Good Clinical Practice Q&A

One of the conditions of an IND exemption is that the sponsor or investigator does not intend to use the results to support significant changes in a product’s approved labeling. But does this mean that, if the sponsor or investigator changes his or her mind, those results cannot later be submitted in a marketing application?

Assuming that the sponsor or investigator acted in good faith in taking the IND exemption, those results can be submitted in a marketing application. In the preamble to the 1987 IND regulations, the agency states, “FDA advises that a study that is conducted in good faith under the terms of the exemption in [FDA regulations] (i.e., without the filing of an IND) will later be acceptable to the agency in support of an IND or marketing application. Therefore, where the agency finds that a study was conducted under the exemption on the reasonable belief that each of the significant elements of the exemption applied, the FDA will not subsequently raise any objections to its acceptance, assuming adequate guarantees of the ethical propriety and scientific validity of the study. On the other hand, where there is evidence that the sponsor had no reasonable basis for concluding that a study should have been exempted, FDA may take other regulatory action, as appropriate... As FDA is willing to discuss and advise sponsors on the applicability of the exemption to planned clinical investigations, the agency believes there should be few occasions for determining after the fact that a study did not qualify for the exemption but should have been conducted under an IND.”

More recently, the agency discussed this issue in its September 2013 final guidance titled, “Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND.” The guidance notes that, “whether a planned clinical investigation will be used to support a new indication, other significant labeling change, or advertising claim may not always be known or apparent at the outset of the investigation. Generally, it seems reasonable to infer that the intent of any well-controlled trial of a marketed drug sponsored by the manufacturer of the drug would be to influence labeling or promotion in some way. On the other hand, the sponsor-investigator of an investigator-initiated study in an academic setting (a study designed and initiated by the investigator, independent of the manufacturer) probably does not intend that his or her study of a marketed drug influence labeling or promotion, even if the sponsor-investigator is receiving some limited support from the drug’s manufacturer. However, certain investigator-initiated research has the potential to influence labeling or promotion, notwithstanding the investigator’s intent (e.g., a controlled trial with an endpoint representing improvement of a serious disease). Similarly, certain studies of effectiveness conducted by government agencies (e.g., National Institutes of Health, Veterans Administration) have the potential to influence labeling. FDA strongly encourages IND submissions for these types of studies so the Agency can have an opportunity to provide advice on study design.”

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