UNIVERSITY OF CALIFORNIA, SAN DIEGO
HUMAN RESEARCH PROTECTIONS PROGRAM
FACT SHEET

Expanded Access – Investigational Device

Definitions

FDA guidance includes the following: "When a patient has a serious or life-threatening condition that is not addressed by current approved treatments, options may exist to use an investigational medical device (i.e., one that has not been approved or cleared by FDA) to treat the patient...there are circumstances under which a health care provider may use an investigational device outside of a clinical study to save the life of a patient or to help a patient suffering from a serious disease or condition for which no other alternative therapy exists. The use of an investigational device outside of a clinical trial for treatment of a patient is called 'expanded access.' If enrollment in an existing clinical trial protocol is not possible (e.g., a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical trials to address the patient's condition), patients/physicians have the potential to receive expanded access to investigational devices under one of three alternative mechanisms."

The three alternative mechanisms include the following

- Treatment Use IDE
- Compassionate Use IDE
- Emergency Use IDE

Treatment Use IDE

The FDA defines "treatment use" as "An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in the study. During the course of the clinical trial, if the data suggest that the device is effective, then the trial may be expanded to include additional patients with life-threatening or serious diseases. This is called treatment use."

The criteria for a Treatment IDE include the following:

- The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition;
- There is no comparable or satisfactory alternative device available to treat or diagnose the disease or condition in the intended patient population;
- The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or all clinical trials have been completed; and
- The sponsor of the controlled clinical trial is pursuing marketing approval/clearance of the investigational device with due diligence.

The FDA notes, "The treatment use provision of the IDE facilitates the availability of promising new devices to desperately ill patients as early in the device development process as possible, before general marketing begins, and to obtain additional data on the device's safety and effectiveness. In the case of a serious disease, a device ordinarily may be made available for

treatment use under this section after all clinical trials have been completed. In the case of an immediately life-threatening disease, a device may be made available for treatment use under this section prior to the completion of all clinical trials."

In addition, the FDA provides the following definition: "An '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. 'Treatment use' of a device includes the use of a device for diagnostic purposes."

Under a Treatment Use IDE, the sponsor and investigator(s) are responsible for meeting all applicable investigator responsibilities under 21 CFR 812, 21 CFR 50, and 21 CFR 56. These responsibilities include FDA approval, review and approval by a convened IRB, and the use of IRB-approved consent document as would be done with "full" IDE protocols.

In addition, as noted by the FDA, "The sponsor of a treatment IDE must submit progress reports on a semi-annual basis to all reviewing IRB's and FDA until the filing of a marketing application. The dates of these reports are based on the period of time since initial approval of the treatment IDE. *After* filing of a marketing application, progress reports must be submitted annually in accordance with the IDE regulations."

Additional information including applying for a Treatment Use IDE can be found in Guidance on IDE Policies and Procedures, Chapter III, *Expanded Access to Unapproved Devices*, at https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm#III. The Treating Physician/Sponsor is responsible for ensuring FDA requirements associated with a Treatment Use IDE are satisfied.

The Treating Physician/Sponsor is responsible for submitting safety reports, outcome reporting including annual reports, etc. to FDA and IRB, as appropriate.

Please note: A "NEW" UCSD Biomedical Research application must be submitted to the UCSD IRB/HRPP for review by a convened IRB. Information about submitting an application can be found at https://irb.ucsd.edu.

A sample treatment consent document for adults can be found here for UCSD and here for RCHSD/UCSD. A sample treatment parent permission document can be found here for UCSD and here for RCHSD/UCSD. A sample treatment adolescent assent document can be found here for UCSD and here for RCHSD/UCSD.

Note: It is the treating physician's responsibility to ensure the information included in the consent is accurate including the costs associated with the treatment such as the cost of the device. Consultation with the Office of Coverage Administration (OCAA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. It also the treating physician's responsibility to ensure any appropriate agreements are in place. Consultation with the Office of Contracts and Grants (OCGA) and/or the Office of Clinical Trials Administration (OCTA) is recommended.

In addition, the Treating Physician must also follow IRB/HRPP post-approval reporting requirements including review and approval of amendments before initiation except where

necessary to eliminate apparent immediate hazard to the subject (see HRPP fact sheet, Submitting an Amendment/Modification to a Research Plan (Protocol) and reporting of adverse events and unexpected problems (see SOPP, section 3.13, Reporting Adverse Events and Unexpected Problems) as well as Continuing Review submission.

Compassionate Use IDE

The FDA provides the following information: "FDA recognizes that there are circumstances in which an investigational device is the only option available for a patient faced with a serious or life-threatening disease or condition…. The compassionate use provision provides a path to accessing investigational devices that have not received FDA approval or clearance for patients for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. Compassionate use can be for devices that are being studied in a clinical trial under an IDE for patients who do not meet the requirements for inclusion in the clinical investigation but for whom the treating physician believes the device may provide a benefit in treating and/or diagnosing their disease or condition. It can also be used for devices that are not being studied in a clinical investigation (i.e., an IDE for the device does not exist). This provision is typically approved for individual patients but may be approved to treat a small group."

The criteria for a Compassionate Use IDE include the following:

- The patient has a life-threatening or serious disease or condition; and
- No generally acceptable alternative treatment for the condition exists.

Prior FDA approval is needed before compassionate use occurs. In addition to FDA approval, the compassionate use cannot proced without written concurrence from an UCSD IRB Chair or the UCSD IRB Chair's designee, in this case, the Director of the UCSD HRPP.

The FDA notes, "Following the compassionate use of the device, a follow-up report should be submitted by whoever submitted the original compassionate use request to FDA. This report should present summary information regarding patient outcome. If any problems occurred as a result of device use, these should be discussed in the follow-up report and reported to the reviewing IRB as soon as possible."

Obtaining FDA approval for a compassionate use include submitting to the FDA a IDE supplement if the device has an IDE or a description of the device, if there is no IDE for the device. Additional information that should be provided in either case includes the following:

- A description of the patient's condition and the circumstances necessitating treatment;
- A discussion of why alternatives therapies are unsatisfactory and why the probable risk of using the investigational device is no greater than the probable risk from the disease or condition;
- An identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient;
- The patient protection measures that will be followed include the following:
    - A draft of the informed consent document that will be used (see below for sample consent);
    - Clearance from the institution as specified by their policies;
    - Concurrence of the IRB chairperson or appropriate designee;
    - An independent assessment from an uninvolved physician; and

- Authorization from the device manufacturer on the use of the device.

Additional information including applying for a Compassionate Use IDE can be found in Guidance on IDE Policies and Procedures, Chapter III, *Expanded Access to Unapproved Devices*, at https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm#III. The Treating Physician/Sponsor is responsible for ensuring FDA requirements associated with a Compassionate Use IDE are satisfied.

The Treating Physician/Sponsor is responsible for submitting safety reports, outcome reporting including annual reports, etc. to FDA and IRB, as appropriate.

Please note: A "NEW" UCSD Biomedical Research application must be submitted to the UCSD IRB/HRPP for review by a convened IRB. Information about submitting an application can be found at https://irb.ucsd.edu.

The Treating Physician should also ensure the patient protections noted above, with the exception of the concurrence of the IRB chairperson, should be submitted, as appropriate, as a completed device supplement that is available here.

A sample treatment consent document for adults can be found here for UCSD and here for RCHSD/UCSD. A sample treatment parent permission document can be found here for UCSD and here for RCHSD/UCSD. A sample treatment adolescent assent document can be found here for UCSD and here for RCHSD/UCSD.

Note: It is the treating physician's responsibility to ensure the information included in the consent is accurate including the costs associated with the treatment such as the cost of the device. Consultation with the Office of Coverage Administration (OCAA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. It also the treating physician's responsibility to ensure any appropriate agreements are in place. Consultation with the Office of Contracts and Grants (OCGA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. Consultation with RCHSD Research Administration for RCHSD studies is also recommended.

In addition, the Treating Physician must also follow IRB/HRPP post-approval reporting requirements including review and approval of amendments before initiation except where necessary to eliminate apparent immediate hazard to the subject (see HRPP fact sheet, Submitting an Amendment/Modification to a Research Plan (Protocol) and reporting of adverse events and unexpected problems (see SOPP, section 3.13, Reporting Adverse Events and Unexpected Problems) as well as Continuing Review submission.

Emergency Use IDE

The FDA defines emergency use as "Emergency use is the use of an investigational device in an emergency situation. It is intended to provide patients and physicians with access to devices intended to treat life-threatening or serious diseases or conditions when there is no available alternative and no time to obtain FDA approval. Emergency use may apply even if the investigational device is being studied in a clinical trial under an IDE: if a physician needs to use the device in a manner inconsistent with the approved investigational plan; or a physician who is

not part of the clinical study, wishes to use the device to treat a patient with a life-threatening or serious disease or condition. Emergency use of an investigational device may occur before an IDE is approved and when a device is not being studied under an IDE."

The criteria for an Emergency Use IDE include the following:

- The patient has a life-threatening or serious disease or condition that needs immediate treatment;
- No generally acceptable alternative treatment for the condition exists; and
- Because of the immediate need to use the device, there is no time to use existing procedures to obtain FDA approval for the use.

The FDA notes that if all the criteria for an emergency use or met, "an unapproved device may be used in an emergency situation without prior approval by the FDA."

The FDA also "…expects the physician to make the determination that the patient's circumstances meet the above criteria, to assess the potential for benefit from the use of the unapproved device, and to have substantial reason to believe that benefits will exist. In the event that a device is used in circumstances meeting the criteria listed above, the physician should follow as many patient protection procedures as possible." These patient protection procedures include the following:

- Informed consent from the patient or a legal representative (see below for sample consent;
- Clearance from the institution as specified by their policies;
- Concurrence of the IRB chairperson;
- An independent assessment from an uninvolved physician; and
- Authorization from the device manufacturer.

The FDA provides this guidance for reporting an emergency use of a device: "If there is an IDE for the device, the IDE sponsor must notify the FDA of the emergency use within 5 days through submission of an IDE Report (§812.35(a)(2)).This follow-up report should include a summary of the conditions constituting the emergency, the patient protection measures that were followed, and patient outcome information. If no IDE exists, the physician should submit a follow-up report on the use of the device (description of device used, details of the case, and the patient protection measures that were followed) to: Food and Drug Administration, Center for Devices and Radiological Health, 10903 New Hampshire Ave., Document Control Center, WO66 Rm G-609, Silver Spring, MD 20993."

Additional information including applying for an Emergency Use IDE can be found in Guidance on IDE Policies and Procedures, Chapter III, *Expanded Access to Unapproved Devices*, at https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080202.htm#III. The Treating Physician/Sponsor is responsible for ensuring FDA requirements associated with an Emergency Use IDE are satisfied.

The Treating Physician/Sponsor is responsible for submitting safety reports, outcome reporting including annual reports, etc. to FDA and IRB, as appropriate.

The Treating Physician should notify the Director of the HRPP at 858-246-4777 and complete and upload the Biomedical Emergency Use Facesheets to allow the HRPP Office to track the

emergency use. Additional information will also need to be submitted including a completed Emergency Use Notification Form and Emergency Use Notification, 5-day Post Use form.

The Treating Physician should also ensure the patient protections noted above, with the exception of the concurrence of the IRB chairperson, should be submitted to the HRPP Office, as appropriate.

A sample treatment consent document for adults can be found here for UCSD and here for RCHSD/UCSD. A sample treatment parent permission document can be found here for UCSD and here for RCHSD/UCSD. A sample treatment adolescent assent document can be found here for UCSD and here for RCHSD/UCSD.

Note: It is the treating physician's responsibility to ensure the information included in the consent is accurate including the costs associated with the treatment such as the cost of the device. Consultation with the Office of Coverage Administration (OCAA) and/or the Office of Clinical Trials Administration (OCTA) is recommended. It also the treating physician's responsibility to ensure any appropriate agreements are in place. Consultation with the Office of Contracts and Grants (OCGA) and/or the Office of Clinical Trials Administration (OCTA) is recommended.

Note that an emergency use of a test article is exempt from prior IRB review and approval. However, the emergency use of a test article must be reported to the IRB within 5 working days of date of the emergency use. The determination to use a test article in an emergency setting is made by the treating physician in concert with the FDA and should not be dependent on the submission of information to the UCSD IRB/HRPP. If possible, the IRB and/or Director of the HRPP should be notified prior to an emergency use of a test article.

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