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109TH CONGRESS
2D SESSION

H. R. 6303

To amend the Federal Food, Drug, and Cosmetic Act to create a new three-tiered approval system for drugs, biological products, and devices that is responsive to the needs of seriously ill patients, and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

SEPTEMBER 29, 2006

Mr. SHAYS introduced the following bill; which was referred to the Committee on Energy and Commerce

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A BILL

To amend the Federal Food, Drug, and Cosmetic Act to create a new three-tiered approval system for drugs, biological products, and devices that is responsive to the needs of seriously ill patients, and for other purposes.

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 ''Access, Compassion, Care, and Ethics for Seriously Ill Patients Act'' or the ''ACCESS Act''.

SEC. 2. FINDINGS.

Congress finds the following:

(1) The necessity of placebo controlled studies has been questioned on both scientific and ethical grounds for seriously ill patients.

(2) The current standards of the Food and Drug Administration for approval of drugs, biological products, and devices deny the benefits of medical progress to seriously ill patients who face morbidity or death from their disease.

(3) Promising therapies intended to treat serious or life threatening conditions or diseases and which address unmet medical needs have received unjustified delays and denials of approval.

(4) Seriously ill patients have a right to access available investigational drugs, biological products, and devices.

(5) The current Food and Drug Administration and National Cancer Institute case-by-case exception for compassionate access must be required to permit all seriously ill patients access to available experimental therapies as a treatment option.

(6) The current emphasis on statistical analysis of clinical information needs to be balanced by a greater reliance on clinical evaluation of this information.

(7) Food and Drug Administration advisory committees should have greater representation of medical clinicians who represent the interests of seriously ill patients in early access to promising investigational therapies.

(8) The use of available investigational products for treatment is the responsibility of the physician and the patient.

(9) The use of combinations of available investigational and approved products for treatment is the responsibility of the physician and the patient.

(10) The development and approval of drugs, biological products, and devices intended to address serious or life-threatening conditions or diseases is often delayed by the inability of sponsors to obtain prompt meetings with the Food and Drug Administration and to obtain prompt resolution of scientific and regulatory issues related to the investigation and review of new technologies.

SEC. 3. TIERED APPROVAL SYSTEM FOR DRUGS, BIOLOGICAL PRODUCTS, AND DEVICES.

Section 506 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356) is amended to read as follows:

"SEC. 506. TIERED APPROVAL SYSTEM.

"(a) IN GENERAL.—Notwithstanding any other provision of law, the sponsor of an investigational drug, biological product, or device may submit an application to the Secretary for Tier I or Tier II approval in accordance with this section.

"(b) TIER I APPROVAL.—

"(1) IN GENERAL.—

"(A) APPLICATION CONTENT.—A sponsor of an investigational drug, biological product, or device applying for Tier I approval of the product shall submit to the Secretary an application as described under section 505(b)(1) or 505(b)(2), section 351(a) of the Public Health Service Act, or section 510(k) or 515(c)(1), as applicable, which shall contain—

"(i) data and information from completed Phase I clinical investigations and any other nonclinical or clinical investigations;

"(ii) preliminary evidence that the product may be effective against a serious or life-threatening condition or disease, which evidence may be based on uncontrolled data such as case histories, information about the pharmacological mecha-

nism of action, data from animal and computer models, comparison with historical data, or other preliminary information, and may be based on a small number of patients; and

"(iii) an assurance that the sponsor will continue clinical investigation to obtain Tier III approval.

"(B) LIMITATION.—Tier I approval shall be primarily based upon clinical evaluation, not statistical analysis.

"(2) DETERMINATION BY SECRETARY.—

"(A) IN GENERAL.—Not later than 30 days after the receipt of an application for Tier I approval, the Secretary shall either—

"(i) approve the application; or

"(ii) refer the application to the Accelerated Approval Advisory Committee.

"(B) RECOMMENDATION.—Within 90 days after receipt of an application for approval, the Accelerated Approval Advisory Committee shall issue a recommendation to the Secretary on whether the Secretary should approve the application.

"(C) FINAL DECISION.—Within 30 days after receipt of the recommendation from the Accelerated Approval Advisory Committee, the Secretary shall either approve the application or shall issue an order setting forth a detailed explanation of the reasons why the application was not approved and the specific data that the sponsor must provide so that the application may be approved.

"(3) APPEAL.—If the Secretary does not approve an application for which the Accelerated Approval Advisory Committee recommended approval, the sponsor of the application shall have the right to appeal the decision to the Commissioner of Food and Drugs. The Commissioner shall provide the sponsor with a hearing within 30 days following the nonapproval of the application and shall issue an order within 30 days following the hearing either concurring in the nonapproval or approving the application. The Commissioner shall not delegate the responsibility described in this paragraph to any other person.

"(4) CRITERIA.—In making a determination under paragraph (2), the Secretary shall consider whether the totality of the information available to

the Secretary regarding the safety and effectiveness of an investigational drug, biological product, or device, as compared to the risk of morbidity or death from a condition or disease, indicates that a patient (who may be representative of a small patient subpopulation) may obtain more benefit than risk if treated with the drug, biological product, or device. If the potential risk to a patient of the condition or disease outweighs the potential risk of the product, and the product may possibly provide benefit to the patient, the Secretary shall approve the application.

''(5) PRODUCT LABELING.—The labeling approved by the Secretary for the drug, biological product, or device—

''(A) shall state that the product is intended for use by a patient whose physician has documented in writing that the patient has—

''(i) exhausted all treatment options approved by Secretary for the condition or disease for which the patient is a reasonable candidate; and

''(ii) unsuccessfully sought treatment, or obtained treatment that was not effective, with an investigational drug, biological product, or device for which such indi-

vidual is a reasonable candidate (which may include consideration of the lack of a source of supply or geographic factors); and

"(B) shall state that every patient to whom the product is administered shall, as a mandatory condition of receiving the product, provide—

"(i) written informed consent, as described under part 50 of title 21, Code of Federal Regulations;

"(ii) a written waiver of the right to sue the manufacturer or sponsor of the drug, biological product, or device, or the physicians who prescribed the product or the institution where it was administered, for an adverse event caused by the product, which shall be binding in every State and Federal court; and

"(iii) consent for the manufacturer of the product to obtain data and information about the patient and the patient's use of the product that may be used to support an application for Tier II or Tier III approval.

''(6) LIMITATION ON CONDITIONS.—Tier I approval may be subject to the requirement that the sponsor conduct appropriate post-approval studies.

''(c) TIER II APPROVAL.—

''(1) IN GENERAL.—A sponsor of an investigational drug, biological product, or device applying for Tier II approval shall submit to the Secretary an application as described under section 505(b)(1) or 505(b)(2), section 351(a) of the Public Health Service Act, or section 510(k) or 515(c)(1), as applicable, which shall contain—

''(A) data and information that the drug, biological product, or device has an effect on a clinical endpoint or on a surrogate endpoint or biomarker that is reasonably likely to predict clinical benefit to a patient (who may be representative of a small patient subpopulation) suffering from a serious or life-threatening condition or disease; and

''(B) an assurance that the sponsor will continue clinical investigation to obtain Tier III approval.

''(2) DETERMINATION BY SECRETARY.—

''(A) IN GENERAL.—Not later than 30 days after the receipt of an application for Tier II approval, the Secretary shall either—

''(i) approve the application; or

''(ii) refer the application to the Accelerated Approval Advisory Committee.

''(B) RECOMMENDATION.—Within 90 days after receipt of an application for approval, the Accelerated Approval Advisory Committee shall issue a recommendation to the Secretary on whether the Secretary should approve the application.

''(C) FINAL DECISION.—Within 30 days after receipt of the recommendation from the Accelerated Approval Advisory Committee, the Secretary shall either approve the application or issue an order setting forth a detailed explanation of the reasons why the application was not approved and the specific data that the sponsor must provide so that the application may be approved.

''(3) APPEAL.—If the Secretary does not approve an application for which the Accelerated Approval Advisory Committee recommended approval, the sponsor of the application shall have the right to

appeal the decision to the Commissioner of Food and Drugs. The Commissioner shall provide the sponsor with a hearing within 30 days following the nonapproval of the application and shall issue an order within 30 days following the hearing either concurring in the nonapproval or approving the application. The Commissioner shall not delegate the responsibility described in this paragraph to any other person.

''(4) LIMITATION ON CONDITIONS.—

''(A) POST-APPROVAL STUDIES.—Tier II approval may be subject to the requirement that the sponsor conduct appropriate post-approval studies to validate the surrogate endpoint or biomarker or otherwise confirm the effect on the clinical endpoint.

''(B) RULE OF CONSTRUCTION.—Nothing in this subsection shall be construed to permit the Secretary to condition Tier II approval on compliance with any other standards, including any standard necessary to meet Tier III approval.

''(d) TIER III APPROVAL.—For purposes of this Act, the term 'Tier III approval' means—

''(1) with respect to a new drug or new biological product, approval of such drug or product under section 505(b)(1) or 505(b)(2) or section 351 of the Public Health Service Act, as the case may be; and

''(2) with respect to a new device, clearance of such device under section 510(k) or approval of such device under section 515(c)(1).

''(e) PROMOTIONAL MATERIALS.—Approval of a product under either Tier I or II may be subject to the requirements that—

''(1) the sponsor submit copies of all advertising and 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, and at least 30 days prior to the dissemination of the materials;

''(2) all advertising and promotional materials prominently disclose the limited approval for the product and data available supporting the safety and effectiveness of the product; and

''(3) the sponsor shall not disseminate advertising or promotional material prior to obtaining written notification from the Secretary that the advertising or promotional material complies with this subchapter.

''(f) EXPEDITED WITHDRAWAL OF APPROVAL.—The Secretary may withdraw Tier I or Tier II approval using expedited procedures (as prescribed by the Secretary in regulations which shall include an opportunity for a hearing) if—

''(1) the sponsor fails to conduct post-approval studies with due diligence, considering all of the circumstances involved;

''(2) a post-approval study fails to verify clinical benefit of the product for even a small patient subpopulation;

''(3) other evidence demonstrates that the product is not safe or effective under the conditions of use for even a small patient subpopulation; or

''(4) the sponsor disseminates false or misleading promotional materials with respect to the product and fails to correct the material promptly after written notice from the Secretary.

''(g) ACCELERATED APPROVAL ADVISORY COMMITTEE.—

''(1) IN GENERAL.—In order to facilitate the development and expedite the review of drugs, biological products, and devices intended to treat serious or life threatening conditions, the Secretary shall

establish the Accelerated Approval Advisory Committee.

''(2) DELEGATION.—The Secretary may delegate authority for the Accelerated Approval Advisory Committee to the Commissioner of Food and Drugs. The Accelerated Approval Advisory Committee shall be staffed and administered in the Office of the Commissioner.

''(3) COMPOSITION.—

''(A) IN GENERAL.—The Committee shall be composed of 11 voting members, including 1 chairperson and 5 permanent members each of whom shall serve a term of 3 years and may be reappointed for a second 3-year term, and 5 nonpermanent members who shall be appointed to the Committee for a specific meeting, or part of a meeting, in order to provide adequate expertise in the subject being reviewed. The Committee shall include as voting members no less than 2 representatives of patient interests, of which 1 shall be a permanent member of the Committee. The Committee shall include as nonvoting members a representative of interests of the drug, biological product, and device industry.

"(B) APPOINTMENTS.—The Secretary shall appoint to the Committee persons who are qualified by training and experience to evaluate the safety and effectiveness of the types of products to be referred to the Committee and who, to the extent feasible, possess skill in the use of, or experience in the development, manufacture, or utilization of, such products. The Secretary shall make appointments to the Committee so that the Committee shall consist of members with adequately diversified expertise and practical experience in such fields as clinical medicine, biological and physical sciences, and other related professions. Scientific, industry, and consumer organizations and members of the public shall be afforded an opportunity to nominate individuals for appointment to the Committee. No individual who is in the regular full-time employ of the United States and engaged in the administration of this chapter may be a member of the Committee.

"(4) COMPENSATION.—Committee members, while attending meetings or conferences of the Committee or otherwise engaged in its business, shall be entitled to receive compensation at rates to be fixed

by the Secretary, but not at rates exceeding the daily equivalent of the rate in effect for grade GS–18 of the General Schedule, for each day so engaged, including traveltime, and while so serving away from their homes or regular places of business each member may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, for persons in the Government service employed intermittently.

''(5) ASSISTANCE.—The Secretary shall furnish the Committee with adequate clerical and other necessary assistance.

''(6) ANNUAL TRAINING.—The Secretary shall employ nongovernmental experts to provide annual training to the Committee on the statutory and regulatory standards for product approval.

''(7) TIMELINE.—The Committee shall be scheduled to meet at such times as may be appropriate for the Secretary to meet applicable statutory deadlines.

''(8) MEETINGS.—

''(A) OPPORTUNITIES FOR INTERESTED PERSONS.—Any person whose product is specifically the subject of review by the Committee shall have—

''(i) the same access to data and information submitted to the Committee as the Secretary;

''(ii) the opportunity to submit, for review by the Committee, data or information, which shall be submitted to the Secretary for prompt transmittal to the Committee; and

''(iii) the same opportunity as the Secretary to participate in meetings of the Committee.

''(B) ADEQUATE TIME; FREE AND OPEN PARTICIPATION.—Any meetings of the Committee shall provide adequate time for initial presentations and for response to any differing views by persons whose products are specifically the subject of the Committee review, and shall encourage free and open participation by all interested persons.

''(C) SUMMARIES.—At all meetings of the Committee, the Secretary shall provide a summary to the Committee of all Tier I and Tier II applications that the Committee did not consider that were approved by the Secretary since the last meeting of the Committee.

''(h) COMMENCEMENT OF REVIEW.—If the Secretary determines, after preliminary evaluation of the data and information submitted by the sponsor, that the product may be effective, the Secretary shall evaluate for filing, and may commence review of portions of, an application for Tier I or Tier II approval before the sponsor submits a complete application. The Secretary shall commence such review only if the applicant provides a schedule for submission of information necessary to make the application complete.

''(i) INAPPLICABILITY OF PROVISIONS.—The following provisions shall not apply to Tier I or Tier II applications and approvals:

''(1) Chapter VII, subchapter C, parts 2 and 3 relating to fees for drugs, biological products, and devices.

''(2) The provisions of the Drug Price Competition and Patent Term Restoration Act of 1984 that authorize approval of abbreviated new drug applications and applications submitted under section 505(b)(2). Market exclusivity and patent term restoration of Tier I and Tier II approved drugs, biological products, and devices shall be determined solely at the time of Tier III approval without regard to prior Tier I or Tier II approval. Prior to

Tier III approval, the Secretary shall not approve any application submitted under section 505(b)(2) or section 505(j) that references a drug approved under subsections (b) or (c) of this section.''.

SEC. 4. ETHICS IN HUMAN TESTING.

Chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended by adding at the end of section 505(i) the following:

''(5) Notwithstanding any other provision of law, the Secretary shall prohibit placebo-only or no-treatment-only concurrent controls in any clinical investigation conducted under this chapter or, in the use of the last-observation-carried-forward convention, in any clinical investigation conducted under this chapter or section 351 of the Public Health Service Act with respect to any life-threatening condition or disease where reasonably effective approved alternative therapies exist for the specific indication.''.

SEC. 5. EXPANDED ACCESS TO INVESTIGATIONAL DRUGS AND DEVICES.

(a) IN GENERAL.—Chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended by adding at the end of section 561 the following:

''(f) EXPANDED ACCESS PROGRAM.—The Food and Drug Administration shall establish a new program to expand access to investigational treatments for individuals with serious or life threatening conditions and diseases. In carrying out this expanded access program, the Secretary shall publish and broadly disseminate written guidance that—

''(1) describes such expanded access programs for investigational drugs, biological products, and devices intended to treat serious or life-threatening conditions or diseases;

''(2) encourages and facilitates submission of Tier I and Tier II applications and approvals; and

''(3) facilitates the provision of investigational drugs and devices to seriously ill individuals without unreasonable delay by recognizing that the use of available investigational products for treatment is the responsibility of the physician and the patient.

''(g) IMPLEMENTATION OF EXPANDED ACCESS PROGRAMS.—

''(1) TRAINING OF PERSONNEL.—Not later than 90 days after the date of enactment of this subsection, the Secretary shall implement training programs at the Food and Drug Administration with

respect to the expanded access programs established under this section.

''(2) POLICIES, REGULATIONS, AND GUIDANCE.—The Secretary shall establish policies, regulations, and guidance designed to most directly benefit seriously ill patients.

''(h) DEVELOPMENT OF SURROGATE ENDPOINTS AND BIOMARKERS.—The Secretary shall—

''(1) establish a program to encourage the development of surrogate endpoints and biomarkers that are reasonably likely to predict clinical benefit for serious or life-threatening conditions for which there exist significant unmet medical needs;

''(2) request the Institute of Medicine to undertake a study to identify validated surrogate endpoints and biomarkers, and recommend research to validate surrogate endpoints and biomarkers, that may support approvals for products intended for the treatment of serious or life-threatening conditions or diseases; and

''(3) make widely available to the public a list of drugs, biological products, and devices that are being investigated for serious or life-threatening conditions or diseases and that have not yet received Tier I or Tier II approval for marketing.''.

(b) CONFORMING AMENDMENT.—Section 561(c) of the Federal Food, Drug, and Cosmetic Act is amended by striking the heading and inserting ''EXPANDED ACCESS TO INVESTIGATIONAL DRUGS AND DEVICES FOR SERIOUSLY ILL PATIENTS''.

SEC. 6. MODERNIZATION OF THE FOOD AND DRUG ADMINISTRATION.

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. 565. POLICIES RELATED TO STUDY EVALUATION INFORMATION.

''(a) IN GENERAL.—

''(1) NONSTATISTICAL MEASURES.—The Secretary shall give equal weight to clinical judgment and statistical analysis in the evaluation of the safety and effectiveness of drugs, biological products, and devices, and shall not disapprove a product application solely on the basis of a statistical analysis or the rigid use of the 95 percent confidence level convention. This policy shall apply—

''(A) in evaluating clinical study designs and endpoints; and

''(B) in making decisions with respect to product applications.

''(2) TYPES OF NONSTATISTICAL MEASURES.—The policy established under paragraph (1), for the purposes described in such paragraph—

''(A) shall include but not be limited to such nonstatistical information as—

''(i) clinical evaluation information, such as case history reports;

''(ii) scientific and clinical studies designed to measure or define mechanisms of action or molecular targeting;

''(iii) data from animal and computer models; and

''(iv) comparison with historical data; and

''(B) shall incorporate the use of—

''(i) evaluations of the adverse effect of delaying the availability of an investigational drug to even a small subpopulation of seriously ill patients; and

''(ii) scientific, observational, or clinical studies designed and conducted to collect well-documented information.

''(b) MEETINGS.—A meeting to address any pending scientific, medical, regulatory, or other issue relating to the development, investigation, review, or other aspect of

a drug, biological product, or device shall ordinarily be held within 15 days of the receipt of a written request for the meeting by the sponsor of the product, which may be extended to 30 days for good cause. Such meetings shall ordinarily be conducted in person, but may be conducted by telephone or other form of communication if both parties agree. In order to reduce the burden of meetings, only those Food and Drug Administration employees who are intended to actively participate in the discussion shall attend a meeting. Minutes of a meeting shall be promptly prepared and exchanged by both parties immediately following the meeting and shall accurately summarize what occurred at the meeting

''(c) RULE OF CONSTRUCTION.—The provisions of chapter V and section 351 of the Public Health Service Act shall be construed to incorporate the policy established in this section.''.

SEC. 7. MEMBERSHIP OF ONCOLOGY DRUGS ADVISORY COMMITTEE.

Membership of the Oncology Drugs Advisory Committee of the Food and Drug Administration shall consist of no less than 2 patient representatives who are voting members of the committee.

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