**From:** OC GCP Questions
**To:** [redacted]
**Subject:** RE: informed consent question
**Date:** Tuesday, September 15, 2015 9:41:40 AM

---

Thank you for bringing your concern to FDA's attention. I am not exactly certain what question you are asking, but presumably you want to know whether what the local Institutional Review Board (IRB) is doing is acceptable from FDA's perspective. FDA generally give IRBs wide latitude in determining the level of risk they believe a given protocol entails and in determining whether capacity assessments should be part of the informed consent process. FDA regulations do not define "significant risk" nor does it describe when capacity assessments should be done. Given the protocol you briefly outlined involves a condition characterized by progressive dementia, it does not seem unreasonable to me for the local IRB to require a capacity assessment be included in the informed consent process. Likewise, given the potential unknown risks associated with an investigational drug product, it does not seem unreasonable to me for a local IRB to characterize the risk as significant. This is especially true for an investigational drug product that will likely need to be taken long-term, as is often the case for conditions such as Alzheimer's disease.

It is not possible for me to assess the "suitability" of the informed consent document without actually reviewing the informed consent document and the associated protocol materials; however, the language you provide about the informed consent document (i.e., "*the LAR that he or she names can consent to their participation in 'significant risk' clinical trials*") suggests the IRB wants to assure prospective subjects understand the extent of the LARs authority. Although it would be a matter of state and local law, it is likely the authority of the LAR extends to all subsequent clinical research decisions related to the trial in question and could allow the LAR to consent to the individual's participation in future unknown clinical investigations. It does not seem unreasonable to me for the IRB to require that prospective subjects be alerted to the extent of the LARs authority.

I hope this information is helpful to you. If further assistance is needed, please feel free to contact us once again at the official OGCP mailbox, gcp.questions@fda.hhs.gov

Thank You,

Kevin

Kevin A. Prohaska, D.O., M.P.H., Captain (USPHS)
Senior Medical Policy Analyst
Office of the Commissioner
Office of Good Clinical Practice

**From:** [redacted]
**Sent:** Saturday, September 12, 2015 8:58 AM
**To:** OC GCP Questions
**Subject:** informed consent question

I am contacting the Office of Good Clinical Practice to inquire about the suitability of an informed consent document in use at a local site for a multi-site clinical trial of an IND for Alzheimer's Disease. A local site requirement is that a psychiatrist will determine whether the prospective subject has capacity to name a Legally Authorized Representative (LAR).

The informed consent document includes a section for this determination along with informing the prospective subject that the LAR that he or she names can consent to their participation in 'significant risk' clinical trials. The informed consent document does not provide a definition of 'significant risk' and the capacity assessment determination is for this single clinical trial.

The local investigator communicated a question from the sponsor to the Institutional Official (IO) designate about the reference to 'significant risk'. The explanation provided by the designate is that this requirement is according to the policies and procedures in the IRB Manual. The designate also explained that; "The language is to alert the prospective subject that the LAR can consent to any risk level research including research that involves 'significant risk' and that 'Greater than minimal risk' does not accurately convey this required concept." The consent document is for this one trial which is greater than minimal risk.

From a regulatory perspective the only reference to a 'significant risk' IND is in Sec. 312.32 IND safety reporting: "The sponsor must report any findings from epidemiological studies, pooled analysis of multiple studies, or clinical studies (other than those reported under paragraph (c)(1)(i) of this section), whether or not conducted under an IND, and whether or not conducted by the sponsor, that suggest a significant risk in humans exposed to the drug." There is no NY State statute addressing 'significant risk' clinical trials.

While this clinical trial is greater than minimal risk, the IO designate states that it is a requirement to reference the trial as 'significant risk'. In reality there is no known, unusual clinical toxicity associated with the study drug. The trial has been underway for some time and no significant potential for serious risk to human subjects has developed. To reference this clinical trial as 'significant risk' seems to purposely misinform prospective subjects (vulnerable population) and their LAR. There is no known, effective treatment for Alzheimer's Disease so despite any serious misgivings or anxiety about taking part in a 'significant risk' clinical trial prospective subjects and LARs will likely consent to participate.

Thank you for you insights on this matter.