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January 30, 2009

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United States Public Health Service
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Submitted via email to discontinueparticipation@hhs.gov

Re: Draft Guidance on Discontinuation of Subject Participation

Dear Dr. Carome:

The American Society of Clinical Oncology (ASCO), the professional society representing more than 27,000 multi-disciplinary oncology specialists engaged in all aspects of cancer research and care, is pleased to offer its comments and advice regarding the draft guidance on discontinuation of subject participation.

We appreciate that OHRP has drafted a guidance on this important topic. Cancer investigators at times encounter situations in which patients suspend participation in a study because they are unable to tolerate the investigational treatment or because they feel the potential benefits no longer outweigh the risks at their stage of disease.

The guidance makes a helpful distinction between those activities that involve the subject's participation (pages 10-11, numbers 1-4) and those activities in which the subject does not participate, but for which the investigator can conduct continued analysis of information and test results, according to the IRB-approved protocol (page 11, number 1-2).

However, ASCO's primary concern with the draft guidance is that the biopsy example does not appear to allow continued analysis of obtained biospecimens, as outlined in the protocol. Once an investigator has obtained a biospecimen, he/she should be able to conduct the testing and analysis that is specified in the protocol. The same should apply for non-specimen related data that has already been collected, as well. This would make the example more consistent with the earlier section that articulates the activities that an investigator can continue to do without subject participation (items 1 and 2 on page 11).

In addition to the concern that an investigator is able to conduct protocol-specified activities, the example creates an unworkable distinction between each step of the

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biospecimen analysis and testing process. It is clear when a research participant has undergone the biopsy, but the specific time that the investigator or lab staff has extracted the DNA, performed the assay, and analyzed the assay results may not be easy to pinpoint. Unless all parties keep careful note of when each testing/analysis step occurs and when the participant informed study staff of their desire to withdraw, it may be difficult to know which steps in the biopsy analysis are permitted. In addition, multi-center trials often require central lab analysis of the biospecimens, so information about the timing of the steps may be outside of the investigator's knowledge or control.

While OHRP notes its belief that the draft guidance is consistent with FDA's final guidance (Data Retention When Subjects Withdraw from FDA-Regulated Clinical Trials), ASCO believes the example provided contradicts FDA's advice. The FDA guidance articulates safety and data integrity reasons for its "longstanding policy ... that all data collected up to the point of withdrawal must be maintained in the database and included in subsequent analyses, as appropriate." This is particularly important if a research participant chooses to withdraw from a study after receiving an investigational treatment. It is necessary in that instance to conduct additional testing and analyze the results of any tests done or data gathered prior to their withdrawal to determine whether the side effect was caused by the investigational drug. For this reason, it might be helpful to include an example that discusses withdrawal after receiving an investigational treatment and the safety issues that the investigator should discuss with the participant. In addition to safety concerns for the participant, the inability to conduct follow-up testing would cause investigators to lose possibly key data to characterize the safety profile of the investigational agent.

The typical experience in oncology clinical trials is that patients choosing to discontinue or discontinuing from a study on advice from the investigator often want to ensure that their experience will nevertheless be useful. Therefore, patients do not typically want to withdraw entirely. As such, we would recommend that OHRP also include an example in the guidance that illustrates how to manage data for a patient who is willing to continue participation in other research activities.

We would be pleased to provide additional information or answer any questions you may have about our comments. Please contact Suanna Bruinooge at 571-483-1613 or suanna.bruinooge@asco.org.

Sincerely,

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