

Fast Track -

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**BY MESSENGER**

Janet Woodcock, MD  
Director, Center for Drug Evaluation and Research  
Food and Drug Administration  
HFD-1  
1451 Rockville Pike  
Rockville, MD 20852-1420

Rebecca A. Devine, PhD  
Associate Director for Policy,  
Center for Biologics Evaluation and Research  
Food and Drug Administration  
HFM-10  
8800 Rockville Pike  
Bethesda, MD 20892-001

**RE: PhRMA Proposal for Guidance on Fast Track Products Under  
Section 112 of the FDA Modernization Act (FDAMA)**

Dear Drs. Woodcock and Devine:

We are writing on behalf of the Pharmaceutical Research and Manufacturers of America (PhRMA) to provide industry input on the fast track provisions of the FDA Modernization Act (Section 112). As you know, Section 112 of FDAMA created a new statutory mechanism for facilitating the development and expediting the approval of drugs and biological products that demonstrate the potential to address unmet medical needs for serious or life-threatening conditions. These statutory provisions codify and expand FDA's existing programs for accelerated approval products in order to facilitate patient access to products that qualify for fast track designation and FDA approval.

Although Section 112 became effective February 19, FDA has until November 21, 1998 to issue regulatory guidance to implement the new provisions. PhRMA is committed to supporting FDA in the implementation of key provisions such as Section 112, and has established a Fast Track Work Group to consider the most workable and effective means of fulfilling Congressional intent regarding fast track. Enclosed for your consideration is a recommended approach for implementing Section 112, in the form of prototype "Guidance for Industry."

98D-0267

*Pharmaceutical Research and Manufacturers of America*

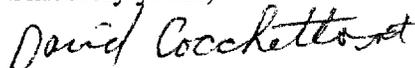
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We believe the proposed guidance fulfills the Congressional intent in enacting Section 112 of facilitating the development and expediting the approval of all drugs and biological products that demonstrate the potential to address unmet medical needs for serious or life-threatening conditions. Products that qualify for a fast track designation and possess efficacy data based on clinical or validated surrogate endpoints sufficient to support conventional approval will receive priority review under the fast track program and be approved according to conventional criteria ("Fast Track A" products). Fast track products with efficacy data based on clinical or surrogate endpoints insufficient to support traditional approval ("Fast Track B" products) will receive priority review and be approved if they satisfy the alternative standard authorized by Section 112(b)(1) (i.e., "reasonably likely to predict clinical benefit"). Only Fast Track B products will be potentially subject to various post-approval requirements, such as post-approval studies, advance submission of promotional materials, and expedited withdrawal.

We hope that you and your staffs, and interested members of the public, find this input useful. The PhRMA Fast Track Work Group is available at your convenience to discuss this proposal and answer any questions. We will be pleased to provide any appropriate assistance to the Agency in furtherance of the timely implementation of this important provision, which promises to provide FDA and pharmaceutical researchers with another useful tool for speeding cures to waiting patients.

Sincerely yours,



David M. Cocchetto, Ph.D.  
Glaxo Wellcome Inc.  
Chair, PhRMA Fast Track Work Group  
919/483-5127



Matthew B. Van Hook  
Deputy General Counsel, PhRMA  
202/835-3513

cc: Jane Axelrad, Associate Director for Policy, CDER

March 31, 1998

**GUIDANCE FOR INDUSTRY**

**THE DESIGNATION AND APPROVAL OF FAST TRACK DRUG AND  
BIOLOGICAL PRODUCTS UNDER SECTION 506 OF THE FEDERAL FOOD,  
DRUG, AND COSMETIC ACT (21 U.S.C. § 356)**

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**GUIDANCE FOR INDUSTRY**

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**I. INTRODUCTION**

Section 112 of the Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105-115, 111 Stat. 2296 (1997), creates a new statutory mechanism for facilitating the development and expediting the approval of drugs and biological products that demonstrate the potential to address unmet medical needs for serious or life-threatening conditions. This new mechanism for so-called “fast track” products codifies and expands FDA’s existing programs for accelerated approval products in order to facilitate patient access to promising new drugs and biological products.

Under the Federal Food, Drug, and Cosmetic Act (FFDCA) and the Public Health Service Act (PHSA) all drugs and biological products must be shown through evidence from adequate and well-controlled clinical studies to be safe and effective in order to obtain FDA marketing approval. Ordinarily, product sponsors establish safety and effectiveness through evidence that treatment produces a beneficial impact on a clinically meaningful endpoint (for example, morbidity or mortality) or on a validated surrogate endpoint (that is, a surrogate endpoint that has been proven to cause or be associated with the desired clinical outcome, such as lowering blood pressure reduces the risk of stroke, or lowering serum cholesterol reduces the risk of coronary artery disease). In contrast, fast track review under

Section 112 of the FDA Modernization Act, codified as section 506 of the FDCA (21 U.S.C. § 356), may be based either on evidence that could support a conventional approval, or on clinical evidence of a product's impact on a clinical or surrogate endpoint that is "reasonably likely" to predict clinical benefit. As Congress explained in enacting the FDA Modernization Act, the latter authority in Section 112 represents "an alternative basis for approving fast track products." H.R. Rep. 105-310, at 55 (1997).

Where a product is approved on the basis of surrogate or clinical endpoints that would be insufficient to support a conventional approval, Section 112 authorizes FDA, in its reasoned discretion, to impose certain conditions on the approval to provide further assurances of the safety and effectiveness of a product once marketed. FDA's determination of whether to impose any post-approval requirements on such products will depend on the nature and strength of the available clinical data for the product.

Sponsors may submit applications under the fast track program for products that qualify for fast track designation (*i.e.*, they have the potential to address unmet medical needs for serious or life-threatening conditions) and have conventional data establishing safety and effectiveness based on clinically significant or validated surrogate endpoints even though such applications could be reviewed and approved under FDA's conventional (*i.e.*, non-fast track) application procedures. If a sponsor of such a product chooses to request a fast track designation and submits an application for approval under the fast program in order to accelerate review and patient access through the expedited procedures of the fast track program, the application can be reviewed and approved according to conventional approval criteria. Fast track products approved under conventional criteria ("Fast Track A Products") will not be subject to any of the post-approval requirements (*i.e.*, commitments to

post-approval studies, pre-submission of promotional materials, and expedited withdrawal of approval) that may apply to fast track products approved on the basis of surrogate or clinical endpoints that are reasonably likely to predict clinical benefit (“Fast Track B Products”).

This Guidance outlines FDA’s current plans for implementing Section 112. The following sections clarify (1) the criteria FDA will apply to determine a product’s eligibility for fast track designation and the process for requesting a fast track designation; (2) the approval of applications for fast track products; (3) the nature and duration of conditions and requirements that FDA might apply to the approval of fast track products based on surrogate or clinical endpoints that reasonably predict clinical benefit (Fast Track B); (4) public reporting of fast track designation; and (5) FDA’s efforts to promote awareness of the new fast track program.

## **II. FAST TRACK DESIGNATION**

### **A. Intended to Treat a Serious or Life-Threatening Condition**

To be eligible for fast track designation, a drug must be intended for the treatment of “a serious or life-threatening condition.” FFDCA § 506(a)(1); 21 U.S.C. § 356(a)(1). FDA has previously provided definition and guidance of its conception of what constitutes a serious or life-threatening illness. The Agency first addressed the definition of serious disease as part of the Treatment IND regulations in 1987. 52 Fed. Reg. 19466 (May 22, 1987). FDA considered as serious diseases or disease stages in which substantial morbidity is present, but in which premature death without early treatment or a high short-term mortality rate is not a consideration. FDA’s examples of serious diseases were Alzheimer’s disease, advanced multiple sclerosis, advanced Parkinson’s disease, transient ischemic attacks (TIAs), progressive ankylosing spondylitis, active advanced lupus erythematosus,

certain forms of epilepsy, nonacidotic or hyperosmolar diabetes, and paroxysmal supraventricular tachycardia.

These concepts were reinforced in 1992 in FDA's discussion in the preamble to its proposed accelerated approval rule:

The seriousness of a disease is a matter of judgment, but generally is 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. Thus, acquired immunodeficiency syndrome (AIDS), all other stages of human immunodeficiency virus (HIV) infection, Alzheimer's dementia, angina pectoris, heart failure, cancer, and many other diseases are clearly serious in their full manifestations. Further, many chronic illnesses that are generally well-managed by available therapy can have serious outcomes. For example, inflammatory bowel disease, asthma, rheumatoid arthritis, diabetes mellitus, systemic lupus erythematosus, depression, psychoses, and many other diseases can be serious for certain populations in some or all of their phases.

57 Fed. Reg. 13235, 13235 (Apr. 15, 1992). Under FDA's regulatory accelerated approval program, products subject to accelerated approval have been indicated to treat a number of diseases and conditions such as HIV infection, various cancers, Mycobacterium avium complex (MAC) infection, cystic fibrosis, multiple sclerosis, symptomatic orthostatic hypotension, AIDS-related wasting and cachexia, and knee cartilage injury. Taken together, the Treatment IND regulations and accelerated approval regulations provide consistent and meaningful guidance on the operational definition of serious disease.

FDA has also provided definition and guidance regarding life-threatening illness. In the Treatment IND regulations, FDA defined an immediately life-threatening disease as "a stage of disease in which there is a reasonable likelihood that death will occur within a matter of months (generally within 6 months) or in which premature death is likely without early treatment." 52 Fed. Reg. at 19467. FDA's examples of immediately life-threatening

diseases were congestive heart failure (New York Heart Association Class IV), advanced AIDS, bacterial endocarditis, metastatic recurrent sustained ventricular tachycardia or ventricular fibrillation, herpes simplex encephalitis, refractory cancer, far advanced emphysema, severe combined immunodeficiency syndrome, bacterial endocarditis, and subarachnoid hemorrhage. The definition and examples in the Treatment IND regulations are instructive, although there is no requirement that fast track products be “immediately” life threatening. Any disease in which there is a reasonable likelihood that premature death will occur unless the course of the disease is altered to reduce that possibility may be considered life threatening.

These definitions and operational examples provide an appropriate basis for use in the fast track designation process. In addition, the flexible case-by-case assessment of each proposal, which FDA has employed in the past, has proven workable and was expressly endorsed by Congress when it enacted Section 112. *See* H.R. Rep. No. 105-310, at 55-56 (1997). Accordingly, FDA will employ the same approach for the fast track program.

**B. Potential to Address Unmet Medical Needs**

Fast track products must also demonstrate the potential to address “unmet medical needs.” FFDCIA § 506(a)(1), 21 U.S.C. § 356(a)(1). Again, it is difficult to formulate a precise definition, and each case will have to be considered on its own merits. Any product that shows the potential to provide some meaningful therapeutic benefit to patients over existing treatments will be considered to possess the potential to address unmet medical needs. For example, a new treatment for patients who are unresponsive to, or intolerant of, available therapy can qualify for fast track designation. Alternatively, a fast track product might demonstrate improved patient response or improved tolerability over available

therapy. Even a therapeutically beneficial change in route of administration (*e.g.*, an orally absorbed version of a previously parenteral product) or a major improvement in impurity profile (*e.g.*, a recombinant protein that may replace a potentially contaminated natural protein) could address an unmet medical need. Products may also meet an unmet medical need in a subpopulation (*e.g.*, pediatric or geriatric patients). Overall, FDA will apply this requirement in a flexible and inclusive manner, consistent with the criteria it has employed for accelerated approval programs. (*See, e.g.*, 57 Fed. Reg. 58942, 58946-47, explaining the concept of “meaningful therapeutic benefit over existing therapy” for accelerated approvals). FDA will expect that the sponsor’s request for a fast track designation will provide a clear and complete summary of each specific basis for the sponsor’s claim that the product has the potential to address unmet medical needs.

### **C. Sponsor Requests**

A sponsor may submit a written request for a product to receive a fast track designation at any point prior to or concurrent with the filing of a marketing application for the product. Requests should be submitted to the appropriate CDER or CBER reviewing division with responsibility for the product.

A sponsor that submits a request for fast track designation of a drug or biological product should submit three copies of a completed, dated, and signed request for designation that contains the following:

- (1) a statement that the sponsor requests fast track designation;
- (2) the name and address of the sponsor; the name of the sponsor’s primary contact person and/or resident agent including title, address, and telephone number;

- (3) the generic and trade name, if any, of the product; and the name and address of the source of the product if it is not manufactured by the sponsor;
- (4) a description of the serious or life-threatening disease or condition for which the product is being or will be investigated, and the proposed indication or indications for use of the product;
- (5) a description of the product and a discussion of the scientific rationale for the use of the product for the serious or life-threatening condition, including all data from nonclinical laboratory studies, clinical investigations, and other relevant data that are available to the sponsor, whether positive, negative, or inconclusive (copies of pertinent unpublished and published papers are also requested) – Note: For products subject to an active IND, the sponsor may incorporate supporting information by reference to specific, previous submissions of technical reports in the IND record; and
- (6) the documentation, with appended authoritative references, to demonstrate that
  - (a) the disease or condition for which the product is intended is serious or life-threatening (documentation is not necessary for diseases that FDA has already identified as obviously serious or life threatening such as those enumerated in Section II.A above, those already the subject of other fast track designations, or those for which accelerated approval has been granted); and
  - (b) the product has the potential to address an unmet medical need.

A sponsor may reference any information previously provided to FDA as part of that sponsor's product application. A sponsor may request a fast track designation for a previously unapproved drug, or for a supplemental application of an already marketed drug.

The reviewing division will determine whether the product qualifies for fast track designation within 60 calendar days after receipt of a request and notify the sponsor in writing. The reviewing division's determination that a drug does not qualify for fast track designation shall constitute final agency action and be subject to judicial review. A sponsor may, at its option, request reconsideration of an adverse determination in accordance with (A) the appeal provisions established for clinical holds on investigational new drugs

provided for in 21 C.F.R. §§ 312.42(f) & 312.48 and MAPP 6030.1, or (B) the dispute resolution procedure set forth in Section V of the PDUFA Reauthorization Performance Goals and Procedures (*See* Cong. Rec., Nov. 13, 1997, at H10888). A sponsor need not pursue such an appeal prior to seeking judicial review.

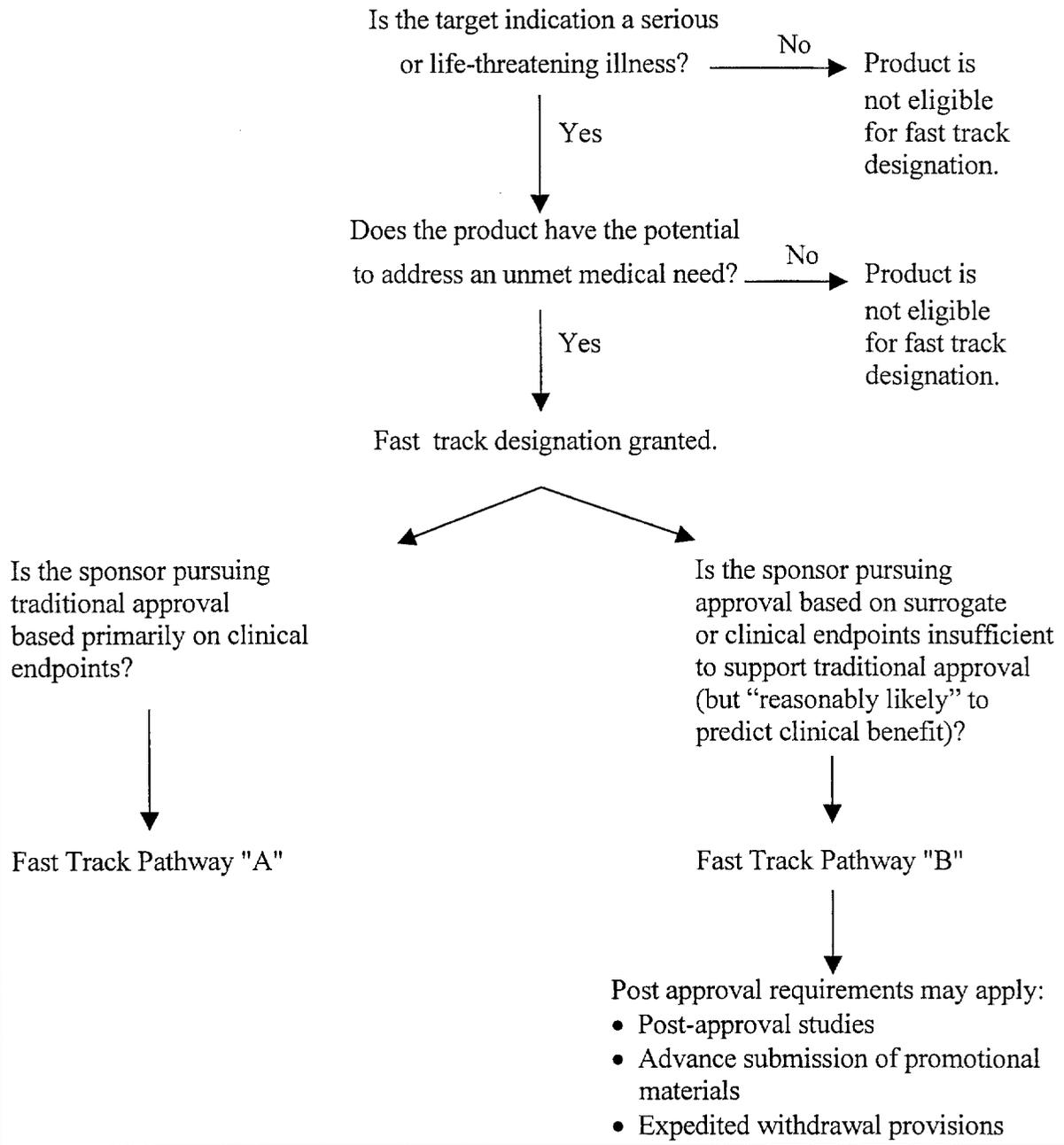
### **III. APPROVAL OF APPLICATIONS FOR FAST TRACK PRODUCTS**

#### **A. Fast Track A Versus Fast Track B --Conventional and Non-Conventional Approvals**

Approval of a fast track product will be based on evidence of the product's effect on either a clinical endpoint or an appropriate surrogate endpoint. Where data on a clinical endpoint are sufficient to establish clinical benefit, and the product sponsor has elected to request fast track designation and utilize the fast track program, review and approval of the product will be based on FDA's traditional approval criteria. If the sponsor seeks approval of a product based on evidence of an effect on a surrogate endpoint or a clinical endpoint that is insufficient to support traditional approval, FDA may approve an application for approval of a fast track product under Section 112(b) of the FDA Modernization Act upon a determination that the effect on the surrogate or clinical endpoint is reasonably likely to predict clinical benefit. FDA may impose post-approval requirements on approvals that are based on surrogate or clinical endpoints that are insufficient to support traditional approval, as discussed further in Section IV below. Conventional approvals of fast track products based on clinically meaningful endpoints are categorized as Fast Track Pathway A, while other approvals are categorized as Fast Track Pathway B, as shown in Illustration 1. Sponsors should clearly indicate in a product application whether they are requesting approval under Fast Track Pathway A or B. Where a sponsor is submitting data on

surrogate endpoints to corroborate data on clinically meaningful endpoints that are sufficient to support traditional approval, it may utilize Pathway A.

**ILLUSTRATION 1 - Schematic Diagram for Fast Track Products**



## **B. Appropriate Surrogate Endpoints**

Various types of evidence can establish that a surrogate endpoint is reasonably likely to produce a desired clinical benefit. As FDA has previously explained, “[a] surrogate endpoint . . . is a laboratory measurement or physical sign that is used in therapeutic trials as a substitute for a clinically meaningful endpoint that is a direct measure of how a patient feels, functions, or survives and that is expected to predict the effect of the therapy.” 57 Fed. Reg. 13234, 13235 (Apr. 15, 1992). Elevated cholesterol and hypertension are validated surrogate endpoints for coronary and cerebral artery disease, although the clinical endpoints associated with the disease remain angina, heart attack and congestive heart failure, stroke and paralysis, and potentially sudden death. Unvalidated surrogate endpoints are suggestive of clinical benefit, but their relationship to clinical benefits such as morbidity and mortality remain less certain. For example, if a drug can be shown to reduce the amount of HIV virus detectable in the blood of AIDS patients, it can be approved on the basis of its short-term effect on this surrogate endpoint, even though the drug’s durable effect on the virus and its ultimate effect on health and survival requires extended studies. Endpoints that FDA has used in its existing accelerated approval program include CD4 cell count, plasma HIV RNA, tumor response rates, low proportion of cisplatin-associated renal damage, indicator lesion response in Kaposi’s sarcoma, and ventricular ejection fraction.

Whether a particular surrogate endpoint is sufficiently likely to predict clinical benefit remains a matter of scientific judgment based on available data, and must be decided on a case-by-case basis in view of the weight of the evidence. Epidemiological, therapeutic, pathophysiologic, or other evidence can provide an appropriate basis to predict clinical benefit from a surrogate endpoint. Some surrogates have been shown not to correspond to

clinical benefit. For example antiarrhythmic agents in the Cardiac Arrhythmia Suppression Trial (CAST) were shown not to improve survival despite reduction in ventricular ectopic beats, and effect on coronary artery patency has not been shown consistently to improve survival in patients with myocardial infarction. In contrast, evidence exists establishing the link between durable complete responses in many cancers and improved survival, as well as between an increase in CD4 cell counts and reduced AIDS-defining illnesses.

By definition, approval based on surrogate endpoints other than those that have been validated will involve some remaining uncertainty regarding a product's clinical benefit. Among the factors FDA will consider in assessing a particular surrogate are (1) whether the surrogate is consistent with what is known about the pathophysiology and pathogenesis of the disease; (2) the prevalence of the surrogate endpoint in people who have the disease; (3) the correlation between the surrogate and disease progression; and (4) the association of the surrogate endpoint with clinical improvement. These criteria and others will not all apply in a given case, and no one consideration will ever likely be determinative. FDA will continue to work (in collaboration with academia, the pharmaceutical industry, and others) to develop greater information on surrogate endpoints and will provide periodic guidance and hold Advisory Committee hearings as information is developed.<sup>1</sup>

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<sup>1</sup> FDA will determine on a case-by-case basis when approval is appropriate based on evidence of a product's effect on a clinical endpoint that is insufficient to support conventional approval. In enacting Section 112, Congress indicated that FDA could approve products "when the evidence of a [product's] effect on a clinical endpoint strongly suggests effectiveness, but is not sufficiently conclusive with respect to the ultimate outcome to warrant ordinary approval." H.R. Rep. No. 105-310, at 55 (1997). Such approvals are categorized as Fast Track Pathway B and may be subject to post-approval requirements.

### **C. Submission and Review of Applications**

If the Agency determines that a product qualifies for a fast track designation, it will take steps to expedite the development and review of the application for approval of the product. FFDCA § 506(a)(3); 21 U.S.C. § 356(a)(3).

A sponsor may submit a complete New Drug Application (NDA) or Biologics Licensing Application (BLA) in components for a product with fast track designation. Under Section 112 of the FDA Modernization Act, FDA may initiate review of an application for a fast track product upon receipt of the first component if it determines after preliminary evaluation of clinical data submitted by the sponsor that the product may be effective. Sponsors are advised to follow the following three steps in pursuing such a process:

- (1) The sponsor should submit to FDA a proposed schedule for submission of each component of the complete NDA or BLA. FDA strongly advises sponsors to submit such a proposed schedule as part of a pre-meeting briefing document in preparation for the Pre-NDA or Pre-BLA meeting.
- (2) The sponsor and FDA should discuss and agree upon the proposed schedule for submission of each component of the complete application. Usually, such discussion and agreement can be completed at the Pre-NDA or Pre-BLA meeting.
- (3) The sponsor should initiate submission of components of the NDA or BLA. Submission of the first such component must be accompanied by payment of the appropriate user fee, as required under Section 736 of the FFDCA. *See* FFDCA § 506(C); 21 U.S.C. § 356(C).

FDA will determine the acceptability of the complete application for filing within 60 days after FDA receives the final component of the application. At that time, FDA may determine that an application is acceptable for filing or not acceptable for filing in accordance with the criteria already described in regulations (*see* 21 C.F.R. § 314.101). The user fee clock for FDA review of an application will start after FDA receives the final component of the application. FDCA § 506(C)(2); 21 U.S.C. § 356(C)(2). Given that fast track products are intended to meet unmet medical needs in the treatment of serious or life-threatening illnesses, an NDA or BLA for a fast track product will, ordinarily, receive “priority” review status.

**IV. POST-APPROVAL REQUIREMENTS FOR FAST TRACK B APPROVALS – THOSE BASED ON SURROGATE OR CLINICAL ENDPOINTS INSUFFICIENT TO SUPPORT CONVENTIONAL OR FAST TRACK A APPROVAL**

Under Section 112, FDA has the discretion to impose post-approval requirements on fast track products approved on the basis of surrogate or clinical endpoints that are insufficient to support conventional approval (Fast Track B Products). FDA will determine whether and to what extent to impose such requirements on a case-by-case basis in light of the availability and strength of clinical evidence of a product’s safety and effectiveness. The stronger the available data, the less need there will be for post-approval requirements.

**A. Post-Approval Studies for Fast Track B Products**

Post-approval studies will generally be required for Fast Track B products, as Congress acknowledged when it enacted the fast track provisions. *See* H.R. Rep. No. 105-310, at 56 (1997). Such studies should be adequate and well-controlled clinical trials designed to obtain confirmatory data of a product’s safety and effectiveness. Sponsors should carry out studies in a timely manner after consultation with FDA. FDA anticipates

that studies will often be already underway, but not yet complete, at the time of approval. Such studies, once complete, should satisfy any post-approval study requirement. The marketing application for the product should include a plan for the timely completion of proposed post-approval studies. Sponsors will be required to provide annual updates on the status of post-approval studies and shall use the NDA or BLA annual report to provide such updates.

**B. Advance Submission of Promotional Materials for Fast Track B Products**

Section 112 authorizes FDA to require a sponsor to submit promotional materials for a product at least 30 days prior to the sponsor's dissemination of the materials following approval on the basis of a surrogate or clinical endpoint that is insufficient to support conventional approval. Congress has indicated that advance submission of promotional materials should only be required when appropriate and "for a period of time necessary for the sponsor to demonstrate that it understands and will comply with the FDA's promotional material requirements." H.R. Rep. No. 105-310, at 56 (1997). Where a sponsor has a demonstrated track record of substantial compliance with applicable advertising and promotion requirements, advance submission of promotional materials following approval will typically be unnecessary. In any case, FDA will only require advance submission for the limited time necessary for a sponsor to demonstrate its understanding and compliance with applicable promotional rules. Ordinarily, advance submission of promotional materials will not be required for longer than six months following approval. Following approval of a product, FDA will not require agency approval of promotional materials, simply advance submission prior to dissemination.

FDA's determination of the need for prior submission of promotional materials is independent from its determination of the need for post-approval clinical studies, and FDA can terminate the requirement for prior submission even if post-approval studies have not yet been completed.

**C. Expedited Withdrawal of Approval for Fast Track B Products**

FDA may withdraw approval of a Fast Track B product using expedited procedures if (1) the sponsor fails to conduct with due diligence a required post-approval study; (2) a post-approval study fails to verify a clinical benefit; (3) other evidence demonstrates that the product is not safe or effective for its intended use or uses; or (4) the manufacturer disseminates false or misleading promotional materials with respect to the product. FFDC § 506(b)(3); 21 U.S.C. § 356(b)(3). The sponsor of a product removed under expedited procedures may request an informal hearing prior to withdrawal. The informal hearing will be held under the procedures FDA has developed for its existing accelerated approval program, as set forth in 21 C.F.R. part 15 and 21 C.F.R. § 314.530.

Under those procedures, the CDER or CBER Director will provide the license holder notice of the Agency's proposed withdrawal of approval of the application and present an opportunity for a hearing on the withdrawal. The notice will state the reasons for the Agency's proposed withdrawal. At the informal hearing, the sponsor will be given an opportunity to present data and information disputing FDA's position regarding the product. The Commissioner or a designee will preside over the hearing with input from advisory committee members in accordance with 31 C.F.R. part 15 & § 314.530. The

Commissioner's determination following the hearing will constitute final agency action from which the sponsor may petition for judicial review.<sup>2</sup>

**D. Termination of Post-Approval Requirements**

As indicated above, any post-approval requirements imposed on a fast track product will be of limited duration. The requirement for post-marketing studies will be satisfied once such studies are completed, and further studies will not be required. The need for advance submission of promotional materials, if required for a particular product, will end as soon as the product's sponsor demonstrates compliance with applicable promotional requirements. Ordinarily, advance submission of promotional materials will not be required for longer than six months following approval. Once post-marketing studies are successfully completed and reported to FDA, no special requirements shall remain on a product's approval, and FDA shall no longer employ expedited withdrawal procedures.

**V. PUBLIC INFORMATION**

Consistent with current practice, FDA will not prohibit a sponsor from reporting publicly its receipt of a fast track designation of a product. In addition, on an annual basis, FDA will publish a cumulative list of all products that have received a fast track designation. This list will include the established name of the drug, specific disease or condition for which the designation was granted, and the name and address of the sponsor.

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<sup>2</sup> When FDA withdraws approval of a Fast Track A product, FDA's conventional withdrawal rules will apply and the holder of the license may request a formal evidentiary hearing under 21 CFR part 12. The formal hearing typically includes written and oral testimony before an administrative law judge, who issues an initial decision that may be appealed to the Commissioner.

**VI. PROMOTING AWARENESS OF THE FAST TRACK PROGRAM**

In an effort to promote awareness of the fast track program described in this guidance, FDA will disseminate this guidance to physicians, patient organizations, pharmaceutical and biotechnology companies, and the public. In addition, FDA will work with other groups and organizations to support the development of appropriate surrogate endpoints that are reasonably likely to predict clinical benefit for serious or life-threatening conditions.