text	Revision 2 05/01/2019	
New Text	Revision 23 059/012 /2019	
Reason for Change	To reflect updated version number and date.	

Page No.: 1	Section: Procedures
Original Text	Every protocol must have one Site Committee designated as the responsible site committee. In some cases, input from other Site Committees may be required, as outlined in this policy. The PRC has the authority to request additional Site Committee reviews other than those outlined below. However, the designated Site Committee always holds review and monitoring authority over the protocol and is responsible for the conduct of all procedures outlined in the PRMS Site Committee Review Policy, as well as any additional responsibilities outlined below. The designated Site Committee is responsible for protocol development, review, monitoring, and conduct [i.e., Protocol Project Manager (PPM) and Clinical Research Coordinator (CRC) support is the responsibility of the designated site committee]. Disagreement as to the appropriate assignment of a protocol to a specific site committee, or requests for exceptions to these rules by a Principal Investigator (PI) or site committee will be adjudicated by the Cancer Center Clinical Research Oversight Committee (CCCROC).
New Text	Every protocol must have one Site Committee designated as the responsible site committee. In some cases, input from other Site Committees may be required, as outlined in this policy. The PRC has the authority to request additional Site Committee reviews other than those outlined below. However, the designated Site Committee always holds review and monitoring authority over the protocol and is responsible for the conduct of all procedures outlined in the PRMS Site Committee Review Policy, as well as any additional responsibilities outlined below. The designated Site Committee is responsible for protocol development, review, monitoring, and conduct [i.e., Protocol Project Manager (PPM) and Clinical Research Coordinator (CRC) support is the responsibility of the designated site committee]. Disagreement as to the appropriate assignment of a protocol to a specific site committee, or requests for exceptions to these rules by a Principal Investigator (PI) or site committee will be adjudicated by the Cancer Center Clinical Research Oversight Committee (CCCROC).
Reason for Change	Sentence regarding PRC's authority to request additional Site Committee reviews outside of what's written in the policy was changed to Bold for increased emphasis.

Page No.: 2	Section: Procedures 1. Disease-Specific Protocols
Original Text	Interventional protocols focused on only one disease type are the purview of the relevant disease-specific Site Committee wherever one exists. E.g., a protocol with eligibility criteria limited to subjects diagnosed with melanoma is the responsibility of the Cutaneous Oncology Site Committee. In some situations, an organ-specific site committee may have purview over more than one organ site in the relevant system. For example, a protocol designed to treat patients with both gastric and colorectal cancer would be in the purview of the Gastrointestinal Site Committee, and a protocol designed to treat subjects with both kidney and bladder cancer is the responsibility of the Genitourinary Site Committee.
New Text	Interventional protocols focused on only one disease type are the purview of the relevant disease-specific Site Committee wherever one exists, <i>unless they meet the criteria for one of the modality-specific Site Committees below.</i> E.g., a <i>phase 3 melanoma treatment</i> protocol <i>which is not using immunotherapy, radiation, radionuclides or imaging</i> with eligibility criteria limited to subjects diagnosed with melanoma is the responsibility of the Cutaneous Oncology Site Committee. In some situations, an organ-specific site committee may have purview over more than one organ site in the relevant system. For example, a protocol designed to treat patients with both gastric and colorectal cancer would be in the <i>responsibility</i> purview of the Gastrointestinal Site Committee, and a protocol designed to treat subjects with both kidney and bladder cancer is the responsibility of the Genitourinary Site Committee.
Reason for Change	Added clarification to this section to make it clear that single-disease protocols only go to the disease-specific Site Committee <i>provided</i> they do not meet any modality-specific Site Committee criteria; used the newly formed Molecular Imaging and Radionuclide Therapy modality Site Committee as an example.

Page No.: 10	Section: Procedures 2. Modality-Specific Protocols E. Molecular Imaging and Radionuclide Therapy Trials
Original Text	Imaging protocols are those using one or more radioactive agents for diagnostic purposes only, with no therapeutic intent. Radionuclide therapy protocols are defined as protocols using one or more radioactive agents to treat a malignancy.
New Text	Imaging protocols are those using <i>diagnostic imaging or</i> one or more radioactive agents for diagnostic purposes only, with no therapeutic intent. Radionuclide therapy protocols are defined as protocols using one or more radioactive agents to <i>either</i> treat a malignancy, <i>or to determine a specific treatment as defined within the protocol.</i>

Reason for Change	Expanded the definition for imaging protocols to allow for protocols using imaging modalities such as MRI. Expanded the definition for molecular therapy protocols to include the nuances referenced in the Chair or Co-Chair Summary of Review form.
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Page No.: 10	Section: Procedures 2. Modality-Specific Protocols E. Molecular Imaging and Radionuclide Therapy Trials i. Molecular Imaging and Radionuclide Therapy Trials with Therapeutic Intent with or without Experimental Systemic Therapies
Original Text	i. Molecular Imaging and Radionuclide Therapy Trials with Therapeutic Intent All trials using an imaging or radiopharmaceutical (radionuclide) agent(s) with therapeutic intent will be overseen by either the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee if it meets any applicable criteria (see 2.A. and 2.B. above), or the relevant disease-specific Site Committee if it does not meet CIP or ETP criteria. Therapeutic intent includes both trials where the radiopharmaceutical is used to directly treat the cancer as in radioligand therapy, and also refers to trials where a molecular imaging agent is used to determine a specific treatment as defined within the protocol.
New Text	i. Molecular Imaging and Radionuclide Therapy Trials with Therapeutic Intent <i>with or without Experimental Systemic Therapies</i> All trials using an imaging or radiopharmaceutical (radionuclide) agent(s) with therapeutic intent, <i>regardless of whether or not it is combined with any form of experimental systemic agents (including chemotherapy)</i> , will be overseen by either the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee if it meets any applicable criteria (see 2.A. and 2.B. above), or the relevant disease-specific Site Committee if it does not meet CIP or ETP criteria. Therapeutic intent includes both trials where the radiopharmaceutical is used to directly treat the cancer as in radioligand therapy, and also refers to trials where a molecular imaging agent is used to determine a specific treatment as defined within the protocol.
Reason for Change	Added a reference to experimental systemic therapies in order to clarify that any use of radionuclide agents with therapeutic intent, with or without experimental systemic therapy, is subject to the same requirements. Revised the header to reflect the same.

Page No.: 10		Section: Procedures 2. Modality-Specific Protocols E. Molecular Imaging and Radionuclide Therapy Trials ii. Imaging Trials with No Therapeutic Intent Alone or Combined with Standard of Care Systemic Therapies
Original Text	ii. Imaging Trials with no Therapeutic Intent All trials using molecular imaging with no therapeutic intent will be overseen by the Molecular Imaging and Radionuclide Therapy Site Committee.	
New Text	ii. Imaging Trials with no Therapeutic Intent <i>Alone or Combined with Standard of Care Systemic Therapies</i> All trials using molecular imaging with no therapeutic intent <i>and with no accompanying systemic agents, and those combined with any form of standard of care systemic agents (including chemotherapy)</i> , will be overseen by the Molecular Imaging and Radionuclide Therapy Site Committee.	
Reason for Change	Added clarification to make clear that all imaging modalities either used alone, or with standard of care systemic therapies, are subject to the same requirements. Revised the header to reflect the same.	

Page No.: 11		Section: Procedures 2. Modality-Specific Protocols E. Molecular Imaging and Radionuclide Therapy Trials iii. Imaging Trials with No Therapeutic Intent Combined with Experimental Systemic Therapies
Original Text	None.	

<p>New Text</p>	<p>iii. Imaging Trials with no Therapeutic Intent Combined with Experimental Systemic Therapies</p> <p>All trials using molecular imaging with no therapeutic intent but combined with any form of experimental systemic agents (including chemotherapy) will be overseen by either the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee if it meets any applicable criteria (see 2.A. and 2.B. above), or the relevant disease-specific Site Committee if it does not meet CIP or ETP criteria.</p> <p>The review process for these trials is outlined below:</p> <ul style="list-style-type: none"> • Formal Full Committee review, approval and prioritization by the disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee. <p style="text-align: center;">AND</p> <ul style="list-style-type: none"> • A Supplemental Site Committee Review form completed by the Molecular Imaging and Therapy Site Committee. • The disease-specific Site Committee, the Cancer Immunotherapy Program (CIP) Site Committee or the Experimental Therapeutics Program (ETP) Site Committee will have responsibility for research management of these trials.
<p>Reason for Change</p>	<p>Added new text to include instructions on how to handle potential imaging trials with no therapeutic intent but which are combined with experimental systemic therapies.</p>

<p>Page No.: 12</p>	<p>Section: Procedures Other Cross-Cutting Site Committees</p>
<p>Original Text</p>	<p>None.</p>
<p>New Text</p>	<p>The Pediatric Oncology/Pediatric Leukemia Site Committee will be the “default” responsible Site Committee for all protocols involving minors. Any other criteria in this policy will not apply if minors are involved – unless the Pediatric Oncology/Pediatric Leukemia Site Committee declines responsibility. If they do, that should be documented and provided to the PRC.</p>
<p>Reason for Change</p>	<p>Added new paragraph to clarify that the Pediatric Oncology/Pediatric Leukemia Site Committee will always oversee studies involving minors; any disease-specific or modality-specific criteria outlined in this policy will not apply to such studies.</p>