Expanded Access to Investigational Drugs for Treatment Use

FDA

U.S. Department of Health and Human Services
Food and Drug Administration

Presentation Outline

- Proposed Rule
- Division of Antiviral Products Experience and Perspective

Proposal

- December 14, 2006, FDA published proposed rule *(press release on 11th)*
  - Expanded Access to Investigational Drugs for Treatment Use

See http://www.fda.gov/cder/regulatory/applications/IND_PR.htm

Background

- Longstanding history of facilitating access to investigational therapies
  - Cardiovascular (metotropol, nifedipine)
  - HIV (pentamadine, AZT)
  - Oncology (group C drugs)

- In 1987 T-IND regs codified approach to large scale access programs

Existing Regulations

- 312.34 - Treatment use of an investigational new drug
- 312.36 - Emergency use of an investigational new drug

Rational and Goals

- Current regulations
  - Do not reflect how we function
  - Do not provide necessary flexibility
  - May promote inequitable access to programs
- New Regulations will
  - Improve access to investigational drugs for patients with serious and life threatening diseases and no satisfactory alternative therapies

Expanded Access to Unapproved Therapies & Diagnostics [FDAMA Sec. 561]

- Provides for access to experimental therapies for individuals and populations
  - A serious or immediately life-threatening disease or condition
  - No satisfactory alternatives
- Standards
  - Evidentiary basis linked to size of population and seriousness of disease
    - Sufficient evidence of safety and effectiveness to support drug use
    - Reasonable basis to conclude the therapy may be effective and would not expose patients to unreasonable and significant risk
  - Access will not interfere with the clinical investigations necessary to support marketing approval

Proposed Rule—Basic Principles

- Goal of expanded access is treatment, as opposed to data development
- Describes 3 different treatment use scenarios based on size of population to be treated to allow for more rigorous requirements with increasing exposure
- In particular, the evidentiary standard necessary to support use will vary with size of population and seriousness of disease

Balancing Competing Interests

Rule must reconcile:

- Facilitating patient access to unapproved therapies
  - Serious or immediately life-threatening disease
  - No satisfactory alternatives
- Minimizing risk to patients
- Potential for access to impede development and marketing of life-saving therapies

Proposed Access Regulation

- 312.300 – General
- 312.305 – Requirements for all expanded access uses
- 312.310 - Individual patient
- 312.315 - Intermediate population
- 312.320 - Treatment IND

§§ 312.300 and 312.305

- Facilitate availability of promising investigational drugs to seriously ill patients with no satisfactory alternatives as early in development as possible
- Potential benefit justifies potential risks
- Access will not interfere with clinical trials
- Safeguards
  - Part 50 (Protection of Human Subjects)
  - Part 56 (IRBs)
  - Part 312 (including Clinical Holds, AR reporting)

Individual Patients

- Physician determines probable risk from drug does not exceed that from disease
- FDA determines potential benefit justifies potential risk and risks are not unreasonable
- FDA determines that the patient cannot obtain access under another type of IND
- Emergency use can be granted
- Additional Safeguards
  - Treatment limited to one course
  - FDA requires report and may require special monitoring
  - FDA may request consolidation of cases into single IND

Intermediate Size Population

- Drug is
  - Not being developed (e.g., disease rare)
  - Being developed (e.g., patients not eligible)
  - Approved or related (e.g., drug withdrawn)
- Sufficient evidence drug is safe at proposed dose/duration to justify size of trial
- Preliminary evidence (clinical or plausible pharmacological) of effect
- Additional Safeguards
  - Require explanation of why drug cannot be developed or why patients cannot be enrolled in clinical trial
  - Annual review to determine whether T-IND would be more appropriate

Treatment IND or Protocol

- Drug is being investigated in clinical trial designed to support marketing, or trials are complete
- Company is actively pursuing marketing approval
- Sufficient evidence of safety and effectiveness
  - For serious disease, would ordinarily consist of data from phase 3 or compelling data from phase 2 clinical trials
  - For immediately life-threatening disease, reasonable basis to conclude that the investigational drug may be effective and would not expose patients to an unreasonable and significant risk
- Additional safeguards
  - 30-day postsubmission wait before initiating trial
  - Monitoring

Stakeholder Interests

- Industry
  - Likely will welcome increased clarity of policies and procedures
  - May have some concerns about increased pressure to make drugs available
- Advocacy groups
  - Are split on whether access is good or bad
  - Believe access should be fair
  - Most recognize common goal of protecting drug development

Overarching Goals

- Protecting the safety of human subjects
- Protecting the interests of society by preserving the integrity of the drug development process
- Facilitating access to investigational therapies for those in need

Division Involvement with EAP Process

- FDA cannot compel a company to provide access to investigational drugs for treatment use
- However, the Division:
  - Encourages EAP during development meetings with sponsors
  - Discusses appropriate timelines for EAPs as to not interfere with drug development process
    - Evidence of safety and efficacy from phase 3 or
    - Compelling phase 2 data may be sufficient to support treatment IND or protocol

Role of EAP data

- Goal is to **provide access** and not answer safety or effectiveness questions about the drug
- Therefore, limited safety data required from Division
  - Death
  - Serious Adverse events
- Limited impact on initial product labeling
  - Uncontrolled data
  - Population with underlying co-morbidities
- Can help further characterize Warning/Precaution statements