1. Purpose
   1.1. To define the process for reviewing a clinical study protocol amendment to determine if the amendment must be submitted to the Food and Drug Administration (FDA) at least 25 days prior to implementation.

2. Scope
   2.1. This standard operating procedure applies to protocols conducted under Center for Cancer Research-held Investigational New Drug (IND) or Investigational Device Exemption (IDE) applications, and Office of Sponsor and Regulatory Oversight (OSRO) oversight.

2.2. Limitation
   2.2.1. Not Applicable.

3. Responsibilities
   3.2. OSRO Safety evaluates protocol amendments for impact on subject safety, study objectives and determines if the FDA must be notified.
   3.3. OSRO Regulatory evaluates protocol amendments for changes to the investigational agents/device and communicates with the FDA regarding protocol amendments.

4. References
   4.1. 202 Protocol Development Policy
   4.2. 21 CFR §312.30: Investigational New Drug Application – Protocol Amendments
   4.3. 21 CFR §812.35: Investigational Device Exemptions – Supplemental Applications

5. Definitions
   Refer to the OSRO Lexicon.

6. Procedure
   6.1. The amendment review process targets specific items in order to determine whether the amendment requires FDA review at least 25 days prior to implementation. It does not constitute a review of the entire amendment, nor does it constitute Sponsor approval of the amendment.
   6.2. OSRO Procedure for Reviewing Protocol Amendments Under an IND
       6.2.1. OSRO Safety and OSRO Regulatory receive notification of a pending protocol amendment from the Protocol Support Office.
       6.2.2. Each OSRO functional group independently assesses the protocol amendment.
6.2.2.1. OSRO Regulatory evaluates for possible changes to the investigational agents/device.

6.2.2.2. OSRO Safety evaluates for changes in the subject risk/benefit ratio.

6.2.2.3. If the proposed protocol change requires FDA submission at least 25 days prior to implementation, then the Protocol Support Office is notified that the protocol amendment must be submitted to the FDA for a 25-day review.

6.2.3. In all cases, the protocol amendment must be submitted to the Institutional Review Board (IRB) for review.

6.3. OSRO Procedure for Reviewing Changes in Protocol Conducted Under an IDE

6.3.1. When a protocol amendment is received, OSRO assesses the changes using the same procedure outlined in Step 6.2 with the following exception:

6.3.1.1. FDA notification must occur within 5-working days of the Sponsor’s knowledge of a minor change.

6.3.2. In all cases, the protocol amendment must be submitted to the IRB for review.

6.4. OSRO Regulatory submits the protocol amendment to the FDA.

6.5. This document shall be reviewed periodically and updated as necessary.

7. Associated Documents

7.1. 202-S03-W01 Protocol Amendment Evaluation for FDA Submission

8. Change Summary

<table>
<thead>
<tr>
<th>Revision Number</th>
<th>Effective Date</th>
<th>Description of Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13NOV2019</td>
<td>New Document</td>
</tr>
<tr>
<td>2</td>
<td>07JUL2020</td>
<td>Changed the 30-day prior to implementation submission to FDA to 25 days. Added Step 6.3, IDE submission process.</td>
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