



for  
*Sponsors*  
and  
*Monitors*

**The Ultimate Step-by-Step  
Guide to Conducting  
Pharmaceutical Clinical  
Trials in the USA**

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## 1.3 Preparing and obtaining approval of a case report form (CRF)

**Goal:** To create a data collection document specific to the protocol and document approval within the sponsor.

What Should Be Done	 The Regulatory Basis	 Relevant Documentation	 Hints
<ol style="list-style-type: none"> <li>1. Review the sponsor's requirements and standard operating procedures for CRF preparation and approval.</li> <li>2. Use the study protocol to generate a list of content areas for which data must be collected (see SAMPLE 1.3.1).</li> <li>3. Establish acceptable ranges and electronic data checks for all variables.</li> <li>4. Create a draft CRF (using templates when available).</li> <li>5. Obtain review and approval of the CRF by all relevant persons, in accordance with the sponsor's SOPs.</li> <li>6. Use the approved CRF to finalize the database setup (see 1.30)</li> </ol>	<ul style="list-style-type: none"> <li>◆ 21 CFR 11 Electronic Records; Electronic Signatures</li> <li>◆ ICH GCP Guideline, Part 5.4 Trial Design</li> <li>◆ ICH GCP Guideline, Part 5.5 Trial Management, Data Handling, Record Keeping, and Independent Data Monitoring Committee</li> </ul>	<ul style="list-style-type: none"> <li>◆ <b>SAMPLE 1.3.1</b> Standard Case Report Form Content</li> <li>◆ Sponsor's CRF templates or electronic modules</li> <li>◆ Sponsor's approved protocol</li> </ul>	<ul style="list-style-type: none"> <li>◆ Most sponsors have "templates" for standard CRF sections. These are often stored electronically. Use of these templates is critical to facilitate consistency and accuracy in data collection within and across studies.</li> <li>◆ When a sponsor conducts multiple studies for a specific indication, it is advisable to define standard variables and methods for data collection within the therapeutic area. This standardization will facilitate integrated data analyses that are required in New Drug Applications.</li> <li>◆ Electronic CRFs (investigator enters the data) generally follow the same principles as paper CRF development, but they also require adherence to additional electronic data capture standards (see 21 CFR 11). An advantage to an electronic CRF is the ability to immediately query data using pre-defined range checks.</li> <li>◆ Refer to the strategy discussed under step 1.1, item 5, for optimal CRF development.</li> </ul>

## Sample 1.12.1 Initiation Letter to an Investigator (with List of Study Initiation Documents and Required Activities)

[Date]

[Investigator name]

[Address]

Subject: Protocol ##-##, Required study initiation documents and activities

Dear Dr. \_\_\_\_\_:

Enclosed are numerous documents and instructions to assist you in completing the required study initiation documents and activities. Please complete the actions required on your part for each document. If you have any questions, please contact me immediately.

Sincerely,

\_\_\_\_\_  
*Clinical Research Manager*

Enclosure: List of Study Initiation Documents and Required Activities

## Sample 1.12.1 Attachment: List of Study Initiation Documents and Required Activities

Document/Activity	Action required by investigator
Final study protocol	<ul style="list-style-type: none"> <li>◆ Sign one copy and return to sponsor</li> <li>◆ Submit to IRB, requesting review and approval</li> <li>◆ Prepare and submit a protocol summary, if requested by your IRB</li> </ul>
Informed consent document	<ul style="list-style-type: none"> <li>◆ Review and make any IRB-specific changes, prior to submitting to the IRB for review and approval</li> <li>◆ Submit to IRB, requesting review and approval</li> <li>◆ Discuss and negotiate any IRB-requested modifications with the sponsor until final resolution and agreement among parties is reached</li> </ul>
FDA Form 1572	<ul style="list-style-type: none"> <li>◆ Complete all sections, sign one copy and return it to the sponsor with your current curriculum vitae</li> <li>◆ Retain the second copy in your study regulatory document file</li> </ul>
Study budget	<ul style="list-style-type: none"> <li>◆ Complete the budget worksheet and return it to the sponsor for approval</li> </ul>
Financial disclosure documents	<ul style="list-style-type: none"> <li>◆ Review the investigator list of financial disclosure requirements</li> <li>◆ Complete and sign the investigator's financial disclosure statement</li> <li>◆ Return one signed copy to the sponsor and retain a copy for your records</li> </ul>

**Note:** All investigator signatures must be original signatures (not copies).