From: OC GCP Questions
To: [redacted]
Subject: Question on pottential discriminative action on illiterate patients
Date: Thursday, May 24, 2018 12:32:00 PM
Attachments: [redacted]

Good afternoon –

We cannot comment on specifics of any study. I suggest you consult the sponsor of the IND/IDE. The sponsor may also contact the FDA regulatory project manager of the IND/IDE for advice as well.

I can give you general information on illiterate and vulnerable subjects.

Illiterate subjects - Here is advice about obtaining documentation of informed consent when a subject is illiterate. (This excerpt was taken from FDA's Information Sheet Guidances, which may be viewed in their entirety by pasting the following URL into your web browser: www.fda.gov/oc/ohrt/irbs/default.htm.)

Illiterate English-Speaking Subjects

A person who speaks and understands English, but does not read and write, can be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law.

A person who can understand and comprehend spoken English, but is physically unable to talk or write, can be entered into a study if they are competent and able to indicate approval or disapproval by other means. If (1) the person retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (still competent) and (2) is able to indicate approval or disapproval to study entry, they may be entered into the study. The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to participate in the study. An impartial third party should witness the entire consent process and sign the consent document. A video tape recording of the consent interview is recommended.

It is not entirely clear to me whether you are asking about an individual who is simply illiterate, or who has impaired decision making, or both. Being illiterate should not be equated with being unable to consent. An individual may be legally competent, but simply unable to read or write, in which case he/she would not have (or need) a legally acceptable representative.

If the individual has impaired decision making, and the individual's legally acceptable representative is not able to visit the clinic in person, it does not necessarily preclude the individual from participating in the study. Nevertheless, these circumstances will require that the clinical investigator take additional steps to ensure that the rights and welfare of this subject are protected. The investigator may be able to speak to the subject's LAR on the telephone and fax documents back and forth. The investigator may also need to consider how to verify that the individual providing the consent is indeed the subject's LAR, and to establish his identify (i.e., that he is who he says he is). It is also important for the investigator to consider the ability of the subject to provide their assent to participate in the study.

You should definitely consult with the IRB or Ethics Committee (EC) that has reviewed and approved the study, so that the IRB/EC can weigh in on the risks of enrolling these types subject.s Because individuals who are illiterate or have impaired decision making ability are a vulnerable population, the IRB/EC needs to carefully consider whether the procedures proposed by the investigator to address these circumstances are appropriate and acceptable.

Finally, you also need to ensure that you understand and comply with the applicable laws and regulations in your country pertaining to obtaining informed consent and protecting the rights of individuals who may be illiterate or who have impaired decision making.

Vulnerable subjects -- Many articles have been written discussing the meaning of "vulnerable subjects" such that additional protections can be afforded those subjects in research. Although, "vulnerable subjects" is difficult to define, it is generally accepted that subjects with impaired consent capacity, an increased susceptibility to undue influence or coercion, or an increased susceptibility to the risks associated with a particular research study may be vulnerable and may need additional safeguards to protect them.

Review by an ethics committee, written standard operating procedures (including those pertaining to vulnerable subjects), and maintenance of ERC records are all routine required activities for all studies and research subjects regardless of whether they involve vulnerable subjects.

There are many additional protections for vulnerable subjects that can be considered depending on the reasons for the vulnerability and the circumstances of the study. For example, for subjects who are unemployed or impoverished, the ethics review committee may ensure that incentives offered to subjects for participating in the study (e.g., payment to subjects) is not so high as to unduly influence the subjects to enroll, or the ethics review committee may include a member with experience working with unemployed/impoverished subjects, or the ethics review committee may ensure that the informed consent document be written using simple language if the subjects are also educationally deprived.

I hope this information is helpful.

Kind regards,

Doreen M. Kezer, MSN
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Office of Good Clinical Practice
Office of the Commissioner, FDA

U.S. FOOD & DRUG ADMINISTRATION

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From: [redacted]
Sent: Thursday, May 24, 2018 7:31 AM
To: OC GCP Questions <gcpquestions@fda.hhs.gov>
Subject: Question on pottential discriminative action on illiterate patients

Dear All,
Hope this finds you well.

I have a question that was raised on monitoring visits anf I'd like to share with you and have your thoughts...

A international clinical trial on a phase III cardiovascular study drug (which requires FDA1572 signed form) is ongoing and Brazil is involved on such protocol.
The sponsor on approved protocol states that patient must comply with study procedures for participation.

On monitoring visits sponsor realized illiterate patients is being recruited. Protocol have several procedures. which includes an Eq-5D. Sponsor want patient itself answer EQ-5D, however illiterate patients does not have capabilities for reading. on Signed ICF sponsor does not state illiterate patients can not participate.
These illiterate patient is being helped by unbiased person (usually patient's relatives) to answer EQ-5D (no clinical research staff involved).
Sponsor sent e-mail through CRO requesting all Brazilian sites to refrain illiterate patients from participation on this protocol, using argument that these patients can not participate due to his/ her illiterate status.
Although EQ-5D is on of procedures of this study, it is not a essential procedure, and having subject relatives helping does not bring us safety concerns, and/ or patient prejudice, and/ or unbalanced equippoise.

Question: It is ethical refrain illiterate subjects from study participation only due to his/ her illiteracy condition? Shall sponsor provides alternatives for EQ-5D participation (eg.: Braile questionnaire for blinded subjects, audio version of such questionnaire for illiterate patients? Shall we avoid a subject with amputated arm (which is not illiterate) to be screened on a pottential study due to impossibility of filling a EQ-5D due to his amputated arm condition? Prohibiting illiterate people, blinded people, amputated arm people from participation on clinical long term follow up study using the argument that their condition fulfills exclusion criteria due to his/ her socio-economical and medical conditions can be interpreted as a discriminative attitude at FDA's perspective?

Hope hear your comments quite soon about these quite challenging situation, I remain,

Sincerely,

[redacted]