RTOG Radiation Therapy Oncology Group	**PHASE I, I/II, or II < 100 PATIENTS CTEP (TREATMENT) TRIAL** **DEVELOPING CONCEPT**
Date of Submission	
Title of LOI	
Phase of Study	
Other Institutions/Groups on Study	
Principal Investigator's Name	
Affiliation and Street Address	
Phone and Fax Numbers	
E-mail Address	
Co-Chairs and their affiliations	
Agent(s) supplied by NCI	
Commercial Agents in Study	
Tumor Type	Solid Tumor ___ Hematologic Malignancy (NOS) ___ Disease-Specific (Specify): _____ _____ _____
Performance Status	
Abnormal Organ Function Permitted (Y/N)?	
Prior Therapy	

SCHEMA:

STRATIFY		**REGISTER**	**or**	**RANDOMIZE**	

RATIONALE/HYPOTHESIS: [100 words or less]

LABORATORY CORRELATES:

PRIMARY OBJECTIVE:

SECONDARY OBJECTIVE(S):

HYPOTHESIZED DIFFERENCE YOUR PROPOSED TREATMENT WILL MAKE:

TO WHAT TREATMENT WILL YOUR PROPOSED TREATMENT BE COMPARED?:

PROTOCOL TREATMENT PLAN:

TO DOCUMENT ACCRUAL RATE, LIST TRIALS WITH PATIENTS WHO HAD SIMILAR TUMOR TYPE/PHASE OF STUDY/PRIOR THERAPY:

Protocol Number/Title/Sponsor (*include NCI# if applicable)*	Trial Activation Date	Trial Completion Date	No. Patients Enrolled

LIST ALL ACTIVE, APPROVED, OR IN REVIEW STUDIES AT YOUR INSTITUTION FOR WHICH THIS PATIENT POPULATION WILL BE ELIGIBLE:

Protocol Number/Title/Sponsor (*include NCI# if applicable*)	Trial Activation Date	Anticipated Trial Completion Date	No. Patients Enrolled to Date	Enrollment Start Date	Anticipated Enrollment End Date	Duration of Patient Enrollment (Months)	Total planned Patient Enrollment (at LOI-relevant sites only)

IF STUDY INCLUDES RT:

- Specify type of image data submission required: [If electronic data, specify optical disk, CD, DAT, DVD; or specify hardcopy data (film)]:
- Specify the imaging modalities utilized for this study:
- Specify if a radiologist and/or other medical expert will perform image evaluation as a part of this study. If yes, specify who will do the reviews:

IS INVOLVEMENT OF the AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK (ACRIN) PROPOSED?

Yes___ No___

If yes:

- Does the Study Chair want ACRIN to collect/archive images? Yes___ No___
- Is the Study Chair also interested in scientific partnership with ACRIN (in which ACRIN investigators have an imaging objective/endpoint and would be responsible for analyzing and publishing data)? Yes___ No___
- Has the Study Chair identified a funding source for ACRIN involvement? Yes___ No___
- If yes, specify the funding_____
- Has contact with ACRIN been made by the Study Chair(s)? Yes___ No___
- If yes, provide contact's name_____

CORRELATIVE STUDIES/SPECIAL OPERATIONAL REQUIREMENTS:

Does the study include **central laboratory review of biomarker(s)**? Yes___ No___

If yes, please list biomarker(s):

If yes, at what point is analysis needed:

Prior to registration___
After registration but prior to treatment___
Other___

If yes, provide any additional information:

PHASE I, I/II, or II < 100 PATIENTS CTEP (TREATMENT) TRIAL DEVELOPING CONCEPT (Continued)

Does the study include a **translational research component**? Yes___ No___
If yes, please provide additional information:

Does the study include a **QOL and/or Outcomes component**? Yes___ No___
If yes, please provide additional information about the objective(s) and possible assessments:

If the study includes a translational research and/or QOL component, does the Study Chair plan to submit a request for BIQSFP funding with the NCI concept/LOI? (BIQSFP funding is for translational research and/or QOL components that are **integral** to the study design (i.e. needed for eligibility or stratification) or **integrated** into the study design (i.e. a major study endpoint depends upon analysis of the component for confirmation of a hypothesis; the component is not hypothesis generating.)
Yes___ No___

Does the study include **neurocognitive function assessment**? Yes___ No___
If yes, please provide additional information:

Does the study include **other special operational requirements**? Yes___ No___
If yes, please identify:

If the study includes correlative studies or special operations, please identify any funding sources (e.g., RO1s, pharmaceutical support) other than BIQSFP funding (e.g. RO1s, pharmaceutical support): _____

RT PRESCRIPTION WORKSHEET

Check one or more item(s) within each category as appropriate.

1. Treatment equipment:
   ☐ Linear accelerator ☐ Tomotherapy ☐ CyberKnife ☐ Gamma Knife
   ☐ Protons ☐ Scatter beam ☐ Scan beam

2. Planning technique:
   ☐ 3D Conformal RT
   ☐ IMRT
   ☐ Both 3D-CRT and IMRT
   ☐ 2D (drawn field outlines using patient anatomy)
   ☐ CyberKnife using inverse treatment planning
   ☐ Gamma Knife using multiple isocenters

3. Describe the proposed prescription method:
   Will sub-regions within the target receive different doses (i.e. “dose painting”)? ☐ Y ☐ N ☐ TBD

   Is it possible to have separate target regions that are not connected? ☐ Y ☐ N ☐ TBD

   Will a boost be used to treat some sub-regions to a higher dose? ☐ Y ☐ N ☐ TBD

   Will this boost be treated simultaneously with the lower dose regions? ☐ Y ☐ N ☐ TBD

   Will 3D-CRT be used followed by IMRT for boost? ☐ Y ☐ N ☐ TBD

4. Proposed Prescribed Dose Coverage:
   Prescribe to a point ☐ Y ☐ N ☐ TBD

   Prescribe to the PTV periphery (selected isodose line touches surface) ☐ Y ☐ N ☐ TBD

   Prescribe to a fixed percentage of the PTV ☐ Y ☐ N ☐ TBD

   What is the % volume of the PTV included? _____%
   Will this % volume remain the same for all the PTVs listed below? ☐ Y ☐ N ☐ TBD

   If No, please elaborate _____

   Will your protocol use IGRT that is integrated into the treatment unit or in-room process? ☐ Yes ☐ No

   Will the use of IGRT be a protocol requirement? ☐ Mandatory ☐ Optional

   Will the use of IGRT be linked to margin reduction? ☐ Yes ☐ No
   Proposed PTV margin without IGRT: _____mm
   Proposed PTV margin with IGRT: _____mm

   Which forms of IGRT will you allow?
   ☐ Integrated cone-beam CT
   ☐ kV
   ☐ MV
   ☐ In-room helical CT (e.g. CT on rails)
   ☐ Tomotherapy
   ☐ 2D kV imaging
   ☐ 2D MV imaging

   Do you intend to use routine repeat imaging (after initial imaging but before treatment) to verify the positioning of treatment fields? ☐ Yes ☐ No

5. Do you intend to use diagnostic imaging as an IGRT method for adapting treatment after an initial course decreases the tumor size?

   ☐ Yes, please elaborate. _____ ☐ No

6. Do you intend to check each institution's treatment approach using any of the following techniques? Check one or more:
   ☐ PI review of sample or benchmark case treatment plan before any patients are entered on the protocol
   ☐ PI review of first patient's treatment plan as a rapid review turnaround
   ☐ PI review of institution's contouring for first case
   ☐ Other (please explain) _____

7. What data do you need for your case review?
   Note: Data submission and archiving is automatic for all 3D and IMRT protocols.
   ☐ Simulation CT
   ☐ Structure contours
   ☐ Dose distributions

7a. Would you like to obtain raw IGRT image data for your review? ☐ Y ☐ N

The comment sections below are completed by RTOG HEADQUARTERS

RESPONSIBLE COMMITTEE:

STATISTICS COMMENTS:

ESTIMATED SAMPLE SIZE:

DATA MANAGEMENT COMMENTS:

RT QUALITY ASSURANCE COMMENTS:

This is an ATC study Yes_____ No_____ RTOG applicable studies:

If RT QA identifies the study as an ATC study, the PA will e-mail the concept sheet to RTOG Physics for feedback.

PHYSICS COMMENTS: [PA: Use the "RTOG Physics Distribution" list in the RTOG mail system]

ACRIN COMMENTS: [PA: If ACRIN involvement proposed, forward to Charles Apgar for review]

HSRO CHAIR'S COMMENTS: [PA: If QOL/Outcomes component, forward to Deb Bruner for review]

CONTRACTS:
Questions to be answered by the Contracts staff for all studies with a drug component and/or intended corporate support:

A. PHARMACEUTICAL SUPPORT
☐ N/A

☐ There will be pharmaceutical support for this study requested as follows:

Company	Agent Provided	Funding

B. INVESTIGATIONAL NEW DRUG (IND)
☐ N/A

The IND will be held by: ☐ Pharma; ☐CTEP/PMB; ☐ RTOG cross file

The individuals at the pharmaceutical company responsible for:

Cross file letter:
Name:
Title:
Mailing Address:
Phone/Fax:
E-mail:

APPROVAL SECTION: Documented by the Protocol Associate

SITE CHAIR APPROVAL:
Date:

RESEARCH STRATEGY DECISION:
Date:

PHASE I, I/II, or II < 100 PATIENTS CTEP (TREATMENT) TRIAL DEVELOPING CONCEPT (Continued)

The purpose of the RTOG developing concept is to gather feedback concerning the proposed trial from RTOG Headquarters and other reviewers and to obtain approval for development of the study from the appropriate sponsoring committee and from the RTOG Research Strategy Committee.

Submitting the Concept Sheet: The Study Chair(s) will e-mail the completed protocol concept sheet (as an e-mail attachment) to the appropriate Protocol Associate, as follows:

***Note**: For all phases of symptom management, cancer prevention, or late effects trials, please follow instructions for the "DCP All Phase Concept Form" on the RTOG web site.*

- Brain: Kathryn Okrent, kokrent@acr.org
- Breast, GYN, GI: Courtney Conroy, cconroy@acr.org
- GU: Dana Robinson, drobinson@acr.org
- Head & Neck, Lung, Sarcoma: Linda Walters-Page, lwalters@acr.org

Concept Process:

- The Director of Protocol Development and Regulatory Compliance (PDRC), e-mails the Disease Site Chairs to provide the date of the next Research Strategy Committee meeting (6 weeks in advance of the meeting) and gives them 3 weeks to submit RTOG developing concepts to the appropriate Protocol Associate (PA).
- The PA circulates the concepts received to the appropriate HQ disease site team, RTOG Contracts, RTOG Physics/RTQA (and ACRIN if appropriate) and the Health Services and Research Outcomes (HSRO) Chair (if a QOL/Outcomes component is identified) for review and feedback (2 week turnaround) and then e-mails the concept with the comments to the appropriate Site Chair for review (1 week turnaround), with a copy to the Study Chair.
- The Site Chair e-mails his/her approval of the concept to the appropriate PA(see above) OR will e-mail the concept to the Study Chair(s) for further discussion.
- The PA e-mails any concepts approved by a Site Chair to the Director of PDRC, who distributes the concept to the RTOG Research Strategy Committee for review in the Committee's next scheduled conference call.
- The PA assigns an RTOG protocol number to concepts approved by the Research Strategy Committee and then e-mails the Study/Site Chairs concerning the development and submission of an NCI LOI or concept.

NOTE: The Research Strategy Committee may defer a decision on the developing concept if the Study or Site Chair (or designee) does not participate in the conference call or if comments from the Team Statistician have not been received.

RTOG Radiation Therapy Oncology Group	PHASE II>100, II/III, or III CTEP (TREATMENT) TRIAL DEVELOPING CONCEPT

I. ADMINISTRATIVE

Date of Submission

Title of Concept:

Study Chair Name:

Study Chair Address:

Study Chair Phone:

Study Chair Fax:

Study Chair E-mail:

Co-chairs and their affiliations:

II. Phase of Study

Specify phase of this study:

2 □ **3** □ **2/3** □

III. PHARMACEUTICAL SECTION

Specify the agent(s) to be used in the study:

Agent Name	Request for CTEP/PMB-distribution?	Is the agent Investigational?	Placebo Controlled?
	[ ]Yes [ ]No	[ ]Yes [ ]No	[ ]Yes [ ]No
	[ ]Yes [ ]No	[ ]Yes [ ]No	[ ]Yes [ ]No
	[ ]Yes [ ]No	[ ]Yes [ ]No	[ ]Yes [ ]No
	[ ]Yes [ ]No	[ ]Yes [ ]No	[ ]Yes [ ]No

If CTEP is being requested to distribute any agents not under a CTEP IND, provide the reason for the request for each agent.

IV. SCIENCE SECTION

1. Specific hypotheses:

2. Objectives:

   2.1 Primary objective:

   2.2 Secondary objective(s):

3. Background Information: [300-1500 words]. This section should include the following:

   3.1 Rationale for selected approach and trial design.

   3.2 Discuss why this trial is important (include summary of clinical issues and competing study questions relevant to the trial setting) and potential impact on, for example, overall survival, quality of life or advances in proof of biologic principles. Also, how would research strategy or future clinical practice be altered by either positive or negative results?

   3.3 Relevant data (include phase 1-3 trial results, and any pilot or confidential data from companies that justify the use of the control and experimental arms).

4. Eligibility (include rationales for selecting or excluding particular cohorts):

5. Arms/Regimens (include schema):

   5.1 Schema

   5.2 Arms/Regimens

6. Feasibility:

   6.1 Competing trials in RTOG:

   6.2 Competing trials in other U.S. or International Groups:

   6.3 Competing industry studies of which you are aware:

V. EMBEDDED CORRELATIVE STUDY SECTION (if applicable)

(Companion laboratory or imaging studies or quality of life studies)

[NOTE: NCI requires completion of this section for NCI concept sheet; see section below for additional details RTOG HQ requires]

1. Correlative study title:

1.1 Correlative study design (to include methods for obtaining samples, administering forms, or performing radiologic studies):

1.2 Specific hypotheses (include relevant background studies):

2.1 Correlative study design (to include methods for obtaining samples, administering forms, or performing radiologic studies):

2.2 Specific hypotheses (include relevant background studies):

CORRELATIVE STUDIES/SPECIAL OPERATIONAL REQUIREMENTS:

Does the study include **central laboratory review of biomarker(s)**? Yes___ No___

If yes, please list biomarker(s):

If yes, at what point is analysis needed:

Prior to registration___
After registration but prior to treatment___
Other___

If yes, provide any additional information:

Does the study include a **translational research component**? Yes___ No___

If yes, please provide additional information:

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Yes___ No___

Does the study include **neurocognitive function assessment**? Yes___ No___

If yes, please provide additional information:

Does the study include **other special operational requirements**? Yes___ No___

If yes, please identify:

If the study includes correlative studies or special operations, please identify any funding sources other than BIQSFP funding (e.g. RO1s, pharmaceutical support):_____

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3. Describe the proposed prescription method:
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Will 3D-CRT be used followed by IMRT for boost? ☐ Y ☐ N ☐ TBD

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Prescribe to a point ☐ Y ☐ N ☐ TBD

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Prescribe to a fixed percentage of the PTV ☐ Y ☐ N ☐ TBD

What is the % volume of the PTV included? _____%
Will this % volume remain the same for all the PTVs listed below? ☐ Y ☐ N ☐ TBD

If No, please elaborate _____

Will your protocol use IGRT that is integrated into the treatment unit or in-room process?	☐ Yes ☐ No
Will the use of IGRT be a protocol requirement?	☐ Mandatory ☐ Optional
Will the use of IGRT be linked to margin reduction?	☐ Yes ☐ No
	Proposed PTV margin without IGRT: _____mm
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Which forms of IGRT will you allow?	☐ Integrated cone-beam CT ☐ kV ☐ MV
	☐ In-room helical CT (e.g. CT on rails)

	☐ Tomotherapy
	☐ 2D kV imaging
	☐ 2D MV imaging
Do you intend to use routine repeat imaging (after initial imaging but before treatment) to verify the positioning of treatment fields?	☐ Yes ☐ No

5. Do you intend to use diagnostic imaging as an IGRT method for adapting treatment after an initial course decreases the tumor size?

   ☐ Yes, please elaborate. _____ ☐ No

6. Do you intend to check each institution's treatment approach using any of the following techniques? Check one or more:
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7. What data do you need for your case review?
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   ☐ Structure contours
   ☐ Dose distributions

7a. Would you like to obtain raw IGRT image data for your review? ☐ Y ☐ N

IS INVOLVEMENT OF the AMERICAN COLLEGE OF RADIOLOGY IMAGING NETWORK (ACRIN) PROPOSED?
Yes___ No___

If yes:
- Does the Study Chair want ACRIN to collect/archive images? Yes___ No___
- Is the Study Chair also interested in scientific partnership with ACRIN (in which ACRIN investigators have an imaging objective/endpoint and would be responsible for analyzing and publishing data)? Yes___ No___
- Has the Study Chair identified a funding source for ACRIN involvement? Yes___ No___
- If yes, specify the funding:
- Has contact with ACRIN been made by the Study Chair(s)? Yes___ No___

If yes, provide contact's name:

COMMENT SECTION: COMPLETED BY RTOG HEADQUARTERS

STATISTICS COMMENTS:

ESTIMATED SAMPLE SIZE:

DATA MANAGEMENT COMMENTS:

RT QUALITY ASSURANCE COMMENTS:

This is an ATC study Yes_____ No_____ RTOG applicable studies:

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ACRIN COMMENTS: [PA: If ACRIN involvement proposed, forward to Charles Apgar for review]

HSRO CHAIR'S COMMENTS: [PA: If QOL/Outcomes component, forward to Deb Bruner for review]

CONTRACTS:
Questions to be answered by the Contracts staff for all studies with a drug component and/or intended corporate support:

A. PHARMACEUTICAL SUPPORT
☐ N/A

☐There will be pharmaceutical support for this study requested as follows:

Company	Agent Provided	Funding

B. INVESTIGATIONAL NEW DRUG (IND)
☐ N/A

The IND will be held by: ☐ Pharma; ☐CTEP/PMB; ☐ RTOG cross file

The individuals at the pharmaceutical company responsible for:

Cross file letter:
Name:
Title:
Mailing Address:
Phone/Fax:
E-mail:

VII. APPROVAL SECTION: Documented by the Protocol Associate

SITE CHAIR APPROVAL:
Date:

RESEARCH STRATEGY DECISION:
Date:

PHASE II>100, II/III, or III CTEP (TREATMENT) TRIAL DEVELOPING CONCEPT (Continued)

The purpose of the RTOG developing concept is to gather feedback concerning the proposed trial from RTOG Headquarters and other reviewers and to obtain approval for development of the study from the appropriate sponsoring committee and from the RTOG Research Strategy Committee.

Submitting the Concept Sheet:
The Study Chair(s) will e-mail the completed protocol concept sheet (as an e-mail attachment) to the appropriate Protocol Associate, as follows:

Note: For all phases of symptom management, cancer prevention, or late effects trials, please follow instructions for the "DCP All Phase Concept Form" on the RTOG web site.

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- Breast, GYN, GI: Courtney Conroy, cconroy@acr.org
- GU: Dana Robinson, drobinson@acr.org
- Head & Neck, Lung, Sarcoma: Linda Walters-Page, lwalters@acr.org

Concept Process:

- The Director of Protocol Development and Regulatory Compliance (PDRC), e-mails the Disease Site Chairs to provide the date of the next Research Strategy Committee meeting (6 weeks in advance of the meeting) and gives them 3 weeks to submit RTOG developing concepts to the appropriate Protocol Associate (PA).
- The PA circulates the concepts received to the appropriate HQ disease site team, RTOG Contracts, RTOG Physics/RTQA (and ACRIN if appropriate) and the Health Services and Research Outcomes (HSRO) Chair (if a QOL/Outcomes component is identified) for review and feedback (2 week turnaround) and then e-mails the concept with the comments to the appropriate Site Chair for review (1 week turnaround), with a copy to the Study Chair.
- The Site Chair e-mails his/her approval of the concept to the appropriate PA (see above) OR will e-mail the concept to the Study Chair(s) for further discussion.
- The PA e-mails any concepts approved by a Site Chair to the Director of PDRC, who distributes the concept to the RTOG Research Strategy Committee for review in the Committee's next scheduled conference call.
- The PA assigns an RTOG protocol number to concepts approved by the Research Strategy Committee and then e-mails the Study/Site Chairs concerning the development and submission of an NCI LOI or concept.

NOTE: The Research Strategy Committee may defer a decision on the developing concept if the Study or Site Chair (or designee) does not participate in the conference call or if comments from the Team Statistician have not been received.

RTOG Radiation Therapy Oncology Group	**Instructions for Completing the Concept Form** **PHASE I, I/II, II, II/III, or III** **CCOP/SYMPTOM MANAGEMENT COMMITTEE DEVELOPING CONCEPT FORM**

Submitting the Concept Sheet to RTOG: The Study Chair(s) will e-mail the completed protocol concept sheet (as an e-mail attachment) to the CCOP/Symptom Management Steering Committee Chairs Deborah Watkins Bruner (wbruner@nursing.upenn.edu), Lisa Kachnic (Lisa.Kachnic@bmc.org), or Lawrence Berk (Lawrence.Berk@moffitt.org).

RTOG CCOP/Symptom Management Committee Concept Approval Process:

- **Concept approval may be a multistep process** depending on the stage of development of the concept. Study Chairs who want to submit a concept early, prior to full development, to obtain feedback and guidance from the committee may submit for this process. However, fully developed concepts must have a full review prior to approval and NCI submission even if partially developed concepts have been previously reviewed. *[Note: Details that are not required for preparation of the concept for Study Chairs who want to submit a concept early, prior to full development, are denoted by an asterisk (*) in the appropriate areas below.]*
- Drs. Bruner, Kachnic, and Berk will forward the concept to at least four external reviewers (content, PRO, TRP, and CCOP) and to the RTOG CCOP/Symptom Management Statistician. Concepts will be reviewed at the January or June RTOG meeting or via conference call in between face-to-face meetings as needed.
- Concept review will follow the NCI Symptom Management and HRQOL Steering Committee review criteria (see Appendix I).
- The CCOP/Symptom Management Committee Chair(s) will communicate the decisions made during the review (e.g., approval; revise and resubmit; disapproval) to the Study Chair:

  1) Approval with or without recommendations: The Committee approves the concept and does not need to evaluate a revised concept. The concept will be presented to RTOG Research Strategy for approval and if approved will be revised based on recommendations (as appropriate) before submission to the NCI Symptom Management and HRQOL Steering Committee.

  2) Revise and resubmit: The committee has determined that the concept requires additional information or has design issues that can be addressed within the next three months and asks that the investigators address that information in a revised concept. "Revise and resubmit" can also be used to indicate that the committee has determined that the concept as written lacks adequate scientific merit or has problems with feasibility, but that relatively modest changes to the study design might address these concerns.

  3) Disapproval: The committee has determined that the concept as written is not feasible and/or lacks adequate scientific merit, and that the changes necessary to address these concerns would result in a study that is substantially different from the study proposed. A future concept from the investigators for such a **"substantially different"** study would be accepted as a new concept for review. "Disapproval" can also indicate that preclinical/early phase studies do not exist to support conduct of the proposed phase II or III trial, in which case a "substantially similar" concept would be accepted as a new concept for review if accompanied by compelling results from relevant preclinical/early phase studies.
- Approved concepts will move forward for further development and presentation to the RTOG Research Strategy Committee.

PHASE I, I/II, II, II/III, or III

CCOP/SYMPTOM MANAGEMENT COMMITTEE
DEVELOPING CONCEPT

Content of Concepts Submitted for Review by the NCI Community Oncology and Prevention Trials Research Group

The concept is the investigator's opportunity to demonstrate that the proposed research answers an important question that will lead to improved clinical care, prevention of cancer, or treatment of precancerous lesions; that the methods and analysis are appropriate to evaluate the research question(s); and that the research is feasible. The concept needs to complete appropriate internal processes at the Research Base before submission to the Division of Cancer Prevention.

NOTE: Some concepts submitted to the Community Oncology and Prevention Trials Research Group are also reviewed by the *Symptom Management and Quality of Life Steering Committee (SxQOL)*. Those concepts are for randomized clinical trials with at least 100 subjects with the objective of preventing or alleviating a medical condition associated with cancer or its treatment. All concepts, including those that will also be reviewed by the steering committee, should follow the guidelines in this document.

The purposes of the concept are to:

- provide basic information to establish the scientific rationale for the proposed study
- describe the value of the study in producing information that will be clinically relevant for cancer symptom management and/or quality of life
- propose clear study objectives and hypotheses
- provide a brief description of the study design and methodology
- provide evidence of the feasibility of recruiting to and conducting a successful study*
- describe the statistical methods to address the primary questions/outcomes.*

*[*Note: This information is not required for preparation of the concept for Study Chairs who want to submit a concept early, prior to full development.]*

Concepts do not need to include consent forms or case report forms. They should, however, include copies of all assessment tools.

All concept proposals are recommended to be 5-7 pages, but cannot be longer than 10 pages. This does not include the title page, schema and references. Submission of appendix materials, other than assessment tools, is discouraged.

The following provides an outline for the concept proposal. All concepts should include the information listed below, as applicable.

Concept Requirements Outline

I. Title page:
Title of study:

Date of document:

Concept Number:

Principal Investigator's Name:

Institution:

Address:

Phone Number:

Fax Number:

E-mail Address:

Full name of research base submitting the study: Radiation Therapy Oncology Group

Co-Chairs and their affiliations:

II. Schema: This one page diagram provides an overview of the study design. A schema that includes eligibility criteria, dose and schedule for intervention, and timing of assessments will aid review.

III. Background

A. Rationale for Proposed Study:
The background is one of the most important sections of the concept and often accounts for the bulk of the concept document. It provides the reviewers with relevant information supporting the rationale for the proposed study. The scientific justification should include a focused review of relevant literature with citations covering significance of the condition to be studied, current knowledge of etiology and pathophysiology, a limited review of studies that have contributed information applicable to the proposed study, and a brief summary of pilot or preliminary data. The background should make the argument that the proposed research is a logical next step in the development of a clinical intervention. The scientific justification for an observational study should include the reason the information is required and the use of that information for developing interventions for cancer prevention and control.

B. Significance of the Study:

The background section should clearly state how the proposed research will further science in cancer prevention, symptom management, and/or quality of life. This should include a brief discussion of the potential clinical utility of the intervention. For example, the investigator should provide evidence that the measurement tool is sufficiently sensitive to detect a clinically important difference. Also, measures of the number needed to treat (NNT) to see an effect or a description of the degree of improvement that a patient would experience, may be relevant to include. Observational studies should describe the gaps in current knowledge and how increasing the knowledge base will facilitate development of interventions.

IV. Study objective(s) and hypotheses

Clearly state all primary and secondary objectives.

V. Study methods

The study design section will outline how the objectives/primary endpoints will be met. This section is a succinct description of the study design and intervention plan, and includes the study population and eligibility criteria, outcome measures, timing of data collection, sample size, and power calculations for the primary study outcomes.* *[Note: study population, eligibility criteria, outcome measures, timing of data collection, sample size, and power calculations are not required for preparation of the concept for Study Chairs who want to submit a concept early, prior to full development.]*

- If the primary outcome is a patient reported outcome (PRO) it is imperative that the PI map the specific intervention to the specific domain or domains in the PRO. For example, it is unacceptable to say that an intervention will improve HRQOL. A specific discussion of how the intervention will improve specific aspects or domains of HRQOL or specific patient-reported symptoms is required.
- Preliminary data on the mechanism of action of an intervention in the population of interest is highly recommended.

In addition, please include the following information as specified by the type of intervention/agent.

A. If a drug treatment trial:

1. Give dose and schedule for intervention together with justification (or potential doses/schedules of agent[s])

2. Identify provider of drug(s), if determined

3. Specify if the drug is currently available to the research base for the trial.

4. If agents are being requested from DCP, provide a listing of each agent by name and NSC number.

5. State whether it is expected that the study will be conducted under an IND.

B. If complementary and alternative medicine agent:

1. Specify probable manufacturer of the product to be used. Include history of company's involvement in clinical trials.

2. Provide information on quality control, shelf life, lot-to-lot variability.

3. Discuss availability of agent in the marketplace.

4. Make a strong argument for the choice of the selected product (e.g. standardization process, use in clinical trials for other indications, preclinical data). Provide pilot data with use of same agent if available.

5. For botanical agents, provide documentation verifying the authenticity of the product and include a plan for obtaining independent analysis to insure that there are no contaminating substances or drugs.

C. If a behavioral intervention is planned:

1. Briefly describe the intervention.

2. Include a brief discussion of the availability of resources in the CCOP setting (e.g. staff, facilities, equipment) to implement the intervention.

3. Provide justification for the proposed control group (if applicable).

D. If study includes biomarker endpoints:

1. Briefly describe the type of biomarker or intended application of the biomarker(s) (risk biomarker, surrogate endpoint biomarker,etc.). Note that biomarkers are not limited to assays of biologic materials but could include fat-free mass, gait speed, blood pressure, etc.

2. Describe the biological material to be analyzed (analyte) and the mode of accessing it, clearly delineating the degree of invasiveness of any procedures.

3. Briefly describe the analytic platforms to be used to assess the proposed biomarkers and the statistical tests that will be applied to the data generated on these platforms. Also, describe the reliability of these technologies for analyzing the proposed biomarkers.

4. Provide justification of the use of the biomarker(s) in the context of the proposed study; cite prior data in support of proposed biomarker application(s). These prior data may come from studies addressing similar clinical issues (e.g. prevention of a given cancer or a set of symptoms) that employed these biomarkers, showing them to add meaningful information on outcomes.

E. If study includes patient reported outcomes (PRO):

1. Describe need for PRO and whether it provides better information than other potential endpoints or complements information obtained from other data.

2. Provide rationale for selection of PRO, to include appropriateness in proposed population, use in previous trials, and psychometric properties.

3. As with all other data collection, justify schedule for data collection and use of data.

VI. Feasibility

Provide data to support the anticipated accrual rate for the proposed target population and the level of interest expressed by the CCOP/MBCCOPs. Provide similar information for studies that will depend predominantly or entirely on participation by academic centers. Address the compatibility of protocol complexity with CCOP resources. List other studies, open or in development, that might compete for patients eligible for this study. Describe the previous experience of the investigators relevant to successful conduct of similar studies. If the study will involve costs in addition to data management, briefly describe them and include a source of funding.

VII. References

VIII. APPROVAL SECTION: ***Documented by CCOP/Symptom Management Committee Chair***

CCOP/SYMPTOM MANAGEMENT CHAIR APPROVAL:
Date:

Appendix I: Concept Evaluation Guidelines and Evaluation Form
GUIDELINES FOR CONCEPT EVALUATORS

These are the NCI Symptom Management and HRQOL review criteria that the RTOG CCOP/Symptom Management Committee will use in the review of your concept prior to voting to approve, revise, or disapprove your concept.

A concept is the investigator's statement demonstrating that the proposed research answers an important question that will lead to improved clinical care, that the methods and analysis are appropriate to evaluate the research question, and that the research is feasible. The primary purpose of the review is to determine whether the concept provides convincing evidence that the study can achieve these goals.

The concept proposal describes a research study systematically so that the review can determine whether the concept has sufficient merit to proceed to the development of a full protocol. Thus, the concept form submitted by the proposed investigators will not have the extensive detail regarding the study design, recruitment, or statistical analyses, for example, as you would find in a complete protocol. Concept review is designed to save investigators time in preparing a complete study protocol on research ideas that are not judged to have sufficient background information to determine the scientific basis for the study, may not be feasible to complete in a community setting, and/or are not a major priority of the Division of Cancer Prevention (DCP)/National Cancer Institute (NCI) given budgetary restrictions and competing research concepts/protocols.

What a concept must contain, and what you are to evaluate the concept on, are the following criteria:

o rationale for the study and its scientific basis

o study's clinical value

o objectives and hypotheses

o appropriateness of the planned study design and analysis plan***** *[Note: This information is not required for preparation of the concept for Study Chairs who want to submit a concept early, prior to full development.]*

o feasibility of conducting the proposed study in multisite, cooperative group institutions and community medical practices.

Concepts are limited to no more than 10 pages, with a recommendation to limit the submission to 5-7 pages. This is to keep the focus of the concept on the scientific basis, the study objectives and hypotheses, and basics of the proposed study design. A restriction on page length means that many details cannot be included in the concept. For example, most concepts will not require text describing the pharmacodynamics of the agent. However, investigators are expected to include important information about an intervention, such as a brief description of the rationale for the dose and schedule, along with documentation regarding availability of the agent for the proposed study.

Please keep the distinctions between a concept and a full protocol in mind when you are completing your review and writing your critique.

CONCEPT EVALUATION FORM

Evaluator's Name:

Date of Evaluation Meeting:

Concept ID Number and Title:

PHASE I, I/II, II, II/III, or III
CCOP/Symptom Management Committee Developing Concept Form

Concept PI Name:

1. **Scientific Rationale** (e.g., How well do the descriptions of current state of knowledge; and adequacy of preclinical and clinical data support the rationale for the study?)

2. **Value of the Research Question in Contributing to Overall Patient Management** (Is the study likely to make a meaningful contribution to patient care or survivorship? Is the research question novel? Is the research question duplicative and/or being appropriately addressed in other research forums? Are the interventions being tested generally applicable to substantial numbers of cancer patients and/or survivors?)

3. **Study Objectives and Hypotheses** (Are the study objectives clear, appropriate, and measurable?)

4. **Study Methodology (including study design, statistical design/QOL measures/etc.)** (Are the study design and intervention plan [study sample, eligibility criteria, outcome measures, timing of data collection, sample size, and power calculations for the primary study outcomes] appropriate for providing information required for addressing the study objectives and hypotheses?)

5. **Feasibility of Conducting the Study in the CCOP Network** (Do previous experience or evidence of the investigators' ability to conduct the intervention support the likelihood of achieving the proposed accrual rates and study duration as specified in the Concept? Have the investigators addressed the issue of compatibility of the intervention and CCOP experience/resources? Is there a source of funding for costs other than data management [e.g. study drug, lab work or behavioral intervention])?

6. **Concept Recommendation (Approval, Revise and Resubmit, or Disapproval)**

Concept recommendation:

1) **Approval with or without recommendations**: The Steering Committee approves the concept and does not need to evaluate a revised concept. The research base can begin to develop the protocol. Certain concept details and minor modifications will be negotiated with the NCI. Major comments from the Steering Committee reviewers may be included in the approval letter sent by DCP to the investigators.

2) **Revise and resubmit**: The Steering Committee has determined that the concept requires additional information or has design issues that can be addressed within the next two to three months and asks that the investigators to address that information in a revised concept. "Revise and Resubmit" can also be used to indicate that the Steering Committee has determined that the concept as written lacks adequate scientific merit or has problems with feasibility, but that relatively modest changes to the study design might address these concerns. The deadline for resubmission will be included in the Consensus Evaluation letter sent to the Research Base/Study PI.

3) **Disapproval**: Concepts should be disapproved when the SC has determined that the concept as written is not feasible and/or lack adequate scientific merit, and that the changes necessary to address these concerns would result in a study that is substantially different from the study proposed. A future concept from the investigators for such a "substantially different" study would be accepted as a new concept for review. "Disapproval" can also indicate that preclinical/early phase studies do not exist to support conduct of the proposed phase II or III trial, in which case a "substantially similar" concept would be accepted as a new concept for review if accompanied by results from relevant early phase studies.

[**Note**: One reason for differentiating between "disapproval" and "revise and resubmit" is to keep the Steering Committee focused on studies that are in active development and require review. A revised concept might be expected for re-review within one to three months, whereas a disapproved concept might require one or more years to conduct early phase studies or to design a new study. Metrics will show shorter time from concept submission to protocol activation if studies with many problems are removed from the queue while they are being redeveloped.]