FOOD & DRUG ADMINISTRATION:
Guidance for Industry on Individual Patient Expanded Access Applications:
Form FDA 3926

OMB Control No. 0910-0814

83-C Change Request to Form FDA 3926, "*Individual Patient Expanded Access Investigational New Drug Application*."

I. Background:

This information collection supports FDA guidance regarding regulations under 21 CFR Part 312.310 – Expanded Access to Investigational Drugs for Treatment Use. Expanded access refers to the use of an investigational drug when the primary purpose is to diagnose, monitor, or treat a patient rather than to obtain the kind of information about the drug that is generally derived from clinical trials. Because of FDA's long history of facilitating expanded access to investigational drugs for treatment use for patients with serious or immediately life-threatening diseases or conditions, our efforts in this regard are ongoing.

Regulation:

On December 14, 2006, FDA published a proposed rule in the Federal Register (71 FR 75147; RIN 0910-AF14) to revise the regulations in 21 CFR part 312. The rule, among other things, intended to increase awareness and knowledge about expanded access and the procedures for obtaining investigational drugs for treatment use for patients with serious or immediately life-threatening diseases or conditions who lack therapeutic alternatives. The rule was also intended to facilitate the availability, when appropriate, of investigational new drugs for expanded access while protecting patient safety and avoiding interference with the development of investigational drugs for marketing under approved applications. Among comments received by FDA were administrative burdens and delay associated with IRB review for treatment use under expanded access protocols, particularly for individual patients.

Public Outreach:

More recently, FDA sought input from the Secretary's Advisory Committee on Human Research Protections (SACHRP, the Committee) on this topic. At the SACHRP meeting of October 4, 2011, FDA representatives asked the Committee to provide feedback on several questions regarding expanded access to investigational drugs/biologics for individual patients, as allowed by 21 CFR 312.305 and 312.310. The questions discussed included: *Does providing for something like expedited IRB review seem a reasonable solution, based on the problem cited*?; and *If a reduction in the number of IRB members to approve an expanded access protocol is satisfactory to the Committee, does the Committee believe that mimicking the expedited review procedure is the best approach*?

Following discussion of these issues, on March 30, 2012, SACHRP submitted recommendations to FDA via a Letter to the Secretary of HHS, "*Attachment B: Recommendation on Single Patient Treatment Use*."[1] In its letter, SACHRP acknowledged the administrative burden and delay incurred by the requirement for full IRB review, which SACHRP felt was unwarranted in cases of individual patient expanded access treatment use, as there is no research risk. SACHRP noted that substantial barriers exist to expanded access to investigational drugs/biologics and provided several recommendations to address this concern. In general, the Committee's recommendations were for FDA to find a way to lessen the burden of full IRB review for expanded access requests for individual patients for treatment use of investigational drugs.[2] Although SACHRP suggested a variety of ways to reduce the administrative burden and delay associated with full IRB review of these expanded access requests while still protecting patients, FDA believes the recommendation to allow expanded access for individual patient treatment use with the concurrence of the IRB chair (or another appropriate board member) would most effectively facilitate access and still provide appropriate ethical oversight.

In addition to input already discussed, FDA also routinely solicits informal input from its stakeholders at various conferences, such as those held by Public Responsibility in Medicine and Research (PRIM&R), Everylife Foundation for Rare Diseases, National Organization for Rare Disorders (NORD), and New York University.

Guidance:

In the Federal Register of May 9, 2013 (78 FR 27115), FDA solicited public comment about the appropriate level of IRB review for individual patient expanded access. Specifically the notice stated "*FDA is particularly interested in receiving comments on this issue, including to what extent the requirement for full IRB review of individual patient expanded access is a*

[1] https://www.hhs.gov/ohrp/sachrp-committee/recommendations/2012-march-30-letter-attachment-b/index.html

[2] SACHRP's recommendations included the following: FDA issuing more specific advice on how to obtain access to treatment use protocols; FDA issuing guidance allowing the chair of the IRB or another appropriate board member to review the expanded access protocol and provide an appropriate opinion; FDA could change the expedited review regulations (21 CFR 56.110) to allow IRBs to review treatment use protocols for individual patients through expedited review; FDA could invoke the IRB waiver (21 CFR 56.105) for these cases; FDA could create an internal or designate an external single patient access IRB; or FDA could modify 21 CFR 312 so that IRB review of a single patient expanded access protocol is not required. FDA has taken steps to address the other SACHRP recommendations, e.g., issuing guidance on the expanded access provisions. See the following guidance documents:

Expanded Access to Investigational Drugs for Treatment Use-Questions and Answers, Guidance for Industry (https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf), Individual Patient Expanded Access Applications: Form FDA 3926, Guidance for Industry (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM432717.pdf), and Charging for Investigational Drugs Under and IND-Questions and Answers, Guidance for Industry (https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351264.pdf?source=govdelivery&utm_medium=email&utm_source=govdelivery).

deterrent to patient access, whether FDA should consider alternatives to full IRB review of individual patient expanded access, and what alternative approaches may better facilitate access while providing appropriate ethical oversight" (see 78 FR 27115-27116). Again public comment recommended that FDA consider expedited IRB review for expanded access use for appropriate cases and requested clarification on the IRB review process for expanded access use.

II. Proposed change:

To satisfy both SACHRP and public comment, FDA is seeking to revise Form FDA 3926 at Question 10. The proposed change allows for an optional waiver to specify that concurrence of an IRB chairperson (or designated IRB member) is sufficient for the individual patient expanded access treatment to proceed. In addition to being responsive to concerns raised by our stakeholders (e.g., individual patients, caregivers, IRB members, and health care professionals) and SACHRP, this change harmonizes with the longstanding medical device policy – *Guidance on IDE Policies and Procedures*[3], which allows for the IRB chairperson's concurrence for individual patient expanded access to an investigational medical device rather than review and approval by the full IRB. FDA is also seeking to make editorial changes within the title box and at Question 11. The requested changes are highlighted in the draft revised form accompanying this request.

[3] https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080203.pdf