INTRODUCTION

Cardiovascular health care professionals (HCPs) bear a heavy professional responsibility. Indeed, the profession itself is defined by the commitment to place the well-being of the patient ahead of the self-interest of the professional. An obligation of professional behavior of cardiovascular HCPs is to encourage the development of new knowledge that can ultimately improve patient care. One way to accomplish this is by participation in clinical research, which involves a complex interaction of multiple parties (including individuals, institutions, commercial organizations, and regulatory agencies). Because cardiovascular disease is the leading cause of death and disability in the technologically developed world (1) and is projected to increase in prevalence over the next 30 years, appropriate ethical behavior by cardiovascular HCPs could have a major impact on the well-being of both individuals and society. Lack of appropriate participation in efforts to improve care could undermine the delicate balance in the clinical research system (2), which ensures the protection of human subjects and forms the basis for the evidence upon which rational clinical practice is based.

Clinical research studies encompass a broad array of activities, ranging from reviews of medical records to small Phase I safety studies to large multicenter clinical trials. The roles and responsibilities of parties to this complex endeavor have not reached a level of complete clarity. For example, the first textbook on the function of data-monitoring committees was just published in the past two years (3). Accordingly, any effort currently to define appropriate behavior of individual investigators must be viewed as a “moving target.”

The most easily identifiable situation in which professional behavior is called into question occurs when the cardiovascular HCP interacts with the industry that invents, manufactures, and sells medical products. The enormous magnitude of the clinical research enterprise and the high financial stakes of transactions between cardiovascular HCPs and the industry provide fertile ground for sensational claims and concerns. Indeed, as technology continues to advance at a rapid pace, the interdependence of cardiovascular HCPs and the medical products industry is increasingly evident. The advances of drugs and devices for diagnostic and therapeutic purposes have been an overwhelmingly positive development for society, but the large impact of technology on health outcomes and cost reinforces the importance of professional conduct in the development and assessment of these new products.

Although the majority of cardiovascular clinical research is funded by the industry, a significant minority is funded from public sources, most notably the National Heart, Lung, and Blood Institute (NHLBI), a division of the National Institutes of Health (NIH). However, the NHLBI and the NIH as a whole are encouraging public-private partnerships for clinical research (www.nihroadmap.nih.gov), in which resources from both sectors are combined to cover the enormous cost of technology development and evaluation. The principles of appropriate investigator participation are applicable across the range of funding sources, including industry, public sources, and public-private partnerships.

For the most part, the medical products industry and cardiovascular HCPs are aligned in a professional manner. Both aim to develop and use technology that will diagnose cardiovascular disease more accurately, treat it when it is present, and prevent its development in people at risk. However, significant tension and/or conflict of interest may occur in the development and evaluation of medical technology by cardiovascular HCPs. Society rightfully expects that, in evaluating medical products and technology, the cardiovascular HCP will act in a professional manner and place the well-being of patients ahead of his or her personal interests. The industry has given attention to the issue of its interaction with HCPs, and the Advanced Medical Technology Association (AdvaMed) has published a code of ethics on interaction with HCPs that became effective in January 2004 (4).

TYPES OF CONFLICT

Conflict of interest in relation to industry is not a monolithic issue. Rather, there are varying levels of conflict, requiring different remedies to ensure that the public trust is being kept. One consideration is whether the conflict relates to an individual cardiovascular specialist or to an institution as a whole. A second consideration is the intensity of the conflict.
Individual conflict. Conflict of interest may begin with an idea for research, regardless of the source of funding. Those who design clinical trials and observational studies almost always have bias in terms of which theories they favor or upon which they may have staked their professional reputations. Accordingly, when considering the relationship between industry and the profession, one should not dismiss non-financial sources of bias and conflict, but should consider the whole spectrum of conflict. In fact, in general the degree of conflict for an individual may have several aspects as described in the Task Force 1 report and in the following text.

When a physician enrolls patients into clinical studies, a number of individual issues may arise, including questions of financial and personal professional gain. Because research is paid for by a public or private sponsor, the potential financial conflict is obvious to almost everyone involved. Fundamentally, the question is: how can the investigator maintain independence of thought and action from the sponsor in the conduct and evaluation of the research? The endorsement of the concepts involved in a study can lead to bias in how research is conducted and interpreted. However, the major issue in industry-sponsored research, as discussed in the following text, is the relationship between payment and the results of the study. Of equal concern, given the intense pressure on individual HCPs to create a revenue stream through efficient procedure-oriented practice, patients may not be offered the opportunity to participate in clinical research studies because it would reduce the income of the HCP or the practice. This could occur because a revenue-generating procedure might not be performed or because the time spent obtaining consent is compensated at a lower rate than direct clinical activity.

Institutional conflict. Until recently, little attention had been paid to institutional conflict of interest. However, recent difficulties with a particular research project—the Gelsinger case (5)—led to a major report by the Association of American Medical Colleges (AAMC) (6) stressing the difficulties when an institution has equity or other major financial interest in the outcome of a study. When an institution stands to benefit in reputation or finance from a research study, a potential conflict exists. Conversely, an institution can discourage investigation when it interferes with normal operation at the hospital. Additionally, clinical investigators are frequently under intense pressure to generate revenue to support the salaries of research nurses because of lack of reserve funds in institutions and practices to cover those salaries during periods of slow enrollment.

Universities, medical centers, and professional organizations have significant financial entanglements with the industry that go well beyond the conduct of research. The majority of continuing medical education (CME) is funded by industry, and significant donations and funding of training and faculty positions are awarded to academic institutions by industry. Both the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) rely on industry funding in the form of direct support, training money, and exhibits at national meetings (7) (see the Task Force 6 report).

Levels of responsibility and potential conflict

Individual clinicians play a variety of roles in the development and assessment of cardiovascular technology, and these roles may be considered according to the degree to which the clinician is financially involved with the sponsor of the research. At the most basic level, when the industry needs to conduct human research, it must contract with a physician-investigator to perform the research. The investigator, in turn, has a dual responsibility: the primary responsibility is to the research subjects to ensure that the research conforms to the ethical standards defined in documents such as the Declaration of Helsinki (8), the Geneva Declaration (9), and the Belmont Report (10). These obligations are spelled out in the informed-consent document, which is a contract between the investigator and the subject or patient. The second responsibility of the investigator is to complete the research in a professional manner. These issues are detailed in the regulatory document from the Food and Drug Administration entitled “Good Clinical Practices” (11,12). The contract between the investigator and the sponsor provides evidence of the seriousness of this obligation. Therefore, cardiovascular HCPs who enroll patients in clinical research studies have a potential conflict because they are paid to conduct the research, but society has also assigned investigators an independent role to act on behalf of the human subject in the conduct of the research.

A researcher may also be involved in disseminating the research findings. Because most CME is paid for by the medical products industry, interactions with industry are common, both in the writing of manuscripts for the peer-reviewed literature and in the preparation and delivery of lecture materials, slide sets, and other CME materials. Although the dissemination of research findings is increasingly recognized as a responsibility of the clinicians participating in research (13), as discussed in the Task Force 1 report, the degree to which the payment for these activities biases the control of the content of the material represents a potential conflict in this situation, and adherence to standards of conduct in CME is essential (see the Task Force 3 report).

The industry depends heavily on consultants from the academic and practice communities. These consultants offer insight into clinical and scientific issues and often provide feedback on dissemination of ideas and technology into the community. Consultancy contracts can vary considerably, as can the financial transactions around consulting.

A significant number of cardiovascular HCPs become inventors of technology. This privileged position is a major source of societal interest and concern. Much of the advancement of cardiovascular medicine in the U.S. has been
driven by ingenious inventor-investigators who were able to combine scientific and engineering insights with knowledge of cardiovascular medicine (14). A cardiovascular specialist with a patented invention that could result in substantial financial and status benefits and who uses that invention to perform procedures or studies on patients perhaps represents the highest level of direct conflict. It is recognized that the participation of the clinician-inventor in the clinical trial can be valuable. However, the clinician-inventor should not be the principal investigator of the clinical trial. Furthermore, special oversight is necessary when the clinician-inventor is involved in the informed-consent process (15).

Finally, a growing number of cardiovascular HCPs work directly in the medical products industry. This may lead to multiple issues of conflict of interest, particularly in conduct of clinical research developing or evaluating medical products. Such individuals may be involved but should not be the principal investigator of a study.

**COMMON ISSUES**

**Declaration of conflict.** When an individual or institution works with the medical products industry, society agrees that disclosure is a minimal standard. Although the issues in CME are discussed in the Task Force 3 report, less energy has been placed on appropriate declarations by investigators enrolling patients in clinical research studies. Recently, the AAMC (6,16,17) guidelines have emphasized disclosure to the patient when the investigator or the institution has equity interest or the potential for royalties in the product being evaluated (6,18). The degree to which these guidelines are being followed has not been quantified. More data needs to be collected in order to evaluate this type of disclosure. At minimum, financial interests must be disclosed to the Institutional Review Board (IRB).

**Publication.** The conduct of clinical research obligatorily involves an agreement between a subject (often a patient) and an investigator that the study is being done “to create generalizable knowledge.” This term has become standard in the definition of clinical research under which institutional ethics committees review and approve protocols under federal guidelines (18). However, the literature is replete with flaws in the approach to creating this body of knowledge. A critical report by Dickersin (19) highlights the degree to which failure to publish results can lead to inaccurate assessments of the balance of risk and benefit of diagnostic and therapeutic technologies. A particularly interesting report from the Johns Hopkins and Oxford universities (20) documented, in a review of all protocols submitted to institutional IRBs in the 1980s, that industry funding of research is an independent and major predictor of failure to publish. Recent publications have emphasized that this problem has not gone away (21–23), and multiple journals and investigators have called for a registry of all clinical trials (24).

Beyond the failure to publish is the issue of determination of the editorial content of publications. The content may be heavily influenced by the commercial sponsor in several ways in addition to simply not releasing the data. The sponsor may control the analysis for, or the writing of, the research publication, or may pressure investigators to portray a particular point of view.

A recent trend in the medical products industry is the assignment of publications managers to product development teams. These managers often are company employees, but increasingly major “medical education” firms are combining CME, project promotion, and the production of scientific articles for peer review into package contracts. This effort may lead to “ghost writing,” in which the publications group manager writes the manuscript while the investigators are listed as the authors. This practice seems commonplace in the production of journal supplements, which are highly valuable to industry because the law allows sales representatives to distribute publications from peer-reviewed journals. In this manner, an investigator can write about an off-label use of a product, and although the company cannot advertise that indication, it can distribute the supplement to practitioners. Perhaps of more concern is the use of names of prominent key opinion leaders on major reports from clinical research without independent input or editorial control from these investigators. There should be formal disclosure in the manuscript, if the manuscript is written, in whole or in part, by an individual or group other than the listed authors. All publication supplements should name the sponsor, anyone other than the listed authors involved in preparing the supplement, and whether or not it was peer-reviewed.

An additional issue is access to data. In most industry-funded research, the investigators are restricted from performing their own analyses. The industry sponsor either directly provides statistical support or contracts with a contract research organization for the purpose of analysis for regulatory and publication purposes. The industry contends that access to printouts of the analyses is sufficient to ensure that investigators have independent access to the data (Bayh-Dole Act of 1980; P.L. 96–517). Others have argued that the conduct of the analyses themselves should be in the purview of statisticians and clinicians free of high-level financial ties with the sponsor (25). Finally, the industry can apply significant pressure to investigators who wish to continue to do research with that company to shade reports favorably for the sponsor. The degree to which this happens has not been assessed, although some highly publicized cases have brought the issue to public attention (15,26,27).

These potential problems must be balanced with the legitimate concerns of industry. Many investigators have neither the capacity to manage complex datasets nor the knowledge of biostatistics to do their own analyses. Without the stimulus of industry support, and at times ghost writing, important research results can languish for months to years because of time constraints on academic investigators or lack of motivation and interest. Additionally, unmonitored ac-
cess to data from a study can allow the data to end up in the hands of individuals without either the in-depth knowledge of the topic or the skills to perform appropriate analyses. Optimally, the database should be shared by both the sponsor and the committee responsible for publication (see the following text).

PROPOSED APPROACHES

Accordingly, we advocate the following set of principles to allay the concerns of both cardiovascular specialty investigators and the medical products industry:

- The primary results of human subjects’ research must be made public. Surveys or analyses conducted for quality assurance purposes are not intended to be included. When the findings have insufficient priority for publication in the peer-reviewed literature, other means of disseminating knowledge should be used, such as through professional meetings, publicly available archives, web sites, or online tutorials. It is acknowledged that the mechanisms for public disclosure are not yet standardized, but the principle is that the default position in human investigation is that the results of the study should be made public so that they can contribute to generalizable knowledge.

- The publication must adhere to the principles regarding authorship, conflict of interest, and publication ethics as expressed in the International Committee of Medical Journal Editors’ “Uniform Requirements” (28).

- A committee responsible for publication should be constituted as part of the contract encompassing multisite human research studies. All decisions regarding development, authorship, and submission of any manuscript, abstract, or other presentation arising from the study should be made by the committee responsible for publication. Such a committee should be comprised of investigators participating in the study who are scientific and medical experts in their respective fields. It is appropriate to include representatives from the sponsor as full voting members of the committee. The committee responsible for publication should act as an independent body to fulfill the professional obligation to subjects participating in the research by representing their interests and by serving the professional mission of developing, improving, and disseminating scientific and medical knowledge. In small studies, this committee may consist of only a few people involved in the study. In larger studies that could inform clinical practice or better define important mechanisms of disease, such a committee should be carefully constructed as a critical component of the trial’s organization.

- The committee responsible for publication should review and approve all analyses and publication topics proposed by participating investigators and institutions, whether based upon the data collected by all participating institutions, by a subset of the participating institutions, or by only a single participating institution.

- The committee responsible for publication should review and constructively critique all proposed submissions that result from an approved analysis or publication topic, and should consider their scientific merit with the aim of promoting the dissemination of scientific and medical knowledge. This should be done in a timely manner before submission for presentation or publication.

- The industry sponsor should ensure that the study data are available for any analysis or publication topic approved by the committee responsible for publication, and the resulting manuscript or presentation should be sent to the sponsor for its timely review and comment. There should be no restrictions on the topics or analytical approaches used in developing manuscripts and presentations. Both the industry sponsor and the investigators should be free to suggest topics and analyses for consideration by the publications committee.

- When the research sponsor chooses to submit publications independent of the committee responsible for publications, the Trial Steering Committee should develop procedures for acknowledgment and disclosure of the publication’s relationship to the study.

- In the case of multicenter studies, the first publication of the results of the study should be a multicenter publication reflecting the results of the study as a whole as specified in the protocol and/or statistical analysis plan.

- The author(s) of the initial and subsequent multicenter publication(s), as approved by the committee responsible for publication, should have access to all of the data from the study and should have the ability to analyze those data, independent of the sponsor, although this principle is subject to review of the capability of the authors to perform appropriate analyses. In the case that the investigators are not capable of independent analysis, it is preferable for a statistician independent of the sponsor to be contracted to either perform the analyses or to check the analyses of the sponsor. This statistician should have a copy of the database.

- The initial multicenter publication should be published as soon as practicable after completion of the study, and the committee responsible for publication should attempt to have the first manuscript submitted to a reputable, peer-reviewed biomedical journal within a reasonable period of time (not more than one year) from the end of the study.

- The committee responsible for publication should promptly provide a copy of a planned submission to the Steering Committee for timely review by that committee and the sponsor within a reasonable period of time.

- The committee responsible for publication should review the documents, including any comments from the Steering Committee and sponsor. If confidential information would be released inappropriately in the manuscript or other presentation, it should be removed if possible, or...
the sponsor should be given appropriate time to protect intellectual property. However, information that the committee responsible for publication finds to be necessary for the accurate presentation and interpretation of the study results, or which is required by the publishing journal to enable other researchers to reproduce those results, should not be withheld beyond this reasonable period of time (typically 90 days).

- In the conduct of industry-funded clinical research, there is a possibility of the discovery of new findings that could be classified as intellectual property. Typically, the sponsor will desire to claim all intellectual property derived from the research. This stance is understandable given that the industry is paying for the research and requires patent protection to enable the investment in research to recoup profits for its employees and investors. However, after a reasonable period of time has elapsed to protect intellectual property, the intellectual property issue should not be used to limit the publication of results. Although formal review of a manuscript by the sponsor is typically provided in the contract for clinical trials, such review should not unduly delay the dissemination of key trial findings.

- The support of the sponsor must be recognized in any publication or presentation arising from the research or the study. If representatives of the sponsor make substantive contributions to the intellectual content of the manuscript or other presentation, as described in the "Uniform Requirements," they should be invited to serve as co-authors of the manuscript or other presentation. Acceptance of this invitation should be at the discretion of the representative.

**CONFIDENTIALITY**

In general, investigators are required to maintain confidentiality with regard to knowledge about the product being evaluated when clinical research is conducted with industry. Given the competitive research environment, this stipulation is quite understandable. Disagreements arise, however, about the scope of confidentiality and the duration of the agreement.

Increasingly, industry has considered confidentiality not only to include intellectual property about the drug or device, but also know-how related to the drug or device and even the protocol itself. This approach has led to extensive delays in the conduct of clinical research because of the requirement to review and sign confidentiality agreements before protocols can be reviewed. Such an approach also inhibits one's ability to discuss a protocol's merits and feasibility among professional colleagues. In general, confidentiality about the drug or device seems reasonable, but clinical know-how may belong to the investigator. Protocols should be considered non-confidential at the point at which they are dispersed to principal investigators at the sites, because broad discussion in the clinical community is required to determine whether the research study is appropriate for the local environment.

Few people in our society are capable of maintaining confidentiality for a lifetime. Accordingly, a time limit is typically placed on the duration of confidentiality. Although there is no objective standard or empirical base on which to make a judgment, confidentiality (except regarding study results—see the following text) should be limited to five years or until the end of the study, whichever is longer.

**INDEMNIFICATION**

Clinical research is no more immune from our societal preoccupation with lawsuits than is any other area of medicine. Indeed, injury occurring to human subjects has become an increasing source of concern and a topic of increasing interest by the legal profession. In general, the sponsor of the research should hold the investigator harmless for injury complications resulting from conduct of the study in accordance with the protocol. Obviously, the sponsor should not be responsible for negligence in the conduct of the protocol by the investigator.

**COMPENSATION**

Clinical research is a complex and demanding endeavor. Accordingly, payment for involvement in many aspects of clinical research activities is reasonable and should be expected. The question arises, however, concerning what should constitute reasonable professional standards for payment. Consulting may occur at several points during medical product development and interpretation of data:

- During the early phases of product development, considerable effort is required to guide decision making on the design of the molecule or device and in the design of animal and human studies. As the human studies are conducted, expert advice often is needed for interpretation of the data.

- In the later phases, product acceptance and message acceptance research is commonly done by marketing groups. Individual investigators should be careful to segregate consulting, marketing efforts, and CME into different categories with different purposes (see the Task Force 3 report).

- Conflict can arise at several levels as a result of consulting. When a cardiovascular HCP cares for an individual patient, decisions on product selection are made every day. It is critical to the public trust that neither patient nor product selection be based on payments occurring for the conduct of clinical research.

At a broader level, key opinion leaders can be identified at local, regional, national, and international levels. These individuals are highly valuable to industry because their opinions have a wide impact on prescribing and product-use decisions by other physicians. A complex issue arises when considering payments for lectures and other CME efforts...
(see the Task Force 3 report). This becomes particularly important for key opinion leaders who also serve on professional society committees that devise clinical practice guidelines and performance measures (see the Task Force 6 report). The level of compensation should be commensurate with the work performed.

THE INVENTOR-INVESTIGATOR DILEMMA

The investment of the NIH in biomedical research has spawned a large number of investigators who make discoveries that may have beneficial applications to human health. The Bayh-Dole Act (29) instructs academic medical centers to support the transformation of these ideas into commercial reality. Similarly, particularly in the device world, physician entrepreneurs have invented new approaches to technology, leading to “start-up” companies.

Recent events in the arena of gene therapy have highlighted the special nature of this situation. In the highly publicized case of Jesse Gelsinger, a research subject with a genetic deficiency (30), the University of Pennsylvania allegedly had supported the commercialization of an approach to gene therapy delivery. The faculty member was the principal inventor, allegedly with major equity in the commercial entity, and the university also allegedly held major equity. In addition, the experimental material apparently was manufactured at the university. When Jesse, an 18-year-old reasonably healthy boy, died as a direct result of the experimental therapy, the lawyers for the family argued that the process of consent and adverse-event reporting was flawed, and that neither the investigator nor the institution could be unbiased about the human experiment being performed.

Avoiding inventor-investigator conflict of interest. Ideally, invention and investigation of new discoveries should maintain rigorous barriers to avoid both the appearance of and the opportunity for bias (see the Task Force 1 report). Typically, this requires physician-scientists to allow other investigators to perform the human testing of their inventions. Although difficult for some inventors, this approach is the only reliable means to protect both the patient and the scientific integrity of the research. It is often simply too difficult to maintain rigorous standards for evidence-based research for drugs or devices in situations in which an involved inventor stands to profit substantially from the success of the project. Even when the scientific integrity of the investigation is impeccable, other physician-scientists, the public, regulators, and the press are likely to question the independence and reliability of the research. In this situation, fairly strict separation of the inventor is most often the best policy. One exception may occur when the inventor is the best or only person with the skill to operate the device in experimental circumstances involving humans (15,25). In this circumstance, special precautions must be taken to independently verify that subjects are fully informed about the issues involved in their participation. As soon as others become facile with the device, the inventor-investigator should be removed from experimental subject contact (26).

AVOIDING BIAS IN REPORTING CLINICAL TRIALS

In recent years, disturbing cases have surfaced in which physician-scientists played a passive or active role in publishing scientific results of clinical trials in which it was claimed major distortion of the findings had occurred (26). These issues may involve selective reporting of results in which findings with unfavorable impact on a commercial drug or device were withheld. Such episodes have a devastating effect on the acceptance of clinical trial results, bringing them all under close scrutiny. Several critical principles should govern the analysis and reporting of all clinical trials:

- The physician-investigator should be critically involved in the design of the trial and selection of the efficacy measures.
- A completely passive role, in which the sponsor designs the trial and the physician is “offered” a role as Study Chair or member of the Steering Committee, is unacceptable; such roles may be acceptable if significant input into final study design and conduct occurs.
- The Study Chair and Steering Committee should be signatories to the protocol and to a formal statistical analysis plan (SAP). Studies should be monitored for safety independent of both the sponsor and the investigators (31).
- In reporting results, the investigators should be guided by the SAP and should disclose any analyses that deviate from this plan.
- The editors of the publishing journal should be supplied with the SAP at the time of submission for publication.
- Full disclosure of negative results is imperative. In the case of an entirely negative study, posting on a public web site may be necessary owing to the well-publicized negative reporting bias of medical journals (see the preceding text). When the primary end point of a study is negative but secondary end points seem to be positive, it is critical to emphasize the negative result before discussing the implications of secondary analyses.
- Delay in reporting results that are unfavorable to a drug or device is equally problematic. Such delays may result in reduced quality of care for individual patients, or may lead to another sponsor conducting a similar trial thereby exposing other patients to unneeded risks.

ETHICAL ISSUES IN TRIAL DESIGN: ADEQUATE STATISTICAL POWER

The purpose of the study design should be clear, and it should be able to answer the question being addressed. In this regard, there are appropriate times for pure superiority trials, for non-inferiority trials, and for combined superiority/non-inferiority trials. The key issue is that the
trial design and sample size should be adequate for the stated purpose.

There are conflicting views in the clinical trial community regarding the ethical considerations in deciding the sample size for a trial. Some authorities believe that a deliberately underpowered trial, particularly when the goal of the trial is to demonstrate “non-inferiority,” is inherently unethical. These arguments center on the principle that all trials involve known and unknown risks to the subject. Accordingly, it is appropriate to expose patients to such risks only when the results are likely to provide significant incremental medical knowledge. According to some, an underpowered “non-inferiority” trial cannot benefit medical science, therefore intrinsically constituting an unacceptable risk to the patient. Opponents of this point of view argue that all trials have the potential to result in unanticipated scientific discoveries, and that an underpowered trial may eventually be included in a useful meta-analysis. Accordingly, this problem represents a “gray zone” in clinical trial ethics in which there is no universal agreement. Non-inferiority trials have a place in medicine, but underpowered non-inferiority trials have questionable value.

**CONCLUSIONS AND RECOMMENDATIONS**

The interaction between cardiovascular HCPs and the medical products industry in the setting of clinical research is complex and evolving. The principles of disclosure are critical. However, continued evaluation, empirical study, and publication of studies examining the “rules of engagement” in clinical research are needed to enable the profession to maintain appropriate independence while participating in a partnership with industry to develop new diagnostic and therapeutic technologies and to assess older ones. Critical principles to be considered by individual investigators are as follows:

- Encouragement for the development of new knowledge is a professional responsibility of cardiovascular HCPs.
- The investigator enrolling patients has an obligation to conduct the study according to the protocol, but also has a legal and ethical responsibility to the human subject from whom consent has been obtained. Thus, although the investigator is obligated to the sponsor he or she has a superseding obligation to act independently from the sponsor if necessary on behalf of the subject.
- Results of human studies must be made public regardless of their outcome. This responsibility can be accomplished preferentially by publication in a peer-reviewed journal, but it may require posting on a public web site or other means of public access.
- In multicenter studies, a formal mechanism for a committee to oversee publication and publish the results should be established by contract before the start of the study. This committee should prevent control of the process either by the sponsor or by individual investigators and should prevent “renegade” publication without due consideration of the interest of the many people who must work together to conduct a clinical research study.
- The complex endeavor of multicenter studies continues to evolve so that standards of conduct and appropriate behavior by all parties will become optimized with continued discussion. Research on methods of performing clinical research and public discussion of the findings of that research should be a high priority for all participants, especially HCPs such as ACCF and AHA members.

**TASK FORCE 2 REFERENCES**


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BACKGROUND

Physicians, scientists, patients, and the public rely on professional organizations to provide an independent, unbiased forum for presentation of research, publications, and educational activities at their scientific sessions and in scientific publications. Attendees at educational activities sponsored by not-for-profit organizations usually incur financial and other costs. The attendees expect to gain information from leading experts that may modify their behavior and result in a change in patient care. Concerns about real or perceived conflicts of interest among organizations, physicians, scientists, patients, and educators regarding their relationships with the medical products industry have been debated in the press and in medical journals (1,2). Concerns about these relationships have been discussed extensively by the Association of American Medical Colleges (AAMC), which issued guidelines for conflict of interest in human subjects’ research based on a consensus of a committee including clinicians, scientists, legislators, ethicists, consumers, and representatives from commercial interests (3).

The Accreditation Council for Continuing Medical Education (ACCME), which accredits continuing medical education (CME) provider organizations, currently requires full disclosure of pertinent commercial relationships. The ACCME has revised the Standards for Commercial Support which were adopted on April 1, 2004. Both the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) policies must be in compliance to maintain their accreditation (Table 1). “Disclosure” must never include the use of a trade name or a product-group message. A provider must disclose this information to learners before beginning the educational activity. The ACCME standards allow for relationships to be disclosed verbally, and for a representative of the CME provider who was in attendance to attest in writing that verbal disclosure did occur.

Medical societies have struggled to define a significant financial relationship that poses a real or perceived conflict of interest. The American Society of Clinical Oncology recently amended its regulations to encompass any money exceeding $100 an investigator received from a firm funding a trial (5). One criticism of this regulation is that the threshold for disclosure is so low that the large number of disclosures might obscure more serious financial relationships. The New England Journal of Medicine has maintained that authors of reviews and editorials must not have any financial interest in a company or its competitor that makes a product discussed in the article. Journal editors relaxed the policy for reviewers in June 2002 because their ability to recruit individuals for review articles and editorials was constrained (6). The new policy prohibits a “significant” financial interest, which the journal defined as a lower limit of $10,000 in accordance with guidelines developed by the National Institutes of Health (7) and the AAMC (3).

The concerns of consumers and professional organizations over conflicts of interest in medical research challenge the ACCF and the AHA to review their policies on conflict of interest, acknowledgment of commercial support, and disclosure of financial relationships with the medical prod-