

January 27, 2010

CUMC Compliance Program for FDA-regulated Human Subjects Research

The CUMC Compliance Program for FDA-regulated human subjects research (the “Program”) is the responsibility of the Executive Vice President for Research, in close collaboration with the P&S Senior Vice Dean. The Program has two arms: oversight and audit, led by the IRB, and education and operational support for investigators, led by the CTO. The IRB and the CTO will continue to work closely together in managing the Program.

The Program is intended to ensure compliance in the conduct of all FDA-regulated human subjects research at CUMC. A principal focus of the Program is on research involving INDs or IDEs when the Principal Investigator (“PI”) is acting as a “sponsor-investigator” or the IND or IDE is held by a member of the Columbia faculty (“S-I Research”). PIs act as sponsor-investigators (“S-Is”) in non-industry sponsored research conducted under an IND or IDE. An IND/IDE Assistance Program has been established to provide S-Is education, training and support on FDA regulations and help ensure appropriate documentation and trial monitoring to satisfy regulatory requirements.

The responsibilities of the IRB, the CTO and the Departments, Centers and Institutes in ensuring compliance are as follows:

A. IRB

1. Oversight. The IRB is responsible for overseeing the conduct of research it approves and is therefore responsible for ensuring that the requirements of the IND/IDE Assistance Program are met. It will continue to include S-I Research in its not-for-cause audit program. In addition, as it already does, the IRB will investigate incidents of FDA non-compliance, and, when necessary, will work with the S-I, the IRB Chairs and the CTO to establish a corrective action plan. If appropriate, the IRB may suspend research studies until the corrective action plan has been implemented. The IRB will strengthen and monitor the Program by having its Compliance Oversight Team focus on auditing S-I research on a regular basis.

2. IND/IDE Determination. As is the current practice, the IRB will make the final determination as to whether an IND or IDE is required for a particular study. The IRB may consult with the Executive Director, the Director of Regulatory Affairs and Trial Development (the “Regulatory Affairs Director”) and/or the Medical Director of the CTO as necessary to make this determination.

3. IRB Controls. The IRB will not approve the enrollment of subjects in S-I research until the CTO notifies the IRB that the mandated prerequisites of the IND/IDE Assistance Program have been met. This process will be implemented in RASCAL at the earliest opportunity. If the study has been approved by the IRB before the CTO has given its sign off, the consent form will be deactivated until that sign off has been received by the IRB.

4. Automatic RASCAL Reminders. Rascal will generate email reminders to S-Is for ongoing FDA filing requirements. However, the PI will remain responsible for ensuring that these requirements have been met.

B. CTO

The CTO is responsible for managing the IND/IDE Assistance Program, which is staffed principally by the Regulatory Affairs Director, under the supervision of the Executive Director and the Medical Director of the CTO. The IND/IDE Assistance Program has the following components:

1. Preliminary Advice. The Regulatory Affairs Director will be available to assist S-Is in making a preliminary determination as to whether an IND or IDE is required and, if so, in preparing the necessary documentation to be submitted to the FDA. S-Is are encouraged to consult with the CTO in the early stages of development of a trial.

2. Protocol Reviews. Rascal will generate on a weekly basis a list of all studies involving an investigational drug or device that do not have an industry sponsor or have an industry sponsor, but the sponsor does not hold the IND or IDE; protocols for those studies will be reviewed by the Regulatory Affairs Director.

3. Mandatory Training. This will involve the following components:

- Mandatory online training course for S-Is and/or other key study personnel to supplement the CITI FDA training module that is already required of investigators new to human subjects research at Columbia and involved in FDA human subjects research. We expect that this training will be available online in the first quarter of 2010.

- Mandatory in-person training in FDA research for clinical research coordinators (“CRC”) will be included as part of the CRC training program that is expected to be rolled out in the first quarter of 2010. There is an extensive discussion of trial management, FDA regulations and FDA audits in the new Clinical Research Handbook that will be used as the textbook for the training course.

4. Mandatory IND and IDE Review. For all new INDs and IDEs, prior in-person consultation with the Regulatory Affairs Director will be required for each S-I. In addition, the application itself and the study’s monitoring plan will be reviewed and approved by the Regulatory Affairs Director prior to submission to the FDA.

All Annual Reports to the FDA by S-Is will be reviewed and approved by the Regulatory Affairs Director prior to submission to the FDA. Evidence that an appropriate monitoring plan is being implemented and documented will be submitted by the S-I to the Regulatory Affairs Director as part of the annual reporting process.

5. Mandatory Document Retention. It is the responsibility of the S-I to retain copies of all documents relevant to S-I IND/IDEs, including all correspondence with the FDA. The CTO and the IRB should be notified of the location of all FDA documents.

6. Master List of Protocols. In order to facilitate the work of the INDE/IDE Assistance Program, the Regulatory Affairs Director will, in close coordination with the IRB, maintain a spread sheet in RASCAL listing all active INDs and IDEs held by Columbia University faculty, with links to the relevant grant identifying information and IRB and JRSC protocol information

C. FDA Inspections

The following provisions apply to all FDA-regulated research:

1. FDA Inspections. If a PI receives notice that a FDA inspection has been scheduled or a FDA representative arrives at CUMC to conduct an unannounced inspection, the PI shall immediately notify the IRB, the CTO and the Office of the General Counsel. The CTO and/or the IRB will review with the PI the required procedures to be followed during the inspection and will be available to provide assistance in preparing for the inspection.

2. FDA Inspection Documentation. It is the responsibility of the PI to retain all correspondence and other documentation relating to FDA inspections. The IRB will maintain a masterfile of all such correspondence and other documentation. Copies of all such correspondence and documentation shall be sent by the PI to the IRB for inclusion in the FDA masterfile.

D. Departments, Centers, and Institutes

It is the responsibility of the Departments, Centers and Institutes to ensure that FDA-regulated human subjects research that is conducted within their administrative units and/or by faculty with their primary appointments in their administrative units is fully compliant as required by University policy. The Departments, Centers and Institutes should ensure that the PIs are competent to be responsible for FDA-regulated research, especially in studies in which they are acting as the S-I, and that they have adequate resources to ensure and document protocol adherence and other regulatory compliance.

E. New York State Psychiatric Institute

1. IRB Coordination. Some S-I Research is conducted by Columbia faculty in the Department of Psychiatry (“NYSPI S-Is”), acting in their capacity as Columbia faculty and/or in Columbia University facilities such as the PET Center or the Hatch Center, and/or through grants to Columbia University, but under review and approval by the New York State Psychiatric Institute IRB (“NYSPI IRB”). As such, CUMC recognizes the need for close coordination between the CUMC IRB and the NYSPI IRB to ensure FDA compliance. It is the responsibility of the two IRBs to provide this coordination.

2. Inclusion in IND/IDE Assistance Program:

- The consultative services of the CTO described in Section B(1) above will be available to NYSPI S-Is and other research staff at NYSPI.
- All NYSPI S-Is and CRCs will be subject to the mandatory training requirements described in Section B(3) above. The CUMC IRB and the NYSPI IRB will coordinate on providing the NYSPI IRB with documentation of training requirements having been met.
- The provisions of Sections B(4) and B(5) and Section C above will apply to all NYSPI S-Is.