SOPP 8203: Evaluation of Cost Recovery Requests for Investigational New Drugs and Investigational Device Exemptions

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I. Purpose

This Standard Operating Policy and Procedure (SOPP) serves as a guide for Center for Biologics Evaluation and Research (CBER) staff to follow for consistent review and administrative oversight regarding requests by sponsors to recover certain costs for a product that is the subject of an investigational new drug application (IND) or investigational device exemption (IDE) under 21 Code of Federal Regulations (CFR) 312.8 and 21 CFR 812.7 respectively.

II. Scope

This SOPP applies to cost recovery requests by sponsors of CBER regulated drugs and medical devices, including biological drugs undergoing clinical investigations, but not yet cleared/approved by the FDA/CBER.

III. Background

A. General

1. Cost recovery enables manufacturers to recoup costs of making drugs or devices available to patients when the product is undergoing clinical investigation but is not yet cleared or approved by the FDA. Regulations for IND cost recovery are codified at 21 CFR 312.8.

2. As explained in the preamble to FDA's 2009 final rule on cost recovery for INDs *Charging for Investigational Drugs Under an Investigational New Drug Application (74 FR 40899)* (see Reference 1) the goal of cost recovery is to "address the situation in which there is a very high cost associated with making a drug available to clinical trial subjects and that drug cost prevents continued development unless the cost of the drug can be recouped during development." A similar rationale applies to cost recovery for IDEs.

3. FDA's cost recovery regulations apply to new unapproved products and, in certain circumstances, to approved products undergoing investigation to obtain approval for additional indications. As described in the 2009 preamble to the final rule, cost recovery for an investigational drug in a clinical trial (21 CFR 312.8(b)(1)) is appropriate when three circumstances are present.

   a. First, cost recovery "should be allowed only to facilitate development of a promising new drug or indication that might not otherwise be developed, or to obtain important safety information that might not otherwise be obtained."

   b. Second, data to be obtained from the clinical trial should be essential to establishing that the drug is safe and effective.

   c. Third, the sponsor must demonstrate that absent cost recovery clinical development of the drug could not be continued because the costs to the individual sponsor due to manufacturing complexity, the large quantity of drug needed, scarcity of a natural resource or a combination of these and other circumstances are "extraordinary" relative to that individual sponsor's resources.

4. Sponsors also may recover costs for implementing an expanded access program (21 CFR 312.8(c)). Expanded access can be for treatment of individual patients, including for emergency use (21 CFR 312.301), intermediate-size patient populations (21 CFR 312.315) or widespread treatment use (21 CFR 312.320)). The intent, as stated in the 2009 preamble, is to "provid[e] a reasonable incentive for sponsors to make investigational drugs available for treatment use."

5. A Table comparing IND and IDE cost recovery requests may be found in the Appendix.

B. Investigational New Drugs (INDs)

1. Cost recovery for INDs was initially added to the IND regulations in 1987 as part of a broader revision of the IND regulations. A proposed rule for cost recovery was issued in 2006 (See Reference 2). In August 2009, FDA finalized the rule stating that sponsors may be eligible for cost recovery to charge for investigational drugs under an IND in two scenarios: clinical trials and expanded access for treatment use.

2. When requesting to charge for an investigational product in a **clinical trial**, sponsors must demonstrate that the IND product has potential clinical benefit superior to current products, that the data obtained from the clinical trial will be essential in moving the product towards FDA approval and that the expenses are so "*extraordinary to the sponsor*" that the clinical trial would not be feasible without cost recovery. The amount the sponsor seeks to charge during the study must be justified to FDA/CBER and sponsors must obtain FDA/CBER written approval prior to implementing cost recovery. Once authorized, sponsors may continue cost recovery through the duration of the clinical trial unless otherwise specified by FDA/CBER.

3. The regulations do not state when along the continuum of drug development submission of a cost recovery request is appropriate. However, consistent with the preambles to the proposed and final rule, the sponsor must demonstrate that the study is essential to establishing that the drug is effective or safe for the purpose of obtaining initial FDA marketing approval. The sponsor therefore should provide evidence of a potential clinical benefit that, if further established by the clinical study, would provide a significant advantage compared to currently approved products.

4. When seeking cost recovery for **expanded access to investigational drugs for treatment use** the sponsor must provide reasonable assurance that cost recovery will not interfere with development of the drug for FDA/CBER marketing approval. However, the preamble to the 2009 final rule states that compared to cost recovery for clinical study INDs, "FDA believes it is less likely that the limited numbers of patients who might obtain individual patient access to an investigational drug (§312.310) or intermediate size patient population expanded access (§312.315) would impede development of a drug or indication."

5. The expanded access regulations also allow access to investigational drugs for treatment use even when the drug is not being actively developed. Sponsors may seek cost recovery under these circumstances but should explain why the drug is not being developed.

6. Sponsors requesting cost recovery under **expanded access/treatment** IND provisions should provide evidence of sufficient enrollment in any ongoing clinical trial; evidence of adequate progress of the drug for marketing approval; and milestones the sponsor plans to meet in the next year (as per 21 CFR 312.23(a)(3)(iv)). The amount charged must be justified to

FDA/CBER and sponsors must obtain prior FDA written approval. In this case, sponsors may continue charging for up to one year as specified by FDA/CBER (or a shorter time period if FDA/CBER so specifies (21 CFR 312.8(c)(4)). After this one-year time period has elapsed, the sponsor must submit a request to continue to charge before FDA may reauthorize cost recovery. Cost recovery by the sponsor in these circumstances may be limited to certain patients authorized to receive the product.

7. Generally, under both the expanded access/treatment IND and clinical trial provisions of 21 CFR 312.8, the sponsor may only recoup **direct costs** associated with making the drug available to subjects in a clinical trial such as the raw materials, labor and non-reusable supplies used to manufacture the amount of IND product specifically intended for the patients from whom cost recovery is sought. Sponsors also may recover costs for shipping and handling of the IND product used in the study and charges for approved drug products which must be purchased from other companies. For cost recovery related to expanded access INDs, in addition to recovering the above expenses, sponsors also may recover monitoring, reporting and administrative expenses necessary for making the product available for expanded access.

8. The 2009 preamble states that "costs incurred at a clinical trial site, including pharmacy costs (e.g., the cost to reformulate a drug for infusion), nursing costs (e.g., costs associated with administering a drug and monitoring study subjects), equipment costs (e.g., intravenous (IV) administration sets), and costs for study-related procedures (e.g., chemistry labs, radiographic procedures), can be recovered without prior authorization from FDA."

9. The sponsor must provide supporting documentation to show justification for all expenses for which cost recovery is sought (21 CFR 312.8(d)(3)). The sponsor's analysis and documentation should be accompanied by a statement from an independent certified public accountant (CPA) that they have reviewed and approved the sponsor's calculations as required by 21 CFR 312.8(d)(3). As stated in the preamble to the final 2009 rule (see comment 59), inclusion of this CPA statement may assist FDA in evaluating the merit of a sponsor's request for cost recovery, especially when supporting documentation relies on financial information or accounting methods that FDA/CBER review staff may "lack [the] expertise" to properly assess.

10. With respect to expenses that are considered 'extraordinary to the sponsor' it is clear from the preambles to both the proposed 2006 rule and final 2009 rule that FDA intended the evaluation of a cost recovery request to be based on the sponsor's particular circumstances. Therefore, what is 'extraordinary' for one company may not be for others. Even though no formal definition of 'extraordinary' expenses is provided in the CFR, FDA stated in the preambles to the proposed and final rules that expenses could be considered to be extraordinary to a sponsor based on such factors as manufacturing

costs/complexity, large quantity of the drug needed, “scarcity of a natural resource,” or a combination of these and other factors. Though the preambles and text of the proposed rule provide some guidance about and examples of direct and indirect cost, in practice these may sometimes be difficult to distinguish since some items (e.g., labor/personnel costs) could potentially fit within either of these categories.

11. Sponsors must notify FDA of changes to approved IND cost recovery protocols, including any requests to increase charges, through an information amendment (21 CFR 312.31).

12. If cost recovery, whether in a clinical trial or under expanded access/treatment IND, interferes with further development of the drug for marketing approval or the company fails to adhere to the requirements for cost recovery, FDA may subsequently withdraw its authorization or decline a sponsor’s request to continue/renew cost recovery (21 CFR 312.8(a)(4)).

C. Investigational Device Exemptions (IDEs)

1. IDE cost recovery regulations (21 CFR 812.7(b)) allow sponsors to implement cost recovery without prior FDA/CBER approval. In contrast to the IND regulations, which explicitly limit cost recovery to sponsors, for IDE cost recovery, a sponsor, investigator or others acting on behalf of a sponsor or investigator are also explicitly permitted to recover costs (See Reference 3).

2. The CFR establishes no specific procedures or explicit limitations on cost recovery for IDEs but does state that sponsors or investigators shall not commercialize an investigational device by charging the subjects or investigators, “a price larger than that necessary to recover costs of manufacture, research, development, and handling.” Sponsors are encouraged to notify FDA/CBER in the original IDE application of the price that they plan to charge per 21 CFR 812.20(b)(8). The amount to be charged and an explanation of why sale does not constitute commercialization of the device should be included.

3. Likewise, as noted in the preamble to these regulations, finalized in 1980, the FDA/CBER is implicitly empowered to determine whether the charge sought by the IDE sponsor is “excessive” (See Reference 3). The preamble suggests FDA/CBER staff should understand device market realities but also remain cognizant of ethical considerations, stating that “[m]any devices, unlike most drugs, are expensive to manufacture, and it is unrealistic to prohibit a sponsor from recovering costs. It is a well-established ethical principle, however, that no profit should be made on experimental drugs or devices.”

4. No specific time limitation for IDE cost recovery is specified in the regulation.

5. Medical devices regulated under IND/BLA should follow the IND cost recovery regulations and procedures discussed above.

IV. Definitions

A. IND - Investigational New Drug Application (21 CFR 312)

B. IDE - Investigational Device Exemption (21 CFR 812.3(g))

C. Cost Recovery - The process through which a sponsor seeks to recover certain costs of permitting expanded access to an investigational drug or device or conducting a clinical study to obtain safety and efficacy data to support FDA marketing approval.

D. Direct costs - "[C]osts incurred by a sponsor that can be specifically and exclusively attributed to providing the drug for the investigational use for which FDA has authorized cost recovery. Direct costs include costs per unit to manufacture the drug (e.g., raw materials, labor, and non-reusable supplies and equipment used to manufacture the quantity of drug needed for the use for which charging is authorized) or costs to acquire the drug from another manufacturing source, and direct costs to ship and handle (e.g., store) the drug." (21 CFR 312.8(4)(i)).

E. Indirect costs - "[C]osts incurred primarily to produce the drug for commercial sale (e.g., costs for facilities and equipment used to manufacture the supply of investigational drug, but that are primarily intended to produce large quantities of drug for eventual commercial sale) and research and development, administrative, labor, or other costs that would be incurred even if the clinical trial or treatment use for which charging is authorized did not occur." (21 CFR 312.8(4)(ii)).

F. Sponsor (21 CFR 812(n-o)); (21 CFR 312.3) and **sponsor-investigator** - (21 CFR 312. 3)-The individual or entity who initiates and takes responsibility for a clinical investigation of a drug or medical device. In some cases, the sponsor also may be the investigator conducting the clinical study and administering the investigational product (sponsor-investigator) while in other cases the entity or individual serving as the clinical investigator will be distinct from the sponsor.

V. Policy

A. The following CBER policy considerations pertain to cost recovery requests for INDs, unless it is specified that they also apply to IDEs.

B. Evaluation of cost recovery requests:

1. Sponsors:

a. Requests for cost recovery may be submitted in the original IND for treatment/expanded access or as an amendment to an active clinical study IND.

b. Sponsors should provide to CBER an estimated dollar amount of the total direct cost of manufacturing a dose calculated on a per patient basis for all patients intended to be treated during the cost recovery period. For INDs, if there is lot to lot variation or if more than one dose of a product is administered, sponsors may express the dollar amount as a range but should show how charges will be assessed for each product lot.

c. Sponsors should provide CBER with justification of direct costs for which cost recovery is sought. Sponsors should be encouraged to provide a separate cost analysis for each clinical protocol within the same IND for which they wish to recover costs.

d. Sponsors are entitled to seek further dialogue with CBER when a cost recovery request is denied in whole or part and to supply additional relevant documentation on cost recovery requests and implementation.

e. For both INDs and IDEs sponsors should be advised to maintain detailed records documenting their cost estimates and actual expenses for all cost recovery requests.

2. CBER Staff:

a. The evaluation of a cost recovery request should be performed in accordance with this SOPP and the relevant regulations and guidances. Staff should be aware of the intention of the cost recovery regulations as discussed in the preambles to the proposed and final rule. Cost recovery is intended to assist the sponsor in moving the product toward FDA/CBER approval.

b. To ensure consistency among CBER offices and between CBER and other FDA Centers, the reviewing office may consult other CBER/FDA sources including other CBER Offices, the CBER Associate Director for Review Management, the CBER Associate Director for Policy, the Center for Drug Evaluation and Research (CDER), the Center for Devices and Radiological Health (CDRH) or the Office of Chief Counsel (OCC), as necessary and appropriate.

i. Bioethicists in the Commissioner's Office also may be consulted to address any ethical issues relevant to evaluation and approval of cost recovery requests such as when there is potential for enrollment bias (i.e., a trial will include only patients with the financial means to participate), questions about informed consent documents or concern as to the vulnerability of the study population(s) (such as those with severe/terminal illness).

ii. The use of placebos in a study for which cost recovery is being sought also may raise ethical issues (e.g., will patients be charged

even if they receive a placebo?) for which further consultation with a bioethicist may be appropriate.

c. For INDs, the basis for CBER's decision to grant or deny cost recovery and the amount granted should be fully documented in a memorandum to the IND file. This memorandum must adequately describe the reasons for the agency decision and record the process used to review the request and the individuals involved in this evaluation. A letter to sponsors denying or approving cost recovery must describe FDA's rationale for its decision and clearly indicate specific conditions/criteria.

d. Cost recovery requests for INDs may be approved or denied by CBER Office Directors or, if Office Directors choose to down-delegate their approval authority, by Deputy Directors, Division Directors and Deputy Division Directors. Sign-off authority for cost recovery requests should not be delegated below the level of Deputy Division Director.

3. Review timeline:

a. Prior FDA written approval is required for IND cost recovery for both clinical studies and expanded access protocols. Under provisions for expanded access for widespread use (21 CFR 312.20), the regulations explicitly state that FDA has 30 days after receipt to review the information amendment or treatment/expanded access IND protocol (312.305(5)(ii)).

b. Though the regulations do not specify a time period to review cost recovery requests for clinical studies, the preamble to the final 2009 rule indicates that FDA anticipates that, in most cases, the agency will be able to make a charging determination for these requests in a 30 day timeframe as well (see p. 40877). This also is consistent with CDER's approach. Therefore, when feasible, reviews for clinical study IND cost recovery requests should be completed and a written response to the company provided within 30 calendar days.

4. Duration of requests:

a. The duration of authorization for IND cost recovery is stated in 21 CFR 312.8. (Duration of IDE cost recovery is not explicitly discussed in the regulations). Unless FDA/CBER specifies a shorter time period, cost recovery for a clinical trial may last for the duration of the clinical trial/study (21 CFR 312.8(2)).

b. Cost recovery for a treatment/expanded access IND may continue only for one year from time of FDA/CBER authorization (unless FDA/CBER has specified a shorter time period). Subsequently, a sponsor may request reauthorization/renewal of their request.

c. Sponsors should be notified by product offices when the time period for an authorized cost recovery request is set to expire.

d. If it is possible that the need for cost recovery may change over time, then product offices may wish to specify a shorter duration for cost recovery from the outset so they may more easily monitor the sponsor's implementation of cost recovery. As a practical matter, it may be easier to limit the initial duration of a cost recovery request then to subsequently withdraw authorization from a sponsor, if necessary, once a cost recovery request has been approved.

5. Reauthorization/withdrawal:

a. Authorization for cost recovery should be withdrawn when product offices determine that cost recovery requirements are no longer met, patient safety or ethical issues develop or the sponsor does not appear to be actively pursuing product approval. In reviewing sponsor requests to renew/reauthorize cost recovery, CBER staff should ensure that the sponsor's justification for cost recovery reflects current circumstances and that the sponsor continues to make good faith progress toward FDA/CBER approval for the product under investigation.

b. FDA/CBER may withdraw authorization for cost recovery when charging for costs interferes with further product development toward approval or the criteria for authorization are no longer being met.

i. Withdrawal is distinct from a decision by FDA/CBER to not renew/reauthorize cost recovery after the initial term has expired.

ii. It is likely that withdrawal will most typically be an issue for clinical trial INDs since expanded access IND cost recovery authorizations expire and must be renewed at least every year.

iii. Withdrawal of authorization for cost recovery could be prompted by changes in sponsor circumstances or concerns about sponsor compliance and intent to seek FDA/CBER approval for its product. For instance, if a small company or academic sponsor were acquired by a much larger company, it may no longer face "extraordinary circumstances" requiring cost recovery for its product during a clinical study and FDA/CBER may then reconsider its cost recovery authorization.

iv. CBER offices may wish to involve the CBER Associate Director for Policy, Associate Director for Review Management and/or OCC in these discussions.

6. Waiver Requests:

a. Under 21 CFR 312.10, FDA may waive certain requirements in 21 CFR Subpart A, including those pertaining to cost recovery (312.8). A sponsor must submit a waiver request as discussed in 21 CFR 312.10.

b. The sponsor's request must explain why:

i. compliance with a given requirement is unnecessary;

ii. compliance with a requirement cannot be achieved by the sponsor; and

iii. an alternative approach may satisfy the purpose of the requirement. Waivers may only be granted when there is no "significant and unreasonable" risk to human subjects and the explanation for the waiver is adequate.

c. 21 CFR 812.10 also permits FDA/CBER to consider waiver requests for IDE requirements, including those pertaining to cost recovery as well. The sponsor must submit a waiver request with supporting documentation. FDA must ensure that granting a request will not undermine the "rights, safety, or welfare of human subjects.

d. Offices may wish to involve the CBER Associate Director for Policy, Associate Director for Review Management and/or OCC in these discussions.

VI. Responsibilities

A. The **Regulatory Project Manager (RPM)**

1. Notifies the review team, including the clinical and chemistry, manufacturing and control (CMC) reviewers, that a cost recovery request has arrived.

2. Communicates with the sponsor on behalf of the review team if more information is needed, including required information omitted from the cost recovery request.

3. Coordinates the review of the request by the assigned reviewer(s).

4. Conveys the Office's final written decision to the sponsor.

B. The primary assigned cost **recovery request reviewer(s)**

1. Evaluates the sponsor's justification as to why charging is necessary in order to undertake or continue the clinical trial or provide expanded access. The clinical and/or CMC reviewers are often assigned this role.

2. Involves other colleagues/experts as needed (e.g., bioethicists, OCC).

3. Seeks concurrence from supervisors about whether to approve or deny the cost recovery request.

C. Office supervisors/management (including team leaders and/or branch chiefs) and other review team members

1. Assists the assigned cost recovery request reviewer(s) and RPMs as needed.

2. Ensures timely review of these requests.

3. The assigned cost recovery reviewer(s) supervisor and/or team leader or branch chief should agree with the final decision to approve or deny the cost recovery request.

D. CBER Office Directors

1. Concurs with decision to approve or deny cost recovery requests based on staff recommendations or initiates further discussion of the request.

2. This responsibility may be delegated to other senior managers, including Office Deputy Directors, Division Directors and Division Deputy Directors.

E. The **CBER Associate Director for Review Management (ADRM)**

1. Ensure CBER review procedures, including those for cost recovery, conform to FDA statutory and regulatory requirements.

F. Other FDA staff from within CBER and other offices/Centers, including the Commissioner's Office (e.g., bioethicists), OCC and Office of Management, are responsible for providing additional expertise when requested to do so by CBER product offices reviewing cost recovery requests.

VII. Procedures

A. Investigational Device Exemptions (IDEs)

1. For IDE requests, no specific documentation is required from the sponsor

2. Any documentation submitted by the sponsor should be shared with appropriate review team members and documented in the appropriate regulatory system.

B. Investigational New Drug Applications (INDs)

1. Ensures the sponsor has submitted relevant documentation including:

   a. (for clinical study INDs) a description of the clinical study for which cost recovery is sought and an explanation as to why the costs the sponsor is

seeking to recover are not simply the cost of doing business and why the study could not proceed without cost recovery; **or**

b. (for treatment INDs/expanded access protocols) an explanation as to why the direct costs identified by the sponsor would not have been incurred even without the treatment use. For all IND cost recovery requests, a written statement signed by an independent CPA supporting the company's cost recovery calculations is required. **[RPM, Primary assigned cost recovery reviewer(s) (e.g., clinical or CMC reviewer)].**

2. If the sponsor's cost recovery request lacks relevant documentation:

a. Notify the review team that there is missing documentation, such as an explanation as to why cost recovery is sought or a CPA statement. [**RPM, Primary assigned cost recovery reviewer(s)**].

b. Request missing **documentation** *from the sponsor* ***such as an explanation as to why cost recovery is sought or a CPA statement.*** [**RPM, Assigned cost recovery reviewer(s)**].

c. Prepare and send a Cost Recovery Denial letter if the missing information is **extensive or significant** citing these deficiencies. Refer to CBER's Review Letter Templates on CBER's Intranet Web page for the most recent approved template. [**RPM/ Primary assigned cost recovery reviewer(s)/Supervisor]**

d. Sign the Cost Recovery Denial Letter [**Office Director or Designee]**

3. Route to appropriate review team member(s) if sufficient documentation has been provided by the sponsor. [**RPM**, **Primary assigned cost recovery reviewer(s)**]

4. Evaluate the merits of the sponsor's written justification as to why charging is necessary in order to undertake or continue the clinical trial (e.g., why the distribution of the test drug to subjects should not be considered the normal cost of doing business, evidence of sufficient enrollment in any ongoing clinical trial; and evidence of adequate progress of the drug for marketing approval). Seek input, when necessary, from others with appropriate expertise. **[Primary assigned cost recovery reviewer(s), other review team members and supervisors or FDA/office staff as necessary]**

5. Evaluation includes:

a. Determination that the drug has a potential clinical benefit that, if established in the clinical study, offers an advantage over available products. [**Primary assigned cost recovery reviewer(s), review team, supervisor]**

b. Determination that the amount to be charged by the sponsor does not exceed the price necessary to recover direct costs based on the manufacturing process and what would be considered reasonable. Seek input, when necessary, from others with medical, legal and financial expertise (e.g., OCC or Office of Management staff). [**Primary assigned cost recovery reviewer(s), other review team members and supervisors or FDA/office staff as necessary]**

6. Interact with the sponsor, as necessary and appropriate, to discuss potential modifications to the sponsor's cost recovery request being evaluated by the office. [**Primary assigned cost recovery reviewer(s), review team, supervisor]**

7. Make a final decision as to whether to approve or deny the cost recovery request. [**Primary assigned cost recovery reviewer(s), review team, supervisor, office director or designee**]

8. Document the Office's decision to grant or deny the cost recovery request in the appropriate regulatory system and import into CBER's Electronic Repository (CER). [**Primary assigned cost recovery reviewer(s), supervisor, office director or designee**]

9. Communicate the Office's decision to the sponsor by preparing a Cost Recovery Denial Letter or a Cost Recovery Approval Letter using the most recently approved letter template on CBER's Intranet Web page. **[RPM or Primary assigned cost recovery reviewer(s)]**

10. If the request is approved:

a. Ensure proper review and routing of any subsequent documentation related to implementation of the approved cost recovery request. [**RPM, assigned cost recovery reviewer(s)]**

b. Ensure sponsors are notified when a time limitation specified by the agency or the one year time limitation for treatment IND/expanded access is set to expire. **[RPM, assigned cost recovery reviewer(s), other office staff]**

11. If the request is denied:

a. Track and route any requests to FDA/CBER to reconsider the cost recovery request that has been denied by the office. [**RPM, assigned cost recovery reviewer(s)]**

12. Sign the Cost Recovery Denial or Approval Letter. [**Office Director or Designee**]

13. Send the Cost Recovery Denial or Approval Letter to sponsor. [**RPM**]

14. Document all communications about the cost recovery request in the appropriate regulatory system. **[RPM, review team, assigned cost recovery reviewer]**

VIII. Appendix

A. Appendix A: Cost Recovery-INDs and IDEs Table

IX. References

A. References below are CBER Internal:

1. CBER Review Template Letters

B. References below can be found on the Internet:

1. Charging for Investigational Drugs Under an Investigational New Drug Application. Final Rule. August 13, 2009, 74 FR 40872
2. Charging for Investigational Drugs. Proposed Rule. December 14, 2006, 71 FR 75168.
3. Charging for Investigational Products - Information Sheet. Guidance for Institutional Review Boards and Clinical Investigators.

X. History

Written/ Revised	Approved By	Approval Date	Version Number	Comment
Monser	N/A	December 11, 2020	3	Technical Update for retirement of EDR and replacement with CER and replace “database” with “system.”
Monser	N/A (Technical Update reviewed by Job Aid Coordinator)	October 9, 2019	2	NO CONTENT CHANGE: Technical Update to correct broken hyperlinks and to update format/font.
Mitchell Berger and RMCC Working Group	Robert A. Yetter, PhD	Dec 20, 2012	1	First Version of SOPP

SOPP 8203: Appendix A: Cost Recovery-INDs and IDEs

	CFR	Prior FDA approval/review needed	Costs recoverable that require prior FDA approval	Time limitation	Who may recover costs
IND-clinical study	21 CFR 312.8	Yes- amount also must be justified, documented and supported by independent CPA. FDA approval for cost recovery must be in writing	Direct costs -Ex. Raw materials, labor and nonreusable supplies and equipment used to manufacture the quantity of product used in the clinical study. Costs to obtain the product from another manufacturer. Shipping/handling costs for the product being investigated in the study.	Can charge throughout clinical study once authorized by FDA unless agency specifies time limitation.	Sponsors/ sponsor-investigators
IND expanded access	21 CFR 312.8	Yes as above.	Direct costs as above. Monitoring, reporting and other administrative requirements related to the expanded access IND also may be included.	One year unless shorter time specified by FDA. Can then be renewed for additional time periods.	As above
IDE	21 CFR 812.7; 21 CFR 820(b)(8)	No- The regulations do not require a separate prior FDA approval before cost	Manufacturing, research, development and handling	None specified except to extent sponsors may not	812.7 applies to sponsors, investigators and/or those

	CFR	Prior FDA approval/review needed	Costs recoverable that require prior FDA approval	Time limitation	Who may recover costs
		recovery begins or a CPA statement. The proposed amount to be charged and the reason why sale does not constitute commercialization may be submitted in the original IDE application.		"unduly prolong" an investigation.	acting on behalf of sponsors

Note: In some cases, as with labor/personnel costs, costs could be considered either direct or indirect depending on the specific product and how it is manufactured and distributed.