A. STATEMENT OF POLICY

It is the policy of Roswell Park Cancer Institute to set forth the policy and procedure for obtaining a compassionate exemption or emergency use IND for treatment of an individual patient(s). (For emergency use of an investigational device, see Policy #204.2)

B. PURPOSE

The purpose of this policy is to facilitate the availability of promising new drugs to desperately ill patients as early in the drug development process as possible, before general marketing begins, and to obtain additional data on the drug’s safety and effectiveness.

The use of an unapproved investigational drug or biologic requires an IND. If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for use under the company's IND.

Or, if there is no existing IND, an application for an IND must be made to the FDA. The FDA has several mechanisms for use of an investigational drug (see below). These include compassionate use, treatment IND and emergency IND.

To provide procedures in order for the IRB to protect the rights and welfare of human subjects who need to be treated in life threatening or a compassionate exemption manner at Roswell Park Cancer Institute.
C. DEFINITIONS

*Immediately life-threatening* - disease means a stage of a disease in which there is a reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.

*Life-threatening* - means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the full IRB is feasible.

*Severely debilitating* - is encompassed in the term life-threatening above and means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

*Emergency use* - is defined as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval [21 CFR 56.102(d)].

D. POLICY

**INFORMATION REGARDING INVESTIGATIONAL NEW DRUG (IND) GUIDELINES FOR COMPASSIONATE EXEMPTION**

Investigational products are sometimes used for treatment of serious or life-threatening conditions either for a single subject or for a group of subjects. When no satisfactory alternative treatment exists, subjects are generally willing to accept greater risks from test articles that may treat life-threatening and debilitating illnesses. The following mechanisms expand access to promising therapeutic agents without compromising the protection afforded to human subjects or the thoroughness and scientific integrity of product development and marketing approval.

**TREATMENT IND**

The treatment IND [21 CFR 312.34 and 312.35] is a mechanism for providing eligible subjects with investigational drugs for the treatment of serious and life-threatening illnesses for which there are no satisfactory alternative treatments. A treatment IND may be granted after sufficient data have been collected to show that the drug "may be effective" and does not have unreasonable risks. Because data related to safety and side effects are collected, treatment INDs also serve to expand the body of knowledge about the drug.
If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company’s IND.

There are four requirements that must be met before a treatment IND can be issued:

1) the drug is intended to treat a serious or immediately life-threatening disease;
2) there is no satisfactory alternative treatment available;
3) the drug is already under investigation, or trials have been completed; and
4) the trial sponsor is actively pursuing marketing approval.

Treatment IND studies require prospective IRB review and informed consent, however, the Roswell Park Cancer Institute IRB requires a review under its policies and procedures.

Treatment use of an investigational drug is conditioned on the sponsor and investigator complying with the safeguards of the IND process, including the regulations governing informed consent (21 CFR Part 50) and institutional review boards (21 CFR Part 56) and the applicable provisions of 21 CFR Part 312, including distribution of the drug through qualified experts, maintenance of adequate manufacturing facilities, and submission of IND safety reports.

TEST ARTICLES
Under DHHS regulations, patients receiving a test article in an emergency / compassionate use as defined by the FDA regulations may not be considered to be a research subject. DHHS regulations do not permit data obtained from patients to be classified as human subjects research, nor permit the outcome of such care to be included in any report of a research activity subject to DHHS regulation.

Under FDA regulations, the emergency use of a test article, other than a medical device, is a clinical investigation, the patient is a subject, and the FDA may require data from an emergency use to be reported in a marketing application.

GROUP C TREATMENT IND

The "Group C" treatment IND was established by agreement between FDA and the National Cancer Institute (NCI). The Group C program is a means for the distribution of investigational agents to oncologists for the treatment of cancer under protocols outside the controlled clinical trial. Group C drugs are generally Phase 3 study drugs that have shown evidence of relative and reproducible efficacy in a specific tumor type. They can generally be administered by properly trained physicians without the need for specialized supportive care facilities. Group C drugs are distributed only by the National Institutes of Health under NCI protocols. Although treatment is the primary objective and patients treated under Group C guidelines are not part of a clinical trial, safety and effectiveness data are collected. Because administration of Group C drugs is not done with research intent, FDA has generally granted a waiver from the IRB review requirements [21 CFR 56.105], however, the Roswell Park Cancer Institute IRB requires a review under its policies and procedures.
A. GENERAL PROCEDURE:

1. The treating physician, who wants to treat a patient through the use of a compassionate exemption (CE), will contact the Office of Research Subject Protection to inform them that a compassionate exemption is being considered for the treatment of a patient.

   *Do not schedule the patient for treatment before IRB approval is received.*

2. Follow directions below for Treatment IND use or Emergency IND use depending on the circumstances.

3. The treating physician should complete the application form F-137a (Appendix A) and submit the required documentation to the Office Research Subject Protection, at least 24 hours prior to when the IRB 02 committee will convene.

REQUIRED DOCUMENTATION:

1. F-137a form is to be completed. (Appendix A)

2. Complete the rationale/justification and risk/benefit assessment form for the treatment proposed. Be sure to explain why standard treatment is not indicated for this patient. (Appendix A)

3. Submit a treatment protocol that is the basis for the treatment. Treatment drugs, doses, routes, and schedule must be given in detail and justified based on published/unpublished experience.

4. Submit a proposed consent (use RPCI model template)

5. Provide recent clinic notes from referring or treating physicians.

6. The Office of Research Subject Protection will assemble the IRB - 02 committee, which is a fully constituted, registered IRB, in order to review the application. The committee will be convened as soon as practicable within 24 - 72 hours of the request.

7. With a quorum and majority vote on the request, the Office of Research Subject Protection will notify the treating physician of the committee’s decision. When the board is convened for Compassionate / Emergency use, quorum will be defined as at least 5 members from existing RPCI IRBs. Minimally, there must be at least one (1) medical doctor, one (1) Registered Nurse, one (1) Pharmacists and one (1) lay person

8. All compassionate requests whether approved or not, are brought to the attention of the full board of the IRB at the next scheduled IRB meeting.
9. For a drug intended to treat a serious disease, a request for treatment use under a treatment protocol or treatment IND maybe denied if there is insufficient evidence of safety and effectiveness to support such use.

B. PROCEDURE For COMPASSIONATE USE/TREATMENT IND:

1. Obtain the permission of the IND holder to treat the specific patient with the investigational new drug. This permission MUST be obtained in writing before the treatment begins. A verbal permission will suffice for the IRB-02 committee to proceed. However, if verbal permission is obtained, the application will be approved pending receipt of the written permission to use the drug.

2. The Vice-President of the Office Research Subject Protection or designee will verify consent from the IND holder of the Investigational agent and authorize the pharmacy to order/release the investigational agent(s).

3. Complete in full and sign the form entitled, “Request for Permission to Treat an Individual Patient” which is available in the Office for Research Subject Protection. (Form F-137a - Appendix A).

4. The submission must be accompanied by the required documentation listed in A. 3. above.

5. If approved, the compassionate exemption approval and the stamped consent are released by the Office Research Subject Protection to the investigator and 2 copies are forward to the Pharmacy for release of drugs for treatment. Only this consent can be used to consent the patient.

6. After obtaining the signature of the patient, the physician, and the witness (if applicable), a copy of the signed consent document should be forwarded to the Office of Research Subject Protection.

7. Within FIVE (5) days of treatment under the compassionate exemption, the investigator is required to submit an interim report to the Office Research Subject Protection for submission to the FDA, if RPCI is the IND holder. A copy will be provided to the IRB at the next scheduled meeting.

8. At termination of the therapy, a final report must be submitted to the Office Research Subject Protection for submission to the FDA, if RPCI is the IND holder. A copy will be provided to the IRB at the next scheduled meeting.

9. If the IND holder is not RPCI, a copy of the approval and interim report and the final report will be forwarded by the P.I. to the sponsor of the IND for submission to the FDA.
C. **PROCEDURE FOR OBTAINING AN EMERGENCY IND FROM THE FDA:**

The emergency use of an unapproved investigational drug or biologic requires an IND.

The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article in advance of the IND submission. Requests for such authorization may be made by telephone or other rapid communication means [21 CFR 312.36].

When an investigator seeks advice from the IRB on the emergency use of a test article, the ORSP staff, IRB Chair or designee will use the emergency use of a test article checklist (Appendix B) to determine whether FDA regulations will be followed and inform the investigator of their conclusion.

The IRB will use the emergency use of a test article checklist (Appendix B) to evaluate whether the FDA regulations were followed and inform the investigator of their conclusions.

The request for such authorization will be transmitted to the FDA by telephone or fax: (use link below for current address and telephone or fax numbers)

* If the treating physician is phoning or faxing the information, a copy MUST be forwarded to the IRB.

http://www.fda.gov/cder/cancer/singleIND.htm

After normal working hours, Eastern Standard Time, the request will be directed to the FDA Division of Emergency and Epidemiological Operations, (202) 857-8400.

The Office Research Subject Protection will make the appropriate IND submission to the FDA as soon as practicable after receiving the authorization. The required documentation as outlined in A.3. above must be completed and forwarded to the IRB within 5 (five) working days from the receipt of the authorization.

* Failure to follow the FDA regulations on emergency use will be treated as non-compliance.

D. **EXEMPTIONS:**

1. **Emergency Exemption from Prospective IRB Approval:**

   a. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The exemption, which may not be used unless all of the conditions described in 21 CFR 56.102(d) exist, allows for one emergency use of a test article without prospective IRB review.
b. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval.

2. **Exception From Informed Consent Requirement:**

   Even for an emergency use, the investigator is required to obtain informed consent of the subject or the subject's legally authorized representative *unless* both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following [21 CFR 50.23(a)]:

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

   If, in the investigator's opinion, immediate use of the test drug/article is required to preserve the subject's life, and if time is not sufficient to obtain an independent physician's determination that the four conditions above apply, the clinical investigator should make the determination and, within 5 working days after the use of the article, have the determination reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. The investigator must notify the IRB within 5 working days after the use of the test article [21 CFR 50.23(c)].

E. **PLANNED EMERGENCY RESEARCH:**

   Roswell Park Cancer Institute does not participate in planned emergency research.

   *Please contact the Office of Research Subject Protections if further information or clarification is needed.*
Appendix A

REQUEST FOR PERMISSION TO TREAT AN INDIVIDUAL PATIENT (F-137a)

PATIENT INFORMATION

Age: ______ Male/Female (circle)

Height: ______ Weight: _______ Body Surface Area: _______

Diagnosis: ______________________________________

REQUESTED TREATMENT Protocol No (if any): _______

Attach copy of protocol and proposed consent form

Drugs name: _____________________________

dose: _________ Frequency: ___________ Route: ___________

duration: _____________________________________

Drugs name: _____________________________

dose: _________ Frequency: ___________ Route: ___________

duration: _____________________________________

Drugs name: _____________________________

dose: _________ Frequency: ___________ Route: ___________

duration: _____________________________________

Concomitant Medications/therapy: _____________________________

IND Holder: Name/Company: _________________ Phone: _________________

Verbal Written (attach)

Justification for Compassionate Exemption:

Is patient’s condition life threatening? Explain.

____________________________________________________________________________

____________________________________________________________________________
Are other therapies available? ______________________________________________________________

Why is standard therapy not available: ____________________________________________________

Medical/Scientific basis for use of the proposed therapy:
_____________________________________________________________________________________

Investigator signature: ________________________________ date: __________

Phone: ________________

cc: Pharmacy
    PI
    IND holder, if applicable
    IRB
COMPASSIONATE EXEMPTION RATIONALE/JUSTIFICATION AND RISK/BENEFIT ASSESSMENT

Patient Name: ____________________________ MR # ____________

1. CLINIC NOTES - Attach most recent pertinent clinic notes that give the following information: (Add more information here if necessary)

   · Previous Medical/Surgical/ Radiation treatments
   · Social History
   · Physical Examination and Clinical Impression
   · Treatment plan

2. TREATMENT OPTIONS AND EXCLUSIONS: (Explain why the standard or other treatments for this disease are not indicated for this particular patient.)

3. PROPOSED TREATMENT PLAN: (Attach any already existing protocols that describe the treatment proposed for this patient. IF none apply, provide a proposed protocol under which to treat this patient.)

4. PATHOLOGY, IF RELEVANT: (Attach any pertinent pathology reports)

5. RATIONALE FOR THE PROPOSED TREATMENT PLAN: (Why is the proposed treatment reasonable for this patient)

6. RISK /BENEFIT PROJECTION FOR THIS PATIENT:
Appendix B

EMERGENCY USE OF A TEST ARTICLE

Physician Name:
Investigational Article:

Evaluation to determine whether emergency use of a test article will be (or was) conducted in accordance with FDA regulations:

The physician has certified the following:

☐ The subject is (was) confronted by a disease or condition that is (was) life threatening meaning:
  - The likelihood of death is high unless the course of the disease is interrupted;
  - A disease or condition with a potentially fatal outcome, where the endpoint of clinical trial analysis is survival;
  - The disease or condition causes major irreversible morbidity.

☐ The situation necessitates (necessitated) the use of the investigational article.

☐ No standard acceptable treatment is (was) available.

☐ There is (was) NOT sufficient time to obtain IRB approval.

☐ The emergency use will be (was) reported to the IRB within 5 working days.

☐ Any subsequent use of the investigational product at Roswell Park Cancer Institute will have prospective IRB review and approval.

☐ The research involves (involved) an investigational drug and the FDA has issued an IND? IND #

☐ The research is (was) NOT subject to DHHS regulations. (See Determining Whether a Proposed Activity is Human Research According to DHHS Regulations or FDA Regulatory Definitions)

☐ One of the following is (was true):
  ☐ Informed consent will be sought from each prospective subject or the subject’s legally authorized representative, in accordance with and to the extent required by 21 CFR §50 and informed consent will be appropriately documented, in accordance with and to the extent required by 21 CFR §50.27.
  ☐ Informed consent is not required because all of the following are true:
Before the use of the test article both the investigator and a physician who is (was) not otherwise participating in the clinical investigation certified in writing that:

- The subject is (was) confronted by a life-threatening situation necessitating the use of the test article.
- Informed consent cannot (could not) be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from the subject.
- Time is (was) not sufficient to obtain consent from the subject’s legal representative.
- There is (was) available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

The above written certification will be (was) submitted to the IRB with 5 working days after the use of the test article.

Reviewed By: ____________________________________________________________  
Name & Title  Date
Informed Consent is not Required Because all of the Following are True:

☐ Immediate use of the test article is (was), in the investigator's opinion, required to preserve the life of the subject.

☐ Time is (was) not sufficient to obtain the independent determination a physician who is (was) not otherwise participating in the clinical investigation.

☐ Before the use of the test article, the investigator will certify (has certified) in writing, all of the following:
  • The subject is (was) confronted by a life-threatening situation necessitating the use of the test article.
  • Informed consent cannot (could not) be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
  • Time is (was not) sufficient to obtain consent from the subject's legal representative.
  • There is (was) available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

☐ After the use of the test article a physician who is (was) not otherwise participating in the clinical investigation will certify (has certified) in writing within 5 working days after the use of the article, all of the following:
  • The subject is (was) confronted by a life-threatening situation necessitating the use of the test article.
  • Informed consent cannot (could not) be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
  • Time is (was not) sufficient to obtain consent from the subject's legal representative.
  • There is (was) available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

The above written certification will be (was) submitted to the IRB within 5 working days after the use of the test article.

Reviewed By: _____________________________

Name & Title ___________________________ Date __________