CONSORTIUM OF
INDEPENDENT REVIEW BOARDS

January 14, 2008

Via E-Mail [impairedcapacityohrp@hhs.gov]

REQUEST FOR INFORMATION ON RESEARCH THAT INVOLVES ADULT INDIVIVIDUALS WITH IMPAIRED DECISION-MAKING CAPACITY
Office for Human Research Protections
The Tower Building
1101 Wootton Parkway
Suite 200
Rockville, MD 20852

Re: Comments on Request for Information and Comments on Research That Involves Adult Individuals with Impaired Decision-making Capacity

Dear Sir or Madam:

The Consortium of Independent Review Boards ("CIRB®") welcomes the opportunity to comment on the Office for Human Research Protections ("OHRP") request for information and comments on the need for additional regulations or guidance in connection with research involving adults with decisional impairment (72 Fed. Reg. 50,966 (September 5, 2007)). As OHRP knows, CIRB is a consortium of independent institutional review boards ("IRBs") located in the United States and Canada. The membership has a central mission of promoting the protection and rights of human research subjects, while providing an understanding of how independent IRBs support this goal. Approximately 75% of clinical research in the United States is conducted in non-academic settings, and independent IRBs review a majority of this research.

As an organization of independent IRBs that regularly provide central review for studies occurring in the 50 states and elsewhere, CIRB is uniquely familiar with the difficulties associated with reviewing clinical research studies that may involve adult individuals with impaired decision-making capacity. Among other things, OHRP seeks information and comments on any problems or concerns in connection with obtaining consent from a legally authorized representative ("LAR") on behalf of a prospective adult research subject with decisional impairments, on the appropriate definition of "adults with impaired decision-making capabilities", and on whether additional guidance or regulations are needed when dealing with certain adult subjects that may develop impaired decision making capacity (e.g. persistent, fluctuating, or progressive decisional impairment) after

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enrolling in a clinical research study. As an initial comment, CIRB believes that these areas are best addressed through the federal guidance process, as opposed to the regulatory process, to assure the flexibility necessary to stay current with best practices in clinical research.

A. Legally Authorized Representatives

While federal regulation allows for surrogate consent through the use of LARs, it provides no guidance on who should be able to serve in this capacity. Instead, states have been left with the task of developing laws and regulations governing who can consent on behalf of a decisionally impaired adult to engage in research. CIRB does not question the states' proper regulation and jurisdiction in this area. However, without a national model to provide guidance to the states, a patchwork of laws and in some cases no laws, address and/or are silent on who can serve as an LAR for clinical research matters. For example, while many states allow a number of individuals to act as LARs, such as guardians, persons with power of attorney, family members, and even attending physicians and surrogates, significant state differences exist that limit the LAR's ability to provide surrogate consent to participate in research. Many states require the LAR to have durable power of attorney or to go through the cumbersome process of becoming a court-appointed guardian. Some state laws are so restrictive that even court-appointed guardians cannot provide surrogate consent to participate in research.

The lack of federal guidance creates two significant problems. Of profound concern, differences in state LAR laws place adults with impaired decision-making capacity at a disadvantage in connection with multi-state, multi-site studies because eligible subjects may be prevented from being enrolled in studies that similarly situated subjects are enrolled in simply because of where the subjects live. Such barriers are particularly troubling when this patient population has the potential to directly benefit from participation in the research. Some level of uniformity in state LAR laws is necessary to achieve parity for decisionally impaired adults.

Further, state law variations present a challenge to the research community, and in particular, the central IRB, in ensuring that current laws and regulations of each state are followed in connection with multi-state research. In an effort to keep up with the constantly changing state laws and regulations, a number of years ago CIRB commissioned the creation of a database that includes all the state requirements regarding legally authorized representatives. Today, the database, called *clinlaw*, is maintained and regularly updated by the Thompson Publishing Group and available online to subscribers. However, the difficulties created by the differing laws can and do lead sponsors and investigators to exclude decisionally impaired adults from protocols that are not specifically designed for this population, potentially affecting the robustness of the research and clearly disadvantaging decisionally impaired adults.

It is CIRB's belief that this community of vulnerable subjects would be better served if variations in state LAR laws governing research were minimal. Thus, CIRB encourages

the development of an ethically and legally sound federal guideline on LARs directed at the states. The proposed guideline would address:

(1) who should be able to act as an LAR, creating a hierarchy as appropriate, and

(2) the types of research for which LARs should be able to provide consent on behalf of decisionally impaired adults.

For practical reasons, CIRB supports a system that does not require court appointed guardians except in extremely limited situations. It is CIRB's hope that a guideline of this nature will provide states with a framework to create uniform laws and regulations and would help ensure that adults with impaired decision-making capacity will have the same opportunities to participate in clinical research regardless of their location. If OHRP decides to pursue this activity, CIRB recommends the active involvement of all stakeholders to allow full consideration of the proper identities, uses, and limits of LARs in the context of clinical research. CIRB also recommends active review of progressive state laws in this area; for example, California legislation enacted in 2003 squarely addresses surrogate consent for the decisionally impaired for both emergency and non-emergency research. *See* California Health and Safety Code § 24178.

B. Definition of "Adults with impaired decision-making capacity"

OHRP is seeking comments on how to define the population of adults with impaired decision-making and offered the following definition:

> "Adults with impaired decision-making capacity are persons who do not have the capacity to give legally effective informed consent to treatments or procedures involved in research/clinical investigation, under the applicable law of the jurisdiction in which the research/clinical investigation will be conducted."

CIRB believes that the proposed definition is workable if OHRP provides useful guidance on when such adults lack "capacity" to give legally effective informed consent. As recognized in OHRP's request for comments, the determination of whether a person has the capacity to provide legally effective consent is a state issue. Even more problematic than the LAR issue, the understanding of when an adult subject does or does not have the "capacity to consent" is not just different from state to state, but also from institution to institution. As in the LAR area, these variable processes for determining "capacity" have broad implications on whether a subject can be enrolled in a study. Thus, CIRB encourages OHRP to issue guidance to assure that any variations in state and institutional standards for evaluating "capacity" are minimal.

OHRP also requested comments on whether guidance or additional regulations are necessary to address the treatment of adult subjects who may develop impaired decision making capacity, or who may no longer be decisionally impaired, after consent has already

been obtained. CIRB supports the development of guidance in this area that would provide investigators with guidelines for:

(1) determining when it would be appropriate to seek consent from an LAR in order to allow a subject who has become decisionally impaired after providing consent to continue to participate in research; and

(2) addressing the special consent issues associated with subjects who fluctuate between being decisionally impaired and being capable of providing legally effective consent.

If OHRP decides to pursue the issuance of guidance to address these issues, CIRB once again recommends the active involvement of all stakeholders in the development of definitions and procedures applicable to this special population. Such involvement will foster the formation of guidelines that assure the level of precautions necessary to protect decisionally impaired adults without unnecessary exclusions.

CIRB believes that addressing the particular needs of the decisionally impaired adult in the context of clinical research is a valuable undertaking and thanks OHRP for the opportunity to provide its comment on this crucial matter.

Sincerely,

Cami Gearhart

Cami Gearhart
Chair

cc: CIRB Membership