The Expanded Access Pathway

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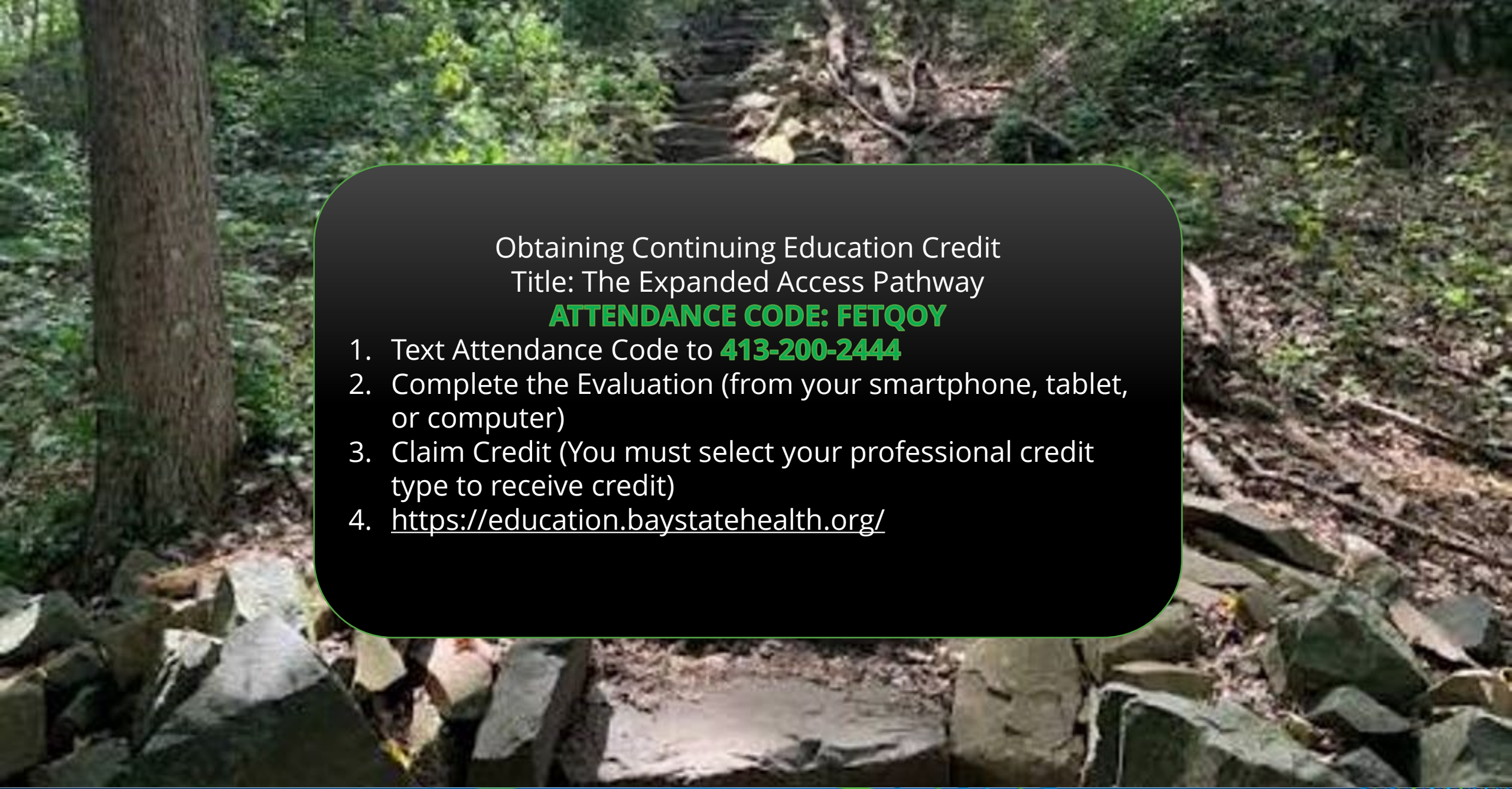
Baystate Health

Disclosure

I have no actual or potential conflict of interest in relation to this presentation.

Baystate Health



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Objectives

- Describe expanded access pathway categories for drugs and biologics as well as devices
- Define immediately life-threatening disease or condition
- Differentiate between expanded access and compassionate use
- Describe the process of initiating a request for expanded access to a drug or biologic/device.



What is Expanded Access?

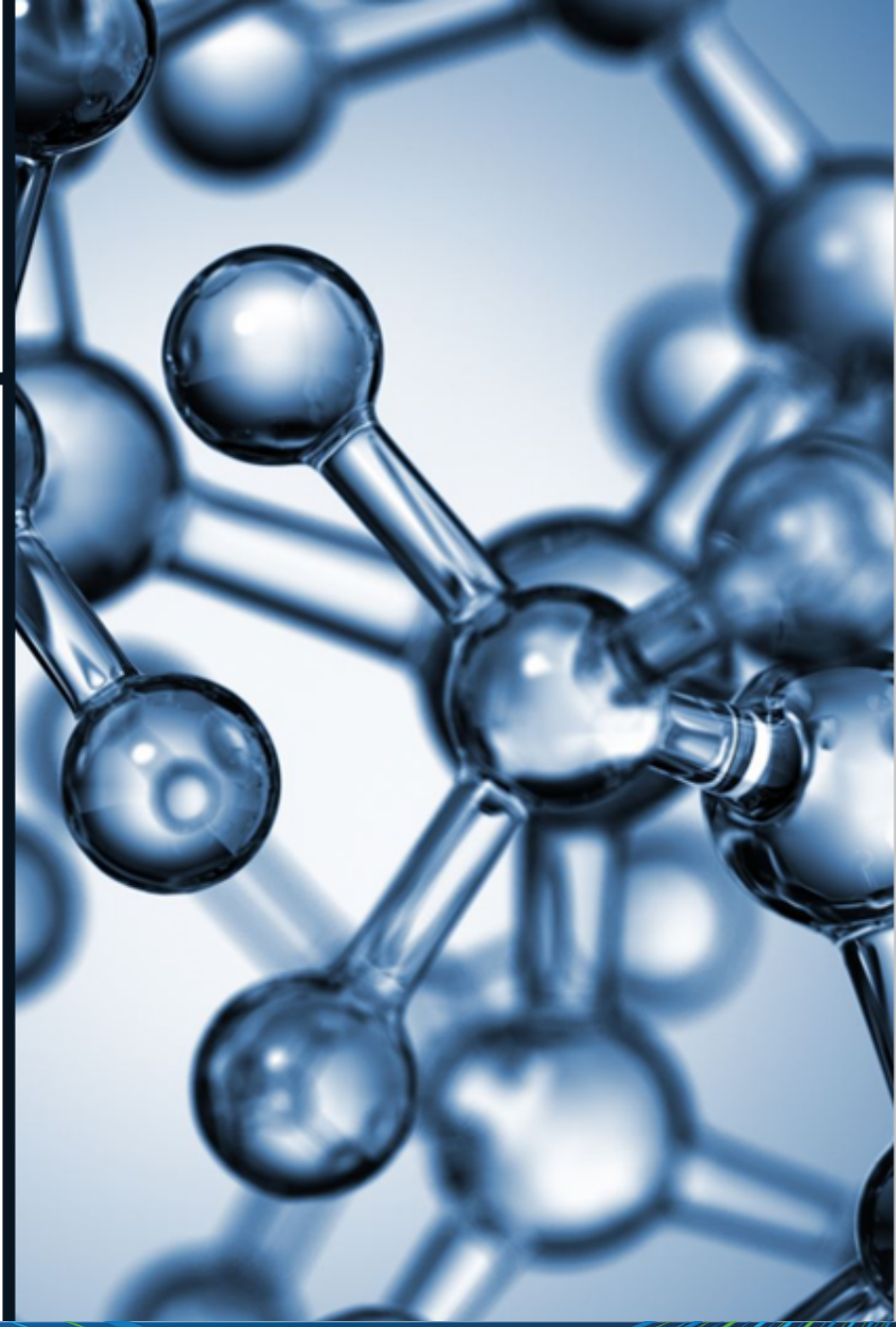
Expanded Access is a process (or pathway) regulated by the Food and Drug Administration (FDA) that allows manufacturers to provide investigational new drugs to patients with immediately life-threatening or serious disease or condition who have exhausted approved therapy and cannot participate in a clinical trial.



How are Serious or Immediately Life-threatening Disease or Condition Defined?

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. (21 CFR 312.300)

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 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 CFR 312.300)



Expanded Access Pathways & Shared Common Requirements

Common Requirements:

1. Patients have a serious or immediately life-threatening disease or condition
2. No comparable or satisfactory alternative therapy
3. Potential benefit justifies the potential risks of the treatment, and those risks are not unreasonable in the context of the disease or condition being treated.
4. Providing drug will not interfere with or compromise development for the expanded access use



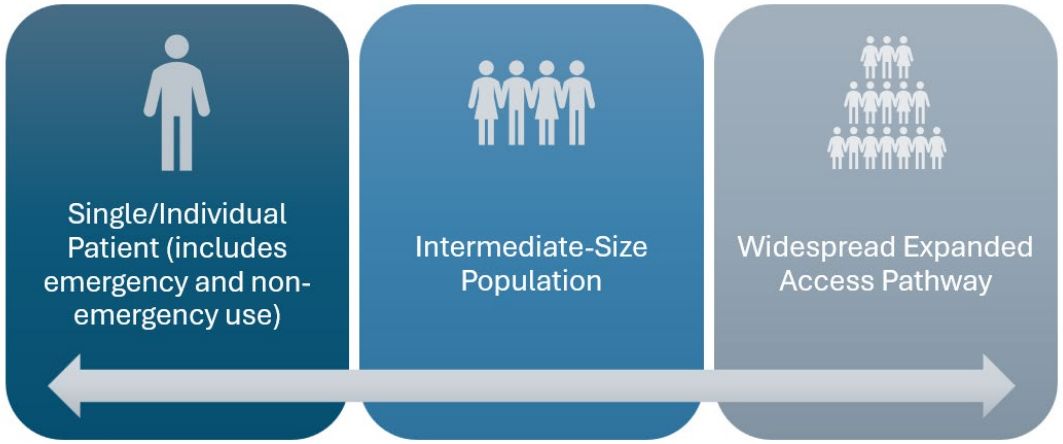
What are Examples of Expanded Access?

- A patient with a genetic mutation that has no treatment
- Compassionate use of a specific device to treat a vascular abnormality.
- Compassionate use of a specific device when all other options have failed in the treatment of a knee replacement.
- The use of convalescent plasma during COVID

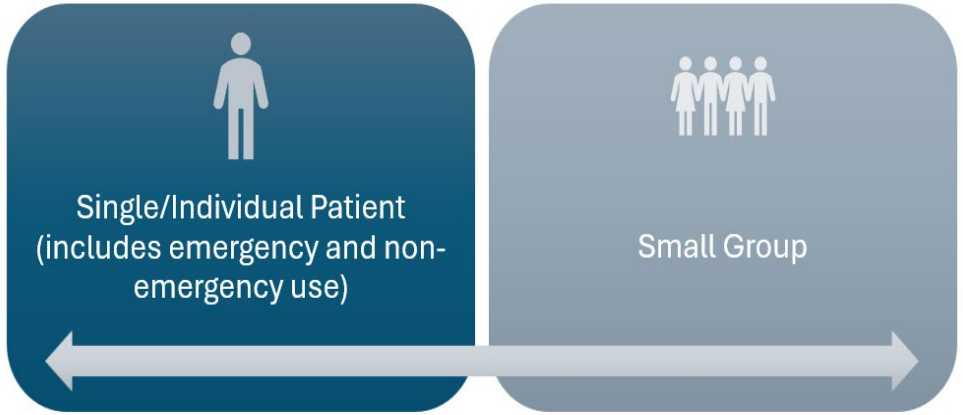


What are the Categories of Expanded Access?

Drugs and Biologics



Devices



Is there a difference?
Expanded Access vs. Compassionate Use



Expanded Access is a general pathway to use an unapproved medical product



Compassionate Use is a specific pathway for us of an unapproved medical device

Common Terminology Associated with Expanded Access Pathways

Sponsor-Investigator – A licensed physician under whose immediate direction an investigational drug is administered or dispensed, and who submits an IND for expanded access use.

Letter of Authorization (LOA) – a letter requested from the pharmaceutical company that makes the investigational drug you wish to obtain. A LOA grants the right of reference to the information contained in the supplier's existing Investigational New Drug (IND) application.

Letter of Agreement – is a type of business document that explains and sets out the terms of a working agreement between two or more parties. This may be an agreement between the institution and a pharmaceutical company.

FDA Form 3926 – a fillable PDF document designed to streamline the individual emergency and non-emergency use of an investigational drug.

IRB Chair Concurrence – A physician submitting an individual expanded access IND using Form 3926 may choose to request authorization to obtain concurrence by the IRB chairperson or by a designated IRB member before the treatment use begins.

Expanded Access Pathway Drugs and Biologics



Single/Individual Patient

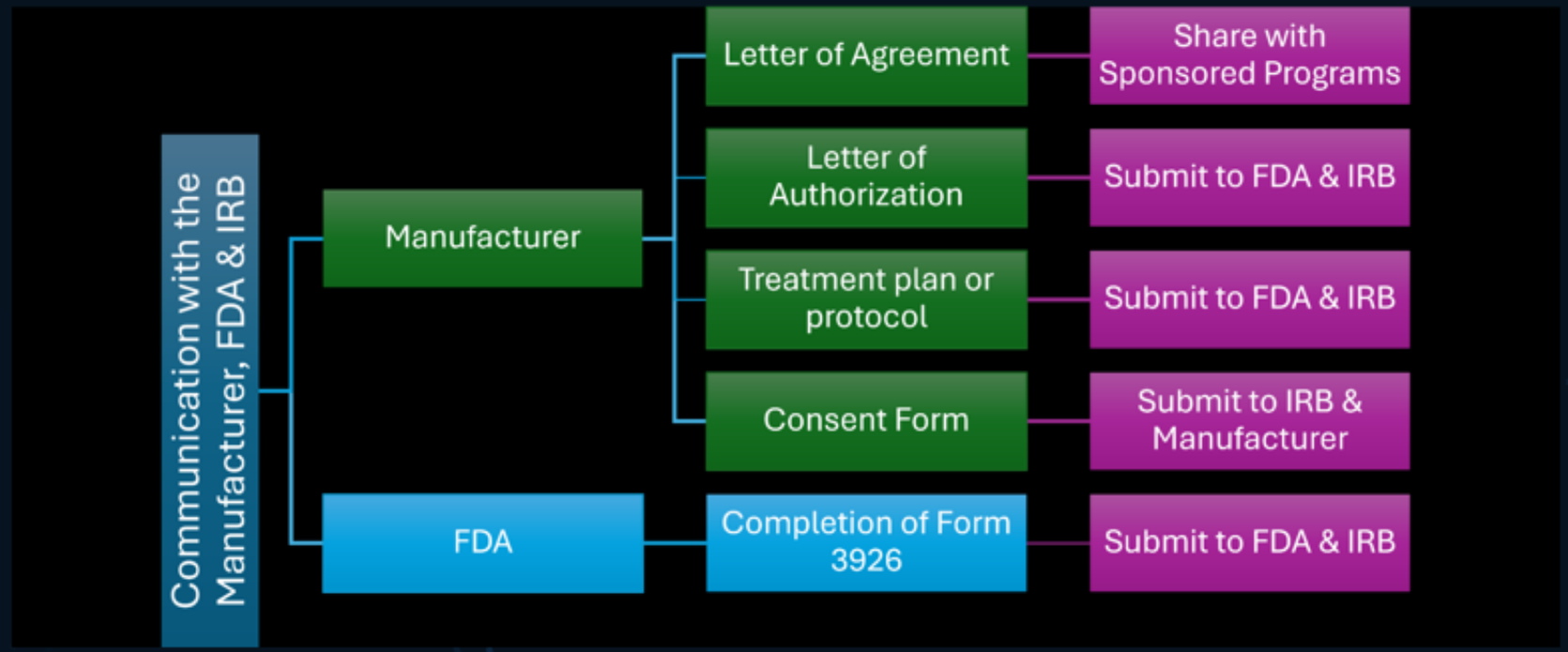
Intermediate-Size Population

Widespread Use

Individual Patient: Emergency and Non-emergency Requests

For Physicians: How to Request Single Patient Expanded Access ("Compassionate Use")

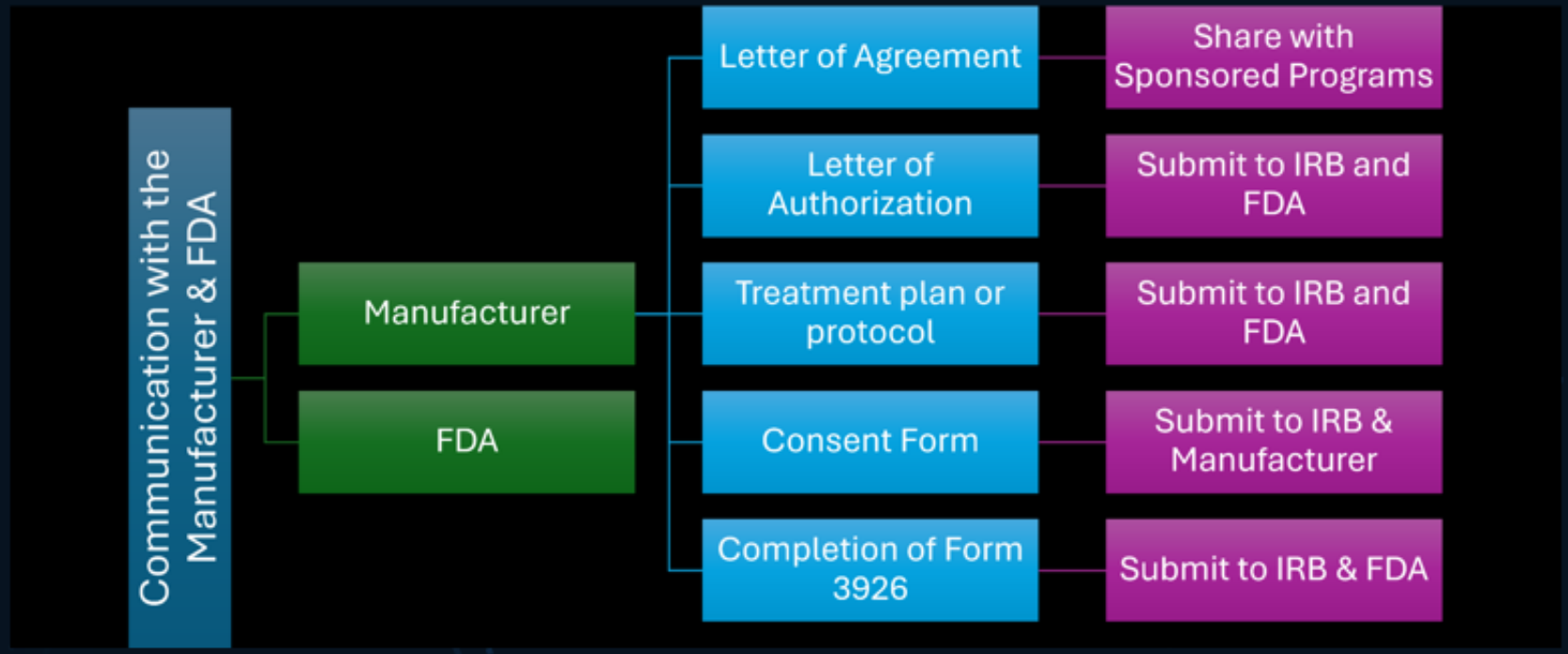
IND Type	FDA Request Process	FDA Processes	IRB Submission	Follow up FDA Reporting
Individual Patient Expanded Access (Non-Emergency)				
New IND New Protocol	Permission for use of IP from Manufacturer	**30-day waiting period** before treatment with the drug may begin unless the FDA notifies the sponsor that the treatment may begin sooner	Approval by IRB prior to IP administration	Yes
Existing IND	Permission for use of IP from FDA	**No 30-day waiting period** before treatment with the IP may begin but the protocol must be received by the FDA and have approval by an IRB.	Approval by IRB prior to IP administration	Yes
Individual Patient Expanded Access (Emergency)				
New IND New Protocol **OR** Emergency Protocol (existing IND by the Sponsor of the existing IND)	FDA Authorization via telephone contact	Immediate Use of IP following phone authorization by FDA.	Yes, within 5 working days of IP administration	Report to the FDA within 15 business days of telephone authorization



What is Next?

Individual Patient Non-Emergency

- If the sponsor holds the IND and possesses a treatment protocol, they will possibly share a protocol, investigator brochure and consent templates.
- If the treating physician holds the IND, they are considered the Sponsor/Investigator and are responsible for the development of the treatment plan that is described in Form 3926.
- IRB and FDA approval to move forward



What is Next?

Individual Patient Emergency

- Telephone permission from the FDA
- Completion of Form 3926 submitted to **FDA within 15 business days.**
- Submission to IRB **within 5 working days of IP administration**

What is Form 3926 (Drugs and Biologics)? Individual Patient

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FDA Guidance: Individual Patient Expanded Access Applications: Form 3926

How to Complete Form FDA 3926 for Initial Submissions

FDA: Expanded Access - Information for Physicians

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Individual Patient Expanded Access Investigational New Drug Application (IND)

(Title 21, Code of Federal Regulations (CFR) Part 312)

Form Approved: OMB No. 0910-0814
Expiration Date: October 31, 2026
See PRA Statement on last page.

1. Physician Name, Name of Institution or Clinical Practice, Address, and Contact Information

Physician Name *(Sponsor)*

Email Address of Physician

Name of Institution or Clinical Practice

Address 1 *(Street address, No P.O. boxes)*

10.a. Request for Authorization to Use Form FDA 3926

☑ I request authorization to submit this Form FDA 3926 to comply with FDA's requirements for an individual patient expanded access IND.

10.b. Request for Authorization to Use Alternative IRB Review Procedures

☑ I request authorization to obtain concurrence by the Institutional Review Board (IRB) chairperson or by a designated IRB member, before the treatment use begins, in order to comply with FDA's requirements for IRB review and approval. This concurrence would be in lieu of review and approval at a convened IRB meeting at which a majority of the members are present.

NOTE: Checking box 4a or 4b will "turn on" ONLY the fields that must be completed.

4.a. Initial Submission

☐ Select this box if this form is an initial submission for an individual patient expanded access IND, enter the Physician's IND Number, if previously issued by FDA, and complete only fields 5 through 8, and fields 10 and 11.

4.b. Follow-Up Submission

☐ Select this box if this form accompanies a follow-up submission to an existing individual patient expanded access IND, and complete the items to the right in this section, and fields 9 through 11.

Physician's IND Number *(if known)*

5. Clinical Information

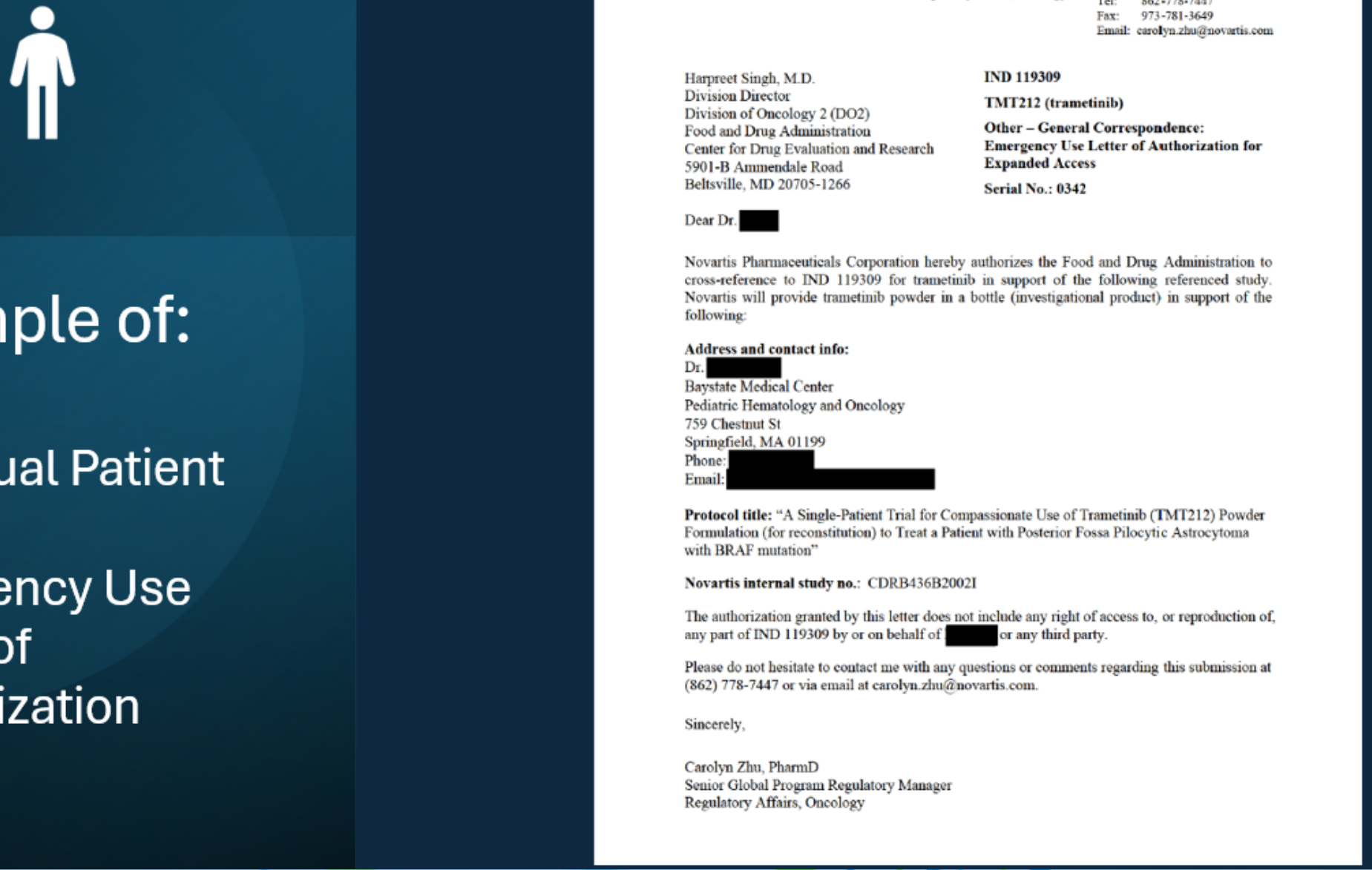
Indication

Brief Clinical History *(Patient's age, sex, weight, allergies or sensitivities, race and ethnicity (optional), diagnosis, prior therapy, response to prior therapy, reason for request, including an explanation of why the patient lacks other therapeutic options)*

Example of:

Individual Patient

Emergency Use Letter of Authorization



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Beltsville, MD 20705-1266

IND 119309

TMT212 (trametinib)

Other – General Correspondence:
Emergency Use Letter of Authorization for Expanded Access

Serial No.: 0342

Dear Dr. [redacted]

Novartis Pharmaceuticals Corporation hereby authorizes the Food and Drug Administration to cross-reference to IND 119309 for trametinib in support of the following referenced study. Novartis will provide trametinib powder in a bottle (investigational product) in support of the following:

Address and contact info:
Dr. [redacted]
Baystate Medical Center
Pediatric Hematology and Oncology
759 Chestnut St
Springfield, MA 01199
Phone: [redacted]
Email: [redacted]

Protocol title: "A Single-Patient Trial for Compassionate Use of Trametinib (TMT212) Powder Formulation (for reconstitution) to Treat a Patient with Posterior Fossa Pilocytic Astrocytoma with BRAF mutation"

Novartis internal study no.: CDRB436B2002I

The authorization granted by this letter does not include any right of access to, or reproduction of, any part of IND 119309 by or on behalf of [redacted] or any third party.

Please do not hesitate to contact me with any questions or comments regarding this submission at (862) 778-7447 or via email at carolyn.zhu@novartis.com.

Sincerely,

Carolyn Zhu, PharmD
Senior Global Program Regulatory Manager
Regulatory Affairs, Oncology

What is the Process When Considering the Intermediate-Size Population Pathway?



1 *Treatment IND*

New IND submitted to the FDA by the Sponsor or Sponsor-Investigator

- IP is not administered until FDA approval **or** after 30 day waiting period without response from FDA
- Full Board IRB Submission and Review
- Informed Consent Required

2 *Treatment Protocol*

Addendum protocol submitted to an existing IND by the IND Sponsor.

- 30 day waiting period is not required.
- IRB submission to Internal or External IRB requiring Expedited or Full Board Review
- Informed Consent Required

Example of:

Intermediate-size Population

Treatment IND/Protocol

NCT05911399

Expanded Access Program for **Tiratricol** in Patients With Monocarboxylate Transporter 8 Deficiency

Conditions

Allan-Herndon-Dudley Syndrome | Monocarboxylate Transporter 8 Deficiency

Massachusetts Locations

Springfield, Massachusetts, United States, 01199
Available
Baystate Medical Center
Contact : Bracha Goldsweig, MD



Expanded Access Pathway
Use of a Device

Emergency

Single/Individual Patient

Small Group

What is the Process When Considering This Pathway?

Compassionate Use of a Device

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



Criteria for Compassionate Use of a Device

- 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
- Potential patient benefit justifies the potential risks of the investigational device.



Investigational Device Exemptions (IDEs)
Existing IDE

The IDE 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 compassionate use under section §812.35(a) to treat the patient.

IDE Supplement to FDA should include:

- 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;
- An identification of any deviations in the approved clinical protocol that may be needed to treat the patient;
- The patient protection measures that will be followed:
  - A draft of the informed consent document that will be used;
  - Clearance from the institution as specified by their policies;
  - Concurrence of the IRB chairperson;
  - An independent assessment from an uninvolved physician; and
  - Authorization from the device manufacturer on the use of the device.

Example of:

Individual Patient Compassionate Use of a Device

March 5, 2017
RE: [redacted]
Page 3

CASE PLAN

[redacted] is an ideal candidate for a silver-impregnated, Modular MUTARS arthrodesis implant. This device has been shown in recent literature in the *Journal of Arthroplasty* to be a largely successful option for patients with chronic, recurrent infections and massive bone loss. I believe for [redacted] this is the ideal device for the following reasons:

1. She has an extraordinarily high risk of recurrent infection given her ongoing urogenital abnormalities and kidney stones and recurrent urinarty tract infections and chronic infections. The silver-impregnated device has a lower risk of recurrent infection.

2. The patient has very challenging anatomy given some bowing of her tibia as well as previous hip fracture with fairly significant osteopenia. The Modularity of this device and the potential for cementing her stems is unique and would allow a combination of her unique anatomical abnormalities.

3. This device does not require bony opposition as is the usual case for a knee fusion and this lack of need for bony opposition given her massive distal femoral bone loss makes this particular implant the ideal device.



Resources

- Reagan-Udall Foundation –The Expanded Access Navigator represents a unique partnership between the Reagan-Udall Foundation for the FDA, Patient advocacy organizations, the pharmaceutical industry, and the federal government to provide clear information on individual patient expanded access.
- clinicaltrials.gov







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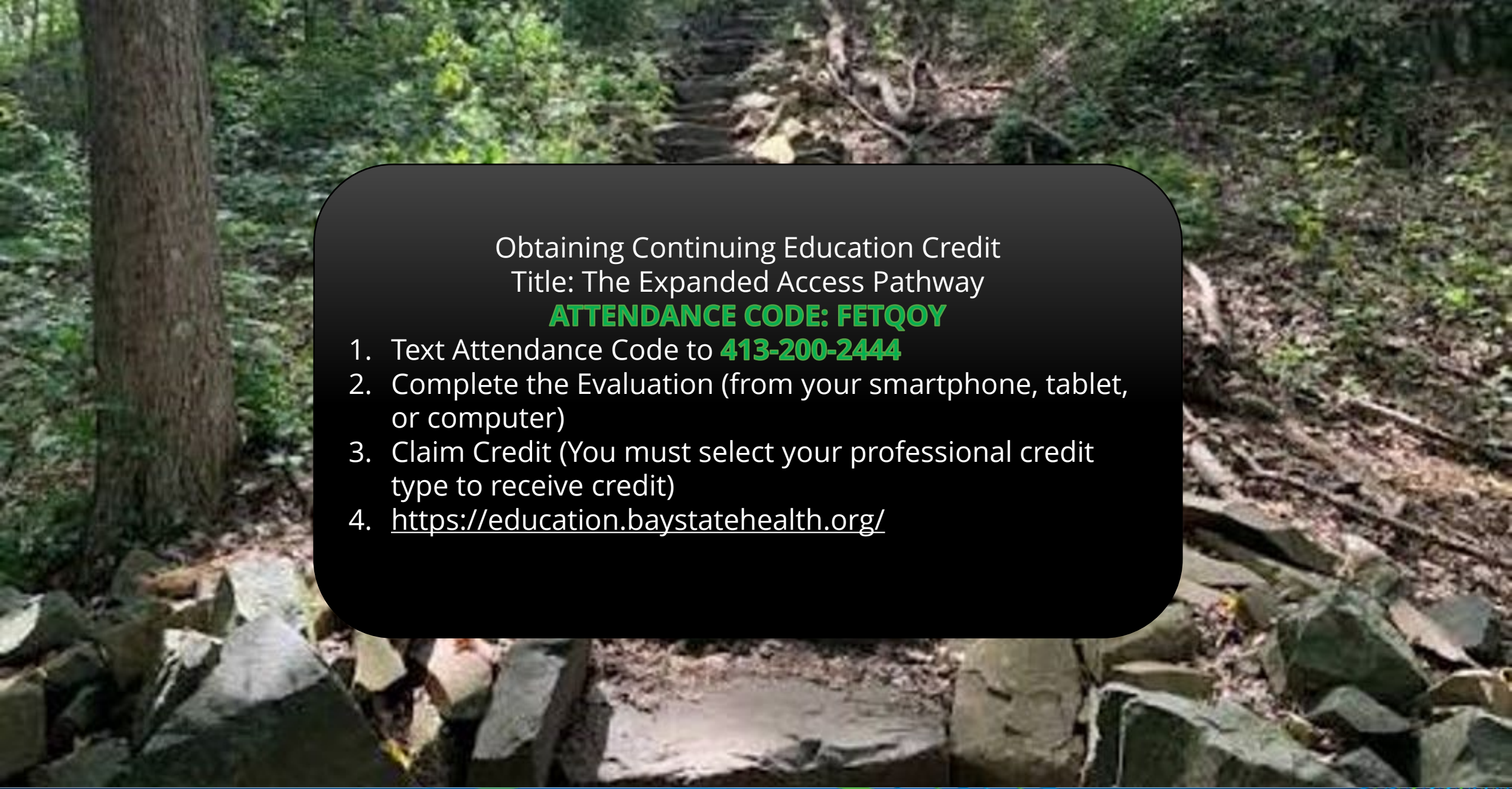

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