Drug Approval and Patient Access

HELP Draft for Stakeholder Discussion

Chairman Harkin & Ranking Member Enzi

April 4, 2012

This discussion draft reflects bipartisan efforts to develop consensus policy proposals to accompany the FDA human medical product user fee legislation. Our goal is to solicit feedback on the policy merits, potential unintended consequences, and potential opportunities to improve the legislative language. We anticipate releasing additional drafts in other policy areas in the upcoming weeks. The discussion drafts will be available on the HELP Committee website. Please submit your written comments to both Kathleen Laird (Kathleen_Laird@help.senate.gov) in Senator Harkin's office and Grace Stuntz (Grace_Stuntz@help.senate.gov) in Senator Enzi's office by April 11, 2012. We will try to meet with as many stakeholders as possible who have submitted written comments. Written comments should accompany meeting requests.

112TH CONGRESS
2D SESSION

S. _____

To amend the Federal Food, Drug, and Cosmetic Act with respect to certain reauthorizations.

IN THE SENATE OF THE UNITED STATES

_____

_____ introduced the following bill; which was read twice and referred to the Committee on _____

A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to certain reauthorizations.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

[This Act may be cited as the "_____ Act of _____".]

SEC. 2. ENHANCEMENT OF ACCELERATED PATIENT ACCESS TO NEW MEDICAL TREATMENTS.

(a) FINDINGS; SENSE OF CONGRESS.—

(1) FINDINGS.—Congress finds as follows:

(A) The Food and Drug Administration (referred to in this section as the "FDA") serves a critical role in helping to assure that new medicines are safe and effective. Regulatory innovation is 1 element of the Nation's strategy to address serious and life-threatening diseases or conditions by promoting investment in and development of innovative treatments for unmet medical needs.

(B) During the 2 decades following the establishment of the accelerated approval mechanism, advances in medical sciences, including genomics, molecular biology, and bioinformatics, have provided an unprecedented understanding of the underlying biological mechanism and pathogenesis of disease. A new generation of modern, targeted medicines is under development to treat serious and life-threatening diseases, some applying drug development strategies based on biomarkers or pharmacogenomics, predictive toxicology, clinical trial enrichment techniques, and novel clinical trial designs, such as adaptive clinical trials.

(C) As a result of these remarkable scientific and medical advances, the FDA should

be encouraged to implement more broadly effective processes for the expedited development and review of innovative new medicines intended to address unmet medical needs for serious or life-threatening diseases or conditions, including those for rare diseases or conditions, using a broad range of surrogate or clinical endpoints and modern scientific tools earlier in the drug development cycle when appropriate. This may result in fewer, smaller, or shorter clinical trials for the intended patient population or targeted subpopulation without compromising or altering the high standards of the FDA for the approval of drugs.

(D) Patients benefit from expedited access to safe and effective innovative therapies to treat unmet medical needs for serious or life-threatening diseases or conditions.

(E) For these reasons, the statutory authority in effect on the day before the date of enactment of this Act governing expedited approval of drugs for serious or life-threatening diseases or conditions should be amended in order to enhance the authority of the FDA to consider appropriate scientific data, methods,

and tools, and to expedite development and access to novel treatments for patients with a broad range of serious or life-threatening diseases or conditions.

(2) SENSE OF CONGRESS.—It is the sense of Congress that the Food and Drug Administration should apply the accelerated approval and fast track provisions set forth in section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356), as amended by this section, to help expedite the development and availability to patients of treatments for serious or life-threatening diseases or conditions while maintaining safety and effectiveness standards for such treatments.

(b) EXPEDITED APPROVAL OF DRUGS FOR SERIOUS OR LIFE-THREATENING DISEASES OR CONDITIONS.—Section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356) is amended to read as follows:

"SEC. 506. EXPEDITED APPROVAL OF DRUGS FOR SERIOUS OR LIFE-THREATENING DISEASES OR CONDITIONS.

"(a) DESIGNATION OF DRUG AS FAST TRACK PRODUCT.—

"(1) IN GENERAL.—The Secretary shall, at the request of the sponsor of a new drug, facilitate the

development and expedite the review of such drug if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. (In this section, such a drug is referred to as a 'fast track product'.)

"(2) REQUEST FOR DESIGNATION.—The sponsor of a new drug may request the Secretary to designate the drug as a fast track product. A request for the designation may be made concurrently with, or at any time after, submission of an application for the investigation of the drug under section 505(i) or section 351(a)(3) of the Public Health Service Act.

"(3) DESIGNATION.—Within 60 calendar days after the receipt of a request under paragraph (2), the Secretary shall determine whether the drug that is the subject of the request meets the criteria described in paragraph (1). If the Secretary finds that the drug meets the criteria, the Secretary shall designate the drug as a fast track product and shall take such actions as are appropriate to expedite the

development and review of the application for approval of such product.

"(b) ACCELERATED APPROVAL OF A DRUG FOR A SERIOUS OR LIFE-THREATENING DISEASE OR CONDITION, INCLUDING A FAST TRACK PRODUCT.—

"(1) IN GENERAL.—

"(A) ACCELERATED APPROVAL.—The Secretary may approve an application for approval of a product for a serious or life-threatening disease or condition, including a fast track product, under section 505(c) or section 351(a) of the Public Health Service Act upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity or rarity of the condition and the availability of alternative treatments. The approval described in the preceding sentence is referred to in this section as 'accelerated approval'.

"(B) EVIDENCE.—The evidence to support that an endpoint is reasonably likely to predict clinical benefit under subparagraph (A) may include epidemiological, pathophysiological, therapeutic or other evidence developed using biomarkers, for example, or other scientific methods or tools.

"(2) LIMITATION.—Approval of a product under this subsection may be subject to 1 or both of the following requirements:

"(A) That the sponsor conduct appropriate post-approval studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit.

"(B) That the sponsor submit copies of all promotional materials related to the product during the preapproval review period and, following approval and for such period thereafter as the Secretary determines to be appropriate, at least 30 days prior to dissemination of the materials.

"(3) EXPEDITED WITHDRAWAL OF APPROVAL.—The Secretary may withdraw approval of a product approved under accelerated approval using expedited procedures (as prescribed by the Secretary

in regulations which shall include an opportunity for an informal hearing) if—

"(A) the sponsor fails to conduct any required post-approval study of the drug with due diligence;

"(B) a study required to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit of the product fails to verify and describe such effect or benefit;

"(C) other evidence demonstrates that the product is not safe or effective under the conditions of use; or

"(D) the sponsor disseminates false or misleading promotional materials with respect to the product.

"(c) REVIEW OF INCOMPLETE APPLICATIONS FOR APPROVAL OF A FAST TRACK PRODUCT.—

"(1) IN GENERAL.—If the Secretary determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective, the Secretary shall evaluate for filing, and may commence review of portions of, an application for the approval of the product before the sponsor submits a complete application. The Sec-

retary shall commence such review only if the applicant—

"(A) provides a schedule for submission of information necessary to make the application complete; and

"(B) pays any fee that may be required under section 736.

"(2) EXCEPTION.—Any time period for review of human drug applications that has been agreed to by the Secretary and that has been set forth in goals identified in letters of the Secretary (relating to the use of fees collected under section 736 to expedite the drug development process and the review of human drug applications) shall not apply to an application submitted under paragraph (1) until the date on which the application is complete.

"(d) AWARENESS EFFORTS.—The Secretary shall—

"(1) develop and disseminate to physicians, patient organizations, pharmaceutical and biotechnology companies, and other appropriate persons a description of the provisions of this section applicable to accelerated approval and fast track products; and

"(2) establish a program to encourage the development of surrogate and clinical endpoints, in-

cluding biomarkers, and other scientific methods and tools that can assist the Secretary in determining whether the evidence submitted in an application is reasonably likely to predict clinical benefit for serious or life-threatening conditions for which significant unmet medical needs exist.

"(e) CONSTRUCTION.—

"(1) PURPOSE.—The amendments made by the [insert short title] to this section are intended to encourage the Secretary to utilize innovative and flexible approaches to the assessment of products under accelerated approval for treatments for patients with serious or life-threatening diseases or conditions and unmet medical needs.

"(2) CONSTRUCTION.—Nothing in this section shall be construed to alter the standards of evidence under subsection (c) or (d) of section 505 (including the substantial evidence standard in section 505(d)) of this Act or under section 351(a) of the Public Health Service Act. Such sections and standards of evidence apply to the review and approval of products under this section, including whether a product is safe and effective. Nothing in this section alters the ability of the Secretary to rely on evidence that does not come from adequate and well-controlled in-

vestigations for the purpose of determining whether an endpoint is reasonably likely to predict clinical benefit as described in subsection (b)(1)(B).".

(c) GUIDANCE; AMENDED REGULATIONS.—

(1) DRAFT GUIDANCE.—Not later than 1 year after the date of enactment of this Act, the Secretary of Health and Human Services (referred to in this section as the "Secretary") shall issue draft guidance to implement the amendments made by this section. In developing such guidance, the Secretary shall specifically consider issues arising under the accelerated approval and fast track processes under section 506 of the Federal Food, Drug, and Cosmetic Act, as amended by subsection (b), for drugs designated for a rare disease or condition under section 526 of such Act (21 U.S.C. 360bb).

(2) FINAL GUIDANCE.—Not later than 1 year after the issuance of draft guidance under paragraph (1), and after an opportunity for public comment, the Secretary shall issue final guidance.

(3) CONFORMING CHANGES.—The Secretary shall issue, as necessary, conforming amendments to the applicable regulations under title 21, Code of Federal Regulations, governing accelerated approval.

(4) NO EFFECT OF INACTION ON REQUESTS.—If the Secretary fails to issue final guidance or amended regulations as required by this subsection, such failure shall not preclude the review of, or action on, a request for designation or an application for approval submitted pursuant to section 506 of the Federal Food, Drug, and Cosmetic Act, as amended by subsection (b).

(d) INDEPENDENT REVIEW.—The Secretary may, in conjunction with other planned reviews, contract with an independent entity with expertise in assessing the quality and efficiency of biopharmaceutical development and regulatory review programs to evaluate the Food and Drug Administration's application of the processes described in section 506 of the Federal Food, Drug, and Cosmetic Act, as amended by subsection (b), and the impact of such processes on the development and timely availability of innovative treatments for patients suffering from serious or life-threatening conditions. Any such evaluation shall include consultation with regulated industries, patient advocacy and disease research foundations, and relevant academic medical centers.

SEC. 3. BREAKTHROUGH THERAPIES.

(a) IN GENERAL.—Section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356), as amended by section 2, is further amended—

(1) by redesignating subsections (a) through (c) as subsections (b) through (d), respectively;

(2) by redesignating subsection (d) as subsection (f);

(3) by inserting before subsection (b), as so redesignated, the following:

"(a) DESIGNATION OF A DRUG AS A BREAKTHROUGH THERAPY.—

"(1) IN GENERAL.—The Secretary shall, at the request of the sponsor of a drug, expedite the development and review of such drug if the drug is intended, alone or in combination with 1 or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on 1 or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. (In this section, such a drug is referred to as a 'breakthrough therapy'.)

"(2) REQUEST FOR DESIGNATION.—The sponsor of a drug may request the Secretary to designate

the drug as a breakthrough therapy. A request for the designation may be made concurrently with, or at any time after, the submission of an application for the investigation of the drug under section 505(i) or section 351(a)(3) of the Public Health Service Act.

"(3) DESIGNATION.—

"(A) IN GENERAL.—Not later than 60 calendar days after the receipt of a request under paragraph (2), the Secretary shall determine whether the drug that is the subject of the request meets the criteria described in paragraph (1). If the Secretary finds that the drug meets the criteria, the Secretary shall designate the drug as a breakthrough therapy and shall take such actions as are appropriate to expedite the development and review of the application for approval of such drug.

"(B) ACTIONS.—The actions to expedite the development and review of an application under subparagraph (A) may include, as appropriate—

"(i) holding meetings with the sponsor and the review team throughout the development of the drug;

"(ii) providing timely advice to, and interactive communication with, the sponsor regarding the development of the drug to ensure that the development program to gather the non-clinical and clinical data necessary for approval is as efficient as practicable;

"(iii) involving senior managers and experienced review staff, as appropriate, in a collaborative, cross-disciplinary review;

"(iv) assigning a cross-disciplinary project lead for the Food and Drug Administration review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor; and

"(v) taking steps to ensure that the design of the clinical trials is as efficient as practicable, when scientifically appropriate, such as by minimizing the number of patients enrolled in the trials and the duration of the trials.";

(4) in subsection (f)(1), as so redesignated, by striking "applicable to accelerated approval" and in-

serting "applicable to breakthrough therapies, accelerated approval, and"; and

(5) by adding at the end the following:

"(g) REPORT.—Beginning in fiscal year 2013, the Secretary shall annually prepare and submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives, and make publicly available, with respect to this section for the previous fiscal year—

"(1) the number of drugs for which a sponsor requested designation as a breakthrough therapy;

"(2) the number of products designated as a breakthrough therapy; and

"(3) for each breakthrough therapy approved in the fiscal year—

"(A) the point in the drug development and review process at which such breakthrough designation occurred;

"(B) the total time from designation as a breakthrough therapy to a final decision on the approvability of the drug; and

"(C) the number of breakthrough therapies approved, including the number approved on the first review out of the total number of such therapies so approved.".

(b) GUIDANCE; AMENDED REGULATIONS.—

(1) IN GENERAL.—

(A) GUIDANCE.—Not later than 18 months after the date of enactment of this Act, the Secretary of Health and Human Services (referred to in this section as the "Secretary") shall issue draft guidance on implementing the requirements with respect to breakthrough therapies, as set forth in section 506(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(a)), as amended by this section. The Secretary shall issue final guidance not later than 1 year after the close of the comment period for the draft guidance.

(B) AMENDED REGULATIONS.—If the Secretary determines that it is necessary to amend the regulations under title 21, Code of Federal Regulations in order to implement the amendments made by this section to section 506(a) of the Federal Food, Drug, and Cosmetic Act, the Secretary shall amend such regulations not later than 2 years after the date of enactment of this Act.

(2) REQUIREMENTS.—Guidance promulgated under this section shall—

(A) specify the process and criteria by which the Secretary makes a designation under section 506(a)(3) of the Federal Food, Drug, and Cosmetic Act; and

(B) specify the actions the Secretary shall take to expedite the development and review of a breakthrough therapy pursuant to such designation under such section 506(a)(3), including updating good review management practices to reflect breakthrough therapies.

(c) INDEPENDENT REVIEW.—Not later than 3 years after the date of enactment of this Act, the Comptroller General of the United States, in consultation with appropriate experts, shall assess the manner by which the Food and Drug Administration has applied the processes described in section 506(a) of the Federal Food, Drug, and Cosmetic Act, as amended by this section, and the impact of such processes on the development and timely availability of innovative treatments for patients affected by serious or life-threatening conditions. Such assessment shall be made publicly available upon completion.

(d) CONFORMING AMENDMENTS.—Section 506B(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356b) is amended by striking "section 506(b)(2)(A)" each

place such term appears and inserting "section 506(c)(2)(A)".

SEC. 4. GUIDANCE DOCUMENT REGARDING PRODUCT PROMOTION USING THE INTERNET.

Not later than 2 years after the date of enactment this Act, the Secretary of Health and Human Services shall issue a guidance document that describes the policy of the Food and Drug Administration regarding the promotion, using the Internet (including social media), of medical products that are regulated by such Administration.

SEC. 5. REAUTHORIZATION OF PROVISION RELATING TO EXCLUSIVITY OF CERTAIN DRUGS CONTAINING SINGLE ENANTIOMERS.

Section 505(u)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(u)(4)) is amended by striking "2012" and inserting "2017".

SEC. 6. REAUTHORIZATION OF THE CRITICAL PATH PUBLIC-PRIVATE PARTNERSHIPS.

Section 566(f) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb–5(f)) is amended by striking "2012" and inserting "2017".

SEC. 7. CONSULTATION WITH EXTERNAL EXPERTS ON RARE DISEASES, TARGETED THERAPIES, AND GENETIC TARGETING OF TREATMENTS.

Subchapter E of chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb et seq.) is amended by adding at the end the following:

"SEC. 568. CONSULTATION WITH EXTERNAL EXPERTS ON RARE DISEASES, TARGETED THERAPIES, AND GENETIC TARGETING OF TREATMENTS.

"(a) IN GENERAL.—

"(1) OPPORTUNITIES FOR CONSULTATION.—The Secretary shall ensure that opportunities exist, at a time the Secretary determines appropriate, for consultation with external experts on the topics described in subsection (c), for the purpose of promoting the efficiency of and informing the review by the Food and Drug Administration of drugs and biologic products for rare diseases and drugs and biologic products that are genetically targeted.

"(2) CONSULTATION.—The Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research shall, when appropriate, seek the opinion of external experts on any topic, including the topics described in subsection (c), by initiating contact with such experts. External experts may also request the opportunity to meet

with a review division regarding any topic described in subsection (c).

"(b) EXTERNAL EXPERTS.—The external experts under subsection (a) may include—

"(1) representatives of patient, consumer, research, and health professional organizations with expertise relevant to the review of rare disease products;

"(2) experts on rare diseases, rare subtypes of rare and other diseases, and genetic targeting of treatments, including experts from academia; and

"(3) experts in innovative clinical trial designs for small target populations.

"(c) TOPICS FOR CONSULTATION.—Topics for consultation may include—

"(1) rare diseases;

"(2) the severity of rare diseases;

"(3) the unmet medical need associated with rare diseases;

"(4) the willingness and ability of individuals with a rare disease to participate in clinical trials;

"(5) an assessment of the benefits and risks, including side effects, of current and investigational therapies;

"(6) the design of clinical trials for rare disease populations and subpopulations, including regulatory and scientific policies affecting the design of such trials; and

"(7) demographics and the clinical description of patient populations.

"(d) CLASSIFICATION AS SPECIAL GOVERNMENT EMPLOYEES.—The external experts who are consulted under this section may be considered special government employees, as defined under section 202 of title 18, United States Code.

"(e) PROPRIETARY INFORMATION.—Nothing in this section shall be construed to create a right for any external expert, as described in subsection (b), to obtain access to proprietary information of a sponsor without the permission of such sponsor.

"(f) NO RIGHT OR OBLIGATION.—Nothing in this section shall be construed to create a legal right for a consultation on any matter or require the Secretary to meet with any particular expert.".

[SEC. 8. ACCESSIBILITY OF INFORMATION IN PRESCRIPTION DRUG LABELING BY VISUALLY-IMPAIRED AND BLIND CONSUMERS.

To be supplied.]