Expanded Access or compassionate use is the use of investigational drug outside of a clinical trial for the sole purpose of treating a patient or patients with serious or life-threatening disease who have no acceptable medical option. Serious diseases or conditions are those associated with morbidity that has a substantial impact on day-to-day functioning. Whether a disease is serious is a matter of clinical judgment. Examples cited by FDA include epilepsy and in situ breast cancer.

Expanded Access includes three options:
- Treatment IND
- Group C treatment IND
- Emergency Use IND

**Expanded Access of Investigational Drugs: Treatment IND (21 CFR 312.320)**

A treatment IND allows patients, whose need for treatment outweighs the risks (e.g. life-threatening illness), to obtain access to investigational treatment prior to completion of pivotal clinical trials. The FDA will allow an investigational drug to be used under a particular Treatment IND if there is a preliminary evidence of drug efficacy, which means that Phase III clinical trials with this drug must be well underway. Typically, such patients are not eligible for the on-going trials, and no alternative therapy is available. Such IND requires IRB review and Informed consent. The list of approved Treatment INDs is posted on the FDA website.

**Expanded Access of Investigational Drugs: Group C Treatment IND**

Group C drugs are Phase III cancer drugs that have shown evidence of reproducible efficacy. These drugs are distributed by the NIH under NCI protocols. Treatment is a primary objective, but safety and effectiveness data are still collected. FDA generally grants the waver from the IRB review requirements.


The need for investigational drug may arise in an emergency situation that does not allow for IND submission and IRB review. A physician who wishes to administer an investigational drug under the Expanded Access: Single-Patient program is responsible for procuring the drug from the sponsor, securing IRB approval and providing informed consent consistent with standard FDA rules (subject to emergency use exceptions provided in those rules), reporting adverse drug events to the sponsor, and maintaining accurate drug accountability and patient case history records. Depending on the
circumstances, additional requirements may apply. A physician who is unable or unwilling to meet these demands should not proceed.

1. First, a treating physician will obtain the permission from the manufacturer to obtain the drug in question. If there is no commercial manufacturer, the drug can be manufactured locally (e.g., at UC Davis cGMP facility), however, the FDA will require detailed manufacturing information.

2. After this permission is granted, a physician contacts the FDA. In an emergency situation, the request to use the drug may be made via telephone or other rapid means of communication, and authorization to ship and use the drug may be given by the FDA official over the telephone. In these emergency situations, shipment of and treatment with the drug may begin prior to FDA’s receipt of the written IND submission that must follow the initial request.

In a non-emergency situation, a written request (IND) for individual patient use of an investigational drug must be received by the FDA before shipment of and treatment with the drug may begin. These non-emergency requests are known as individual patient INDs. For information to be included in this IND click here or use the worksheet at the end of the document. Briefly, the physician must specify that he or she is seeking an emergency IND/a single-patient IND, provide information about the patient’s history and prognosis, treatment plan, and proposed intervention, and attach a completed IND application. It is unnecessary to prepare a formal research protocol designed to obtain meaningful scientific data – FDA fully recognizes that the purpose of the expanded access program is primarily to diagnose, monitor, or treat a patient’s condition; and expects very limited data collection (described in further detail below).

The IRB approval is required for single-patient INDs even though the purpose of the use of the test article is for clinical care and not research. In the event of an emergency (a life-threatening or severely debilitating situation where no standard acceptable treatment is available and there is not sufficient time to obtain IRB approval), the investigator may rely on an emergency use exemption from IRB approval under 21 C.F.R. § 56.104(c). “Life-threatening” includes diseases or conditions where the likelihood of death or major irreversible morbidity such as blindness, loss of limb, loss of hearing, paralysis, or stroke is high if promising treatment is delayed until the IRB can convene. In this case, the investigator must report the emergency use to the IRB within five (5) days of administration. This exemption to the IRB approval requirement applies only to a single use of the test article; any subsequent use requires prospective IRB review and approval. However, FDA has acknowledged that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle was that the IRB had not had sufficient time to convene a meeting to review the issue. Once IRB approval has been secured, standard rules for conducting clinical trials generally apply.

3. The informed consent requirements found at 21 C.F.R. part 50 apply to emergency and single-patient INDs. Emergency use may justify the exception to the informed consent requirements. For emergency cases both the investigator and an independent physician certify in writing to FDA and the IRB, under 21 C.F.R. § 50.23(a) that:
   • The patient is confronted by a life-threatening situation necessitating the use of the test article.
   • Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective informed consent from, the subject.
   • Time is not sufficient to obtain consent from the subject’s legal representative.
• No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject’s life.

What if, in the investigator’s opinion, immediate use is required to preserve the patient’s life, and time is not sufficient to obtain an independent physician’s determination that the above conditions apply? In these cases of extreme emergency, the investigator may make the determination and, within five (5) working days after use of the product, will have the determination reviewed and evaluated in writing by an independent physician.

UC Davis IRB does not have a specific Consent Form template for single-patient treatments. CTSC recommends that a Standard Biomedical Consent Form or a sample consent form provided below. Note that patients may be responsible for the costs of an investigational drug administered through the expanded access program.
INFORMED CONSENT FOR TREATMENT WITH AN UNAPPROVED DRUG

You have been diagnosed with: _______________________________.
This is a serious or life-threatening disease. You and your doctor have discussed your options. Your doctor believes that:

√ There is no FDA-approved drug available to treat your condition because:
   o No such drug exists; or
   o Approved drugs have been tried but not worked; or
   o Approved drugs cause side-effects that you cannot tolerate.

√ You cannot find or get into a clinical trial of an experimental drug that might help.

√ There are no other acceptable medical options.

Your doctor has told you that an unapproved drug, _______________________________, might help. This drug has not been proven to be safe or effective for your treatment. The Food and Drug Administration (FDA), however, has given your doctor permission to treat you with this unapproved drug under its "expanded access" program. More information about the program is online at: http://tinyurl.com/UCM176098 and http://tinyurl.com/UCM177138. If you cannot access these articles on a computer, please ask your doctor to print them out for you.

The known risks of the unapproved drug include: _______________________________.

Your doctor has a financial interest in the drug or its manufacturer as: ☐ an inventor (may receive royalties if the drug is approved and marketed); ☐ a consultant/advisor/spokesperson (receives or in the last 12 months has received professional service fees); ☐ an officer or director or employee; ☐ other: _______________________________; ☐ none (your doctor has no financial interest in the drug or its manufacturer).

Your doctor has told you that treatment with this unapproved drug is not the same as regular drug treatment:

√ While the drug may help you, it may not. There is no guarantee.

√ The drug has not been approved by FDA. Treatment may cause unknown side effects. These may include serious injury or pain, disability, or death. No compensation is available for these side effects.

√ Your insurance may not cover the cost of the drug or treatment for its side effects. These are costs you may need to pay. To find out more about possible costs, contact your health plan.

You may want to discuss your options further with your doctors, your family, your friends, or others before you decide what to do. You may also contact the [IRB NAME/NUMBER] with questions about your rights. If you choose to receive the unapproved drug, please sign below.

I understand my diagnosis and my options. I know that information about my treatment and response will be kept confidential, but may be given to the drug’s manufacturer and/or FDA as required by law. My questions have been answered. I would like to receive the unapproved drug. This decision is voluntary and I understand that I can discontinue treatment at any time without penalty or loss of benefits to which I may otherwise be entitled.

Patient Name: ____________________________________________ MRN: __________________________ Date: __________________________

Signature: ____________________________________________ Date: __________________________

If the patient is unable to consent (a minor, incompetent, or incapacitated), please add the following information and signature:

Name of Legally Authorized Representative (“LAR”): ________________________________

LAR’s Authority to Sign: ☐ Parent (of Minor) ☐ Legal Guardian ☐ Other: ____________________________

Signature of LAR: ____________________________________________ Date: __________________________

I have explained the proposed treatment to the above patient/LAR, including risks, potential benefits, and alternatives, as well as any financial interest I may have in the treatment.

Physician Name: ____________________________________________ Tel.: __________________________

Signature: ____________________________________________ Date: __________________________
REQUEST FOR EMERGENCY OR INDIVIDUAL PATIENT IND (COVER SHEET)


Request Type (check one): ☐ Emergency IND ☐ Individual Patient IND

Drug Name:

Brief Clinical History

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Disease Status</th>
<th>Prior Therapy</th>
<th>Response to Prior Therapy</th>
<th>Rationale*</th>
</tr>
</thead>
</table>

* Include a list of available therapeutic options that would ordinarily be tried before the investigational drug or an explanation of why use of the investigational drug is preferable.

Treatment Plan

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Route of Administration</th>
<th>Planned Duration</th>
<th>Monitoring Procedures</th>
<th>Modifications for Toxicity†</th>
</tr>
</thead>
</table>

† Describe dose reduction, treatment delay, or other modifications that may be made.

Narrative:
To the extent not already addressed above, describe the justification for the proposed treatment plan, explain the basis of the determination that there are no comparable or satisfactory therapeutic alternatives to the unapproved drug or biologic, and confirm that you have determined that the probable risk to the patient from the investigational drug is not greater than the probable risk from the patient’s disease or condition.

Chemistry, Manufacturing, and Controls Information and Pharmacology and Toxicology Information:
Include a description of the manufacturing facility. The requirement for this information may be met by providing a Letter of Authorization (LOA) to refer to this information if it has been previously submitted to FDA (for example, to an existing IND or NDA). The treating physician should contact the sponsor of the previously submitted information for such authorization and letter. The letter of authorization should include relevant identifying information, such as the sponsor’s relevant application (e.g., IND) number.

References:
Reference a published protocol or journal article (or articles) if appropriate.

Informed Consent and IRB Approval:
☐ Informed consent and approval of the use by an appropriate Institutional Review Board (IRB) will be obtained prior to initiating treatment. This is an emergency use request. An appropriate IRB will be notified of the emergency treatment within 5 working days of the treatment. Informed consent will be sought unless the requirements of 21 C.F.R. § 50.23 are met and appropriately documented.

Physician Information

<table>
<thead>
<tr>
<th>Name</th>
<th>E-Mail</th>
<th>Phone</th>
<th>Fax</th>
<th>Qualifications§</th>
<th>Signature</th>
</tr>
</thead>
</table>

§ Describe training, experience, and licensure or attach relevant portions of the physician’s curriculum vitae.