Single Patient and Emergency Use Investigational New Drug (IND)/ Investigational Device Exemption (IDE) Process Guidance

This guidance is intended to document the internally agreed upon process between VCU and VCU Health (VCUH) related to how single patient (s) and emergency use (e) IND/IDEs will be managed and how the responsibility will be divided. sIND/IDEs and eIND/IDEs can also be referred to as compassionate use protocol. This differs from an expanded access protocol that is intended to allow for multiple patients to enroll versus just one patient.

sIND/IDEs or eIND/IDEs are a potential pathway/regulatory mechanism by which an investigational drug, biologic or device can be made available outside of a clinical trial to treat a patient with serious or life-threatening conditions for which there are no satisfactory treatment options. This may be appropriate when all the following apply:

- Patient has a serious disease/condition, or life is immediately threatened by their disease or condition
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the condition
- Patient enrollment in a clinical trial is not possible
- Potential patient benefit justifies the potential risks of treatment
- Providing the product will not interfere with investigational trials that could support development or marketing approval for the treatment indication
- Specific to eIDEs: Independent assessment from an uninvolved physician of need for eIDE

Emergency use IND/IDEs are utilized when it isn't practical or possible to obtain IRB approval prior to administering the product to the patient. OVPRI's FDA program should be consulted, when possible, prior to using an investigational device as an emergency use as there are additional requirements for devices.

Once a treating physician has identified a patient in need of an FDA-unapproved product and there is no commercially available alternative nor is there any available clinical trial (including an expanded access protocol we can be added to as a site), the treating physician must reach out to the company of the desired product for approval to use the product in a single patient or emergency use IND/IDE. OVPRI can provide assistance in determining whether this can be done as a single patient IND/IDE versus an emergency use IND/IDE. The treating physician will obtain approval from the company, a letter of authorization for the use of the FDA-unapproved product in an FDA submission, and a contract (if required by the company). Please provide a copy of all documents from the company to the Office of Vice President for Research and Innovation (OVPRI)'s FDA program to facilitate the IRB and FDA submissions; they may be included in the email to the company to facilitate document exchange. The contract should then be provided directly to the Division of Sponsored Programs (DSP) at ospred@vcu.edu via submission in RAMS-SPOT by SOM-CT or Massey CTO staff.

If an eIND/IDE is needed, the treating physician will need to call the FDA (numbers provided below in appendix 2) for authorization after the company agrees to provide the product. The treating physician CANNOT delegate this task to a resident, fellow, nurse or other staff because the FDA will put the IND/IDE in the name of the individual who calls for authorization and the treating physician is the one who will be ultimately responsible; nurses, residents and fellows may rotate off service or off the patient's care.

For both sIND/IDE and eIDE/INDs, FDA regulations require that the patient or legally authorized representative (LAR) consents to treatment using an informed consent. OVPRI's FDA program is able to quickly produce a consent form when provided with the necessary information which is

why it is important to include them in this process as early as possible. Regulations do allow informed consent to be waived if both the treating doctor and an uninvolved doctor certify all of the following in writing:

- The patient is confronted by a life-threatening situation necessitating use of the product
- Informed consent can't be obtained because of an inability to communicate with or obtain legally effective consent from the patient
- Time is not sufficient to obtain consent from the patient's LAR
- No alternative method of approved or generally recognized therapy is available to provide an equal or greater likelihood of saving the patient's life

If in the treating doctor's opinion, there isn't sufficient time to obtain an independent physician's determination that the above criteria are met, the treating doctor should make the determination and subsequently obtain (within 5 working days) a review of their determination by an independent physician. Documentation of this process is required to be submitted to the IRB within 5 working days.

OVPRI's FDA program should be notified as early as possible with the latest possible notification after the company provides approval (and after the FDA approval for emergency use IND/IDEs) at indide@vcu.edu. OVPRI will draft the initial FDA and IRB submissions. Once drafted, OVPRI will obtain signatures from the treating physician and then proceed with submitting to the FDA and IRB. OVPRI will manage all subsequent FDA and IRB submissions. OVPRI will proactively reach out to the treating physician and the assigned staff prior to the continuing review and annual report being due to get patient updates needed for the submissions. The treating physician and/or assisting staff should notify OVPRI immediately if the patient discontinues treatment, has an adverse event (AE) or if a protocol deviation occurs. This will enable OVPRI to timely complete FDA and IRB submissions as applicable according to regulations, policies and within the required submission timelines. If the patient never initiates treatment after the initial IRB and/or FDA submission is submitted, OVPRI must be notified so they can proceed to withdraw the IND/IDE.

The treating physician and staff (ex: coordinator) will be responsible for ensuring regulatory compliance by maintaining the regulatory binder for this IND/IDE. This may include, but is not limited to:

- Form FDA 1572
- Staff training
- Delegation of authority log

The treating physician and staff (ex: coordinator) will be responsible for maintaining patient level information. This may include, but is not limited to:

- Signed Informed Consent Form
- Drug accountability
- Adverse Event (AE) logs

In the event that a physician has multiple single patient or emergency use IND/IDEs utilizing the same investigational product under the same indication or anticipates having more in the near future, the physician should make every effort to open either the company's expanded access protocol (if one exists) or discuss with the company if they would allow VCU to initiate their own expanded access protocol for the investigational product in an effort to reduce administrative burden. OVPRI is able to help facilitate these conversations with the company.

Any questions or concerns regarding this process should be directed to:

- VCU FDA program: indide@vcu.edu
- VCUHS research: clinical.research@vcuhealth.org

Appendix 1: Responsibility assignment matrix

	Treating Physician (Sponsor-investigator)	OVPRI	Staff (ex: Coordinator, research nurse)	OnCore team	SOM-CT/ Massey CTO
Confirm no other options available for patient	X				
Contact company to obtain approval for research use of drug (Letter of Authorization LOA)*	X	X	X*		
Contact FDA by phone for authorization (**emergency use only**)	X (CAN ONLY BE ATTENDING)				
Contract submission to DSP (if applicable)					X
Register study in OnCore				X	
IRB submissions (initial and subsequent)		X			
FDA submissions (initial and subsequent)		X			
Other regulatory or patient obligations (ex: staff training log, delegation of authority log, documenting informed consent, etc.)	X		X		
Notification to OVPRI for any treatment related SAEs, discontinuation of treatment, never initiating treatment after this process has started or protocol deviations (to trigger appropriate FDA/IRB submissions)	X		X		
Provide Care to patient	X				
Maintain Patient Documents	X		X		
Monitoring of IND/IDE		X			

*Every effort of the treating physician should be made to contact the company

Appendix 2: Important Contacts

Food and Drug Administration (FDA)
Exception from informed consent requirements for emergency research (FDA 21 CFR 50.24)
https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50/subpart-B/section-50.24

Drugs using CDER:
Division of Drug Information, Center for Drug Evaluation and Research
8:00 AM – 4:30 PM, Monday through Friday
301-796-3400 or 888-463-6332
druginfo@fda.hhs.gov

Biologics using CBER:
Office of Communication, Outreach, and Development, Center for Biologic Evaluation and Research
8:00 AM – 4:30 PM, Monday through Friday
240-402-8020 or 800-835-4709
Industry.biologics@fda.hhs.gov

Devices using CDRH:
Division of Industry and Consumer Education, Center for Devices and Radiological Health
8:00 AM – 4:30 PM, Monday through Friday
CDRHExpandedAccess@fda.hhs.gov or DICE@fda.hhs.gov

Drugs, biologics and devices after normal working hours and on weekends
Office of Crisis Management & Emergency Operations Center
866-300-4374 or 301-796-8240

Center for Disease Control (CDC)
CDC Emergency Operations Center
770-488-7100

VCU/VCUHS Contacts

VCU Health Investigational Drug Service (IDS)
Phone: (804) 828-7901
Fax: (804) 827-0181
Investigational.drug@vcuhealth.org
IDS pharmacist on-call for urgent issues
Emergency ONLY Pager: (804) 628-9000
Ask operator to page 9089 (Investigational Pharmacist On-Call)

Office of the Vice President for Research and Innovation (OVPRI)
FDA program: Compassionate, Expanded Access and Emergency Use of Drugs/Devices

- Includes templates needed for sIND/IDEs and eIND/IDEs

Lauren Wallace: kanigherl@vcu.edu
Liz Kissell: kisselle@vcu.edu
Group email: indide@vcu.edu

VCU Health System (VCUHS) Clinical Staff Support
Joan Greer & Mary Harmon
clinical.research@vcuhealth.org

Appendix 3: Letter of Authorization Template (To be used if product manufacturer doesn't have one)

[COMPANY LETTERHEAD PROVIDING COMPANY NAME, ADDRESS, AND TELEPHONE NUMBER]

[DATE]

[FDA ADDRESSEE]

Re: Letter of Authorization to Cross Reference to IND [INSERT DRUG NAME AND IND NUMBER]

Dear [NAME OF ADDRESSEE]:
This letter of authorization (LOA) authorizes [INSERT PHYSICIAN SPONSOR'S NAME] to reference and rely on [INSERT COMPANY'S NAME] IND [INSERT IND NUMBER] in connection with [INSERT PHYSICIAN SPONSOR'S NAME] individual patient expanded access IND [INSERT RELEVANT INFORMATION DESCRIBING PHYSICIAN SPONSOR'S IND].

FDA is authorized to refer to [INSERT COMPANY'S NAME] IND [INSERT IND NUMBER] for the purpose of FDA's review of the IND submitted by [INSERT PHYSICIAN SPONSOR'S NAME] and described above.

As indicated by my signature below, I am authorized to provide this LOA on behalf of [INSERT COMPANY NAME], and my full name, title, address, email address, telephone number, and facsimile number are set out below for verification.

If you have any questions, please contact me at [INSERT TELEPHONE NUMBER].

Sincerely,

[INSERT SIGNATURE OF RESPONSIBLE OFFICIAL]

[INSERT NAME OF RESPONSIBLE OFFICIAL]
[INSERT RESPONSIBLE OFFICIAL'S TITLE]
[INSERT RESPONSIBLE OFFICIAL'S FAX NUMBER]
[INSERT RESPONSIBLE OFFICIAL'S E-MAIL ADDRESS]