

***IRB Policy Single Patient Use of an Investigational Agent or Device /  
Compassionate Use of an Investigational or Label Drug (CIND)/Emergency Use of  
a Test Article***

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**PURPOSE**

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**21 CFR § 312.36** The need for an investigational drug may arise in an emergency situation that does not allow time for submission of an IND in accordance with Sec. 312.23 or Sec. 312.34. In such a case, FDA may authorize shipment of the drug for a specified use in advance of submission of an IND. A request for such authorization may be transmitted to FDA by telephone or other rapid communication means.

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**POLICY**

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**MD Anderson Policy:** A Compassionate Investigational New Drug (CIND) application is MD Anderson's term for authorization to give a single patient investigational or unusual treatment for a condition that is considered refractory to all appropriate conventional therapy and for which no approved experimental research protocol exists. This authorization is provided out of compassion for the patient's need and not as a mechanism for conducting any type of clinical research. The following procedures have been devised for the approval of such therapy. It is to be emphasized that regular protocols must be prepared if multiple patients are expected to need this treatment.

**Guidance for CIND:**

If the agent has been commercially approved by the FDA (e.g., FDA-approved), and the treating physician would like to use the agent for an off-label indication to treat a single patient, the treating physician may prescribe the agent as part of best medical practice. In this situation, the treating physician does not need to submit a protocol or CIND form to the IRB.

The treating physician should note that treating a series of patients in a novel or innovative manner and analyzing results for publication does require IRB approval prior to treatment.

- The treating physician, research nurse, or a staff person from the physician's section will complete the CIND form in the Protocol Document On-Line (PDOL) system. If the test article is being supplied by the National Cancer Institute (NCI), a copy of the Special Exception Protocol form needs to be included with the CIND form.
- If the test article is under an Investigational New Drug (IND) application or an

Investigational Device Exemption (IDE) from the FDA, the sponsor must contact the FDA to obtain approval for the use of the test article. The FDA Approval for the use of the test article must be in writing.

- Under certain circumstances, the test article may be supplied by an industry sponsor that will request that MD Anderson Cancer Center file the IND. In these situations, the MD Anderson Office of Research Education and Regulatory Management (ORE&RM) will contact the FDA to obtain approval for the use of the test article as described in the CIND protocol. Please contact the ORE&RM Office at (713) 745-5572.

If the test article supplier has requested that MD. Anderson file the IND application with the FDA, M. D. Anderson will act as the regulatory Sponsor.

**Procedures for submitting a CIND protocol:**

In order to submit a CIND protocol, via PDOL, follow the steps outlined below:

1. Click "Begin a New Protocol" in PDOL
2. Select CIND as the protocol type
3. Complete the requested template information, create an Informed Consent Document and obtain the appropriate electronic signatures, which include signatures of the treating physician and Division or Department Head.
4. Attach all supporting documents as appendices, if applicable
5. 5. Submit the CIND to OPR

After the CIND has been electronically submitted OPR will:

1. Assign a protocol number (e.g., CIND08-XXXX)
2. Perform an administrative review for completeness
3. Check for any Conflict of Interest
4. Review the Informed Consent Document (ICD) for readability and appropriate content
5. If FDA approval is required, OPR will upload FDA correspondence and/or other ancillary committee approvals as appendices in PDOL.

OPR will then request a review of the CIND protocol from the IRB Chair or designee. The IRB Chair or designee may perform one of the following actions on the submission:

- Approve
- Approve with contingencies
- Defer
- Send for full board review

The treating physician must respond to all outstanding issues for a CIND protocol that receives contingent approval or has been deferred or sent for full board review. After the CIND protocol has been unconditionally approved by the IRB Chair, the Full Board or designee, an OPR will perform the following steps:

1. Activate the CIND protocol in PDOL and the Clinical Oncology Research (CORe) systems
2. Issue an IRB approval/activation memo

3. Set a continuing review due date of at least 30 days from the date of IRB approval (see MDACC Policy for Continuing Review, Chapter 11.012 IRB Continuing Review of Research)
4. Alert Investigational Pharmacy Services that the IRB has approved the release of the test article for the CIND protocol, when appropriate.
5. The treating physician or research nurse must print the ICD from the PDOL

Informed Consent Database to be used during the consenting process.

The physician must maintain a regulatory binder which includes, at a minimum: 1) a copy of the IRB approved CIND protocol; 2) copies of documentation of FDA, Sponsor and Institutional approvals; and 3) a copy of the signed ICD.

The original signed ICD should be forwarded to the Health Information Management (HIM) department to be included as part of the patient's official medical record.

### **Continuing Review Requirements for the CIND Protocol**

The treating physician will submit the continuing review form to the IRB for review by the designated due date. At this time, the investigator may request termination or justify why the compassionate use treatment should continue.

The requirements for continuing review will follow the MD Anderson IRB Policy for Continuing Review of Research. (Chapter 11.012 IRB Continuing Review of Research) M.D. Anderson Cancer Center operates under the assumption that FDA regulatory requirements for informed consent (21 CFR Part 50) and IRB review (21 CFR Part 56) remain in effect. M.D. Anderson recognizes that in some circumstances there will be insufficient time to obtain approval of a CIND. Under these circumstances, emergency use of a test article may be utilized.

### **Emergency Use of a Test Article**

An exemption under FDA regulations at 21 CFR 56.104(c) permits the emergency use of an investigational drug, device, or biologic on a one-time basis per institution without IRB review and approval. All of the following conditions must be met for this type of emergency use:

- i. A human subject is in a life-threatening situation.
- ii. No standard acceptable treatment is available.
- iii. There is insufficient time to obtain IRB approval.
- iv. The emergency use must be reported to the IRB within five working days. This reporting must not be construed as an approval for the emergency use by the IRB. Any subsequent use of the investigational new drug at the institution requires IRB review and approval.
- v. Ordinarily, the investigator must obtain the informed consent of the subject for such an emergency use, except as described below.

(a) **Emergency Use of Drugs.** Emergency use of an investigational new drug occurs when the emergency situation does not allow time for submission of an IND. Use of the drug requires a request to FDA to authorize shipment of the drug for the emergency use. Such authorization is conditioned on the sponsor making an appropriate IND submission as soon as practicable (21 CFR 312.36). The emergency use of an investigational new drug may take place without IRB review and approval, provided that the use is reported to the IRB within 5 working days. Informed consent is required unless the situation is life-threatening, the criteria at 21 CFR 50.23(a) or 50.23(b) have been met, and the IRB is notified within 5 working days. (See section below on Emergency use w/o consent.)

(b) **Emergency Use of Devices.** Emergency use of an unapproved device may occur in an emergency situation when (i) an IDE for the device does not exist, (ii) a physician wants to use a device in a way not approved under an existing IDE, or (iii) when a physician is not an investigator under the existing IDE.

The device may be used if (i) the patient has a life-threatening condition that needs immediate treatment, (ii) there is no generally acceptable alternative treatment, and (iii) there is no time to obtain FDA approval. Such uses require as many of the following patient protections as possible (FDA Center for Devices and Radiological Health Guidance on IDE Policies and Procedures, January 20, 1998): (i) informed consent; (ii) clearance from the institution; (iii) concurrence of the IRB chairperson (this concurrence does not constitute IRB approval); (iv) an independent assessment of an uninvolved physician; and (v) authorization from the IDE sponsor (if an IDE exists). Follow-up reports should be provided to the Sponsor if an IDE exists or to FDA if no IDE exists. Such use is limited to a few patients.

### **Emergency Use of a Test Article without Informed Consent**

An exception under FDA regulations at 21 CFR 50.23 permits the emergency use of an investigational drug, device, or biologic without informed consent where the investigator and an independent physician who is not otherwise participating in the clinical investigation certify in writing all four of the following specific conditions:

- i. The subject is confronted by a life-threatening situation necessitating the use of the test article.
- ii. Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from, the subject.
- iii. Time is not sufficient to obtain consent from the subject's legally authorized representative.
- iv. No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life.

### **Procedures for reporting Emergency Use to the IRB:**

1. Consult the IRB Chairperson for guidance in the event of emergency use of drugs and medical devices.
2. An independent assessment, from a physician that is not involved in the clinical investigation, should be provided in writing, if time permits. If this assessment cannot

be obtained before treatment is administered, then it should be obtained within five working days after treatment administration and submitted to the IRB with the notification of emergency use.

3. An adequately informative Informed Consent is required unless the situation is life-threatening. (The criteria at 21 CFR 50.23(a) or 50.23(b) have been met)
4. If informed consent could not be obtained, this information should also be described in the report of Emergency Use to the IRB.

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## REFERENCES

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Date	Action	Initials	Description
01/02/2017	Approval	WQ	
06/27/2019	Rev	JH	Updated format

v.

Office of Human Subjects Protection