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January 4, 2015

Sylvia M. Burwell
Secretary
Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201

RE: Federal Policy for the Protection of Human Subjects; Proposed Rules [HHS-OPHS-2015-0008]

Dear Secretary Burwell:

The American College of Cardiology (ACC) is pleased to offer the Department of Health and Human Services (HHS) comments on proposed changes to the *Federal Policy for the Protection of Human Subjects* (the Common Rule) as published in the *Federal Register* on Sept. 8, 2015. The ACC is a 49,000-member medical society that is the professional home for the entire cardiovascular care team. The mission of the College is to transform cardiovascular care and improve heart health. The ACC leads in the formation of health policy, standards and guidelines. The College operates national registries to measure and improve care, provides professional medical education, promotes cardiovascular research and bestows credentials on cardiovascular specialists who meet stringent qualifications. The ACC appreciates the opportunity to provide input as HHS considers these important issues.

The College's key recommendations regarding the proposed revisions to the Common Rule are:

- **Extend the application of the Common Rule to all research conducted by institutions receiving federal funding and all clinical trials other than those regulated by the Food and Drug Administration (FDA).**
- **Exclude low-risk research from IRB review, including**
  - **Program improvement activities, such as internal monitoring**
  - **Quality assurance and quality improvement activities**
  - **Public health surveillance activities**
  - **Activities covered under HIPAA**
- **Develop a decision support tool to assist investigators and research administrators in making exemption qualification determinations**
- **Align the Common Rule's privacy safeguards and security requirements with the requirements of the HIPAA Privacy and Security rules**
- **Allow the use of individually identifiable information for secondary purposes without requiring notice in certain circumstances**
- **Develop an informed consent program that is truly meaningful and interactive for potential research participants, including the creation of a template for a standardized informed consent form that is written in plain language and digestible to potential research participants**
- **Align and harmonize the research-related requirements of the Common Rule, FDA and HIPAA so we may realize the benefits of a learning health system**
- **Require the use of single IRBs for multi-site research conducted in domestic institutions**

Research is essential to the progression of society as a whole. It forces us to look critically at accepted truths and can have effects far beyond the individual researcher's original intentions. Medical research, in particular, has effects that are far-reaching, regardless of whether the question is one of basic science, translational science, clinical care or otherwise. Despite the amount of research already conducted into the inner workings of the human anatomy, there is still much to learn. Each discovery leads to new answers, but also new questions. As such, it is critical that we continue to push forward and enable research to occur in a manner that allows for innovative examinations but also protects research subjects from potential harms.

The College notes that the research environment has changed a great deal since the Federal Policy for the Protection of Human Subjects, also referred to as the Common Rule, was first promulgated in 1974, in response to specific concerns that arose with respect to the treatment of human research subjects. The current policies themselves have been in place since 1991, more than 20 years ago. Those policies do not address a number of questions at issue today, namely questions pertaining to biospecimens, appropriate levels of consent by human subjects, increased levels of interest by research participants in engaging in all aspects of research, determinations pertaining to level of risk by type of research and the ability of researchers to determine level of risk without oversight by a third party. Additionally, the current regulations presuppose that most, if not all, biomedical research is conducted in the academic medical center setting. The biomedical research model is evolving, with an increasing shift from the academic medical center to the clinical care setting, particularly as more attention is paid to health services research and electronic health records are deployed throughout the healthcare environment. Given the evolution of the field of bioethics, in addition to the changes in science and medicine, it is more than appropriate for an examination of the Common Rule at this point in time.

Despite the millions of dollars poured into research each year, cardiovascular disease remains the number one cause of death in the US. Continued research into various types of cardiovascular disease is desperately needed to reduce those numbers. Research has already taught us a great deal about the causes of cardiovascular disease, but there is still more to be learned in order to prevent the development of cardiovascular disease. Additional research is also needed into new therapies once cardiovascular disease has been diagnosed. And equally important is research into questions of cardiovascular care protocols, the quality of clinicians and methods for improving cardiovascular care.

The ACC is committed to improving the quality of care that cardiovascular patients receive. In 1997, the College launched the National Cardiovascular Data Registry (NCDR®) as a result of its exploration of various strategies for collecting and implementing clinical data to improve cardiovascular care. The outgrowth of that effort focused on quality patient care through standardized measurement of clinical practice and patient outcomes. Then, and now, NCDR is committed to including clinicians and care providers in its leadership and using standardized, clinically relevant data elements and scientifically appropriate methods to collect, analyze and report clinical outcomes.

Today, more than 2,200 hospitals nationwide participate in the NCDR's six, soon to be eight, inpatient registries, in addition to the 4,285 clinicians participating in the NCDR's two outpatient registries. As the US' preeminent cardiovascular data repository, the NCDR provides evidence-based quality improvement solutions for cardiologists and other medical professionals who are committed to measurement, improvement and excellence in cardiovascular care. The NCDR, a trusted patient-centered resource, has also developed clinical modules, programs and information solutions that support the areas of cardiovascular care where quality can be measured, benchmarked and improved to make a difference in patients' lives.

NCDR data has been studied for a variety of purposes, including consistency with guidelines,[1] appropriateness,[2] and comparative effectiveness,[3] to name a few. The Food and Drug Administration has long collaborated with NCDR, providing funding for the Improving Pediatric and Adult Congenital Treatment (IMPACT) Registry and development of an atrial fibrillation registry. NCDR also participates in the Food and Drug Administration's (FDA's) Sentinel Initiative, looking at methods of drawing on registry data as a mechanism of providing safety signals to the FDA. More recently, the College has collaborated with The Society of Thoracic Surgeons (STS) and the FDA to develop the STS/ACC Transcatheter Valve Therapy (TVT) Registry™ for use as a vehicle for quality improvement by physicians and for post-approval studies on novel technologies and ongoing postmarket surveillance. Representatives from various stakeholders, including the FDA, the National Institute for Heart, Lung and Blood Institute, Centers for Medicare and Medicaid Services, industry and the public, have been invited by the ACC and STS as key stakeholders in the TVT Registry. Other efforts are underway to use other NCDR registries in a similar fashion.

This past year, the College took the next step in demonstrating its commitment to research, adopting three key principles that will guide its advocacy on research issues:

- Increase the availability of funding for research
- Remove barriers to research
- Develop and implement a learning health system

The first principle is indirectly relevant to the Common Rule in that streamlined administrative requirements free up resources for research operations. Proposals to reduce review requirements for low-risk research necessarily implicate the second. The implications of the Common Rule for this third principle are worth additional discussion.

It is safe to say that improving the quality of care for and outcomes for patients is the principal goal of the healthcare community. Particularly with the increasing use of electronic data collection through a wide range of sources, there is a wealth of information that could be used to accomplish this goal, allowing clinicians and biomedical researchers to learn about care being provided today, not just about drugs and devices, but also care plans, clinician training and competence, ideal patient characteristics for specific therapies and more. However, current rules and regulations impose barriers, both real and imagined, for realizing a "learning health system" as advocated by the US Institute of Medicine.[4] Under the current system, clinical research is separate and distinct from the provision of care. New models for conducting clinical trials, such as the "pragmatic clinical trial," reimagine them as integrated within the ongoing care process and the existing care system. These new models are designed to take advantage of existing data streams, reducing the costs and burdens of research and the amount of time it takes to enroll patients into clinical trials, encouraging the move of research from academic medical centers based largely in urban environments into broader clinical practice and better enabling the transition of new guidelines for improved care practices into the healthcare system. **As such, the College believes that it is critical that revisions be made to the Common Rule that allow for the development and implementation of a true learning health system.**

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[1] Chan PS, Patel MR, Klein LW, et al. Appropriateness of Percutaneous Coronary Intervention. JAMA 2011; 306(1):53-61.

[2] Al-Khatib SM, Hellcamp A, Curtis J, et al. Non-evidence-based ICD implantations in the United States. JAMA 2011; 305(1):43-49.

[3] Weintraub WS, Grau-Sepulveda MV, Weiss JM, O'Brien SM, Peterson ED, Kolm P et al. **Comparative effectiveness of revascularization strategies.** *N Engl J Med.* 2012;**366**:1467-76.

[4] Institute of Medicine. Best Care at Lower Cost: The Path to Continuously Learning Health Care in America. Washington, DC: The National Academies Press, 2013. Doi:10.17226/13444.

Application of the Common Rule

The College strongly supports extending the application of the Common Rule to all research conducted by institutions receiving federal funding and all clinical trials other than those regulated by the Food and Drug Administration (FDA). As an organization that receives federal funding for research, the ACC has long opted to apply the Common Rule to all of its research, and based on anecdotal evidence that this holds true for most organizations conducting research subject to the Common Rule. The rationale for this determination is two-fold. First and foremost, it is of the utmost importance to the College and its members that any subjects of research that it conducts be treated in an ethical manner. For the College, research participants are not simply research subjects whose purpose is to expand the knowledge base and to improve care for society; they are also individual patients who deserve to receive the best possible care and to be treated with the utmost respect.

Additionally, from an organizational compliance perspective, it is easier to administer and conduct research when all of that research is governed by the same set of rules and regulations. The College receives funding to conduct research from a wide array of sources. Often times, individual research projects receive funding from multiple sources, a situation not uncommon today given the difficulty researchers face in obtaining funding. Rather than parsing out the research funded by the federal government and regulated by the Common Rule and developing multiple sets of operating guidelines, all of the College's research is governed by one set of rules. In so doing, the College has simplified its operations for its research administrator, researchers and other individuals engaged in the research enterprise. The ACC believes that other institutions and researchers would similarly benefit from such simplification.

Exclusions

HHS proposes to create a new category for research, that is, research that is "excluded" from regulation by the Common Rule. Under this proposal, there are 11 categories of exclusions, including some that would no longer be considered "research" as defined by the Common Rule, some that would be considered to constitute low-enough risk so as not to require review by an IRB and one that would apply to research involving the secondary use of non-identified specimens. **The rationale for this proposal is that the current regulatory schema creates unnecessary layers of review, increasing the burden and costs of conducting research beyond that which is appropriate. Overall, the College supports this proposal and the rationale.** The ACC believes that there are certain types of research that involve such low levels of risk so as not to require oversight by a third party, nor would they require extensive regulations to ensure research subjects are treated ethically.

Throughout this section, HHS requests comment on the reasonableness of relying on investigators to make the determination regarding the applicability of exclusions, as well as the appropriateness of imposing documentation and document retention requirements for excluded research. In general, the College believes that investigators are ethical and well-intentioned. That said, **the ACC would support a requirement that research administrators be involved in making determinations regarding the applicability of exclusions.** The Common Rule and other relevant research regulations are quite complex. Often times, investigators are not as well-versed in all of the elements of these regulations as is needed to make such determination, whereas research administrators are generally immersed in this universe. **The College would also support the implementation of documentation and document retention requirements for excluded research.** For compliance purposes, it is essential that investigators and research administrators are able to demonstrate their review of regulations and consideration of biomedical ethics concerns before beginning a research study. Additionally, as is noted in the discussion of the transparency principle in the preamble to the proposed regulation, it is important

for researchers to be able to demonstrate to research study participants that their well-being has been considered thoroughly.

Exclusion of activities that are not deemed research

Program improvement activities

The first exclusion proposed in this Notice of Proposed Rulemaking (NPRM) is for the collection and analysis of data for an institution's own internal operational monitoring and program improvement purposes. These are essentially program evaluation activities that organizations conduct on a routine basis to assess their own performance, rather than to develop generalizable knowledge, and could include activities required by other federal programs. For example, under the federal Electronic Health Records Incentive Program, participating hospitals and medical practices are required to solicit feedback on their performance from patients. Under current law, the Common Rule would be triggered. However, it is widely acknowledged that the risk to individuals completing such a survey is extremely low, rendering it unnecessary and burdensome to consult with an Institutional Review Board (IRB) to review the parameters of such research. **The ACC strongly supports the adoption of this proposal in the interests of streamlining the evaluation of program activities and enabling institutions, medical practices and IRBs to focus resources on higher risk activities.**

Quality assurance and quality improvement activities

Also proposed for exclusion are quality assurance and improvement activities. However, the definitions of quality assurance and quality improvement activities remain clouded, making it difficult to evaluate the validity of this newly proposed exclusion. Based on one reading of the preamble, it could be argued that HHS has proposed limiting "quality assurance and improvement activities" to primarily quality assurance activities. **The College would strongly oppose such a definition and urges HHS to further clarify these definitions before finalizing this rule.**

Public health surveillance

HHS also proposes to create an exclusion category for research conducted for public health surveillance purposes. **The College supports this proposal, particularly in light of the clear attempt by HHS to align the Common Rule with the public health requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA).** It is critical that the requirements of the Common Rule not interfere with the mission imposed on public health agencies. Excluding public health surveillance activities from the Common Rule accomplishes this goal without exposing affected individuals to increased risk.

Exclusion of activities that are low-risk and already subject to independent controls

Certain activities covered by HIPAA

As is noted in the proposed rule, there are a number of overlapping regulations that govern research and the use of healthcare data for research purposes. HIPAA is one of those regulations that overlaps with the Common Rule in instances where "protected health information" is "used" or "disclosed" by a "covered entity" as defined by HIPAA. In recognition of this overlap, HHS proposes to have HIPAA govern in such instances, rather than the Common Rule, in order to minimize confusion, as well as in recognition of the strength of HIPAA's requirements with respect to privacy, confidentiality and security. Given that HIPAA specifically focuses on questions of privacy and security of data, the ACC believes that, in many instances, HIPAA is actually more protective of human subjects than the Common Rule. As such, **the College agrees with HHS' rationale and supports this proposal, particularly if it is limited to data**

collected or generated in the course of clinical practice, rather than in the collection of new information.

Applicability of exclusions to the subparts

The College believes that the proposed exclusions addressed herein should be applied broadly to all of the subparts. The research described in the exclusions is of such low risk that even studies involving human subjects in need of greater care such as children, prisoners and pregnant women do not warrant increased oversight. Instead, this research is either already subject to oversight as is the case with HIPAA-covered activities or is designed to evaluate education or programmatic activities, rather than designed to focus on research that includes the real potential for harm to the subject.

Exemptions

Making exempt research determinations

While exempt studies do not require administrative review, current federal recommendations do include such review as one option. Because of this, most institutions conduct administrative reviews for exempt studies. Under the current proposal, this recommendation would be removed. Instead, researchers would complete a decision tool that would demonstrate that their proposal meets the requirements for an exemption or rely on their institution's designated official(s) to make the determination on their behalf. Given that the categories of exempt studies have been defined as such because of their low risk of harm to subjects, there are few reasons for requiring administrative review of all such studies. With clearer definitions of what constitutes an exempt study and the new exclusions, the risks are even lower that studies with greater risk will escape review. Thus, the benefits outweigh the risks. **The ACC supports this change and appreciates the efforts by HHS to reduce the administrative burden. The ACC would urge HHS to provide the opportunity to comment on a draft version of any federally-developed decision tools to ensure that they truly reduce the administrative burden imposed by the current administrative reviews.**

Exemptions subject to documentation requirements but not privacy safeguards

<u>Research involving benign interventions in conjunction with collection of data from adult subjects</u>

In the NPRM, HHS proposes to create a new exemption for research involving benign interventions in conjunction with the collection of data from an adult subject through verbal or written responses or video recording where prospective agreement is obtained from the subject in certain circumstances. Research of this type is clearly so low risk as to render IRB involvement unnecessary, particularly in light of the agreement that the subject prospectively authorize his or her own participation and the requirements regarding the nature and duration of the intervention. Membership-based organizations like the College regularly conduct studies of its members to better understand their needs, as well as their interests, areas of expertise and the like. The ACC has a standing panel, CardioSurv, consisting of a representative sample of members who agree to regularly respond to questions regarding their needs, interests, and awareness level and knowledge of various subjects. The risks associated with this research, as described in the proposal, are minimal and lack short-term, let alone long-term effects on individual participants. **As such, the College supports the creation of this new exemption.**

Exemptions subject to documentation requirements and privacy safeguards

The lack of alignment between the Health Insurance Portability and Accountability Act (HIPAA) regulations and the Common Rule has been a long-standing concern for the College. **This proposal takes significant steps towards addressing that concern, and the College strongly supports this effort. To**

that end, the ACC supports efforts by HHS to align the HIPAA Security Rule with HHS's requirements for the security and privacy of data protected by the Common Rule for healthcare research. Alignment of the Common Rule with HIPAA and the requirements for data security and privacy imposed by HHS' Office of Civil Rights (OCR) would make compliance easier for covered entities without reducing the privacy and security afforded to human subjects and their data. Additionally, imposing such a standard should diminish the subjectivity in determining which security practices should be in place and aid healthcare researchers in developing an adequate security infrastructure to protect subjects from informational risks. The College would recommend that it be clearly enumerated in regulations that covered entities and business associates would not be subject to both the HIPAA requirements and the safeguards promulgated by the Secretary; instead, they should only be measured against the HIPPA Privacy and Security regulations. To require both could create the potential for confusion and conflicts, so it is essential that the regulatory language is clear on this matter. As mentioned previously, the protections afforded by HIPAA are adequately stringent.

With respect to the obligations of IRBs, most IRBs that review healthcare research also have experts on HIPAA and function as a Privacy Board. For these institutions, this would not constitute a broadening of IRB responsibilities. However, where the IRB does not already review research where HIPAA remains relevant, this could constitute a change in their responsibilities, requiring the hiring of additional staff and development of new expertise. The College offers no comment on the merits of these changes, but merely offers the comment that it could potentially require some change for existing IRBs.

While the research carried about by the ACC and the cardiovascular care team would generally meet the requirements for HIPAA compliance and not the proposed Secretary's list of privacy safeguards, the College believes that eight years is too long between reviews of the privacy safeguard measures included on the Secretary's list. Given the rapid pace of technology's evolution, it is essential that privacy safeguards evolve in a similar manner. As such, **the ACC recommends that the Secretary's list be reviewed at least every three years**. Three years should be sufficient to capture any significant changes in technology and related concerns, but it is also not so frequent as be overly burdensome for HHS, IRBs or investigators.

<u>Secondary research use of identifiable private information</u>

Currently, the secondary use of identifiable private information for research is subject to IRB review and approval. As noted in the NPRM, the expedited review procedure is frequently used, and the requirement for informed consent is typically waived. The proposal for a new exemption for the secondary use of identifiable private information that has been or will be acquired for non-research purposes would require that:

- Subjects have received notice that their information could be used for research
- The secondary use of identifiable private information be limited to the specific purposes for which the investigator requests access to such information.
- The new privacy safeguards and security requirements addressed above are met

The College opposes the addition of the proposed requirement that patients receive notice prior to allowing individually identifiable information to be used for secondary purposes.

With the imposition of these new requirements, the standards for this exemption would actually be raised from current law and functionally render most such research difficult, if not impossible. Although this exemption would eliminate the need for IRB oversight, the proposed requirements potentially place greater burdens on the research than are currently imposed by law. For example, observational registries are operated generally by either the quality improvement department or the cardiovascular service line within an institution. Because the maintenance of the registry is not in and of itself considered "research,"

the department operating the registry often does not intersect with the research department within an institution. Thus, the staff operating the registry do not realize that the data being collected will be used for research purposes. Additionally, many institutions that participate in observational registries have no infrastructure for conducting research, and therefore, lack appropriate research oversight. Generally, registry participation does not require an institution to identify a principal investigator to oversee the activity, a study coordinator does not follow the subject through the course of treatment and some institutions' internal control functions are limited to assessing the quality of registry data. As a result, many of the institutions participating in the registry do not have the capabilities to engage in research. A new requirement imposing requirements on an institution to inform subjects of the specific purposes of such secondary use may place more burdens on institutions, discouraging such institutions from participating in observational registries.

One solution that has been suggested is the incorporation of study consent language into procedural consent forms. Unfortunately, procedural consent forms used by participating institutions in the registry are generally not standardized, making it challenging to incorporate standardized study consent language into them. Additionally, procedural consent forms must be approved in accordance with institutional requirements; some institutions may be unwilling or unable to accommodate the inclusion of study informed consent language into their procedural consent forms. A requirement to do so would likely hamper their ability to participate and could potentially reduce participation in the registry if this became a requirement for participation.

The ACC does support educating patients and potential subjects on the importance of research and encouraging their participation in it. If HHS concludes that some notice is necessary, despite strong evidence that it is frequently waived by IRBs, the College would recommend requiring that broad, general notice be given to patients that their institutions may be participating in activities that could lead to patient data being used for research. This could be in the form of a sentence included in the general forms completed by patients or visible signage posted throughout patient areas of the institution. If HHS adopts this requirement, the ACC recommends that the Department develop sample standardized language that participating institutions could use. **Additionally, the College encourages the development by HHS of a broad education campaign about the benefits of participating in healthcare research.**

Exemptions subject to documentation requirements, privacy safeguards, limited IRB review and broad consent

The exemptions proposed under this section address the biospecimens or identifiable private information. From the preamble discussion pertaining to those exemptions and the regulatory language, it appears as though these exemptions are intended to apply not only to biospecimens and identifiable private information related to those biospecimens, but also to identifiable private information not related to biospecimens. However, based on the preamble discussion pertaining to other proposals addressing identifiable private information and the public meeting held this past September to discuss the NPRM, there are indications that HHS only intended these proposed new exemptions and other proposals pertaining to "biospecimens and identifiable private information" to apply to biospecimens and identifiable private information connected to those biospecimens. **The College urges HHS to clarify its intentions and the resulting regulatory language to address this question.**

Given the lack of clarity regarding the implications of these provisions on identifiable private information not connected to biospecimens, the ACC urges HHS to delay implementation of any provisions pertaining to this type of information unless and until clarification is made and the public has the opportunity to thoroughly review and comment in light of the revisions.

Proposed changes to obtaining, waiving and documenting informed consent

The overly complex, legalistic and lengthy nature of informed consent forms is a longstanding complaint of clinicians and research participants alike. **The College strongly supports efforts to make the informed consent process one that is truly interactive and meaningful to research participants.** Despite plain language requirements, institutions routinely fail at making consent documents understandable for patients. Instead, such documents are routinely aimed at addressing liability concerns. To that end, the ACC believes that a template generated by HHS will be greatly appreciated by investigators and IRBs and clearly demonstrate what is expected. Such government-generated templates are frequently used and become the standard against which similar documents are measured.

Elements of informed consent

The ACC strongly supports the proposal to allow institutions to streamline the consent process by combining the consent required for these proposed exemptions with HIPAA-required authorization.

The College also supports efforts to incorporate patients and research subjects into the research process itself by requiring the return of results to participants. However, the ACC does have concerns about such a requirement where the entity or individual conducting the research does not have a direct relationship with the participants. It may be more harmful than helpful for individuals or entities to contact study participants particularly in situations where the research is being conducted using the data secondarily. Additionally, in situations where de-identified data is used for the research study, it would be impossible for the entity or individual conducting the research to notify participants of the study results. **In such cases, the College urges general publication of study results to constitute the return of research study results to participants.**

Waiver or documentation of informed consent

The College appreciates the proposed rule's clarification that waivers of informed consent may not be permitted for research that is subject to FDA regulations. However, this distinction is potentially harmful in a learning health system where we are continually learning and improving not only the quality of care being provided to patients by clinicians, but also the therapies being used to treat them. A system that is constantly using data collected for a variety of purposes that may or may not be within the jurisdiction of one particular agency requires harmonization of the regulations governing the use of that data, particularly in the case of secondary uses for that data. Anything else will limit the use of that data and the efficiency of the system, increasing burdens and costs. **In the strongest terms possible, the ACC urges that HHS bring together the agencies and offices under its purview to agree on a single set of regulations and rules affecting the collection and use of clinical data for a wide variety of purposes.** The College believes that it is to the benefit of all patients that real world evidence be used to improve the quality of care patients receive, as well as the quality of the products and therapies available to them. Imposing unnecessary regulatory hurdles only impedes the accomplishment of this sorely needed harmonization.

The College supports the proposal to allow IRBs to approve research proposals where investigators obtain identifiable private information from prospective human subjects without informed consent where that information is to be used for the purpose of screening and recruiting subjects for clinical trials. Recruitment for clinical trials is a source of significant cost and burden and frequently delays the completion of clinical trials. This is one potential method for addressing this problem. Additionally, as is referenced repeatedly in these comments, the College strongly supports the harmonization of federal research regulations. This proposal would align the Common Rule with FDA regulations on this matter.

Posting of consent documents

The College supports requirements to post research study consent documents. Currently, information on ongoing clinical studies is posted at clinicaltrials.gov. The ACC recommends that HHS consider posting informed consent documents there, as well. Additionally, the College would support requirements to post revised consent documents on clinicaltrials.gov, as well, to ensure that anyone interested in learning more about the study and its requirements has access to the most current information.

Alignment of federal regulations

Uses for and maintenance of patient data are regulated by numerous government agencies, depending on the purpose for which the data is being collected or circumstances under which it is being studied. While there are frequently similarities among the requirements, there are times where inconsistencies exist and confusion reigns. The ACC urges HHS to work with the agencies and offices within the Department, such as the Office of Human Research Protection (OHRP), FDA, OCR and the Centers for Medicare and Medicaid Services, to align regulations and guidance on issues where there are similar concerns.

Before taking steps to standardize or harmonize all of the federal regulations and guidance in the area of research, the ACC urges HHS to work with the other federal agencies that regulate this area, as well as affected internal offices and agencies, to identify and map out issues of overlapping jurisdiction and concern. The different federal agencies perform separate albeit related functions. While standardization of federal regulations and guidance may be beneficial in many instances, this may not always be the case. Thus, such efforts should be undertaken methodically and thoughtfully. For example, as described above, the conflicting regulations and guidance pertaining to consent for secondary use of data for research are particularly troublesome in light of the FDA's desire to use registry data originally collected for quality improvement purposes for its own purposes that may or may not permit the waiver of informed consent for research. **The College recommends that HHS specifically publish this information, identifying key areas where federal statutes prevent harmonization of regulations and guidance and work with stakeholders and Congress to address those concerns.** The Administration has taken some positive steps towards identifying and reducing regulatory burdens in this proposal, but the College believes that there is more that can be done.

Cooperative research and proposal to cover unaffiliated IRBs

Among the important changes that occurred during the 20th century was the rise of biomedical ethics and the recognition that the research participants have rights that require perhaps even more protection than patients receiving approved therapies. IRBs are critical to ensuring that clinical trials and other research involving human subjects respect those rights. That said, interpretations of the regulations governing human subjects and IRBs have evolved to require reviews by multiple IRBs when the studies involve multiple sites. Rather than offering additional protection for the research subjects, the requirement for the multiple IRB approvals increases the administrative burden and delays the implementation of studies, increasing the costs of clinical trials and potentially delaying access to new therapies. **As such, the ACC supports efforts to reduce the number of IRBs required to review multi-site research.**

NCDR relies on an accredited, centralized IRB, Chesapeake IRB, to review its research proposals and ongoing operations as a purveyor of observational studies. Additionally, the NCDR has committed to compliance with the Common Rule for all of its research, not just its federally funded research. This commitment and centralized IRB review is not sufficient for many participating sites. Instead, those sites also require their own IRBs review NCDR research proposals, requiring an investment of ACC staff time and resources to assist with these reviews, as well as to address inquiries from potential participants determining whether additional IRB review is required. These reviews and inquiries hinder the efforts of interested parties to begin registry participation. By and large, these additional IRB reviews reach the

identical conclusions to the NCDR's IRB. Where the conclusions are not identical, only minor changes are required for the site to participate, changes that are imposed solely on that site. **The College believes that single IRB review for multi-site research is sufficient and urges the HHS to adopt its proposal to require that all institutions located in the United States engaged in cooperative research rely on a single IRB as the reviewing IRB for that study. In that vein, the ACC also supports the extension of HHS's authority over IRBs to ensure compliance with the requirements of the Common Rule.**

The ACC does have concerns regarding HHS's proposal to allow three years before institutions are required to comply with this policy. The College does not believe that it will take three years for institutions to develop and implement policies allowing for compliance with this requirement and urges HHS to implement this provision at the same time and recommends that HHS adopt a shorter compliance period.

Changes to promote effectiveness and efficiency in IRB operations

The proposals addressed in this section are aimed at reducing burdens for IRBs, allowing them to focus their resources on reviewing higher risk research proposals. The College is largely supportive of such efforts and agrees that the proposed changes, such as eliminating requirements for annual review of continuing research unless there is specific justification for it, would accomplish these goals.

Minimal risk studies

Under current regulation, OHRP draws clear distinctions between levels of scrutiny placed on research posing "minimal" risk versus other types of research activities in a number of different ways. For instance, research posing minimal risk is identified in a list approved by the Secretary and is eligible for expedited review. Unfortunately, this list has been static, remaining unchanged for a number of years. The proposal would require that OHRP update the minimal risk research list upon promulgation of the regulation and then at regular intervals, using appropriate data regarding risks to the extent possible. **The ACC would recommend reviewing the list on an annual basis, based on the constant evolution of technology and the effects this may have on what constitutes minimal risk.** Given the constant change in technology and science, the College supports reconsideration of what constitutes minimal risk research on an ongoing basis and as such, would encourage OHRP to regularly update the minimal risk list as appropriate.

Conclusion

The ACC is a firm champion of the rights of human subjects in research studies and ensures ethical reviews of studies it sponsors and supports. To that end, the College believes that the comments above will further these shared goals. The ACC appreciates the opportunity to comment on this draft policy and would welcome the opportunity to discuss this draft policy further. We look forward to working with HHS on this and future matters. Please direct any questions or concerns to Lisa P. Goldstein, ACC's Regulatory Policy Counsel, at (202) 375-6527 or lgoldstein@acc.org.

Sincerely,

Kim A. Williams, MD, FACC, FASNC