

**MASAC STATEMENT ON THE ROLE AND RESPONSIBILITIES OF
THE PRINCIPAL INVESTIGATOR IN BLEEDING DISORDER
CLINICAL TRIALS**

The following statement was approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation on June 7, 2003, and adopted by the NHF Board of Directors on October 19, 2003.

A critical element of clinical research is the relationship between the trial participant and the Principal Investigator (PI). Subjects involved in clinical research programs are dependent on the PI for guidance and education as well as for their medical treatment. Because the advocacy role of the PI in clinical research is integral to its success, and because the complexity of the PI's role can potentially lead to conflicts, MASAC recommends the following guidelines for PIs participating in clinical bleeding disorder research endeavors:

1. The research interests of a trial should never take priority over the primary role of the PI as physician to any individual subject. Recruitment of subjects into a clinical study is in essence an endorsement of that study as a reasonable effort toward the ultimate goal of improving treatment or providing a cure for bleeding disorders and is also an endorsement of the subject's participation in that program.
2. As individuals within the bleeding disorders community represent a precious scientific resource, PIs should make every effort to assure that the design of a trial for which he/she enrolls such individuals will give rise to definitive and significant results that may be published upon completion of the trial.
3. The PI, as physician, is the primary person responsible for education of trial participants. The PI should ensure that all subjects considering enrollment in a clinical research study understand the procedures involved and the implications of all pre-clinical research involving the intended procedures as well as results from other trials or programs involving related research. This includes both an objective appraisal of potential benefits to the individual and/or the community as well as a frank evaluation of the risks and uncertainties that exist in the proposed protocol.
4. In some institutions the PI may not be the primary discussant of a trial. In order to avoid the possibility of subtle coercion felt by a subject and in an

effort to maintain objectivity, an institutional surrogate may perform some of the functions normally performed by a PI. Such functions may include: discussing trial specifics, providing continuing education, or obtaining informed consent. While the PI is primarily responsible for adhering to the guidelines in this document, in situations where an institutional surrogate is utilized, there is a shared responsibility for both the PI and the surrogate to adhere to these guidelines.

5. The PI should ensure that the subject has made a determined effort to understand the nature of the research and that his or her “informed consent” does in the view of the PI in fact represent a reasonably informed choice. As part of the informed consent process, investigators must inform subjects of other research protocols for which they may qualify in accordance with federal regulations.
6. As the trial proceeds, the PI remains responsible for providing continuing education to trial participants, both in terms of a subject's own clinical response to the procedure and the responses of others in the same or comparable trials. It is particularly important that the PI ensure that subjects enrolled in clinical research trials are promptly and fully informed of any serious adverse events that arise in the trial in which they are participating or in other similar trials. Additionally, serious adverse events must be promptly reported to all appropriate regulatory and review bodies including the National Institutes of Health, the FDA, and local institutional review boards.
7. The PI retains primary responsibility for providing medical follow-up on all trial participants even after the initial treatment period has ended. The PI must accept responsibility for ensuring that the procedures for implementing this long-term follow-up are well established and are carried out in accordance with FDA guidelines.
8. All PIs and their research team members must become familiar with their local institutional guidelines and federal agency policies and regulations pertaining to clinical research. Specifically, PIs and their team members must adhere to local IRB policies, OPRH federal regulations, and HIPAA compliance requirements when engaged in clinical research protocols.
9. PIs, scientists, clinicians, and their institutions must make full disclosure of any conflict of interest, consistent with MASAC Document #136,¹ which endorses the Association of American Medical Colleges' Conflict of Interest Guidelines and the requirements of the Office for Human Research

Protections. PIs involved in hemophilia-related gene transfer trials should adhere to all relevant American Society of Gene Therapy guidelines regarding such trials, particularly those relating to potential conflicts of interest.²

10. The PI should provide the trial participant with appropriate contact information that will allow the participant to have any trial-related questions answered. The list of contacts should include the PI, the nurse overseeing the study, and the Chief of the Consumer Affairs Branch at the Office of Communication, Training & Manufacturers Assistance of the Center for Biologics Evaluation and Research of the FDA.

References:

1. Medical and Scientific Advisory Council of the National Hemophilia Foundation. MASAC Standard on Disclosing Conflicts of Interest for Individuals Conducting Clinical Research on Bleeding and Clotting Disorders. MASAC Document #136, November 3, 2002.
2. American Society of Gene Therapy. Policy of the American Society of Gene Therapy on Financial Conflict of Interest in Clinical Research. *Molecular Therapy* 2000;1:384.

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