Textbox: Definitions of Selected Regulatory Terms

Orphan Drug: A drug intended for use in "a rare disease or condition." [21 C.F.R. 316.3(10).] A "rare disease or condition" is defined in section 526(2) of the Federal Food, Drug, and Cosmetic Act "as any disease or condition which (A) affects less than 200,000 persons in the United States, or (B) affects more than 200,000 in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for such disease or condition will recovered from sales in the United States of such drug."

The Prescription Drug User Fee Act (PDUFA): Law that was enacted in 1992 and renewed in 1997 (PDUFA II), 2002 (PDUFA III), and 2007 (PDUFA IV). It authorizes FDA to collect fees from companies that produce certain human drug and biological products

Fast Track Program: ***As described on FDA's webpage,*** http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm**,** *the fast track programs* of the Food and Drug Administration (FDA) are designed to facilitate the development and expedite the review of new drugs that are intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs (fast track products)**.** The purpose is to get important approved new drugs to the patient earlier. Fast track programs should be distinguished from expanded access programs for investigational drugs such as the treatment investigational new drug (IND) regulations codified as 21 CFR 312.34. Expanded access programs are intended to facilitate access to investigational drugs prior to approval for patients with serious and life-threatening conditions and without therapeutic alternatives.

Standard and Priority Review: Prior to approval, each drug marketed in the United States must go through a detailed FDA review process. In 1992, under the Prescription Drug User Act (PDUFA), FDA agreed to specific goals for improving the drug review time and created a two-tiered system of review times – *Standard Review* and *Priority Review*. *Standard Review* is applied to a drug that offers at most, only minor improvement over existing marketed therapies. The 2002 amendments to PDUFA set a goal that a *Standard Review* of a new drug application be accomplished within a *ten-month* time frame. A *Priority Review* designation is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A *Priority Review* means that the time it takes FDA to review a new drug application is reduced. The goal for completing a Priority Review is *six months*. *See* http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm.

Accelerated Approval (AA): In 1992 FDA instituted the ***Accelerated Approval*** regulation, allowing earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint or a clinical endpoint other than

survival or irreversible morbidity. The studies that demonstrate the effect of the drug on these endpoints must be "adequate and well controlled". Approval of a drug based on such endpoints is given on the condition that post marketing clinical trials verify the anticipated clinical benefit. *See* http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/SpeedingAccesstoImportantNewTherapies/ucm128291.htm.

Adequate and well-controlled clinical studies: 21 CFR 314.126(b) defines adequate and well-controlled clinical studies. See http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=314.126.

Sponsor: Sponsor, as defined in 21 C.F.R. 310.3(j), means the person or agency that assumes responsibility for an investigation of a new drug, including the responsibility for compliance with applicable provisions of the Federal Food, Drug, and Cosmetic Act and regulations. A sponsor may be an individual, partnership, corporation, or government agency and may be a manufacturer, scientific institution, or an investigator regularly and lawfully engaged in the investigation of new drugs.

Applicant: The term "applicant" is not defined in the orphan drug or new drug regulations. However, in some instances, this term is used interchangeably with the term "sponsor." For purposes of this paper, "applicant" means any person who submits an application or abbreviated application or an amendment or supplement to them to obtain FDA approval of a new drug and any person who owns an approved application or abbreviated application.

New Molecular Entity (NME): As described on the FDA's webpage, http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm, an active ingredient that has never before been marketed in the United States in any form.

Efficacy Supplement: "Efficacy supplement," defined in 21 C.F.R. 314.3(b), means a supplement to an approved application proposing to make one or more related changes from among the following changes to product labeling: (1) Add or modify an indication or claim; (2) Revise the dose or dose regimen; (3) Provide for a new route of administration; (4) Make a comparative efficacy claim naming another drug product; (5) Significantly alter the intended patient population; (6) Change the marketing status from prescription to over-the-counter use; (7) Provide for, or provide evidence of effectiveness necessary for, the traditional approval of a product originally approved under subpart H of part 314; or (8) Incorporate other information based on at least one adequate and well-controlled clinical study.