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Adults with Impaired Decision-Making Capacity

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COGR comments on research that involves adult individuals with impaired decision-making capacity.

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COUNCIL ON GOVERNMENTAL RELATIONS

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January 14, 2008

Julie Kaneshiro
Office for Human Research Protections
Department of Health and Human Services
1101 Wootton Parkway
Suite 200
Rockville MD 20852

SUBJECT: Request for Information on Research that Involves Adult
Individuals with Impaired Decision-Making Capacity

Dear Ms. Kaneshiro:

The Council on Governmental Relations (COGR) is an association of more than 175 research universities and their affiliated academic medical centers and research institutes. COGR concerns itself with the influence of federal regulations, policies and practices on the performance of research and other sponsored activities conducted at its member institutions. COGR's member institutions conduct much of the biomedical and behavioral human subjects research supported by the Department of Health and Human Services (HHS). These organizations share the Office for Human Research Protection's (OHRP) commitment to ensuring the protection of all research participants but particularly those likely to be vulnerable to coercion or undue influence.

Our comment is directed to the central question posed by OHRP: Does the current regulatory provision [45 CFR 46.111(b)] provide sufficient protections for adult individuals with impaired decision-making capacity or are additional regulatory safeguards needed? (Q 3a)

No New Regulation

We believe the current regulatory provision is sufficient. Additional guidance can be useful but new regulations will not necessarily lead to greater protections and may limit research. Over the past few years, many observers have called for reviews of the additional protections for children, pregnant women and neonates and prisoners built into the regulations noting that the resulting exclusion from research of populations defined as vulnerable has had the unintended effect of prohibiting them from enjoying the benefits of some biomedical and behavioral research. Absent compelling evidence of systemic unacceptable practices with regard to adult individuals with impaired decision-making capacity as research subjects, it would be unwise to introduce a new set of regulations that may

While we recognize that the current straightforward regulatory requirement for an Institutional Review Board (IRB) determination on whether additional safeguards should be included in a study protocol to protect vulnerable subjects may seem inadequate, the other subparts for children, pregnant women and neonates and prisoners offer a cautionary lesson in the challenge of establishing additional regulations.

Lessons from Current Vulnerable Population Subparts

As an example, the debate over Subpart C that provides additional protections for prisoners (45 CFR 46 Subpart C) demonstrates the problems that can arise with the introduction of regulations for a class of subjects. The question of how to manage research with prisoners has been the subject of study and reports by the Secretary's Advisory Committee on Human Research Protections (SACHRP) and National Human Research Protections Advisory Committee (NHRPAC). These examinations have grappled with questions like those raised in this Request for Information (RFI) reaching less than clear and satisfactory conclusions. What is clear from the examination of Subpart C is that the research environment is dynamic, reflecting changes in the population it attempts to protect. As a consequence, setting definitions of prisoner, in the case of Subpart C, or adults with impaired decision-making capacity in the case of this RFI in regulation as opposed to guidance makes the regulations too static and unresponsive to change. Thus, the question of whether the definition of "prisoner" includes someone on probation status or under house arrest is akin to asking whether impaired decision-making is a persistent or progressive condition. As scientists study cognition and decision-making capacity, our understanding will change. Moreover, defining adults with impaired decision-making capacity will likely generate more ambiguity than clarity. For example, there are over 10 Federal definitions of "disability" currently in effect. These sometimes conflicting definitions require protracted resolution processes before eligibility within any given standard can be determined. This type of ambiguity and complexity would likely lead to the unintended effect of prohibiting adults with impaired decision-making capacity from enjoying the benefits of some biomedical and behavioral research.

The introduction of new regulations modeled after those used for prisoners that limit the types of research or using the model for children that introduces the tiered system of risk assessment will not ensure greater protection. Setting up a tiered, risk-based menu of permissible categories is workable but this approach can be equally frustrating at times. IRB members can be diverted from thoroughly discussing whether the relationship between risks and benefits is reasonable and whether the risks are reasonable with respect to the importance of the knowledge to be gained, etc., to a focus instead on picking a category. It is better for the subjects if the IRB remains focused on identifying the appropriate criteria to apply and inclusion of safeguards applicable on a case-by-case basis and wrestling with mitigating the risks as weighed against the anticipated benefits without the oversimplification of such a menu.

IRB's Role in Setting Local Context

This is an area in which thoughtful and careful deliberations and the creation of safeguards on a case-by-case basis likely provides the best protection for this vulnerable population. A case-by-case approach permits a truly customized set of protections to be developed by the investigator in cooperation and collaboration with the IRB. This approach will more directly and effectively

achieve the goal of greater protections. The case-by-case approach is particularly important in this area because of the range of state and local statutes defining the responsibilities of the Legally Authorized Representative (LAR). Some states address research specifically in statutes describing LARs; others do

not and rely on the statutes governing clinical care; and still others remain silent. National or Federal standards will inevitably spawn greater confusion particularly when dealing with multi-site clinical trials. Deferring to a case-by-case approach reflecting the local context allows IRBs to do their own local and particular thinking – an approach at the heart of the American human research protection system.

For example, the State of California Health & Safety Code Section 24178 clarifies who may serve as a research subject's LAR to provide surrogate consent for the potential research subject. To meet these requirements, the state institutions have developed guidelines for the investigators and IRBs to aid them in the process of review and the conduct of research. The guidance addresses the meaning of a cognitive impairment and offers IRBs and investigators thoughtful criteria to use in determining the use of a LAR. In states where the laws are silent on research per se, IRBs look to the state statutes addressing proxy consent for medical treatment for cognitively impaired patients. States set different standards for a LAR to use to make a determination – either substituted judgment or best interest, or both in a specific set of circumstances. These types of issues are appropriately a state question and federal definitions can add an unnecessary layer of confusion.

Guidance for Investigators and IRBs

Additional guidance may be useful and a reasonable next step in this area. OHRP's *IRB Guidebook* provides a helpful discussion and "Points to Consider" (Chapter IV), which work well for IRBs. The National Bioethics Advisory Committee report and follow-up by the HHS Working Group and NHRPAC referenced in the notice provide valuable contextual considerations and recommendations that can be implemented in the review and determination by local IRBS. As an example, guidance synthesizing existing literature would assist institutions and their IRBs in developing procedures for handling consent/assent with decisionally impaired persons that fit their own cultures and resources. Such guidance could help IRBs to explore some of the complexities and nuances of consent and assent for decisionally impaired persons in research or whether assent is ever justified in such cases.

We are concerned with the HHS Working Group's suggestion that certain physical disorders or conditions that may result in impaired decision-making capacity might fall under new regulations. Setting aside the likelihood that this type of condition would either prevent enrollment or terminate enrollment in most studies, this suggestion demonstrates the dangerous elasticity of the definitions proposed.

We also note the distinction or, in some cases the lack thereof, throughout the discussion of research targeted to adult individuals with impaired decision-making capacity versus research that involves these adults. This is a very important distinction if OHRP were to propose a new regulatory framework. In the former case – targeted research – the range of possible elements, e.g., definitions and risk-based assessment, etc., could be examined. In the latter case, a broad epidemiological study or disease survey should include a broad representation of adults and may include those with impaired decision-making capacity. In this case, submitting the entire study to

special requirements would likely frustrate the research and lead to adults with impaired decision-making capacity being excluded unnecessarily.

We urge OHRP to use the information gathered from this request to enhance the guidance available to IRBs to use in their deliberations and review of additional safeguards for vulnerable populations as required in 45 CFR 46.111(b). New regulations are not needed to ensure the protection of adult individuals with impaired decision-making capacity. As NBAC noted in its report, the system is not broken and does not need a regulatory fix.

Sincerely,

Anthony P. DeCrappeo
President