REVIEW OF AN INVESTIGATOR'S REQUEST FOR A WAIVER OF SELECTED INCLUSION/EXCLUSION CRITERIA FOR A SINGLE PERSON

4/3/2021

Investigators are responsible for conducting research with humans according to the signed investigator statement, the investigational plan and applicable federal regulations (as stated in 21CFR312.60) and institutional policies. Sponsors and investigators occasionally use waivers of specific inclusion / exclusion (I/E) criteria for clinical investigations without a sound regulatory basis or prior IRB approval. There is no FDA policy or guidance permitting or precluding this practice, although a common finding reported by FDA compliance auditors is the inappropriate use of such waivers. The DUHS IRB does not support the routine use of waivers of objective I/E criteria for clinical investigations involving an FDA regulated product (drug, device or biologic).

An investigator may encounter a potential research participant who does not satisfy all of the I/E criteria of a research protocol. Examples include a patient being considered for inclusion into a study involving an investigational drug or device, and whose qualifying radiologic images were obtained days to a few weeks earlier than permitted by the protocol, or whose blood chemistry values fall slightly outside of the protocol's required ranges, or who is slightly older or younger than permitted by the protocol. If the investigator concludes that such a person is so close to meeting I/E criteria that the person's inclusion would not place him/her at an increased risk of harm from study participation, and participation in the study would be in the person's best interest because alternatives are limited to less favorable options, often the investigator will consult with the study sponsor and the IRB about obtaining a waiver to permit inclusion of the person. The IRB is asked to approve this waiver, usually after the sponsor has approved it. But often neither the investigator nor the sponsor intends to submit an amendment to incorporate such broadened I/E criteria so as to include both the current person and similar people in the future. Or if such an amendment were to be submitted, the timing of its submission would not permit inclusion of the current person.

Federal regulations and DUHS IRB policy permit use of the expedited review procedure to approve a change in previously approved research only when the proposed change is minor and occurs during the period (one year or less) for which approval was authorized. The IRB defines a change as "minor" if:

a. the change does not adversely alter the overall risk/benefit ratio;
b. the change will not potentially adversely affect the willingness of current participants to remain in the study or the willingness of potential participants to enroll in the study;
c. the change will not diminish the scientific validity of the study,
d. any added revision or procedure involves no more than minimal risk to subjects, and
e. any added procedure falls into one of the categories (1) - (7) of research that can be reviewed using the expedited procedure.

Please refer to the DUHS IRB policy on "Amendments to Previously Approved Research", for examples of changes that may be approved using the expedited procedure and those that may not.

If an investigator encounters a potential research participant who does not satisfy all of the inclusion/exclusion (I/E) criteria of a research protocol, and the investigator concludes that such a person is so close to meeting I/E criteria that the person's inclusion would not place him/her at an increased risk of harm from study participation, and participation in the study would be in the person's best interest because alternatives are limited to less favorable options, and the research is not DHHS regulated, the investigator has several choices:

1) Not recruit the person;
2) Obtain IRB approval of an amendment to alter the I/E criteria to permit inclusion of the person and other such people; or
3) If time does not permit the investigator to submit such an amendment, or if the sponsor chooses not to amend the overall study, but does approve the change in I/E criteria for this single person, the investigator must provide the IRB with the following:

a. assurance that the proposed research is not subject to DHHS regulations;
b. confirmation from the study's principal investigator and sponsor that the potential research participant may be included and will not be unevaluable based on not meeting I/E criteria;
c. declaration that participation in the study would be in the person's best interest because alternatives are limited to less favorable options;
d. confirmation from a colleague uninvolved in the care of the person that alternatives are limited to less favorable options;

The investigator will request, through submitting an amendment in iRIS, to include this subject, with a justification to the IRB that the person's inclusion represents appropriate medical practice. The IRB will then approve/disapprove the amendment.

Only with final approval may the investigator seek the person's consent for research participation.

The investigator is reminded that if the study involves the use of an FDA-regulated product, all FDA reporting requirements must be met, including reporting to the IRB, sponsor and FDA of any unanticipated problems involving risks to the ineligible person or to others.

The investigator must submit all of his/her related correspondence with the sponsor, uninvolved colleague and/or the IRB by uploading all (electronic) documents into iRIS. This correspondence becomes part of the IRB-approved protocol file.

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