1. PURPOSE

The purpose of this document is to discuss considerations for establishing institutional oversight, including review, support, and tracking of expanded access requests at academic medical centers.

2. INSTITUTIONAL OVERSIGHT OF EXPANDED ACCESS

While FDA authorization of expanded access is required by federal law, academic medical centers or institutions may wish to establish separate oversight to ensure compliance with federal regulations. Depending on the goal of instutitional oversight, processes or procedures can be established to:

(1) Review cases to verify FDA criteria have been met;
(2) Track expanded access cases at the institution;
(3) Assist with requests to product manufacturers;
(4) Assist with contractual agreements;
(5) Assist with regulatory applications and obligations;
(6) Assist with receipt, storage, and ordering of the investigational product; and/or
(7) Train physicians on sponsor and investigator responsibilities.

Importantly, hospitals and health systems may have existing policies on the use of unapproved medications within their facilities and these policies should be considered when establishing institutional support of expanded access cases and/or programs.

3. INSTITUTIONAL REVIEW

FDA's Expanded Access Program offers access to investigational medical products for patients with serious or immediately life-threatening conditions when no comparable or satisfactory approved therapies are available. While FDA's authorization of expanded access is required by federal law, institutions may wish to establish separate oversight by implementing a review and/or approval process for the use of investigational medical products at their centers.

Listed below are some considerations that expanded access committees may wish to consider in their review process. The make-up of the committee may vary based on the purpose and goals of the review. Thus, example commitees are provided.

Purpose of review commitee:

- Verify case meets FDA's expanded access criteria
- Ensure adequate resources exist to support the treatment/program
- Confirm clinical capabilities for product administration and monitoring exist
- Assess benefit/risk of investigational product use
- Verify necessary approvals have been granted
- Ensure compliance with regulatory and institutional guidelines, as applicable

Examples of review committees and/or members:

- Independent physician(s) with expertise in therapeutic field
- Individual(s) familiar with expanded access
- Regulatory affairs personnel or office
- Investigational pharmacy staff

- Hospital adminstration
- Institutional Review Board (IRB)
- Clinical research oversight personnel or office

If an institution chooses to implement a review of expanded access cases and/or programs, it is advised that a policy be developed that defines the responsibilities, procedures, and timelines of the expanded access review and that this policy be made available to faculty and staff at the institution.

4. INSTITUTIONAL SUPPORT

4.1 In order to aid expanded access requests in being processed efficiently and consistently, the institution should develop processes for handling expanded access requests and share this information with treating physicians and involved staff.

4.1.1 Start by creating an institutional workflow that defines offices, oversight committees, and key contacts involved in processing expanded access requests.

4.1.1.1 List of offices and oversight committees that may be involved:

- Regulatory affairs personnel to assist with FDA regulatory submissions
- Legal or contracts personnel to assist with confidentiality and expanded access use agreements
- Institutional Review Board (IRB) or other independent ethics committee to ensure protection of the rights, safety, and well-being of human subjects
- Clinical research personnel familiar with IRB applications to assist with IRB submissions
- Investigational Pharmacy or related entitity (e.g., Pharmacy and Therapeutics Committee, Investigational Device Review Committee) to asssit with the receipt, storage, dispensing, and return/disposition of the investigational product

4.1.2 Since the the level of support and/or oversight may differ based on the needs of the institution, it is important to define roles and responsibilities of involved offices and personnel.

4.1.3 To ensure personnel understand their roles and responsibilities and how offices may interact when processing expanded access requests, it is advised that the institution conduct training with the implementation of any expanded access support programs.

5. INSTITUTIONAL TRACKING

To ensure the institution or oversight committee is aware of the use of investigational medical products under expanded access, the institution should develop processes for tracking expanded access requests and associated regulatory applications. Centralized tracking is advised since it offers many advantages, including the ability to:

- Quantify requests and track progress (e.g., approved, ongoing, withdrawn);
- Monitor activities for compliance with federal regulations and oversight committees;
- Determine institutional demands and resources needed for support; and
- Obtain information on patients seeking access outside of a clinical trial

5.1 Requests (and Institutional Workflow)

5.1.1 Institutions may track expanded access requests due to the critical interfaces required, which may need to be considered in line with institutional guidelines. These include:

5.1.1.1 Intractions between physicians and regulatory bodies

- All expanded access requests must be vetted by the FDA, and in most single-patient cases, the physician will be the sponsor for this submission and will be directly responsible for complying with the regulations for investigational drugs or devices.
- Care activities associated with the administration of an investigational product will in many cases require reimbursement by Medicare or Medicaid.

5.1.1.2 Interactions between physicians and product manufacturers.

- Expanded access requires direct interactions between the treating physician and the manufacturer of the investigational product. The provision of product at no cost to the patient is occompanied by contractual terms that may obligate the physician or institution to certain levels of data sharing, financial liability, or access to patients.
- Some manufactures provide funding to offset some costs of the administration of an investigational product.

5.1.1.3 Interactions between clinics and pharmacy/investigational pharmacy

- Like other uses of investigional products, expanded access requires drug or device accountability. As such, it is critical that the institution facilitate interactions between clinical settings and pharmacy to prevent the unauthorized storage and distribution of these products.

5.1.2 It is advised to track the following information for the purposes of this institutional oversight:

- Requesting physicians and specialties
- Products requested
- Number of requests
- Number of patients for whom EA is requested
- Regulatory sponsorship (physician or industry)
- Manufacturer funding if applicable

5.1.3 Institutions can track the work associated with expanded access requests to determine institutional costs associated with supporing requests, as applicable.

5.2 Regulatory Applications

5.2.1 Institutions should track regulatory applications sponsored by physicians or their center, including the FDA regulatory application and the institutional review board (IRB) application.

5.2.2 It is advised to track the following information and use it to remind the sponsor of annual reporting requirements:

- FDA Center, Review Division, and Project Manager's Name
- FDA Application Number
- Effective/Approval Date
- IRB of Record
- IRB Application Number
- IRB Approval Date

5.3 Tracking Platform

5.3.1 The platform used for tracking depends upon information technology infrastructure at the institution. Regardless of the platform, hosting this information on a platform that has the ability to be shared between personel supporting expanded access requests is suggested.

5.3.1.1 Example platforms:

- Spreadsheet prgrams (e.g., Microsoft Excel)
- Web based databases (e.g., REDCap)
- IRB electronic management software
- Clinical research management sofware

5.4 Record Keeping

5.4.1 It is advised that all regulatory applications resulting from expanded access requests be documented according to institutional procedures for FDA regulatory applications.

5.4.2 Regulatory sponsors should track all submissions and communication with the FDA, including but not limited to:

- The original submission and any supplements, reports, or amendments
- Acknowledgement letter
- Safe to proceed/approval notification
- Clinical hold/disapproval notification
- Any requests for information
- All phone calls and emails exchanged with the FDA
- Original signed consent forms should be stored in an appropriate and secure area.

5.4.3 Per federal regulations, a sponsor is required to maintain records and reports on the use of the investigational product for a minimum of 2 years after the expanded access use is completed. Institutional record retention policies that pertain to the protection of human subjects may differ and could be dependent on the product or patient treated. Thus, local policies should be consulted and considered in the development of any record keeping procedures that will be applied to expanded access cases.