Tier Reimbursement System for Federally Funded Ancillary Studies in Cooperative Groups Trials

The purpose of this tier reimbursement system for ancillary payments to sites participating in NCI-sponsored clinical trials is to harmonize these payments on Cooperative Group studies that may be federally funded by CTEP, DCP, or other NIH sources. In order to harmonize payments made to sites for participating in ancillary and companion studies (including biospecimen procurement for correlative studies and HRQOL, cancer control and other ancillary studies) along with follow-up payments, each Lead Group will prospectively evaluate their phase III NCI-sponsored studies for the appropriate payment(s) to be made to each participating site, regardless of their Group affiliation. This new system will also cover Intergroup phase II trials. The Lead Group will determine the tier level and recommend the specific dollar amount within a tier range for each study. Reimbursement amounts will initially be decided at the time of protocol approval, but will be reviewed at the time of study activation so that the most recent version of the protocol is appropriately classified. For DCP funded HRQOL and cancer control studies, final determination of the tier level will be made by the NCI in consultation with the Lead Group.

The scope of this document applies to federal funding of ancillary studies and does not address capitation or funding sources for the base payment of treatment studies. While the majority of Group treatment trials have the same base federal capitation payment, there are some studies with registry or screening arms that have been allocated a smaller federal capitation payment for that particular aspect of the study due to the lesser amount of site effort required. As these trials may vary widely as to how much effort is required of the sites, these types of studies are decided on a case by case basis. Each lead Group sets the capitation rate for the screening or registry arms of the trial and discusses the rate with CTEP. Generally the capitation payments have been less for the registry or screening arms as compared to the randomization or treatment arms. Trials with a registry or screening arm that may have a different capitation payment will require enhanced methods of communication to ensure that all Groups, institutions and sites are fully aware of the reimbursement amounts. It is anticipated that the methods of communication developed for the ancillary study reimbursements could also be utilized to assist groups in implementing studies with differential payments based on enrollment to registry/screening arms.

Tier Payment Categories for Ancillary Studies

I. Payments for Correlative Science & Specimen /Imaging Study Submissions

Tier classification for this ancillary study category is based on the type of biospecimen(s) being procured or imaging study being performed, level of difficulty in obtaining and processing the biospecimen(s) or obtaining/interpreting the imaging study, the increased amount of work to explain and consent patients to participate in the correlative studies, and may also be used to optimize enrollment for studies with highly important biospecimen collection that is critical for a scientific objective of the study. Further, some studies may require a one-time biospecimen submission or require serial sampling. Imaging studies can also have a one-time submission

requirement vs. serial scans, and may or may not require specialized equipment and specialized interpretation. Obviously, the level of work at the site and patient involvement varies with these different scenarios. Some biospecimens are collected solely for banking purposes for future studies; while others may involve complex analyses that may be needed prior to patients beginning protocol treatment and may need further work by the site to explain these results to the patient. Protocols may also require pre-registration collection of biospecimens to determine eligibility and/or treatment assignment and these factors may be included in the Lead Group's assessment of protocol tier assignment. Some studies might also require other family members to participate and be consented. An analysis of all these issues will be employed by the Lead Group in determining which "tier" the study will be assigned.

Tier System for Correlative Science & Specimen / Imaging Study Submissions

Tier 1 ($50-250)

A collection of a biospecimen at a single time point, such as blood, serum, urine, sputum, buccal cells (lavage), genital swab etc., or a single research imaging study. This Tier would also include the routine submission of an archival paraffin block in situations where this submission will not affect patient eligibility or treatment assignment. Standard level of effort is needed to describe the specimen collection process/ imaging study, the purpose for the specimen collection/ imaging study, consent study participants, and obtain the specimen/imaging study. Higher dollar amounts within this tier may be used for multiple single-time-point collections of these types of samples or imaging studies (e.g., one sample each of blood and urine, and a single imaging study).

Tier 2 ($250 -400)

A biospecimen collection requiring a higher level of complexity of work to obtain the biospecimen, such as bone marrow, cerebral spinal fluid, tissue biopsy (paraffin block), etc., or a more complex imaging study than tier 1. This Tier could also include the required urgent submission of archival tissue blocks where real-time testing of such submission will affect patient eligibility or treatment assignment. All marrow/tissue samples are collected at the time of a clinically indicated procedure. Standard level of effort needed to describe the specimen collection process/imaging study, the purpose for the specimen collection/ imaging study, and to consent study participants.

Tier 3 ($400-1000)

(I.) A single biospecimen collection from tier 1 AND a single biospecimen collection from tier 2;
(II.) Serial biospecimen sampling required by protocol; or
(III.) A single biospecimen may be required, but procurement is more complex (e.g. fresh frozen tissue). All biospecimens are collected at the time of a clinically indicated procedure.

Typically, this tier will require a higher level of effort to describe the specimen collection process/complex imaging studies, describe the purpose for the specimen collection/imaging studies, consent study participants, and obtain the biospecimen(s)/imaging studies. The coordinating group may elect to use partial payments for studies requiring serial samples, e.g., $200 for the pre-treatment sample and an additional $200 for the post-treatment sample.

Tier 4 ($1000+)

This tier will include correlative studies requiring biospecimen collection or imaging studies outside of clinically indicated procedures, or stand alone biospecimen collection or imaging protocols. An upper limit is not specified as the amount necessary to cover costs of the non-standard of care procedures will vary. Reimbursement in this tier will include an amount to cover the process of the biospecimen collection /imaging studies similar to tiers 1, 2, and 3.

Tier 4 A

Studies requiring additional procedures to obtain biospecimens or imaging studies that are not part of usual/routine clinical care. The informed consent process requires significantly more time and is more challenging to explain the biospecimen collection process or imaging studies, describe the purpose for the biospecimen collection or imaging studies, and to consent study participants due to issues regarding additional procedures to obtain specimens that are not needed for the patient's clinical care. This tier does not include paying the standard or routine clinical costs of the procedure or imaging study itself, even if it is not clinically indicated, unless it is clearly specified.

Tier 4 B

The study is a stand-alone biospecimen collection protocol or stand-alone imaging protocol and collection of patient clinical outcome data is required for the study. The patient may or may not be enrolled on any other CTEP-supported treatment study. Since collection of clinical data, including outcome data, are required, these studies can involve a significant increased amount of work at the site to recruit, consent and collect data from the study participant, in addition to the specialized requirements for obtaining and processing the biospecimen(s) or imaging study.

II. Payments for Follow-Up Data Collection

For each phase III Cooperative Group treatment trial, each Lead Group will prospectively evaluate their studies for the appropriate follow-up payment to be made to each participating site, regardless of their Group affiliation. These payments acknowledge the work of the sites in providing annual follow-up reporting and data submission for all patients still considered "on study". Given that follow-up requirements often change over the course of the study, studies may begin in one tier and move to another as the follow-up requirements decrease over time. Each lead Group should specifically list which tier payment is required during each year for long term studies that may assign varying payments over the life of the study.

Tier System for Follow-Up Payments per Site Accrual:

Tier 1 ($50 per year)

Study requires submission of annual follow-up data for patients on study and this will be the base payment for each accrual in phase III cancer treatment trials that require minimum follow-up. Typically, this would require one follow-up data form, with no more than 2 submissions required per year.

Tier 2 ($100-200 per year)
Study requires moderate increase in level of effort and work at the site to obtain follow-up data, for example, collection and submission of multiple case report forms. Typically, 3-4 reports or forms per year that require a higher level of expertise and effort to obtain the data.

Tier 3 ($200-1000+)
Study requires significant increase in level of effort and work at the site to obtain follow-up data, including collection and submission of a highly complex group of case report forms or more challenging and time consuming work to obtain the needed follow-up data.

- This tier is intended to accommodate long term studies being considered by some groups that require follow up of increased complexity, for example, not only clinical data, but survivorship issues, resource utilization, medical record review, secondary malignancies or late side effects, etc. Requires significant effort to obtain the required data. It is anticipated that a higher amount will be paid for the initial year of enrollment and lesser amounts in subsequent years for these types of studies.

III. Payments for HRQOL, Cancer Control, Health Services, and other Ancillary Studies

These guidelines apply to funding for Health-Related Quality of Life (HRQOL), Patient Reported Outcome (PRO) Assessments and other Ancillary Studies – e.g. health services, epidemiology, psychosocial, and/or behavioral studies-- that are either companion studies to or embedded studies within NCI-CTEP sponsored phase III treatment trials and may also apply to Intergroup phase II studies. These guidelines exclude ancillary studies that are specimen-based or imaging studies.

The NCI's Division of Cancer Prevention (DCP) may assign credit to cancer control companion studies to phase III trials, whether incorporated within the trial or as a stand-alone companion protocol. DCP does not award credit for companion studies to phase I and II trials due to their small sample sizes and lack of comparison groups. For HRQOL ancillary studies, the investigators need to make compelling arguments for including a HRQOL endpoint, selecting the particular study measure, and deciding on the sample size. Appropriate justification and an analytic plan for the collection points should be defined in the protocol document. The studies will be assessed by DCP for their ability to enhance the treatment endpoints and add information regarding the underlying disease or symptoms.

The Lead Group will prospectively evaluate each study in this category for the appropriate payment to be made to each participating site. Tier classification and the dollar amount within the tier will be assigned based upon the merit of the study, the DCP credit assigned (if applicable), the complexity of work necessary to carry out the study at each site, and the site level of effort. For any ancillary study awarded DCP credit, the Lead Group will use the dollar amount as determined by the level of credit awarded. Some studies may include a short, one-time questionnaire. Since these questionnaires require such a limited amount of work at the site, the lead Group may choose neither to consider them for additional ancillary funding nor to rate them according to these tiers.

The tiers below incorporate criteria used by NCI's Division of Cancer Prevention (DCP) to assign credit to an ancillary study (shown in parentheses for each tier). Ranges are provided within each tier to accommodate other federally funded ancillary studies in this category and to provide the Groups with funding flexibility.

Tier System for HRQOL, Cancer Control, Health Services, and other Ancillary Studies

Tier 1 - $100-200 (DCP Tier 1 - 0.1 credit/ $200)

HRQOL, PROs and other data are collected centrally. Work at the sites is limited to fulfilling HIPAA & local IRB requirements, providing names/contact information to those collecting the data and/or entering this data into a database.

Tier 2 - $250-600 (DCP Tier 2- 0.3 credit/ $600)

HRQOL, PROs and other data collected at the site on one or two occasions. The average site involvement time per subject per evaluation point does not exceed 20 minutes. Dollar assignment within this tier will take into account the level of staff assistance required to explain the study. In addition, the level of effort required to conduct the informed consent process and to obtain completed questionnaires would also be considered.

Tier 3 - $600-1000 (DCP Tier 2- 0.5 credit/ $1,000)

HRQOL, PROs and other data are collected at the site on more than two occasions. Alternatively, the average site involvement time per subject per evaluation point exceeds 20 minutes. Dollar assignment within this tier will take into account the level of staff effort required to explain, conduct, and/or implement the study. In addition, the level of effort required to conduct the informed consent process and to obtain completed questionnaires would also be considered. Additional training may be necessary to successfully implement the study or consent the patients. Justification for the amount and timing of data to be collected must be provided.

Tier 4 - $1,000-2,000 (DCP Tier 4 – 1.0 credit/ $2,000)

An intervention for a symptom outcome is included within a phase III treatment trial as a separate primary endpoint; the trial would either have two randomizations or be a factorial design trial that would include one treatment endpoint and one cancer control endpoint. It is expected that the tested cancer control intervention will enhance (e.g. toxicity reduction) the treatment outcome. Completion of the study may require training of sites and/or coordination with the study-coordinating center.

This tier may also be used for registry-type studies that collect data at multiple time points and/or on an ongoing basis in multiple areas of interest, e.g., health care costs, survivorship issues, late complications, etc., and also involve a significant level of effort at the site to consent, collect data, and maintain ongoing contact with participants.

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