Requirements for Participation in RTOG Clinical Trials for Non-North American Sites

RTOG member sites from countries outside North America have several additional requirements that must be met prior to participation in RTOG clinical trials.

Requirements for All Non-North American Sites

- **US State Department Approval** – RTOG will need to obtain US State Department approval before an international member institution can begin participation in RTOG clinical trials.
- **Country-Specific Approvals** – The participating institution will need to obtain Ministry of Health and any other required country specific regulatory body approval to have the RTOG clinical trial open in its member state
- **LOI Submission –** Non-North American sites must receive prior approval from RTOG for participation in each protocol prior to patient entry. This step is required to ensure the ability to provide study drug to specific countries and in order to meet regulatory requirements. Sites must complete and submit a Letter of Intent (LOI) for each trial in which they would like to enter patients. The LOI application and instructions for completion and submission is available at the following link: http://www.rtog.org/LinkClick.aspx?fileticket=3PpIhF1mkNw%3d&tabid=117
- **Translation** – Translation of documents is critical. The cost of all translation is the participating institution's responsibility. All regulatory documents, including the REC approved consent must be provided in both English and the native language of the member state. Certification of the translation is optimal but due to the prohibitive costs RTOG will accept at a minimum a verified translation. A verified translation consists of the actual REC approved consent document in both English and the native language along with a letter on letter head with the credentials and signature of a qualified translator as well as signed documentation of review and verification of the translation by a third qualified neutral party also noting their title and credentials.
    - Because the QOL portion could involve translation and cultural issues this correlative component is optional for sites outside of North America. If you choose to participate in the QOL Assessment the required translation will be the participating institution's responsibility.
- **Correlative Study Participation** – The participating institution is required to offer the correlative study components defined in the protocol such as blood & tissue banking to each patient. Participation in these portions of the study can only be declined by the patient. Central pathology review is often a study requirement and cannot be declined
    - The creation of a Material Transfer Agreement (MTA) to satisfy your ministry of health or institutional policies regarding the required provision and banking of tissue will be the responsibility of the participating institution.
    - Biospecimen materials not needed for eligibility determination or stratification should be submitted to the RTOG Biospecimen Repository at UCSF in batched shipments containing all of the materials collected for the patient.
- **Patient Registration Requirements** – The participating institution will need to document compliance with all pre-registration requirements noted in Section 5.0 of the RTOG protocol
- **RPC Certification** – Annual participation by the participating institution in the Radiological Physics Center (RPC) Auditing Program is required. Additional information on the RPC Auditing Program is available on their website at: http://rpc.mdanderson.org.The RPC can be contacted via e-mail at rpc@mdanderson.org
- **Study Drugs** – RTOG will attempt to obtain a source for any drug noted as provided in the protocol. This is not always possible and is often the reason for denying Non North American participation in

RTOG trials. The participating institution will be required to obtain any drug noted as commercially supplied in the protocol.

European Union (EU) Participating Sites

The EU Clinical Trial Directive (EUCTD) adds another layer of complexity to Non North American member participation in RTOG clinical trials. Below in is a list of additional important information for our EU members to consider before requesting participation in current or future RTOG studies.

- In compliance with the EUCTD, the participating institution will need to identify a legal representative in the EU for your member state.
  - Any cost or additional requirements (e.g., monitoring, etc.) associated with EUCTD mandates will be solely the responsibility of the participating institution
  - No additional funds outside of the study specific per case payment provided by the NCI will be provided by RTOG to the participating institution
- The participating institution Investigators who are part of the European Union (EU) must prepare and submit a Clinical Trials Application (CTA) for all cancer clinical trials, except those involving only products with a marketing authorization that are to be prescribed in the usual manner and used in accordance with the authorization. The CTA is submitted to the Competent Authority (CA) of each EU member state participating in the clinical trial in the member state's official language. The preparation, submission and verification of CA approval will be handled by the EU member state collaborating institution. A copy of the CTA approval must be provided in English as an e-mail attachment to RTOGDrug@.acr.org
- Indemnity Insurance through an EU Company or a reciprocal agreement with a US company will need to be in effect for the participating institution

Please note: The above issues can take some time to resolve. It is RTOG's goal to make our Non North American members proactively aware of these hurdles so we can work together to resolve them as quickly and as efficiently as possible.

It is important to note that in addition to the pre-registration requirements noted in Section 5.0 the protocol, the items noted above and any specific points noted in your LOI approval response letter from RTOG there is the potential for the identification of other country/member state specific issues, which may also need to be addressed before participation can begin.

All requirements noted above must be fulfilled after RTOG LOI Approval but prior to enrolling patients into the study.