The Christ Hospital IRB
Section: 13
Effective Date: 01/07
Revised/Reviewed Date: 09/22
AAHRPP Element: 1.7.A, 1.7.B, 1.7.C

IRB REFERENCE MANUAL
SECTION 13
EXPANDED ACCESS TO INVESTIGATIONAL MEDICAL PRODUCTS

13.0 EXPANDED ACCESS TO INVESTIGATIONAL MEDICAL PRODUCTS

Expanded access (sometimes called "compassionate use") is a potential pathway for patients with a serious or immediately life-threatening disease or condition to gain access to an investigational medical product (medical device, drug, or biologic) for treatment outside of clinical trials when no comparable or satisfactory alternative therapy options are available.

Expanded access may be appropriate when all the following apply:

1. The patient has a serious or immediate life-threatening disease or condition;
2. There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition;
3. Patient enrollment in a clinical trial is not possible;
4. Potential patient benefit justifies the potential risks of treatment;
5. Providing the investigational medical product will not interfere with investigational trials that could support a medical product's development or marketing approval for the treatment indication.

Ref. U.S. Food & Drug Administration (FDA) Expanded Access

13.1 Investigational Devices

An unapproved medical device may normally be used on human subjects only through an approved clinical study in which the research subjects meet certain criteria and the medical product is used only in accordance with the approved protocol by a clinical investigator participating in the clinical trial. However, there may be circumstances under which a health care provider may wish to use an unapproved medical device (not approved or cleared by the FDA) to save the life of a patient or to help a patient suffering from a serious disease or condition for which no alternative therapy exists. Patients and physicians faced with these circumstances may have access to an investigational device through one of three mechanisms administered by the FDA:

1. Emergency use
2. Compassionate use
3. Treatment Investigational Device Exemption (IDE)
4. Continued Access

These mechanisms can be utilized during a certain timeframe in the IDE process if certain criteria are met. FDA approval is required for all mechanisms except in the case of emergency use.

13.1.1 Emergency Use

Emergency situations may arise in which an investigational medical device that has not received the FDA's approval, or clearance is needed for use (1) in a manner inconsistent with the approved investigational plan, and/or (2) by a physician who is not part of the clinical study investigating the device. In such cases, emergency use of an unapproved medical device may occur before the device is approved.

a. **Criteria**
   i. Life-threatening or serious disease or condition
   ii. No comparable or satisfactory alternative
   iii. Because of the immediate need to use the device, there is no time to use existing procedures required for FDA approval for the use of the device.

b. **Timeframe**
   i. Before initiation of the clinical trial
   ii. After initiation of the clinical trial

c. **Emergency Research**

There are special cases under emergency research in which the human research subject is in a life-threatening situation, in need of emergency medical intervention, and it is not feasible to obtain informed consent. Permitting certain clinical trials involving human subjects who are confronted by life-threatening situations and who are unable to give informed consent because of their medical condition, allows the individuals in these situations access to potentially life-saving therapies, potentially resulting in advancement in knowledge and improvement of treatments used in emergency medical situations that currently have poor clinical outcome (ref. Protection of Human Subjects; Informed Consent and Waiver of Informed Consent Requirements in Certain Emergency Research | FDA.).

In order to allow such research to proceed, special provisions for exception from informed consent requirements must be met.

The conditions required to conduct this type of research with exception from informed consent are described in 21 CFR 50.24 including the IRB's approval (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation).

d. **Documentation**
The sponsor must submit a separate IDE application to the FDA within 5 business days after the sponsor learns of the use of the investigational medical device. The report should include circumstances of the case and measures followed for patient protection including
   i. Informed consent,
   ii. Institutional clearance,
   iii. Concurrence of IRB Chairperson,
   iv. Independent assessment from an uninvolved physician
   v. Authorization from the IDE sponsor (if an IDE exists) or manufacturer
   vi. Monitoring plan and follow-up information.

13.1.2 Compassionate Use

The FDA recognizes that there are circumstances in which an investigational device is the only option available to 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 diagnosing, monitoring, or treating 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 or diagnosing their disease or condition. It can also be used for devices that are not being studied in a clinical investigation (such as 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, if the small group request is under an IDE. (Ref FDA Expanded Access for Medical Devices)

a. **Criteria**
   i. Serious disease or condition
   ii. No comparable or satisfactory alternative treatment

b. **Timeframe**
During the clinical trial

c. **Requesting Approval for Compassionate Use of a Device**
Prior FDA approval is needed before compassionate use occurs according to a 30-calendar-day review timeframe. In order to obtain FDA approval on **an existing IDE** to treat the patient(s), the sponsor (who may be the device manufacturer or a physician who has submitted the IDE to conduct the clinical study for the device) should submit an IDE supplement requesting approval for a protocol deviation under section 21 CFR 812.35(a). The IDE supplement must include:

i. A description of patient's (or patients') condition and circumstances necessitating treatment;
ii. A discussion of why alternative therapies are unsatisfactory and why the probable risk of using the investigational device is not greater than the probable risk from the disease or condition;
iii. Identification of any deviations in the approved clinical protocol that may be needed in order to treat the patient, and
iv. Patient protection measures that will be followed including
    1) informed consent,
    2) concurrence of the IRB chair,
    3) clearance from the institution,
    4) independent assessment from uninvolved physician,
    5) authorization from IDE sponsor.

If there is **no IDE** for the device, a compassionate use request for a single patient may be submitted by the physician or manufacturer with the above information, along with a description of the device provided by the manufacturer, to the FDA at:

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

For assistance, physicians and manufacturers may contact CDRHExpandedAccess@fda.hhs.gov.

The physician should not treat the patient identified in the IDE supplement until the FDA approves use of the device under the proposed

circumstances. When there is an IDE for the device, compassionate use request IDE supplements have the same statutory 30-day review cycle as other IDE submissions; however, the patient need is considered when reviewing these requests as well as whether the preliminary evidence of safety and effectiveness justifies such use and whether such use would interfere with the conduct of a clinical trial investigating support of marketing approval.

If the request is approved, the attending physician should devise a schedule for monitoring the patient, taking into consideration the investigational nature of the device and the specific needs of the patient. The patient should be monitored to detect any problems arising which could be possibly associated with the use of the device. Following the compassionate use of the device, a follow-up report should be submitted to the FDA as an IDE supplement within 45 days of using the investigational device in which summary information regarding patient outcome is presented. If any problems occurred as a result of device use, these should be discussed in the supplement and reported to the reviewing IRB as soon as possible.

13.1.3 Treatment Use

An approved IDE specifies the maximum number of clinical sites and the maximum number of human subjects that may be enrolled in a study. During the course of the clinical trial, if the data suggests that the device is effective, the trial may be expanded under a new IDE to include additional patients with life-threatening or serious diseases.

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. 21 CFR 812.36(a)

a. **Criteria**

The FDA shall consider the use of an investigational device under a treatment IDE if:

i. The device is intended to treat or diagnose a serious or immediately life-threatening disease or condition

ii. There is no comparable or satisfactory alternative device or other therapy available to treat or diagnose the stage of the disease or condition in the intended patient population

iii. The device is under investigation in a controlled clinical trial for the same use under an approved IDE, or such clinical trials have been completed, and

iv. The sponsor of the investigation is actively pursuing marketing approval/clearance of the investigational device with due diligence

Ref. 21 CFR 812.36(b)

b. **Timeframe**
During the clinical trial

A device that is not approved for marketing may be under clinical investigation for a serious or immediately life-threatening disease or condition in patients for whom no comparable or satisfactory alternative device or other therapy is available. During the clinical trial or prior to final action on the marketing application, it may be appropriate to use the device in the treatment of patients not enrolled in the trial under the provisions of the Treatment Use of an investigational device exemption (IDE). Ref. 21 CFR 812.36

The Treatment Use provision 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.

c. **Applications for Treatment Use**
A treatment IDE application shall include, in the following order (ref. 21 CFR 812.36(c)):

i. Name, address and telephone number of the sponsor of the treatment IDE;
ii. The intended use of the device, criteria for patient selection, and a written protocol describing the treatment use;
iii. An explanation of the rationale for use of the device, including, as appropriate, either a list of the available regimens that ordinarily should be tried before using the investigational device or an explanation of why the use of the investigational device is preferable to the use of available marketed treatments;

iv. A description of clinical procedures, laboratory tests, or other measures that will be used to evaluate the effects of the device and to minimize risk;
v. Written procedures for monitoring the treatment use and the name and address of the monitor;
vi. Instructions for use for the device and all other labeling as required under § 812.5(a) and (b);
vii. Information that is relevant to the safety and effectiveness of the device for the intended treatment use (information from other IDE's may be incorporated by reference to support the treatment use);
viii. A statement of the sponsor's commitment to meet all applicable responsibilities under federal regulations 21 CFR 812.36(c)(1)(vii) and 21 CFR 56, and to ensure compliance of all participating investigators with the informed consent requirements of 21 CFR 50;
ix. An example of the agreement to be signed by all investigators participating in the treatment IDE and certification that no investigator will be added to the treatment IDE before the agreement is signed; and
x. If the device is to be sold, the price to be charged and a statement indicating that the price is based on manufacturing and handling costs only.

A licensed practitioner who receives an investigational device for treatment use under a treatment IDE is an "investigator" under the IDE and is responsible for meeting all applicable investigator responsibilities under 21 CFR 812, 21 CFR 50, and 21 CFR 56. (Ref. 21 CFR 812.36(c)(2))

Address for IDE Correspondence
If you are sending an application, supplemental application, report, request for waiver, request for import or export approval, or other correspondence relating to matters covered by this part, you must send the submission to the appropriate address as noted in 21 CFR 812.19.

Applications should be identified on the outside envelope as a treatment IDE application and Reference the IDE number. The original and two copies should be mailed to:

U.S. Food and Drug Administration
Center for Devices and Radiological Health
Document Control Center (DCC) – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Additional information for submission of applications and most IDE supplements, amendments and reports may be found at IDE Application | FDA including instructions for electronic submission.

d. **FDA Action on Treatment IDE Applications**

i. **Approval of Treatment IDEs**

Treatment use may begin 30 days after FDA receives the treatment IDE submission at the address specified in 21 CFR 812.19, unless FDA notifies the sponsor in writing earlier than the 30 days that the treatment use may or may not begin. FDA may approve the treatment use as proposed or approve it with modifications.

ii. **Disapproval/Withdrawal of Approval of Treatment IDEs**

FDA may disapprove or withdraw approval of a treatment IDE if:

1) The required criteria 812.36(b) are not met or the treatment IDE application does not contain the required information 812.36(c);
2) FDA determines that any of the grounds for disapproval or withdrawal of approval apply 812.30(b)(1) through (b)(5);
3) The device is intended for a serious disease or condition and there is insufficient evidence of safety and effectiveness to support such use;
4) The device is intended for an immediately life-threatening disease or condition and the available scientific evidence, taken as a whole, fails to provide a reasonable basis for concluding that the device:
    - May be effective for its intended use in its intended population; or
    - Would not expose the patients to whom the device is to be administered to an unreasonable and significant additional risk of illness or injury
5) There is reasonable evidence that the treatment use is impeding enrollment in, or otherwise interfering with the conduct or completion of, a controlled investigation of the same or another investigational device;

6) The device has received marketing approval/clearance or a comparable device or therapy becomes available to treat or diagnose the same indication in the same patient population for which the investigational device is being used;
7) The sponsor of the controlled clinical trial is not pursuing marketing approval/clearance with due diligence;
8) Approval of the IDE for the controlled clinical investigation of the device has been withdrawn; or
9) The clinical investigator(s) named in the treatment IDE are not qualified by reason of their scientific training and/or experience to use the investigational device for the intended treatment use.

iii. **Notice of Disapproval or Withdrawal**
If the FDA disapproves or proposes to withdraw approval of a treatment IDE, the FDA will follow the procedures set forth in the IDE regulations 812.30(c).

e. **Safeguards** (ref. 21 CFR 812.36(e))
Treatment use of an investigational device is conditioned upon the sponsor and investigators complying with the safeguards of the IDE process and the regulations governing informed consent (21 CFR 50) and IRB's (21 CFR 56).

f. **Reporting Requirements** (ref. 21 CFR 812.36(f))
The sponsor of a treatment IDE shall submit progress reports on a semi-annual basis to all reviewing IRBs and FDA until the filing of a marketing application. These reports shall be based on the period of time since initial approval of the treatment IDE and shall include the number of patients treated with the device under the treatment IDE, the names of the investigators participating in the treatment IDE, and a brief description of the sponsor's efforts to pursue marketing approval/clearance of the device. Upon filing of a marketing application, progress reports shall be submitted annually in accordance with § 812.150(b)(5). The sponsor of a treatment IDE is responsible for submitting all other reports required under §812.150.

Additional Information:

Type of Expanded Access	Brief Definition	FDA approval required?	Follow-up Reports to the FDA
Emergency use	Use of an investigational device when an **individual patient is in a life-threatening situation and needs immediate treatment** (there are no alternative options and no time to use existing procedures to get FDA approval for the use)	No	Yes
Compassionate use	Use of an investigational device to **treat or diagnose an individual patient or a small group of patients** with a serious disease or condition when there are no available alternative options	Yes	Yes
Treatment Investigational Device Exemption	Use of an investigational device to **treat or diagnose a group of patients** with a serious or immediately life-threatening disease or condition when the device is also being studied for the same use under an approved Investigational Device Exemption.	Yes	Yes

(Ref. FDA Expanded Access for Medical Devices)

13.1.4 Continued Access

In order to allow access to an investigational medical device while the marketing application is being prepared by the sponsor or reviewed by the FDA, the FDA may allow continued enrollment of subjects after the controlled clinical trial under an IDE has been completed.

a. **Criteria**
   i. Public health need for the device, or
   ii. Preliminary evidence that the device is likely to be effective and no significant safety concerns have been identified for the proposed indication.

b. **Timeframe**
   After completion of the clinical trial

The continued enrollment of subjects in an investigation while a marketing application is being prepared by the sponsor and/or reviewed by ODE is known as an "extended investigation." Extended investigations permit patients and/or physicians continued access to investigational devices while also allowing the collection of additional safety and effectiveness data to support the marketing application or to address new questions regarding the investigational device. The Continued Access mechanism may be applied to any clinical investigation that meets the identified under **13.1.4** (a) above. However, continued access is intended to be applied late in the device development process (i.e., after the controlled clinical trial has been completed).

c. **IDE Supplement Guidelines**

A sponsor's request for an extended investigation should be submitted as an IDE supplement and include:

i. Justification for the extension;
ii. Summary of the preliminary safety and effectiveness data generated under the IDE;
iii. A brief discussion of the risks posed by the device;
iv. The proposed rate of continued enrollment (the number of sites and subjects);
v. The clinical protocol, if different from that used for the controlled clinical trial, as well as the proposed objectives for the extended study; and
vi. A brief discussion of the sponsor's progress in obtaining marketing approval/clearance for the device.

d. **Determining Continued Access or Treatment Investigational Device Exemption**

There is significant overlap between the mechanisms Continued Access and Treatment IDE. Both Continued Access and the Treatment IDE are intended to provide additional access to an unapproved device once preliminary evidence regarding safety and effectiveness is available to the FDA. However, because a Treatment IDE can be submitted earlier in the IDE process (i.e., once promising evidence of safety and effectiveness has been collected under the IDE but while the clinical study is ongoing), Treatment IDE could provide access to a wider group of patients at an earlier stage in the IDE process. However, the Treatment IDE regulation has a narrower application than the Continued Access policy in that treatment used is intended to address only those patients who have an immediately life-threatening or serious disease or condition whereas Continued Access, applied after completion of the clinical trial, may be considered for any clinical investigation.

13.2 Investigational Drugs and Biologics

The FDA describes three distinct categories of expanded access to investigational drugs and biologics based on the number of people who need access and the level of risk:

1. Expanded access for individual patients (including for emergency use)
2. Expanded access for intermediate-size patient groups
3. Expanded access for widespread treatment use

An expanded access IND submission is required for each of the three types of expanded access. The submission may be a ***new IND*** or a protocol amendment to an ***existing IND***. Ref. FDA Guidance Expanded Access Categories for Drugs (Including Biologics)

13.2.1 Individual Patient Access

Commonly held by the treating physician or investigator for treatment of an individual patient. Ref. 21 CFR 312.310

a. **Individual Patient Expanded Access IND (Single Patient IND)**

Requests access to an investigational drug (including a biologic) for use by a single patient submitted as a protocol ***under a new IND***. The investigational product may or may not be under development. Unless FDA notifies the sponsor that treatment may begin earlier, there is a 30-day waiting period before treatment with the drug may begin.

b. **Individual Patient Expanded Access Protocol (Single Patient Protocol)**

Access to an investigational drug (including a biologic) for use by a single patient submitted as a new protocol *to* ***an existing*** **IND** ***by the sponsor of the existing IND***. Typically, several patients may follow the same protocol. The investigational product may or may not be under development. There is no 30-day waiting period before treatment with the investigational product may begin, but the protocol must be received by the FDA and have approval by the IRB before treatment may begin.

c. **Individual Patient Access in an Emergency**

i. **Emergency IND**

Access to an investigational drug (including a biologic) for use by a single patient in an emergency situation (i.e., a situation that requires a patient to be treated before a written submission can be made) submitted as a protocol under a ***new IND***. Treatment is initially requested and authorized by telephone or other rapid means of electronic communication and may start immediately upon FDA authorization. The written submission (i.e., the individual patient expanded access IND) must be submitted within 15 business days of the telephone authorization.

ii. **Emergency Protocol**

Individual Patient Expanded Access Protocol for Emergency Use providing access to an investigational

drug (including a biologic) for use by a single patient in an emergency situation (i.e., a situation that requires a patient to be treated before a written submission can be made) submitted as a new protocol to an ***existing IND*** by the sponsor of the existing IND. Treatment is initially requested and authorized by telephone or other rapid means of communication, and treatment may start immediately upon FDA authorization. The written submission (i.e., the individual patient expanded access protocol) must be submitted within 15 business days of the telephone authorization.

In an emergency situation where there is not sufficient time to secure IRB review prior to beginning treatment, the emergency use of the investigational drug must be reported to the IRB within 5 working days, as required under 21 CFR 56.104(c).

Note: If a physician has determined that an emergency exists, instructions can be followed on FDA's Expanded Access Contact Information. For additional information regarding emergency requests (phone submissions, other forms of rapid communication such as e-mail) made by a licensed physician after receiving agreement from industry to provide the investigational medical product for expanded access use, refer to FDA publication Emergency Use of an Investigational Drug or Biologic.
Ref. FDA guidance: Expanded Access | Information for Physicians

13.2.2 Intermediate-Size Patient Population Access (ref. 21 CFR 312.315)

a. **Intermediate-size Patient Population Expanded Access IND**
Access to an investigational drug (including a biologic) for use by more than one patient, but generally fewer patients than are treated under a typical treatment IND or protocol, submitted as a protocol under a new IND. The investigational product may or may not be under development for marketing. Unless FDA notifies the sponsor that treatment may begin earlier, there is a 30-day waiting period before treatment may begin.

b. **Intermediate-size Patient Population Expanded Access Protocol**
Access to an investigational drug (including a biologic) for use by more than one patient, but generally fewer patients than are

treated under a typical treatment IND or protocol, submitted as a protocol to an existing IND by the sponsor of the existing IND. The investigational product may or may not be under development for marketing. There is no 30-day waiting period before treatment with the investigational product may begin, but the protocol must be received by FDA and have IRB approval before treatment may begin.

An intermediate-size patient population protocol may also be requested to allow access to treatment with an approved drug (including a biologic) or a related product that is not available through marketing channels because of failure to meet the conditions of approval or a drug shortage, provided the drug and the patient meet the general criteria for expanded access as well as the criteria specific to use in an intermediate-size patient population.

13.2.3 Expanded Access for Widespread Use (Ref. 21 CFR 312.320)

a. **Treatment IND**
Access to an investigational drug (including a biologic) for treatment use by a large (widespread) population, submitted as a protocol ***under a new IND***. The investigational product must be under active development for marketing. Unless FDA notifies the sponsor that treatment may begin earlier, there is a 30-day waiting period before treatment may begin.

b. **Treatment Protocol**
Access to an investigational drug (including a biologic) for treatment use by a large (widespread) population, submitted as a protocol ***to an existing IND by the sponsor of the existing IND***. The investigational product must be under development for marketing. Unlike other access protocols submitted to existing INDs, there is a 30-day waiting period before treatment may begin, unless FDA notifies the sponsor that treatment may begin earlier.

Additional Resources

- SOP 1.24 Expanded Access - Investigational Devices
- SOP 1.11, Expanded Access - Investigational New Drugs
- Federal Regulations 21 CFR 312.305, Requirements for All Expanded Access Uses