MEMORANDUM

TO: Members of the Southwest Oncology Group

FROM: SWOG Operations Office

DATE: April 2009

SUBJECT: Policy Revisions

The following Southwest Oncology Group policies have been revised as summarized below. These and all policies can be viewed and printed from the Group's web site at http://swog.org/Visitors/Policies.asp.

Revision Summations

Policy 2 – Constitutions/Bylaws
The Early Therapeutics Committee is now a subcommittee under Translational Medicine.

The Bone Marrow and Stem Cell Transplantation Committee was moved from a Disease & Research Committee to an Administrative Committee.

The title of the Nurse Oncologist Committee was changed to Nursing Committee.

Policy 13 – Protocol Guidelines
In the Concept Development section on page 5 of the policy, pages 10-12 and 13-17 were deleted.

On page 6, several committee priority slots were changed.

On page 9, revisions in the Post-Activation/Amendment now states:

a. Amendment: A change to the protocol that directly affects patient care or treatment and may substantively increase the patient's risk/benefit ration.
b. Revision: An administrative or editorial change that does not affect patient care of treatment, or a scientific or medical change that does no substantively increase the patient's risk benefit ratio.
e. Permanent Change: The accrual goal has been met for the study, or the required tumor response has not been seen o reopen a study that was temporarily closed, or a decision has been made that the accrual goal for the study is not likely to be met.

Also on page 9, the following sentence now reads:

Phase I studies will be developed within the Early Therapeutics Subcommittee of the Translational Medical Committee.

The following two forms were deleted from Policy 13:

Phase I, II or I/II LETTER OF INTENT Submission Form v2.0
Phase III Trial Concept Submission, Version 2

Policy 18 – Quality Control / Data Evaluation Policy and Procedure
The Quality Control Policy is now titled DATA EVALUATION POLICY AND PROCEDURE. In addition to the title change, the policy itself was revised as noted in the first two paragraphs as follows:

POLICY

The Southwest Oncology Group Data Operations Center performs evaluations on data, submitted for every patient registered to a protocol coordinated by the Southwest Oncology Group.

The purpose of data evaluation is to ensure that patients are eligible, properly stratified, and treated according to protocol requirements. The data are further evaluated to assess response to treatment, conduct consistency checks across forms for accuracy and completeness, and identify protocol deviations. Results of this review are communicated to the registering institution in writing. If an error is made in documentation, the institution may correct the error and submit an amended form.

Policy 19 – Quality Assurance Program

The Quality Assurance Site Visits now reads:

2) For Member and CCOP institutions a number of patients equal to 10% of SWOG and CTSU accruals since the last audit, with a minimum of ~~six~~ three will be randomly selected.

Under item 8, page two, item "i" – "copies of the protocols including model consent forms", was deleted:

Policy 23 – Serious Adverse Events

On page 2 of the policy, the following paragraph was deleted:

DELETED: A specialized SAE report form is used for the Selenium and Vitamin E Cancer Prevention Trial (SELECT). This form reflects that the information collected and the timing of patient contact for this large prevention trial is different than for Group therapeutic studies. SELECT serious adverse event reports are not to be submitted in AdEERS, but should be sent to the Operations Office as prescribed in the protocol."

On page 3 of the policy, first sentence, this second paragraph was added:

Investigators or their study personnel are encouraged to contact the Operations Office for guidance on whether immediate AdEERS reporting is required before submitting the on-line report.

On page 4, the section titled EVALUATION OF SERIOUS ADVERSE EVENTS, was entirely revised. The new section now reads:

Preliminary evaluations of SAEs will be done by the Physician Reviewer as AdEERS reports are received.

For SWOG-held IND studies, additional data is always required on submitted SAEs. The Physician Reviewer's evaluation will be completed on receipt of the required data. For NCI-held IND studies and commercial drug studies, supporting data will be requested from the reporting institution only as needed, and the Physician Reviewer's evaluation will be completed once this data is received.

In all cases, the Physician Reviewer evaluates the report, the supporting data if required, and the reporting investigator's description of the event, adverse event code(s), grade(s), expectedness, and attribution(s). If the initial evaluation of a report suggests that a protocol violation may be implicated in the adverse event(s) being reported, the report and supporting data will be reviewed for protocol compliance by a nurse SAE consultant. Based on this review, the Physician Reviewer may recommend changes in SAE code(s), grade(s), and attribution(s).

If the Physician Reviewer recommends a changes in SAE **code(s)** and **grade(s)**, or **expectedness**, these recommendations will be provided to the submitting investigator, giving him/her the opportunity to challenge any changes the Physician Reviewer may have made to his/her assessment of the event. The Physician Reviewer recommendations will also be sent to the Study Coordinator for comment. If no challenge to the recommended changes is received within 7 calendar days, the judgment of the Physician Reviewer will be reflected in the entries made in the SWOG database.

If the Physician Reviewer recommends a change in SAE **attribution** that would shift the event from a related (definitely, probably, or possibly) to an unrelated (unlikely, not) category, or from an unrelated to a related category, these recommendations will be provided to the submitting investigator with an urgent request for response. The recommendations will also be sent to the Study Coordinator for comment. If the submitting investigator does not respond in agreement with the change in attribution within 7 calendar days, the Executive Officer will be asked to adjudicate the attribution. The Executive Officer may elect to consult with the Study Coordinator and others, as needed to make a determination. No changes in attribution will be made in the SWOG database unless either 1) the investigator agrees with the change; or 2) the Executive Officer agrees with the change. No changes in the investigator's attribution will be considered if the change does not shift the SAE from a related to an unrelated category, or from an unrelated to a related category.

For adverse events below grade 5, differences in SAE attributions entered into AdEERS (by the investigator) and the SWOG database (following Physician Review) will not be resolved. For all grade 5 events, the coding, grading, and attribution must be reconciled between AdEERS and the SWOG database.

Policy 25 – Drug Ordering Policy

The Drug Ordering Policy now reads:

To order study drug, the principal investigator or ordering designee must refer to the Drug Information Section of the protocol to identify the supplier of the study drugs. All study drug orders where drug is supplied through the NCI should be sent directly to the Pharmaceutical Management Branch (PMB) according to the policy and procedures set forth by the PMB. For study drugs that are not supplied by the NCI, consult the protocol for drug ordering procedures. It is not necessary to route any drug orders through the Operations Office.

Drug procurement of PMB-distributed agents must be requested using the NCI Clinical Drug Requests NIH Form 986 (CDRs). The form must be signed by the NCI-registered investigator in whose name the agent is ordered or by the shipping designee or one of the ordering designees whom the Investigator has listed on their most recent Supplemental Investigator Data Form 3_052303 (IDF) on file with PMB. Study drugs must not be redistributed or transferred to another institution or site, with the exception of satellite or affiliated facility distribution. Satellite or affiliated facilities are defined as institutions that are located on the same campus or in proximity where transportation can be provide by the institution courier service. See http://ctep.cancer.gov/requisition/index.html for more information.

The Pharmaceutical Management Branch has in operation an electronic procedure to receive drug requests. This system can reduce the turn around time to less than one week. Should you be interested in this electronic system, please call the Pharmaceutical Management Branch at (301) 496-5725.

For protocols where commercially available agents are being used, acquisition of the drugs should be handled as other non-protocol drugs. However, always refer to the protocol or check with the study coordinator to determine whether a drug accountability form (DARF) should be kept to track the usage of the drugs.

Policy 30 – Responsibility for Patient Follow-Up
Sections 6, 7 and 8 now read as follows:

6. If an investigator moves from one institution to another within the Group and the patient does not follow the investigator, or an investigator leaves the Group, follow-up responsibility should be transferred to another active investigator at the institution who knowingly accepts such responsibility. If the investigator does not transfer follow-up responsibility to another active investigator within the Group, the follow-up responsibility will fall to the institutional Principal Investigator. In the case of an Affiliate investigator, the Member institution may, in some cases, be willing to assume responsibility for clinical follow-up once the patient is being seen annually (or less frequently) for study purposes.

7. Notification of transfers of the follow-up responsibility must be made in writing to the Statistical Center using the Patient Transfer Form. This form is available on the web (www.swog.org) in the CRA Workbench, under 'Tools of the Trade'.

8. If the transfer of follow-up responsibility is made to a new institution, verification of IRB oversight is required. The new institution must have current IRB approval of the protocol prior to accepting a transfer of a new patient that is currently on treatment. Transfer of a patient on long term follow-up may occur prior to IRB approval of the protocol as long as the new institution pursues approval in timely manner. In this case, expedited review of the protocol for follow-up activities only is sufficient.

Policy 38 – Dosing Principles for Patients on Clinical Trials
The following paragraph was added to the third paragraph on page 1:

Several recent published studies continued to support the findings of the previous studies use of actual body weight in dosing chemotherapy for the obese patients (defined as BMI $\geq$ 30), especially in the adjuvant setting where the treatment intent is curative. These studies showed that obese patients do not have poorer prognosis if they are treated with optimal doses of chemotherapy based on actual body weight and no increased toxicity was observed (Barrett, et al. Annal of Oncology 2008;19(5): 898-902, Meyerharsdt, et al. Journal of Clinical Oncology 2004;22(4):648-57). A review article (Hunter et al. Cancer Treatment Review 2009;35(1):69-78), a pharmacokinetic study by Sparreboom et al (Journal of Clinical Oncology 2007;25(30):4707-4713), and an editorial by Gurney et al (Journal of Clinical Oncology 2007;25(30):4703-04) strongly discouraged the use of capped BSA in the dosing of chemotherapy drugs in obese patients.

Policy 40 – Membership of Non-United State Institutions
This policy was revised in Section 10 and Section 12 was added:

10. Before any funds are paid on a trial involving a Federal-wide Assurance (FWA) to a non-U.S. institution(s), the institution(s) requires clearance by the U.S. Department of State. This includes subcontracts, consortia and purchase service agreements (PSAs) supporting Southwest Oncology Group research and patient accrual.

12. The following information must be submitted to the Operations Office, who must in turn forward such to the State Department Clearance prior to their initiating any funding action:

    Name of Principal Investigator of Subcontract
    Institute Name
    City, Country
    OHRP Federalwide Assurance (FWA) #

Identify preferred auditing process (e.g., Group auditors or alternate contract auditor-provide alternate contractor information).

Identify any issues or potential obstacles related to regulatory documentation, IND requirements, contracts, drug shipment, shipment of patient materials (including specimens and images), etc.

Estimated annual Total Cost dollar award for the non-US component

Research Objectives at the site

If human subjects are involved include the following, as applicable:

- The demographics (age-range, gender, etc.)
- The number of subjects (and how they will be recruited, if known)
- What participation will entail (clinic visit, questionnaire, blood sample, treatment, etc.)
- How long subjects will participate (e.g., one clinic visit a month for a year)
- Statement on protection of welfare of humans subjects (describe informed consent and confidentiality procedures to be used or use general statement if suitable)
    - e.g. “Informed consent for participation will be obtained from all human subjects and confidentiality of subjects will be protected, in compliance with NIH and in-country guidelines under the assurance number provided.”

If human subjects data or samples are pre-collected:

- State that data/samples were collected under another project.
- State that data/samples are anonymous or how confidentiality will be ensured if not anonymous.

If data/samples collected under another project *and* are anonymous: State that the study is not considered “human subjects research” because data/samples were previously collected and anonymous