

Expanded Access: Sample Information Sheet

HRP is providing the following information as part of its ongoing responsibility to assist clients in navigating their research programs through the COVID-19 pandemic. This sample information sheet describes the various categories of Expanded Access available under U.S. FDA regulations and summarizes the requirements associated with each. HRP encourages organizations to modify this sample so that it incorporates the organization's processes and requirements. The regulatory information within this sample comes from FDA's websites, guidance documents, and dialogue with the FDA, and so should be modified with caution. This sample does not address HIPAA.

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I. What is Expanded Access?

Expanded Access describes the pathways available within U.S. FDA regulations for the treatment or diagnosis of patients with an immediately life-threatening or serious disease or condition with an investigational or unapproved or uncleared drug, biologic, or medical device when:

- The patient is unable to obtain access through participation in a clinical trial; and
- There are no comparable or satisfactory alternative therapy or diagnostic options.

Expanded Access is sometimes referred to as "compassionate use" and includes everything from emergency use of an investigational or unapproved/uncleared product for a single patient to use for large numbers of people. The FDA has made substantial efforts to streamline the procedures and requirements associated with each type of Expanded Access but there are important differences in requirements based upon the type of Expanded Access and the type of medical product.

This information sheet summarizes the categories of Expanded Access and the initial requirements associated with each. For detailed information, please visit the FDA's Expanded Access webpages, which can be navigated to from this homepage: <https://www.fda.gov/news-events/public-health-focus/expanded-access>.

[Organization name's] HRPP/IRB policy and procedure manual (available here: [hyperlink]) provides additional detail about [Organization name's] initial submission and follow-up requirements. Providers are encouraged to contact the HRPP/IRB office [insert contact information] when contemplating expanded access so that we can facilitate the process.

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Manufacturers of Investigational Drugs are required to make their policy and procedures for expanded access requests readily available, most do so via their public websites. The same requirement does not apply to medical devices, but many manufacturers do make the information available.

II. FDA's Key Contact Information and Mailing Addresses for Expanded Access

- [Drugs, biologics, and medical devices](#)
- [Antiviral Products](#)
- [Convalescent Plasma](#)

III. How is serious or immediately life-threatening defined?

For the purposes of expanded access, the FDA defines serious or immediately life-threatening as follows:

- Immediately life-threatening disease or condition means a stage of disease in which there is reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.
- Serious disease or condition means a disease or condition associated with morbidity that has substantial impact on day-to-day functioning. Short-lived and self-limiting morbidity will usually not be sufficient, but the morbidity need not be irreversible, provided it is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one.

FDA references the following definitions as examples of severe or immediate life-threatening COVID-19 on its website about [Emergency INDs for COVID-19 Convalescent Plasma](#):

- Severe disease is defined as dyspnea, respiratory frequency ≥ 30 /min, blood oxygen $\leq 93\%$, partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300 , and/or lung infiltrates $> 50\%$ within 24 to 48 hours.
- Life-threatening disease is defined as respiratory failure, septic shock, and/or multiple organ dysfunction or failure.

IV. Expanded Access – Drugs and Biologics Classified as Drugs

The Expanded Access pathways for drug products include:

- Single Patient Expanded Access (which includes Emergency Uses)
- Intermediate-Size Patient Population Access
- Treatment INDs and Protocols for widespread access

Historically, most Expanded Access requests at [organization name] have been for single patient access. However, with the COVID-19 pandemic we are anticipating an increase in Intermediate-Size and Treatment INDs and Protocols as industry sponsors seek to make their investigational products available to patients who are unable to participate in a clinical trial.

a. Single Patient Expanded Access:

Providers interested in seeking expanded access for a single patient should do the following: *(Insert any organizational requirements (e.g., physician leader sign-off, independent physician assessment, engaging a clinical trials or regulatory support unit, advance notification to HRPP/IRB, etc.) at the appropriate timepoint.)*

- Evaluate the potential risks and benefits
- Confirm that the patient meets the following criteria:
 - The patient has a **serious or immediately life-threatening disease or condition** as defined by the FDA:
 - There is no available comparable or satisfactory alternative therapy available for the patient
 - There are no available clinical trials for the patient (e.g., because of a lack of open trials, because the patient is ineligible, because of the location of the trials, etc.)
- Confirm that the manufacturer or sponsor will provide the drug/biologic for the patient and, if so, whether they will be the sponsor (by adding the patient on to an existing IND) or you will need to serve as such and submit the request to the FDA (this is more common)
- If you will be the sponsor:
 - Obtain a Letter of Authorization (LOA) from the manufacturer and, if available, a sample treatment protocol and/or informed consent form (if the manufacturer does not have one, a template is available [[insert link or instructions](#)])
 - Find out if the manufacturer will provide the drug/biologic free of charge and, if not, what the cost will be
 - Submit the expanded access request to the FDA following their instructions for either an [Non-Emergency](#) or [Emergency](#) Individual Patient IND. When using Form FDA 3926 (preferred method), be sure to check the 10.b. box for Alternative IRB Review Procedures (this permits review by the IRB Chair instead of the convened IRB). In an emergency, FDA may authorize the use via phone, fax, or email with a requirement to submit the application and LOA within 15 business days.
- Regardless of the FDA IND type (emergency or non-emergency), submit to the [[Organization](#)] IRB for **prior approval** whenever possible. Emergency Use Exemption procedures may only be used when review by the IRB Chair or designee cannot be obtained prior to the use and the remaining criteria for emergency use are satisfied. Submission instructions are available [[insert link or instruction](#)]. You may submit to the IRB at the same time you are submitting to the FDA, but we won't be able to finalize approval of the use until FDA's approval is obtained. If you need help or have questions, please don't hesitate to contact the IRB office at [[insert contact information](#)].
- Treatment may begin as soon as FDA and IRB approval have been obtained.
- When serving as the sponsor-investigator, follow up reports must be submitted to the FDA in accordance with their requirements as well as any proposed modifications to the treatment and safety monitoring plan. FDA's follow up requirements are summarized on this [website](#).

b. Intermediate-Size Patient Population Access:

Intermediate-Size Patient Population Access is available for use when it is expected that the product will be needed for more than one patient but generally fewer patients than a Treatment IND or Protocol (which are intended for widespread access). Use of this mechanism improves efficiency by reducing duplicative reviews. There are two pathways for intermediate-size patient populations available under FDA regulations:

- Intermediate-Size Patient Population Expanded Access INDs
 - Submitted to FDA as a new IND by either a sponsor or a sponsor-investigator
 - Unless FDA notifies the sponsor otherwise, there is a 30-day waiting period before treatment may begin
- Intermediate-Size Patient Population Expanded Access Protocols
 - Submitted to FDA as an addendum protocol to an existing IND by the sponsor of the existing IND
 - May also be used to allow access to treatment with an approved drug that is not available through marketing channels (e.g., because of restrictions on use or because of a drug shortage)
 - No 30-day waiting period, but the protocol must be received by the FDA and approved by the IRB before treatment can begin

Intermediate-Size Patient Population Expanded Access INDs and Protocols must be reviewed and approved by the convened IRB, alternative review by the IRB Chair is not allowed under FDA regulations for these pathways. Please contact the HRPP/IRB office at [insert contact information] when contemplating an Intermediate-Size Patient Population Access protocol so that we can facilitate the process. If the IND or Protocol has already been approved by another IRB, IRB Reliance may be possible.

FDA's [expanded access websites](#) and guidance "[Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers](#)" provides information to help determine which pathway is most appropriate when multiple patients may be treated with the same product and the FDA submission requirements associated with each. FDA may also be contacted with questions (see links in [Section II](#) above).

c. Treatment INDs and Protocols for Widespread Use

Expanded Access Treatment INDs and Protocols are available when widespread use of an investigational drug is anticipated. Unlike the other expanded access pathways, [additional criteria](#) apply, including that the investigational product must be under active development for marketing. A 30-day waiting period applies after application to the FDA before treatment can begin, unless the FDA notifies the sponsor that treatment may begin earlier.

- Treatment INDs are submitted as a protocol under a new IND. Treatment INDs may be submitted by either industry sponsors or sponsor-investigators (but this is unusual)
- Treatment Protocols are submitted as a protocol to an existing IND by the sponsor of the existing IND. This path is preferred because having all of data under a single IND facilitates the identification of safety concerns and the product review process

Treatment INDs and Protocols must be reviewed and approved by the convened IRB, alternative review by the IRB Chair is not allowed under FDA regulations for these pathways. Please contact the HRPP/IRB office at [insert contact information] when considering expanded access for patients under a Treatment IND or Protocol so that we can facilitate the process. If the IND or Protocol has already been approved by another IRB, IRB Reliance may be possible.

We anticipate increased use of these pathways by sponsors during the COVID-19 pandemic so that access to potentially life-saving products can be made available to patients unable to participate in a clinical trial and to facilitate the sponsor's and FDA's ability to gather safety data. It is our understanding that FDA is actively working with sponsors to accelerate FDA review and approval, as appropriate.

d. Informed Consent

Informed consent that fully complies with FDA's requirements for such at [21 CFR 50](#) is required for all expanded access uses of investigational drugs, unless the use meets the requirements for a consent exception at 21 CFR 50.23(a)-(c). Industry sponsors frequently provide investigators seeking expanded access use with a consent template that can be adapted for use by the investigator. [Organization name] HRPP/IRB also has a consent template available at [insert link or instruction]. Consent forms must be reviewed and approved by the IRB prior to use.

Emergency Consent Exception Criteria:

- Both the investigator and an independent physician must determine and certify in writing that all of the following are true:
 - The patient is confronted by a life-threatening situation necessitating the use of the test article;
 - Informed consent cannot be obtained from the patient because of an inability to communicate with, or obtain legally effective consent from the patient;
 - Time is not sufficient to obtain consent from the subject's legal representative; and
 - There is no alternative method of approved or generally recognized therapy available that provides an equal or greater likelihood of saving the life of the subject
- The certification must be made in advance of the use unless immediate use is, in the investigator's opinion, required to preserve the life of the patient, and time is not sufficient to obtain the independent physician certification in advance. In this case, the investigator must make the above determinations and, within 5 working days after the use of the article, have the determinations reviewed and evaluated in writing by an independent physician
- Documentation of the investigator's and independent physician's certifications must be submitted to the IRB within 5 working days after the use of the test article.

Documentation of consent exceptions should be submitted to the IRB by [insert instructions].

V. Expanded Access – Medical Devices and Biologics Classified as Devices

The Expanded Access pathways for medical device products include:

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- Emergency Use
- Compassionate Use (for individual patients or small groups)
- Treatment Investigational Device Exemption (IDE)

While there are similarities between the expanded access pathways for drugs and devices, there are also important differences in processes and requirements that providers should be aware of. FDA provides information about expanded access for medical devices on this website: <https://www.fda.gov/medical-devices/investigational-device-exemption-ide/expanded-access-medical-devices>. Physicians may also contact FDA for assistance using the contact information linked to in [Section II](#) above or by emailing CDRHEExpandedAccess@fda.hhs.gov.

e. Emergency Use

The Emergency Use pathway for medical devices is intended to provide access to investigational or unapproved/uncleared medical devices when a patient is confronted with an immediately life-threatening situation. Physician's contemplating emergency use of an investigational or unapproved/uncleared medical device are expected to:

- Assess the potential for benefit from the use of the device;
- To have substantial reason to believe that benefits will exist;
- Determine that the use meets the following criteria:
 - The patient has a life-threatening 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 obtain FDA approval
- Follow as many patient protection procedures as possible, including obtaining:
 - An independent assessment from an uninvolved physician;
 - Authorization from the device manufacturer;
 - Clearance from the institution as specified by their policies. At [Organization name] this includes: [insert description];
 - Concurrence of the IRB Chairperson; and
 - Informed consent from the patient or their legal representative

These procedures differ substantively from those for emergency use of drugs in that FDA approval does not need to be obtained in advance of the use, but IRB Chair concurrence must. FDA does not consider the single-patient emergency use of an investigational medical device to be research and therefore does not issue an IDE for the use. The IRB Chair should use the criteria at 21 CFR Parts 50 and 56 as guidelines when assessing the proposed use and informed consent.

The Emergency Use must be reported to the FDA within 5 days by the IDE sponsor, when one exists. If no IDE exists, the physician responsible for the use should submit a report to the FDA within 5 days of the use including a description of the device, the details of the case, and the patient protection measures that were followed. The mailing information for the report is available on the FDA's [Expanded Access for Medical Devices](#) website.

[Describe any institutional requirements (e.g., for submission of follow up reports).]

f. Compassionate Use

FDA's Compassionate Use pathway is available for the use of an investigational or unapproved/uncleared medical device to treat or diagnose a single patient or a small group of patients with a serious disease or condition when there are no acceptable alternatives. The criteria for Compassionate Use are as follows:

- The patient has a life-threatening or serious disease or condition;
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; and
- The potential patient benefit justifies the potential risks of the use of the investigational device

Approval must be obtained prior to the use from the medical device company, the FDA and the IRB. The responsibility for submission to the FDA depends on whether there is an existing IDE. When there is an IDE sponsor, the sponsor is responsible for submitting an IDE supplement requesting approval for the compassionate use. If there is no IDE for the device, the physician or device manufacturer should submit the following information to the FDA at the address noted on the FDA's [Expanded Access for Medical Devices](#) website:

- A description of the device provided by the device manufacturer;
- A description of the patient's condition and the circumstances necessitating treatment;
- A discussion of why alternative 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;
- The patient protection measures that will be followed, including:
 - An independent physician assessment;
 - Authorization for the use from the device manufacturer
 - Clearance from the institution as specified by their policies. At [Organization name] this includes: [insert description];
 - IRB Approval (see note below); and
 - A draft of the informed consent form; [If available, describe where a consent template may be found]
- A patient monitoring plan; and
- For small group access, the number of patients and the protocol to be followed

[If needed, modify the following statement to reflect organizational practice.] The IRB Chair may approve single-patient compassionate use, proposals for small group use will be reviewed by the convened IRB. The [organization name] IRB typically does not finalize approval for the use of the device until FDA approval has been obtained. Physician's should indicate in the submission to the FDA that IRB approval will be obtained before the use of the device. A copy of the IRB approval will need to be provided to the FDA in the follow-up report.

A follow-up report should be submitted to the FDA by whichever party (physician, IDE holder, device manufacturer) within 45 days of the use (or after use in all patients for small group access). The report should include summary information regarding patient outcome and any problems that occurred as a result of the use of the device. Such problems should be reported to the IRB as soon as possible after occurrence. [Describe process and timeline for reporting problems to the IRB and whether the FDA follow up report should also be submitted to the IRB.]

g. Treatment IDEs

Treatment IDEs are used to provide patients with a serious or immediately life-threatening condition access to an investigational device when the data from the clinical trial(s) suggest that the device is effective. The following criteria must be satisfied for a Treatment IDE:

- 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 trials have been completed; and
- The sponsor of the controlled clinical trial is pursuing marketing approval or clearance of the investigational device with due diligence

Treatment IDEs must be reviewed and approved by the convened IRB, alternative review by the IRB Chair is not allowed under FDA regulations for this pathway. Please contact the HRPP/IRB office at [insert contact information] when considering expanded access for patients under a Treatment IDE so that we can facilitate the process. If the Treatment IDE has already been approved by another IRB, IRB Reliance may be possible.

h. Informed Consent

Other than Emergency Use, informed consent that fully complies with FDA's requirements at [21 CFR 50](#) is required for expanded access use of investigational devices. For Emergency Use, informed consent should be obtained as a patient protective measure whenever possible and the requirements at 21 CFR 50 should be used as guidelines. Industry sponsors frequently provide investigators seeking expanded access use with a consent template that can be adapted for use by the investigator. [Organization name] HRPP/IRB also has a consent template available at [insert link or instruction]. Consent forms must be reviewed and approved by the IRB prior to use.

VI. PREP Act Declaration for COVID-19

The Secretary of the Department of Health and Human Services has issued a [Public Readiness and Emergency Preparedness Act \(PREP Act\) for Medical Countermeasures Against COVID-19](#) declaration.

The Declaration was effective as of February 4, 2020 and provides liability immunity to the United States and those that "manufacture, distribute, administer, prescribe, or use Covered Countermeasures."

Covered Countermeasures include, among other things, "drugs, devices, or biological products used to diagnose, mitigate, prevent, treat or cure a pandemic or epidemic or limit the harm such a pandemic or

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epidemic might otherwise cause.” The PREP Act does not provide protection for claims involving willful misconduct.

Individuals, or their beneficiaries, who experience serious physical injuries or die as a direct result of the administration or use of Covered Countermeasures may be eligible for benefits under the [Countermeasures Injury Compensation Program](#) (CICP).

When Expanded Access includes the administration or use of a Covered Countermeasure for COVID-19, patients should be informed about the potential limitations on their right to sue under the PREP Act and about the CICP by including the following information should be included in the consent form:

[Insert organizational language for consent or reference its availability within a consent template]

When consent is not obtained prospectively for an emergency use, patients or their LARs should be provided with this information when informed of the emergency use. [If an information sheet is to be provided in such circumstances, reference it here. Organizations should also consider whether subjects who previously consented (before the above language was made available) should be informed via an information sheet or other means.]

VII. Resources

[Add links for organizational resources such as the IRB website, submission forms, consent templates, COVID-19 information]

- [FDA Expanded Access Information for Physicians](#)
- [FDA Expanded Access for Medical Devices](#)
- [FDA Emergency IND Applications for Antiviral Products](#)
- [FDA Investigational COVID-19 Convalescent Plasma – Emergency INDs](#)
- [DHHS Declaration Public Readiness and Emergency Preparedness Act \(PREP Act\) for Medical Countermeasures Against COVID-19](#)
- [HRSA Countermeasures Injury Compensation Program \(CICP\)](#)