New CTMB Guidelines Synopsis of Changes

1) The quality assurance and monitoring guidelines are the minimum set of guidelines that must be met by Cooperative Groups. While the Groups must meet the minimum standards of the CTMB audit guidelines, more stringent policies and procedures may be established and enforced by the Cooperative Groups.

2) If the NCI Central Institutional Review Board (CIRB) is utilized by the local IRB through facilitated review, all documentation of CIRB approvals must be obtained by the local site. Since the local IRB has assumed responsibility through facilitated review, these documents (hard copy) must be present at the time of the audit

3) A re-audit should be done no later than a year after an Unacceptable audit for IRB, Informed Consent or Pharmacy. For Patient Case, a re-audit should be done when sufficient patients have been accrued (3-5 patients).

4) Amendments must be approved by the IRB of record within 90 days of the Group's notification.

5) Administrative updates are exempt from the 90 day requirement.

6) **External safety reports for adverse events that are unexpected and ≥ Grade 3 (attribution of possible, probable or definite) must be submitted to the local IRB within 90 days of the Group's notification (unless the institution's policy does not require such events to be reported and documentation of the institution's policy on external safety report review can be provided at the time of the audit).

7) NCI supplied agents must be returned to the Pharmaceutical Management Branch within 90 days of study closure and all treatment completed.

8) Patient returns of IND supplied agents are not recorded on DARFs unless agents are supplied as double blinded.

9) If records are not in English then a qualified translator chosen by the audit team or institution must be present.

10) Documentation identified as missing at the time of the audit and requested by the audit must be supplied within a maximum of two weeks following the audit to clarify patient case findings. This does not apply to missing IRB, Informed Consent or Pharmacy documentation.

   a. RTOG new policy: Missing documentation for patient case findings must be forwarded to the auditor within one week.

11) **Delinquent data submission

   a. > 6 month delinquency is considered a major deficiency
   b. 3-6 month delinquency is considered a lesser deficiency)

12) **6.3.1 **Suspension of Participating Institutions**

If an audited institution fails to provide a corrective action plan for one or more audit components rated as acceptable needs follow-up or unacceptable within the required time limit, the following actions will be imposed by the Group.

- The Group will provide written notice to the Principal Investigator at the institution that the response/corrective action plan is overdue and a <u>five working day grace period</u> will be granted for the submission of the response/corrective action plan.

- If follow-up or a corrective action plan is not received by the Group during the five day grace period, the Group will immediately suspend patient registrations from that institution.

- If the audited institution is an affiliate of a Main Member institution or a component of a CCOP, or a CTSU, <u>all</u> new patient registrations will be suspended from both the Main Member/CCOP and the affiliate/CCOP component.

- No registrations will be accepted by the Group through any mechanism.

- If follow-up or a corrective plan is not submitted during the 5 working day grace period, a written explanation from the Principal Investigator detailing the reason for the delay must be included. Patient registration will not be lifted until the institution submits the response/corrective action plan to the Group and the response/corrective action plan is forwarded to and reviewed by CTMB. CTMB must receive written notification of the suspension and of the reinstatement (if applicable) of the institution.

- On subsequent audits, the failure to submit a timely response/corrective action plan may result in permanent termination from participation in NCI sponsored clinical trials through the Cooperative Group.

13) **6.3.2 **Probation of Participating Institutions**

- If a participating institution is deemed unacceptable for the same audit component(s) on two consecutive audits, the institution will be placed on probation.

- During the probationary period, accrual will be closely monitored by the Group with increased utilization of quality control procedures at the time of patient registration and timely review of data submission.

- The institution may also be assigned a mentor by the Group.

- The institution site improvement plan should address key infrastructural issues contributing to poor performance.

- If improved performance is not documented at the time of the second re-audit, the institution may be permanently terminated from the Group, this action will be done in consultation with CTMB.