POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

Emergency Investigational New Drug Application Process During and After Normal Working Hours

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PURPOSE

- This Manual of Policies and Procedures (MAPP) describes the policies and procedures established in the Center for Drug Evaluation and Research (CDER) for managing and processing applications for individual patient expanded access for emergency use (henceforth referred to as emergency investigational new drug applications (EINDs)) for physicians licensed in accordance with State law (hereafter referred to as "physician") seeking access to an investigational drug for treatment use in an individual patient in an emergency situation, both during and after normal working hours.[1, 2, 3]

- Although access to an investigational drug for an individual patient in an emergency may be requested and authorized through submission of a protocol for such use by an Investigational New Drug application (IND) holder (e.g., pharmaceutical company) to its existing IND, this situation is not common and is

[1] Section 561(b) of the FD&C Act (21 U.S.C. 360bbb(b)) provides that any person "acting through a physician licensed in accordance with State law" may request access to an investigational new drug under the expanded access pathway.
[2] For the purposes of this MAPP, all references to *drugs* include human drugs and therapeutic biological products regulated by CDER.
[3] For EIND requests, normal working hours are 8:00 AM to 4:30 PM EST, Monday through Friday (refer to 21 CFR 312.310(d)(1)).

not addressed in this MAPP. Most emergency access is requested and authorized through submission of a protocol/treatment plan under a new EIND. This scenario (emergency access requested and allowed under an EIND) is addressed in this MAPP.

- This MAPP does not describe the policies and procedures for managing and processing submissions for access to an investigational drug for an individual patient in a nonemergency situation.

BACKGROUND

- FDA's expanded access regulations are found in 21 CFR 312, subpart I (Expanded Access to Investigational Drugs for Treatment Use).[4] "This subpart contains the requirements for the use of investigational new drugs and approved drugs where availability is limited by a risk evaluation and mitigation strategy (REMS) when the primary purpose is to diagnose, monitor, or treat a patient's disease or condition. The aim of this subpart is to facilitate the availability of such drugs to patients with serious diseases or conditions when there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the patient's disease or condition."[5]

- Subpart I describes the requirements for expanded access to an investigational drug for treatment use (henceforth referred to as access or expanded access), including access for individual patients in emergencies. Whereas 21 CFR 312.305 describes the requirements for all expanded access uses, 21 CFR 312.310 specifically describes the requirements unique to individual patient access, and 21 CFR 312.310(d) describes the procedures for requesting and authorizing access to an investigational drug for use in an individual patient in an emergency.

- As explained in 21 CFR 312.305(c), a patient may obtain access to an investigational drug for treatment use, including in an emergency, through a licensed physician. A licensed physician under whose immediate direction an investigational drug is administered or dispensed for an expanded access use is considered an investigator. An individual or entity that submits an expanded access IND is considered a sponsor. A licensed physician under whose immediate direction an investigational drug is administered or dispensed and who submits an IND for expanded access is a sponsor-investigator and must comply with the regulatory requirements for sponsors and investigators.

- FDA cannot compel a pharmaceutical company to provide access, including emergency access, to its investigational drug for treatment use. When a company provides access to its investigational drug for treatment use, it does so voluntarily.

[4] Refer to 21 CFR 312.300 – 320.
[5] Refer to 21 CFR 312.300(a).

- FDA has issued the following expanded access guidances for industry:[6]

  – *Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers* (November 2022). This draft guidance provides information to industry, researchers, physicians, and patients about the implementation of FDA regulations on expanded access to investigational drugs for treatment use.

  – *Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products* (September 2023). This guidance provides recommendations regarding the key factors and procedures IRBs should consider when reviewing expanded access submissions for individual patient access to investigational drugs.

  – *Individual Patient Expanded Access Applications: Form FDA 3926* (October 2017). This guidance describes a streamlined alternative form for the submission of an IND by a physician for individual patient expanded access.

POLICY

- Because of the inherent urgency of EINDs, CDER reviews requests for EINDs immediately upon receipt. CDER determines if the request meets the regulatory requirements for an EIND. If the EIND meets the requirements, CDER authorizes or denies the request. FDA may authorize the emergency expanded access use to begin without a written submission.[7]

- CDER receives requests for EINDs by telephone, fax, or other means of electronic communication, although the Office of New Drugs (OND) generally does not monitor (and therefore may not respond promptly to) fax transmissions or other electronic communications received after normal working hours. After normal working hours, CDER receives requests for EINDs by telephone or email through either FDA's Emergency Call Center or the CDER Emergency Coordinator (CEC), which are operational 24 hours a day, 7 days a week.

- EINDs are managed by the following CDER offices:

  – Office of Communications (OCOMM), Division of Drug Information (DDI) – only during normal working hours.

[6] For the most recent versions of a guidance, refer to the *Search for FDA Guidance Documents* webpage at https://www.fda.gov/regulatory-information/search-fda-guidance-documents.
[7] Refer to 21 CFR 312.310(d).

  - OND Clinical review divisions and aligned OND Office of Regulatory Operations (ORO), Divisions of Regulatory Operations (DRO) – only during normal working hours.

  - Counterterrorism and Emergency Coordination Staff (CTECS) – only after normal working hours, including weekends and holidays.

- As described under 21 CFR 56.104(c), emergency use of an investigational drug is exempt from the institutional review board (IRB) review requirement if the emergency use is reported to the IRB within five working days of treatment initiation. Subsequent uses of the same investigational drug at the same institution typically require prior IRB review and approval. However, when prior IRB review and approval is not feasible for a subsequent expanded access emergency use of the same investigational drug at the same institution, FDA will not deny the subsequent request for emergency access because of a lack of prospective IRB review. FDA advises the sponsor to report the use to their IRB within five working days of treatment initiation.[8]

- All necessary forms and information must be submitted to FDA within 15 working days of FDA authorization of the EIND.[9] Failure to provide the necessary documentation within 15 working days may result in the EIND being cancelled.

- OND accepts a single copy (instead of the standard three copies) of original EIND submissions or subsequent amendments to EINDs from physicians who submit individual patient expanded access INDs, including EINDs. FDA typically accepts submission of a completed Form FDA 3926 to comply with the IND submission requirements in 21 CFR 312.23, 312.305(b), and 312.310(b).

- If an emergency requires a patient to be treated before a written submission can be made, FDA may authorize the expanded access use to begin without a written submission. The decision to authorize or deny emergency access will be communicated to the licensed physician.

  - Because EINDs are authorized only in emergency situations and some may be authorized after normal working hours (normal working hours are 8:00 AM – 4:30 PM EST, Monday through Friday), there may not be sufficient time for FDA to generate written documentation of the authorization of the EIND.

  - FDA may authorize emergency access prior to receipt of a written submission. However, all information required under FDA's regulations must still be sent to the review staff for authorization. The physician must submit a complete

[8] Draft Guidance for Industry: *Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers* (November 2022).
[9] Refer to 21 CFR 312.310(d)(2)

expanded access submission within 15 working days of EIND authorization, including either:

- Form FDA 3926, available for licensed physicians to use for expanded access requests for individual patient INDs; or
- Form FDA 1571 and the information required by Form FDA 1572.

RESPONSIBILITIES

OCOMM, Division of Drug Information (DDI) staff:

- For EIND requests received during normal working hours, collect preliminary information from the physician (an abbreviated version of the information in Appendix 1). If DDI has authorization from the OND Clinical review division to act on their behalf (when certain conditions established by the OND Clinical review division are met), determine if an EIND request should be authorized and inform the physician. In cases when DDI does not provide authorization, DDI will forward the information from the physician to the ORO staff aligned with the appropriate OND Clinical review division for a determination.
- Inform the physician their request is authorized or forward the request to the appropriate review staff. DDI provides ORO staff the physician's contact information and after-hours contact information for CTECS.
- When DDI provides authorization, DDI sends the OND Clinical review division a summary email with all communication and attachments pertaining to the EIND.
- Follow-up with ORO staff to confirm ORO has contacted the physician.

Counterterrorism and Emergency Coordination Staff (CTECS):

- For EIND requests received during normal working hours, forward the physician's request to DDI, or forward to ORO if covering for DDI temporarily. Inform the physician the request was forwarded to the appropriate CDER staff.
- For EIND requests received after normal working hours, collect preliminary information from the physician, identify the appropriate OND Clinical review division. Relay available information to the appropriate on-call after-hours individual in the OND Clinical review division by telephone and email, using the CDER Emergency Contact List maintained by CTECS.
- If CTECS has permission by the OND Clinical review division to act on its behalf (when certain conditions established by the OND Clinical review division are

met), determine if an EIND request should be authorized or denied, and inform the physician. Send the OND Clinical review division a summary email with all communication and attachments pertaining to the EIND request. Upload a copy of the authorization email sent to the sponsor-investigator to the EIND file in the appropriate CDER Electronic Records Keeping System (ERKS).[10]

OND Clinical Review Division Staff:

- If received by the OND Clinical review division, direct the EIND inquiries to the appropriate individuals in the OND Clinical review division and aligned ORO staff, as determined by the division's policy on the management of EIND requests.

- Assess the need for other review disciplines (e.g., product quality) involvement. Engage other groups in the EIND review, if appropriate.

- Determine if an EIND request is an emergency, requiring patient treatment before a written submission can be made.[11] If yes, determine if the request should be authorized or denied.

OND ORO Staff:

- If received by ORO staff aligned with the OND Clinical review division, direct the EIND inquiries to the appropriate individual in the OND Clinical review division, as determined by the division's policy on the management of EIND requests.

- Facilitate engagement of other review disciplines (e.g., product quality) involvement in the EIND review, if appropriate.

- Ensure and confirm a new IND has been created in the appropriate ERKS for each EIND request. Update the status as appropriate.

- Submit requests for additional information to the physician. Ensure the requests and information received from the physician are appropriately documented in the appropriate ERKS.

[10] Refer to CDER MAPP 7600.11, *CDER Electronic Record Keeping Systems*. For the most recent version of a CDER MAPP, refer to the *CDER Manual of Policies and Procedures* website at https://www.fda.gov/about-fda/center-drug-evaluation-and-research/cder-manual-policies-procedures-mapp.

[11] Refer to 21 CFR 312.305(a) and 312.310(a) for specific criteria.

- Provide any required communication (e.g., *Acknowledge Emergency IND* template) to the physician in a timely manner.[12]

- Ensure all communication and attachments pertaining to the EIND request provided by DDI or CTECS are appropriately archived in the appropriate ERKS.

PROCEDURES

1. *EIND Requests Received During Normal Working Hours*

For EIND requests initiated during normal working hours, FDA's *Expanded Access* webpage (https://www.fda.gov/news-events/public-health-focus/expanded-access) directs physicians to contact the appropriate OND Clinical review division, if known, or the Division of Drug Information (DDI) at DRUGINFO@fda.hhs.gov, if not known. If both are unavailable, physicians are directed to contact the FDA's Emergency Call Center at 866-300-4374, who in turn contacts CTECS.[13]

a. **For EIND requests received by DDI:**

i. Collect the necessary patient and treatment information (see Attachment 1) from the physician or someone requesting access on their behalf (hereafter, physician).

ii. Confirm whether the pharmaceutical company has agreed to provide the investigational drug to the physician.[14] If the physician has not contacted the company, advise them to do so and to contact DDI again after they have agreement from the company to provide the investigational drug.

iii. Determine if the request meets the definition of an emergency.

iv. If the EIND does not meet the definition of an emergency, but it is determined the treatment is appropriate under another type of expanded access IND or under a research IND, DDI informs the physician of the rationale and provides instructions on how to submit the appropriate type of IND.

[12] The applicable templates referenced in this MAPP can be found in the internal *CDER Standard Templates (CST) Library*.
[13] Refer to the *FDA's Expanded Access Contact Information* webpage at https://www.fda.gov/news-events/expanded-access/fdas-expanded-access-contact-information.
[14] Because the existence of and information in an IND are confidential, FDA may not provide or disclose the name of the sponsor of the IND under which an investigational drug is being studied to a third party, such as an EIND sponsor. It is the responsibility of the EIND sponsor to identify the entity developing the investigational drug and to request and obtain that entity's permission to access the investigational drug to treat their patient before contacting FDA to request an EIND.

v. For EIND requests where the OND Clinical review division has provided pre-established criteria by which DDI can authorize the request on the Division's behalf, DDI:

1. Communicates with the physician to verify the EIND request meets all the criteria pre-established by the OND Clinical review division for authorizing the EIND request on their behalf.

2. Informs the physician the EIND is authorized. Direct the physician to the *Information for Physicians* section (https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians) of the FDA's *Expanded Access* webpage (https://www.fda.gov/news-events/public-health-focus/expanded-access) for follow-up submission requirements, and for their responsibilities as a sponsor-investigator of an EIND.

3. Documents all available information in an email to the OND Clinical review division, copying CTECS. For EINDs authorized by DDI on behalf of the OND Clinical review division, the ORO staff uploads a copy of the authorization email sent by DDI to the sponsor-investigator to the EIND file in the appropriate ERKS.

vi. In cases when the pre-established criteria are not met and the EIND request is NOT authorized or for EIND requests where the OND Clinical review division has NOT provided pre-established criteria by which DDI can authorize the request on the division's behalf, DDI:

1. Forwards the information collected to the ORO staff aligned with the appropriate OND Clinical review division, with a request to contact the physician.

2. Provides the physician with contact information for DDI, the ORO staff, and CTECS for follow-up during and after normal working hours.

3. Directs the physician to the *Information for Physicians* section (https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians) of the FDA's *Expanded Access* webpage (https://www.fda.gov/news-events/public-health-focus/expanded-access) for follow-up submission requirements, and for their responsibilities as a potential sponsor-investigator of an EIND.

vii. If the follow-up EIND paperwork is received by DDI, forward the paperwork to the ORO staff aligned with the appropriate OND Clinical review division.

b. **If request is received by CTECS:**

i. Identifies the ORO staff aligned with the appropriate OND Clinical review division and forward the physician's request to ORO. Inform the physician the request is being forwarded to the appropriate OND Clinical review division staff.

ii. Instructs the physician to contact CTECS again if they do not receive a timely response from the OND Clinical review division.

c. **If request is received by an OND Clinical Review Division:**

i. Direct the EIND inquiries to the appropriate individuals in the OND Clinical review division and aligned ORO staff, as determined by that division's policy on the management of EIND requests.

ii. Assess the need for other review disciplines (e.g., product quality) involvement and engage these other groups in the EIND review, as appropriate.

iii. Assess the EIND request to determine if it is an emergency that requires the patient to be treated before a written submission can be made.

1. If an emergency, determine if the request should be authorized or denied.

2. If authorizing the EIND, inform the ORO staff to contact the physician and communicate the decision and IND number.

3. If denying the EIND, inform the ORO staff to contact the physician and communicate the decision and rationale for the denial.

4. If not an emergency, determine if the access to the investigational drug is appropriate under another type of expanded access IND or under a research IND, and inform the ORO staff so that ORO may communicate the rationale and provide additional submission instructions.

d. **If the request is received by ORO staff:**

i. Collect the necessary patient and treatment information from the physician (see Attachment 1). ORO Staff may also direct the physician to the *Information for Physicians* section (https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians) of the

FDA's *Expanded Access* webpage (https://www.fda.gov/news-events/public-health-focus/expanded-access).

ii. Confirm the pharmaceutical company has agreed to provide the investigational drug to the physician. If confirmation is not obtained, inform the physician that the pharmaceutical company will need to agree to provide the investigational drug, if the company has not already done so.[15] If the physician has not contacted the company, advise them to do so and to contact the ORO staff aligned with the appropriate OND Clinical review division after they have agreement from the company to provide the investigational drug.

iii. Provides the EIND information (collected from the physician) to the appropriate individual in the OND Clinical review division, as determined by that division's policy on the management of EIND requests.

iv. Facilitates engagement of other review disciplines (e.g., product quality) involvement in the EIND review, as appropriate.

v. Obtains the EIND decision from the appropriate OND Clinical review division staff.

1. **If the EIND is authorized:**

a. Create or have a new IND created in the appropriate ERKS for the EIND request with a status of "Active." Ensure it is identified as an EIND.

b. Provide the physician with their IND number and instruct the physician to include this IND number in the designated area on the FDA form that accompanies the EIND written submission.

c. Remind the physician of their obligation to report the emergency use to their IRB within five working days (as per 21 CFR 56.104(c)).

d. Provide instructions to the physician on the location of the EIND paperwork in the *Information for Physicians* section (https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians) of the FDA's *Expanded Access* webpage (https://www.fda.gov/news-events/public-health-focus/expanded-access). Remind the physician the EIND paperwork must be completed and submitted to the OND Clinical

[15] Refer to footnote #14.

review division within 15 working days of FDA authorizing access to the investigational drug.

e. When there is an existing IND to reference, ORO Staff reminds the physician to include the Letter of Authorization (LOA) from the pharmaceutical company that permits them to refer to the company's IND to support their EIND.

f. Within five working days of authorization of the EIND, issue the *Acknowledge Emergency IND* template including the official IND number to the physician. Complete the entry of data in the appropriate ERKS, as needed.

g. If the follow-up EIND paperwork is received by the OND Clinical review division instead of the Central Document Room (CDR), identify the receipt date on the paperwork and deliver it to the CDR.

h. In the event an EIND was authorized, and the physician subsequently notifies FDA that treatment is completed and requests to withdraw the EIND, issue an *Acknowledge Withdrawal* template to the physician. In the appropriate ERKS, confirm the status change of the EIND to "Withdrawn."

i. In the event an EIND was authorized, and the physician subsequently notifies FDA that the drug was never administered, issue a *Cancel Emergency IND* template to the physician. In the appropriate ERKS, confirm the status change of the EIND to "Cancelled."

2. **If the EIND is denied:**

   a. ORO staff creates a new IND in the appropriate ERKS for the EIND request with a status of "Denied."

   b. ORO staff informs the physician of decision and the rationale.

3. If the EIND does not meet the definition of an emergency, but it is determined the treatment is appropriate under another type of expanded access IND or under a research IND:

   a. ORO staff informs the physician of the rationale and provides instructions on how to submit the appropriate type of IND.

2. ***EIND Requests Received After Normal Working Hours***

EIND requests initiated after normal working hours or on Federal Holidays, will be managed by CTECS.[16]

a. **When request is received by CTECS:**

i. Collects the necessary patient and treatment information from the physician (see Attachment 1).

ii. Confirms the pharmaceutical company has agreed to provide the investigational drug to the physician.[17] If the physician has not contacted the company, CTECS advises them to do so, and to contact CTECS after they have agreement from the company to provide the investigational drug.

iii. For EIND requests **where the OND Clinical Review Division has provided pre-established criteria by which CTECS can authorize the request on the Division's behalf**, CTECS:

1. Through communication with the physician, verifies that the EIND request meets all the criteria pre-established by the OND Clinical review division for authorizing the EIND request on their behalf.

2. Emails the physician that the EIND request is being authorized (i.e., sponsor is granted permission for the emergency administration of an investigational drug to one patient for the treatment of a specific disease) on behalf of the OND Clinical Review Division Director (provide specific name) to serve as a placeholder for the IND number. Provide the physician with the contact information for ORO staff or Chief, Project Management Staff (CPMS) aligned with OND Clinical review division and instruct the physician to contact ORO the following business day for additional information.

3. Documents all available information in an email to the OND Clinical review division contact(s), copying the FDA's Office of Emergency Operations. Unless otherwise noted by the OND Clinical review division, this email is sent to the appropriate Division Director, Deputy Director, and aligned ORO staff.

4. Uploads a copy of the authorization email sent to the sponsor-investigator to the EIND file, identified as an "After-Hours EIND," in the appropriate ERKS.

[16] Refer to footnote #3.
[17] Refer to footnote #14.

5. If the follow-up EIND paperwork is received by CTECS instead of the CDR, forwards the paperwork to the appropriate ORO staff.

iv. For EIND requests **where CTECS determines the request does NOT meet the criteria pre-established by the OND Clinical Review Division for authorizing the EIND request on their behalf**, CTECS:

1. Contacts the appropriate on-call after-hours individual in the OND Clinical review division by telephone, using the CDER Emergency Contact List maintained by CTECS. Relays all available information regarding the request.

2. Documents all available information in an email to the OND Clinical review division contact(s), copying the FDA's Office of Emergency Operations. Unless otherwise noted by the OND Clinical review division, this email is sent to the appropriate Division Director, Deputy Director, and aligned ORO staff.

3. Uploads a copy of CTECS's email communication sent to the sponsor-investigator, identified as "After-Hours EIND" to the EIND file in the appropriate ERKS.

v. For EIND requests **where the OND Clinical Review Division has NOT provided pre-established criteria by which CTECS can authorize the request on the Division's behalf**, CTECS:

1. Contacts the appropriate on-call after-hours individual in the OND Clinical review division by telephone, using the CDER Emergency Contact List maintained by CTECS. Relays all available information regarding the request.

2. Documents all available information in an email to the OND Clinical review division contact(s), copying the FDA's Office of Emergency Operations. Unless otherwise noted by the OND Clinical review division, this email should be sent to the appropriate Division Director, Deputy Director, and aligned ORO staff.

3. Uploads a copy of CTECS's email communication sent to the sponsor-investigator, identified as "After-Hours EIND" to the EIND file in the appropriate ERKS.

vi. For EIND requests **where CTECS determines the request does not meet the definition of an emergency**, CTECS:

1. Records the physician's contact information and the investigational drug being sought.

2. Informs the physician that the criteria for emergency single patient expanded access are not met, but that the criteria for non-emergency single patient expanded access may be met.

3. If needed, advises the physician on the process for submitting a request for non-emergency single patient expanded access (such as directing to the FDA's Expanded Access webpage (https://www.fda.gov/news-events/public-health-focus/expanded-access)) and informs the physician that CTECS will forward the request to the appropriate OND Clinical review division for consideration on the next business day.

4. Documents all available information in an email and sends to the aligned ORO staff. ORO will determine on the next business day if the treatment is appropriate under another type of expanded access IND or a research IND and will communicate further with the physician regarding rationale and instructions.

b. **The OND Clinical Review Division on-call after-hours individual, after being notified by CTECS of an EIND request:**

i. Contacts the physician to confirm patient information (see Attachment 1).

ii. Assesses the EIND request to determine if it is an emergency that requires the patient to be treated before a written submission can be made.

iii. If an emergency, determines if the request should be authorized or denied.

1. If authorizing the EIND:

a. Informs (or request CTECS to inform) the physician of the decision.

b. Provides (or request CTECS provide) the physician with their name to serve as a placeholder for the IND number and ORO CPMS name and contact information.

c. Directs (or request CTECS direct) the physician to contact ORO the following business day for additional information.

d. Emails CTECS and FDA's Office of Emergency Operations to confirm that the EIND request was authorized.

2. If denying the EIND:

a. Informs (or request CTECS to inform) the physician of the decision and rationale.

b. Emails CTECS and FDA's Office of Emergency Operations to confirm the EIND request was not authorized.

iv. If not an emergency:

1. Determines if the treatment is appropriate under another type of expanded access IND or under a research IND.

2. Emails the CTECS and FDA's Office of Emergency Operations to confirm that the EIND request is not an emergency and if another IND type is appropriate.

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3. Informs (or requests CTECS to inform) the physician of the determination.

4. Directs (or requests CTECS to direct) the physician to contact ORO or DDI the following business day for additional submission instructions.

c. **ORO staff will, on the following business day, for all EIND requests:**

i. **If EIND is authorized**:

1. Create a new IND in the appropriate ERKS for the EIND request with a status of "Active" and ensure that it is identified as an EIND.

2. Provide the physician with their IND number. Instruct the physician to include this IND number in the designated area on the FDA form that accompanies the EIND written submission.

3. Remind the physician of their obligation to report the emergency use to their IRB within five working days (21 CFR 56.104(c)).

4. Provide instructions to the physician on the location of the EIND paperwork in the *Information for Physicians* section (https://www.fda.gov/news-events/expanded-access/expanded-access-information-physicians) of the FDA's *Expanded Access* webpage (https://www.fda.gov/news-events/public-health-focus/expanded-access). Remind the physician the EIND paperwork is to be completed and submitted to the OND Clinical review division within 15 working days of FDA authorizing access to the investigational drug.

5. When there is an existing IND to reference, remind the physician to include the LOA from the pharmaceutical company to reference the company's IND to support their EIND.

6. Inform CTECS of the IND number so CTECS may file communication in the EIND file.

7. Within five working days of authorization of the EIND, issue the *Acknowledge Emergency IND* template including the assigned IND number, and complete the entry of data in the appropriate ERKS.

8. If the follow-up EIND paperwork is received by the division instead of the CDR, identify the receipt date on the paperwork and deliver it to the CDR.

9. In the event an EIND was authorized, and the physician subsequently notifies FDA that treatment is completed and requests to withdraw the IND, issue an *Acknowledge Withdrawal* template to the physician. ORO staff confirms the status of the EIND is updated to "Withdrawn."

10. In the event an EIND was authorized, and the physician subsequently notifies FDA that the drug was never administered, ORO staff issues a *Cancel Emergency IND* template to the physician and confirms the status of the EIND is updated to "Cancelled."

ii. **If EIND is denied:**

1. ORO staff creates a new IND in the appropriate ERKS for the EIND request with a status of "Deny".

2. ORO staff informs CTECS of the IND number. CTECS files the communication in the EIND file.

iii. **If the EIND did not meet the definition of an emergency, but it has been determined that the treatment is appropriate under another type of expanded access IND or under a research IND:**

1. ORO staff contacts the physician with instructions for submitting the appropriate type of IND.

REFERENCES

- Federal Food, Drug, and Cosmetic (FD&C) Act (as amended).
- 21 CFR 56: *Institutional Review Boards*.
- 21 CFR 312: *Investigational New Drug Application*.

- Guidance for Industry: *Institutional Review Board (IRB) Review of Individual Patient Expanded Access Submissions for Investigational Drugs and Biological Products* (September 2023).
- Draft Guidance for Industry: *Expanded Access to Investigational Drugs for Treatment Use – Questions and Answers* (November 2022).
- Guidance for Industry: *Individual Patient Expanded Access Applications: Form FDA 3926* (October 2017).
- CDER MAPP 7600.11: *CDER Electronic Record Keeping Systems*.

DEFINITIONS

- **Emergency Expanded Access Use** – Expanded Access to an investigational drug for a single patient that is authorized by FDA without a written submission when there is an emergency that requires a patient to be treated before a written submission can be made by the expanded access sponsor.

- **Investigational New Drug** – A new drug or biological drug that is used in a clinical investigation. The term also includes a biological product that is used in vitro for diagnostic purposes. The terms "investigational drug" and "investigational new drug" are deemed to be synonymous.[18]

- **Investigator** – An individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. "Subinvestigator" includes any other individual member of that team.[19]

- **Institutional Review Board (IRB)** – Any board, committee, or other group formally designated by an institution to review, to approve the initiation of, and to conduct periodic review of, biomedical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects. The term has the same meaning as the phrase institutional review committee as used in section 520(g) of the FD&C Act.[20]

- **Letter of Authorization (LOA)** – A letter from the company developing an investigational drug that permits FDA to refer to that company's IND to provide certain necessary information about the investigational medical product (e.g., chemistry, manufacturing, controls) to support the individual patient expanded access IND submitted by the applying physician. The company should include the IND number for its investigational medical product in the letter of authorization.

[18] Refer to 21 CFR 312.3(b).
[19] Refer to footnote #19.
[20] Refer to 21 CFR 56.102(g).

- **Serious Disease or Condition** – 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.[21]

- **Sponsor** – A person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.[22]

- **Sponsor-Investigator** – An individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.[23]

EFFECTIVE DATE

- This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
08/15/2017	Initial	N/A.
09/05/2018	n/a	Recertified, via S. Lowke signature.
1/13/2024	R.1	Updated to align with current OND organizational structure, applicable user fee act (UFA) commitments, and contemporary CDER workflow policies, procedures and best practices.

[21] Refer to 21 CFR 312.300(b).
[22] Refer to footnote #18.
[23] Refer to footnote #19.

ATTACHMENT 1: Patient and Treatment Information to be Collected for an EIND

1. The physician's name, work address, email address, and office, cellular, and fax numbers, and a brief summary of qualifications.

2. When the requestor is a person other than the physician, the requestor's name, work address, email address, and office, cellular and fax numbers, and a brief summary of their qualifications and relationship to the physician.

3. The patient's initials, age, sex, weight, allergies, and diagnosis.

4. The indication for which the investigational drug is being requested and when treatment is intended to begin.

5. A brief patient medical history (e.g., a history of the patient's illness, including stage and prior therapy, response to prior therapy, concomitant conditions, medications (including previous medications), and any laboratory results that may affect dosing.

6. The rationale for the request for treatment with the investigational drug (as opposed to treatment with available therapy) and request for emergency access (as opposed to enrollment in a clinical study or other type of expanded access).

7. Whether the Institutional Review Board (IRB) has been contacted, or if the IRB will be contacted prior to treatment with the investigational drug.

8. The name, dosage form, and manufacturer of the investigational drug being requested.

9. Indication that the manufacturer or sponsor of the investigational drug has agreed to provide the investigational drug to the physician (e.g., letter of authorization or other indication of verbal or written authorization).

10. The intended dose, dosing regimen, duration of treatment, and route of administration for the investigational drug. List of other concomitant medication intended to be used with the requested investigational drug for the same indication.

11. The clinical plan for following patient outcomes (e.g., monitoring procedures, plan for modification to treatment plan in event of toxicity).