

PRESCRIPTION DRUG USER FEE REAUTHORIZATION AND
DRUG REGULATORY MODERNIZATION ACT OF 1997

OCTOBER 7, 1997.—Committed to the Committee of the Whole House on the State
of the Union and ordered to be printed

Mr. BLILEY, from the Committee on Commerce,
submitted the following

R E P O R T

together with

ADDITIONAL VIEWS

[To accompany H.R. 1411]

[Including cost estimate of the Congressional Budget Office]

The Committee on Commerce, to whom was referred the bill (H.R. 1411) to amend the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act to facilitate the development and approval of new drugs and biological products, and for other purposes, having considered the same, report favorably thereon with an amendment and recommend that the bill as amended do pass.

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The amendment is as follows:

Strike out all after the enacting clause and insert in lieu thereof the following:

SECTION 1. SHORT TITLE; REFERENCES; TABLE OF CONTENTS.

(a) **SHORT TITLE.**—This Act may be cited as the “Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997”.

(b) **REFERENCES.**—Except as otherwise specified, whenever in this Act an amendment is expressed in terms of an amendment to a section or other provision, the reference shall be considered to be made to that section or other provision of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321 et seq.).

(c) **TABLE OF CONTENTS.**—The table of contents for this Act is as follows:

Sec. 1. Short title; references; table of contents.
Sec. 2. Fees relating to drugs.
Sec. 3. Pediatric studies of drugs.
Sec. 4. Expediting study and approval of fast track drugs.
Sec. 5. Expanded access to investigational therapies.
Sec. 6. Information program on clinical trials for serious or life-threatening diseases.
Sec. 7. Dissemination of information on new uses.
Sec. 8. Studies and reports.
Sec. 9. Approval of supplemental applications for approved products.
Sec. 10. Health care economic information.
Sec. 11. Clinical investigations.
Sec. 12. Manufacturing changes for drugs.
Sec. 13. Streamlining clinical research on drugs.
Sec. 14. Data requirements for drugs.
Sec. 15. Content and review of applications.
Sec. 16. Scientific advisory panels.
Sec. 17. Dispute resolution.
Sec. 18. Informal agency statements.
Sec. 19. Positron emission tomography.
Sec. 20. Requirements for radiopharmaceuticals.
Sec. 21. Modernization of regulation.
Sec. 22. Pilot and small scale manufacture.
Sec. 23. Insulin and antibiotics.
Sec. 24. FDA mission and annual report.
Sec. 25. Information system.
Sec. 26. Education and training.
Sec. 27. Centers for education and research on drugs.
Sec. 28. Harmonization.
Sec. 29. Environmental impact review.
Sec. 30. National uniformity.
Sec. 31. FDA study of mercury compounds in drugs and food.
Sec. 32. Notification of discontinuance of a life saving product.

SEC. 2. FEES RELATING TO DRUGS.

(a) **FINDINGS.**—Congress finds that—

(1) prompt approval of safe and effective new drugs and other therapies is critical to the improvement of the public health so that patients may enjoy the benefits provided by these therapies to treat and prevent illness and disease;

(2) the public health will be served by making additional funds available for the purpose of augmenting the resources of the Food and Drug Administration that are devoted to the process for review of human drug applications;

(3) the provisions added by the Prescription Drug User Fee Act of 1992 have been successful in substantially reducing review times for human drug applications and should be—

(A) reauthorized for an additional 5 years, with certain technical improvements; and

(B) carried out by the Food and Drug Administration with new commitments to implement more ambitious and comprehensive improvements in regulatory processes of the Food and Drug Administration; and

(4) the fees authorized by amendments made in this title will be dedicated toward expediting the drug development process and the review of human drug applications as set forth in the goals identified in the letters of _____, and _____, from the Secretary of Health and Human Services to the chairman of the Committee on Commerce of the House of Representatives and the chairman of the Committee on Labor and Human Resources of the Senate, as set forth at ____ Cong. Rec. _____ (daily ed. _____, 1997).

(b) **DEFINITIONS.**—Section 735 (21 U.S.C. 379g) is amended—

(1) in the second sentence of paragraph (1)—

(A) by striking “Service Act, and” and inserting “Service Act,”; and

(B) by striking “September 1, 1992.” and inserting the following: “September 1, 1992, does not include an application for a licensure of a biological product for further manufacturing use only, and does not include an application or supplement submitted by a State or Federal Government entity for a drug that is not distributed commercially. Such term does include an application for licensure, as described in subparagraph (D), of a large volume biological product intended for single dose injection for intravenous use or infusion.”;

(2) in the second sentence of paragraph (3)—

(A) by striking “Service Act, and” and inserting “Service Act.”; and

(B) by striking “September 1, 1992.” and inserting the following: “September 1, 1992, does not include a biological product that is licensed for further manufacturing use only, and does not include a drug that is not distributed commercially and is the subject of an application or supplement submitted by a State or Federal Government entity. Such term does include a large volume biological product intended for single dose injection for intravenous use or infusion.”;

(3) in paragraph (4), by striking “without” and inserting “without substantial”;

(4) by amending the first sentence of paragraph (5) to read as follows:

“(5) The term ‘prescription drug establishment’ means a foreign or domestic place of business which is at one general physical location consisting of one or more buildings all of which are within 5 miles of each other and at which one or more prescription drug products are manufactured in final dosage form.”.

(5) in paragraph (7)(A)—

(A) by striking “employees under contract” and all that follows through “Administration,” the second time it occurs and inserting “contractors of the Food and Drug Administration.”; and

(B) by striking “and committees,” and inserting “and committees and to contracts with such contractors.”;

(6) in paragraph (8)—

(A) in subparagraph (A)—

(i) by striking “August of” and inserting “April of”; and

(ii) by striking “August 1992” and inserting “April 1997”;

(B) in subparagraph (B), by striking “1992” and inserting “1997”; and

(C) by striking the second sentence; and

(7) by adding at the end the following:

“(9) The term ‘affiliate’ means a business entity that has a relationship with a second business entity if, directly or indirectly—

“(A) one business entity controls, or has the power to control, the other business entity; or

“(B) a third party controls, or has power to control, both of the business entities.”.

(c) AUTHORITY TO ASSESS AND USE DRUG FEES.—

(1) TYPES OF FEES.—Section 736(a) (21 U.S.C. 379h(a)) is amended—

(A) by striking “Beginning in fiscal year 1993” and inserting “Beginning in fiscal year 1998”;

(B) in paragraph (1)—

(i) by striking subparagraph (B) and inserting the following:

“(B) PAYMENT.—The fee required by subparagraph (A) shall be due upon submission of the application or supplement.”;

(ii) in subparagraph (D)—

(I) in the subparagraph heading, by striking “NOT ACCEPTED” and inserting “REFUSED”;

(II) by striking “50 percent” and inserting “75 percent”;

(III) by striking “subparagraph (B)(i)” and inserting “subparagraph (B)”;

(IV) by striking “not accepted” and inserting “refused”; and

(iii) by adding at the end the following:

“(E) EXCEPTION FOR DESIGNATED ORPHAN DRUG OR INDICATION.—A human drug application for a prescription drug product that has been designated as a drug for a rare disease or condition pursuant to section 526 shall not be subject to a fee under subparagraph (A), unless the human drug application includes indications for other than rare diseases or conditions. A supplement proposing to include a new indication for a rare disease or condition in a human drug application shall not be subject to a fee under subparagraph (A), if the drug has been designated pursuant to section 526 as

a drug for a rare disease or condition with regard to the indication proposed in such supplement.

“(F) EXCEPTION FOR SUPPLEMENTS FOR PEDIATRIC INDICATIONS.—A supplement to a human drug application for an indication for use in pediatric populations shall not be assessed a fee under subparagraph (A).

“(G) REFUND OF FEE IF APPLICATION WITHDRAWN.—If an application or supplement is withdrawn after the application or supplement is filed, the Secretary may waive and refund the fee or a portion of the fee if no substantial work was performed on the application or supplement after the application or supplement was filed. The Secretary shall have the sole discretion to waive and refund a fee or a portion of the fee under this subparagraph. A determination by the Secretary concerning a waiver or refund under this paragraph shall not be reviewable.”;

(C) by striking paragraph (2) and inserting in lieu the following:

“(2) PRESCRIPTION DRUG ESTABLISHMENT FEE.—

“(A) IN GENERAL.—Except as provided in subparagraph (B), each person that is named as the applicant in a human drug application, and after September 1, 1992, had pending before the Secretary a human drug application or supplement, shall be assessed an annual fee established in subsection (b) for each prescription drug establishment listed in its approved human drug application as an establishment that manufactures the prescription drug product named in the application. The annual establishment fee shall be assessed in each fiscal year in which the prescription drug product named in the application is assessed a fee under paragraph (3) unless the prescription drug establishment listed in the application does not engage in the manufacture of the prescription drug product during the fiscal year. The establishment fee shall be payable on or before January 31 of each year. Each such establishment shall be assessed only one fee per establishment, notwithstanding the number of prescription drug products manufactured at the establishment. In the event an establishment is listed in a human drug application by more than 1 applicant, the establishment fee for the fiscal year shall be divided equally and assessed among the applicants whose prescription drug products are manufactured by the establishment during the fiscal year and assessed product fees under paragraph (3).

“(B) EXCEPTION.—If, during the fiscal year, an applicant initiates or causes to be initiated the manufacture of a prescription drug product at an establishment listed in its human drug application—

“(i) that did not manufacture the product in the previous fiscal year;

and

“(ii) for which the full establishment fee has been assessed in the fiscal year at a time before manufacture of the prescription drug product was begun;

the applicant will not be assessed a share of the establishment fee for the fiscal year in which the manufacture of the product began.”.

(D) in paragraph (3)—

(i) in subparagraph (A)—

(I) in clause (i), by striking “is listed” and inserting “has been submitted for listing”; and

(II) by striking “Such fee shall be paid” and all that follows through “section 510.” and inserting the following: “Such fee shall be payable for the fiscal year in which the product is first submitted for listing under section 510, or for relisting under section 510 if the product has been withdrawn from listing and relisted. After such fee is paid for that fiscal year, such fee shall be payable on or before January 31 of each year. Such fee shall be paid only once for each product for a fiscal year in which the fee is payable.”; and

(ii) in subparagraph (B), by striking “505(j).” and inserting the following: “505(j), under an abbreviated application filed under section 507, or under an abbreviated new drug application pursuant to regulations in effect prior to the implementation of the Drug Price Competition and Patent Term Restoration Act of 1984.”.

(2) FEE AMOUNTS.—Section 736(b) (21 U.S.C. 379h(b)) is amended to read as follows:

“(b) FEE AMOUNTS.—Except as provided in subsections (c), (d), (f), and (g), the fees required under subsection (a) shall be determined and assessed as follows:

“(1) APPLICATION AND SUPPLEMENT FEES.—

“(A) FULL FEES.—The application fee under subsection (a)(1)(A)(i) shall be \$250,704 in fiscal year 1998, \$256,338 in each of fiscal years 1999 and 2000, \$267,606 in fiscal year 2001, and \$258,451 in fiscal year 2002.

“(B) OTHER FEES.—The fee under subsection (a)(1)(A)(ii) shall be \$125,352 in fiscal year 1998, \$128,169 in each of fiscal years 1999 and 2000, \$133,803 in fiscal year 2001, and \$129,226 in fiscal year 2002.

“(2) FEE REVENUES FOR ESTABLISHMENT FEES.—The total fee revenues to be collected in establishment fees under subsection (a)(2) shall be \$35,600,000 in fiscal year 1998, \$36,400,000 in each of fiscal years 1999 and 2000, \$38,000,000 in fiscal year 2001, and \$36,700,000 in fiscal year 2002.

“(3) TOTAL FEE REVENUES FOR PRODUCT FEES.—The total fee revenues to be collected in product fees under subsection (a)(3) in a fiscal year shall be equal to the total fee revenues collected in establishment fees under subsection (a)(2) in that fiscal year.”.

(3) INCREASES AND ADJUSTMENTS.—Section 736(c) (21 U.S.C. 379h(c)) is amended—

(A) in the subsection heading, by striking “INCREASES AND”;

(B) in paragraph (1)—

(i) by striking “(1) REVENUE” and all that follows through “increased by the Secretary” and inserting the following: “(1) INFLATION ADJUSTMENT.—The fees and total fee revenues established in subsection (b) shall be adjusted by the Secretary”;

(ii) in subparagraph (A), by striking “increase” and inserting “change”;

(iii) in subparagraph (B), by striking “increase” and inserting “change”; and

(iv) by adding at the end the following flush sentence:

“The adjustment made each fiscal year by this subsection will be added on a compounded basis to the sum of all adjustments made each fiscal year after fiscal year 1997 under this subsection.”;

(C) in paragraph (2), by striking “October 1, 1992,” and all that follows through “such schedule.” and inserting the following: “September 30, 1997, adjust the establishment and product fees described in subsection (b) for the fiscal year in which the adjustment occurs so that the revenues collected from each of the categories of fees described in paragraphs (2) and (3) of subsection (b) shall be set to be equal to the revenues collected from the category of application and supplement fees described in paragraph (1) of subsection (b).”; and

(D) in paragraph (3), by striking “paragraph (2)” and inserting “this subsection”.

(4) FEE WAIVER OR REDUCTION.—Section 736(d) (21 U.S.C. 379h(d)) is amended—

(A) by redesignating paragraphs (1), (2), (3), and (4) as subparagraphs (A), (B), (C), and (D), respectively and indenting appropriately;

(B) by striking “The Secretary shall grant a” and all that follows through “finds that—” and inserting the following:

“(1) IN GENERAL.—The Secretary shall grant a waiver from or a reduction of one or more fees assessed under subsection (a) where the Secretary finds that—”;

(C) in subparagraph (C) (as so redesignated by subparagraph (A)), by striking “, or” and inserting a comma;

(D) in subparagraph (D) (as so redesignated by subparagraph (A)), by striking the period and inserting “, or”;

(E) by inserting after subparagraph (D) (as so redesignated by subparagraph (A)) the following:

“(E) the applicant is a small business submitting its first human drug application to the Secretary for review.”; and

(F) by striking “In making the finding in paragraph (3),” and all that follows through “standard costs.” and inserting the following:

“(2) USE OF STANDARD COSTS.—In making the finding in paragraph (1)(C), the Secretary may use standard costs.

“(3) RULES RELATING TO SMALL BUSINESSES.—

“(A) DEFINITION.—In paragraph (1)(E), the term ‘small business’ means an entity that has fewer than 500 employees, including employees of affiliates.

“(B) WAIVER OF APPLICATION FEE.—The Secretary shall waive under paragraph (1)(E) the application fee for the first human drug application that a small business or its affiliate submits to the Secretary for review. After

a small business or its affiliate is granted such a waiver, the small business or its affiliate shall pay—

“(i) application fees for all subsequent human drug applications submitted to the Secretary for review in the same manner as an entity that does not qualify as a small business; and

“(ii) all supplement fees for all supplements to human drug applications submitted to the Secretary for review in the same manner as an entity that does not qualify as a small business.”.

(5) ASSESSMENT OF FEES.—Section 736(f)(1) (21 U.S.C. 379h(f)(1)) is amended—

(A) by striking “fiscal year 1993” and inserting “fiscal year 1997”; and

(B) by striking “fiscal year 1992” and inserting “fiscal year 1997 (excluding the amount of fees appropriated for such fiscal year)”.

(6) CREDITING AND AVAILABILITY OF FEES.—Section 736(g) (21 U.S.C. 379h(g)) is amended—

(A) in paragraph (1), by adding at the end the following: “Such sums as may be necessary may be transferred from the Food and Drug Administration salaries and expenses appropriation account without fiscal year limitation to such appropriation account for salaries and expenses with such fiscal year limitation. The sums transferred shall be available solely for the process for the review of human drug applications within the meaning of section 735(6).”;

(B) in paragraph (2)—

(i) in subparagraph (A), by striking “Acts” and inserting “Acts, or otherwise made available for obligation.”; and

(ii) in subparagraph (B), by striking “over such costs for fiscal year 1992” and inserting “over such costs, excluding costs paid from fees collected under this section, for fiscal year 1997”; and

(C) by striking paragraph (3) and inserting the following:

“(3) AUTHORIZATION OF APPROPRIATIONS.—There is authorized to be appropriated for fees under this section—

“(A) \$106,800,000 for fiscal year 1998;

“(B) \$109,200,000 for fiscal year 1999;

“(C) \$109,200,000 for fiscal year 2000;

“(D) \$114,000,000 for fiscal year 2001; and

“(E) \$110,100,000 for fiscal year 2002,

as adjusted to reflect adjustments in the total fee revenues made under this section and changes in the total amounts collected by application, supplement, establishment, and product fees.

“(4) OFFSET.—Any amount of fees collected for a fiscal year which exceeds the amount of fees specified in appropriation Acts for such fiscal year shall be credited to the appropriation account of the Food and Drug Administration as provided in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be authorized to be collected under appropriation Acts for a subsequent fiscal year.”.

(7) REQUIREMENT FOR WRITTEN REQUESTS FOR WAIVERS, REDUCTIONS, AND FEES.—Section 736 (21 U.S.C. 379h) is amended—

(A) by redesignating subsection (i) as subsection (j); and

(B) by inserting after subsection (h) the following:

“(i) WRITTEN REQUESTS FOR WAIVERS, REDUCTIONS, AND REFUNDS.—To qualify for consideration for a waiver or reduction under subsection (d), or for a refund of any fee collected in accordance with subsection (a), a person shall submit to the Secretary a written request for such waiver, reduction, or refund not later than 180 days after such fee is due.”.

(8) SPECIAL RULE FOR WAIVER, REFUNDS, AND EXCEPTIONS.—Any requests for waivers, refunds, or exceptions for fees assessed prior to the date of enactment of this Act shall be submitted in writing to the Secretary of Health and Human Services within 1 year after the date of enactment of this Act.

(d) ANNUAL REPORTS.—

(1) PERFORMANCE REPORT.—Beginning with fiscal year 1998, not later than 60 days after the end of each fiscal year during which fees are collected under part 2 of subchapter C of chapter VII of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379g et seq.), the Secretary of Health and Human Services shall prepare and submit to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report concerning the progress of the Food and Drug Administration in achieving the goals identified in the letter described in subsection (a)(4) during such fiscal

year and the future plans of the Food and Drug Administration for meeting the goals.

(2) FISCAL REPORT.—Beginning with fiscal year 1998, not later than 120 days after the end of each fiscal year during which fees are collected under the part described in subsection (a), the Secretary of Health and Human Services shall prepare and submit to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate a report on the implementation of the authority for such fees during such fiscal year and the use, by the Food and Drug Administration, of the fees collected during such fiscal year for which the report is made.

(e) EFFECTIVE DATE.—The amendments made by this section shall take effect October 1, 1997.

(f) TERMINATION OF EFFECTIVENESS.—The amendments made by subsections (b) and (c) cease to be effective October 1, 2002, and subsection (d) ceases to be effective 120 days after such date.

SEC. 3. PEDIATRIC STUDIES OF DRUGS.

Chapter V (21 U.S.C. 351 et seq.) is amended by inserting after section 505 the following:

“PEDIATRIC STUDIES OF DRUGS

“SEC. 505A. (a) MARKET EXCLUSIVITY FOR NEW DRUGS.—If, prior to approval of an application that is submitted under section 505(b)(1), the Secretary determines that information relating to the use of a drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), and such studies are completed within any such timeframe and the reports thereof submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)—

“(1)(A) the period during which an application may not be submitted under subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of section 505 shall be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of section 505 to four years, to forty-eight months, and to seven and one-half years shall be deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

“(B) the period of market exclusivity under subsections (c)(3)(D)(iii) and (iv) and (j)(4)(D)(iii) and (iv) of section 505 shall be three years and six months rather than three years; and

“(2)(A) if the drug is the subject of—

“(i) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

“(ii) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

“(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

“(b) SECRETARY TO DEVELOP LIST OF DRUGS FOR WHICH ADDITIONAL PEDIATRIC INFORMATION MAY BE BENEFICIAL.—Not later than 180 days after the date of enactment of this section, the Secretary, after consultation with experts in pediatric research shall develop, prioritize, and publish an initial list of approved drugs for which additional pediatric information may produce health benefits in the pediatric population. The Secretary shall annually update the list.

“(c) MARKET EXCLUSIVITY FOR ALREADY-MARKETED DRUGS.—If the Secretary makes a written request to the holder of an approved application under section 505(b)(1) for pediatric studies (which shall include a timeframe for completing such studies) concerning a drug identified in the list described in subsection (b), the holder agrees to the request, the studies are completed within any such timeframe and the reports thereof are submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)—

“(1)(A) the period during which an application may not be submitted under subsection (c)(3)(D)(ii) or (j)(4)(D)(ii) of section 505 shall be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of section 505 to four years, to forty-eight months, and to seven and one-half years shall be deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

“(B) the period of market exclusivity under subsections (c)(3)(D)(iii) and (iv) and (j)(4)(D)(iii) and (iv) of section 505 shall be three years and six months rather than three years; and

“(2)(A) if the drug is the subject of—

“(i) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

“(ii) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

“(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

“(d) CONDUCT OF PEDIATRIC STUDIES.—

“(1) AGREEMENT FOR STUDIES.—The Secretary may, pursuant to a written request for studies, after consultation with—

“(A) the sponsor of an application for an investigational new drug under section 505(i);

“(B) the sponsor of an application for a drug under section 505(b)(1); or

“(C) the holder of an approved application for a drug under section 505(b)(1),

agree with the sponsor or holder for the conduct of pediatric studies for such drug.

“(2) WRITTEN PROTOCOLS TO MEET THE STUDIES REQUIREMENT.—If the sponsor or holder and the Secretary agree upon written protocols for the studies, the studies requirement of subsection (a) or (c) is satisfied upon the completion of the studies and submission of the reports thereof in accordance with the original written request and the written agreement referred to in paragraph (1). Not later than 60 days after the submission of the report of the studies, the Secretary shall accept or reject such studies were or were not conducted in accordance with the original written request and the written agreement and reported in accordance with the requirements of the Secretary for filing and so notify the sponsor or holder.

“(3) OTHER METHODS TO MEET THE STUDIES REQUIREMENT.—If the sponsor or holder and the Secretary have not agreed in writing on the protocols for the studies, the studies requirement of subsection (a) or (c) is satisfied when such studies have been completed and the reports accepted by the Secretary. Not later than 90 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary’s only responsibility in accepting or rejecting the reports shall be to determine, within the 90 days, whether the studies fairly respond to the written request, whether such studies have been conducted in accordance with commonly accepted scientific principles and protocols, and whether such studies have been reported in accordance with the requirements of the Secretary for filing.

“(e) DELAY OF EFFECTIVE DATE FOR CERTAIN APPLICATIONS; PERIOD OF MARKET EXCLUSIVITY.—If the Secretary determines that the acceptance or approval of an application under section 505(b)(2) or 505(j) for a drug may occur after submission of reports of pediatric studies under this section, which were submitted prior to the expiration of the patent (including any patent extension) or market exclusivity protection, but before the Secretary has determined whether the requirements of subsection (d) have been satisfied, the Secretary shall delay the acceptance or approval under section 505(b)(2) or 505(j), respectively, until the determination under subsection (d) is made, but such delay shall not exceed 90 days. In the event that requirements of this section are satisfied, the applicable period of market exclusivity

referred to in subsection (a) or (c) shall be deemed to have been running during the period of delay.

“(f) NOTICE OF DETERMINATIONS ON STUDIES REQUIREMENT.—The Secretary shall publish a notice of any determination that the requirements of subsection (d) have been met and that submissions and approvals under section 505(b)(2) or (j) for a drug will be subject to the provisions of this section.

“(g) DEFINITIONS.—As used in this section, the term ‘pediatric studies’ or ‘studies’ means at least one clinical investigation (that, at the Secretary’s discretion, may include pharmacokinetic studies) in pediatric age groups in which a drug is anticipated to be used.

“(h) LIMITATION.—The holder of an approved application for a new drug that has already received six months of market exclusivity under subsection (a) or (c) may, if otherwise eligible, obtain six months of market exclusivity under subsection (c)(1)(B) for a supplemental application, except that the holder is not eligible for exclusivity under subsection (c)(2).

“(i) RELATIONSHIP TO REGULATIONS.—Notwithstanding any other provision of law, if any pediatric study is required pursuant to regulations promulgated by the Secretary, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.

“(j) SUNSET.—No period of market exclusivity shall be granted under this section based on studies commenced after January 1, 2002. The Secretary shall conduct a study and report to Congress not later than January 1, 2001, based on the experience under the program. The study and report shall examine all relevant issues, including—

“(1) the effectiveness of the program in improving information about important pediatric uses for approved drugs;

“(2) the adequacy of the incentive provided under this section;

“(3) the economic impact of the program on taxpayers and consumers, including the impact of the lack of lower cost generic drugs on lower income patients; and

“(4) any suggestions for modification that the Secretary deems appropriate.”.

SEC. 4. EXPEDITING STUDY AND APPROVAL OF FAST TRACK DRUGS.

(a) IN GENERAL.—Chapter VII is amended by adding at the end the following:

“SUBCHAPTER D—FAST TRACK PRODUCTS

“SEC. 741. FAST TRACK PRODUCTS.

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

“(1) IN GENERAL.—The Secretary shall facilitate the development and expedite the review of new drugs that are intended for the treatment of serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs for such conditions. In this section, such products shall be known as ‘fast track products’.

“(2) REQUEST FOR DESIGNATION.—The sponsor of a 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)(4) of the Public Health Service Act.

“(3) DESIGNATION.—Within 30 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) APPROVAL OF APPLICATION FOR A FAST TRACK PRODUCT.—

“(1) IN GENERAL.—The Secretary may approve an application for approval of a fast track product under section 505(b) or section 351 of the Public Health Service Act (21 U.S.C. 262) upon a determination that the product has an effect on a clinical endpoint or a surrogate endpoint that is reasonably likely to predict clinical benefit.

“(2) LIMITATION.—Approval of a fast track product under this subsection may be subject to the requirements—

“(A) that the sponsor conduct appropriate post-approval studies to validate the surrogate endpoint or otherwise confirm the effect on the clinical endpoint; and

“(B) that the sponsor submit copies of all promotional materials related to the fast track product during the preapproval review period and, following approval and for such period thereafter as the Secretary deems appropriate, at least 30 days prior to dissemination of the materials.

“(3) EXPEDITED WITHDRAWAL OF APPROVAL.—The Secretary may withdraw approval of a fast track product 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 fast track drug with due diligence;

“(B) a post-approval study of the fast track product fails to verify clinical benefit of the product;

“(C) other evidence demonstrates that the fast track 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 Secretary 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 applicable to fast track products established under this section; and

“(2) establish a program to encourage the development of surrogate endpoints that are reasonably likely to predict clinical benefit for serious or life-threatening conditions for which there exist significant unmet medical needs.”

(b) GUIDANCE.—Within 1 year after the date of enactment of this Act, the Secretary shall issue guidance for fast track products (as defined in section 741(a)(1) of the Federal Food, Drug, and Cosmetic Act) that describes the policies and procedures that pertain to section 741 of such Act.

SEC. 5. EXPANDED ACCESS TO INVESTIGATIONAL THERAPIES.

Chapter V (21 U.S.C. 351 et seq.) is amended by adding at the end the following:

“SUBCHAPTER D—UNAPPROVED THERAPIES AND DIAGNOSTICS

“**SEC. 551. EXPANDED ACCESS TO UNAPPROVED THERAPIES AND DIAGNOSTICS.**

“(a) EMERGENCY SITUATIONS.—The Secretary may, under appropriate conditions determined by the Secretary, authorize the shipment of investigational drugs (as defined in regulations prescribed by the Secretary) for the diagnosis or treatment of a serious disease or condition in emergency situations.

“(b) INDIVIDUAL PATIENT ACCESS TO INVESTIGATIONAL PRODUCTS INTENDED FOR SERIOUS DISEASES.—Any person, acting through a physician licensed in accordance with State law, may request from a manufacturer or distributor, and any manufacturer or distributor may provide to such physician after compliance with the provisions of this subsection, an investigational drug (as defined in regulations prescribed by the Secretary) for the diagnosis or treatment of a serious disease or condition if—

“(1) the licensed physician determines that the person has no comparable or satisfactory alternative therapy available to diagnose or treat the disease or condition involved, and that the risk to the person from the investigational drug is not greater than the risk from the disease or condition;

“(2) the Secretary determines that there is sufficient evidence of safety and effectiveness to support the use of the investigational drug in the case described in paragraph (1);

“(3) the Secretary determines that provision of the investigational drug will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval; and

“(4) the sponsor, or clinical investigator, of the investigational drug submits to the Secretary a clinical protocol consistent with the provisions of section 505(i) and any regulations promulgated under section 505(i) describing the use of investigational drugs in a single patient or a small group of patients.

“(c) TREATMENT INDS.—Upon submission by a sponsor or a physician of a protocol intended to provide widespread access to an investigational drug for eligible patients, the Secretary shall permit such investigational drug to be made available for expanded access under a treatment investigational new drug application if the Secretary determines that—

“(1) under the treatment investigational new drug application, the investigational drug is intended for use in the diagnosis or treatment of a serious or immediately life-threatening disease or condition;

“(2) there is no comparable or satisfactory alternative therapy available to diagnose or treat that stage of disease or condition in the population of patients to which the investigational drug is intended to be administered;

“(3)(A) the investigational drug is under investigation in a controlled clinical trial for the use described in paragraph (1) under an effective investigational new drug application; or

“(B) all clinical trials necessary for approval of that use of the investigational drug have been completed;

“(4) the sponsor of the controlled clinical trials is actively pursuing marketing approval of the investigational drug for the use described in paragraph (1) with due diligence;

“(5) the provision of the investigational drug will not interfere with the enrollment of patients in ongoing clinical investigations under section 505(i);

“(6) in the case of serious diseases, there is sufficient evidence of safety and effectiveness to support the use described in paragraph (1); and

“(7) in the case of immediately life-threatening diseases, the available scientific evidence, taken as a whole, provides a reasonable basis to conclude that the product may be effective for its intended use and would not expose patients to an unreasonable and significant risk of illness or injury.

A protocol submitted under this subsection shall be subject to the provisions of section 505(i) and regulations promulgated under section 505(i). The Secretary may inform national, State, and local medical associations and societies, voluntary health associations, and other appropriate persons about the availability of an investigational drug under expanded access protocols submitted under this subsection. The information provided by the Secretary, in accordance with the preceding sentence, shall be of the same type of information that is required by section 402(j)(3) of the Public Health Service Act.

“(d) TERMINATION.—The Secretary may, at any time, with respect to a sponsor, physician, manufacturer, or distributor described in this section, terminate expanded access provided under this section for an investigational drug if the requirements under this section are no longer met.”

SEC. 6. INFORMATION PROGRAM ON CLINICAL TRIALS FOR SERIOUS OR LIFE-THREATENING DISEASES.

(a) IN GENERAL.—Section 402 of the Public Health Service Act (42 U.S.C. 282) is amended—

(1) by redesignating subsections (j) and (k) as subsections (k) and (l), respectively; and

(2) by inserting after subsection (i), the following:

“(j)(1) The Secretary, acting through the Director of the National Institutes of Health, shall establish, maintain, and operate a program with respect to information on research relating to the treatment, detection, and prevention of serious or life-threatening diseases and conditions. The program shall, with respect to the agencies of the Department of Health and Human Services, be integrated and coordinated, and, to the extent practicable, coordinated with other data banks containing similar information.

“(2)(A) After consultation with the Commissioner of Food and Drugs, the directors of the appropriate agencies of the National Institutes of Health (including the National Library of Medicine), and the Director of the Centers for Disease Control and Prevention, the Secretary shall, in carrying out paragraph (1), establish a data bank

of information on clinical trials for drugs for serious or life-threatening diseases and conditions.

“(B) In carrying out subparagraph (A), the Secretary shall collect, catalog, store, and disseminate the information described in such subparagraph. The Secretary shall disseminate such information through information systems, which shall include toll-free telephone communications, available to individuals with serious or life-threatening diseases and conditions, to other members of the public, to health care providers, and to researchers.

“(3) The data bank shall include the following:

“(A) A registry of clinical trials (whether federally or privately funded) of experimental treatments for serious or life-threatening diseases and conditions under regulations promulgated pursuant to sections 505 of the Federal Food, Drug, and Cosmetic Act that provides a description of the purpose of each experimental drug, either with the consent of the protocol sponsor, or when a trial to test effectiveness begins. Information provided shall consist of eligibility criteria, a description of the location of trial sites, and a point of contact for those wanting to enroll in the trial, and shall be in a form that can be readily understood by members of the public. Such information must be forwarded to the data bank by the sponsor of the trial not later than 21 days after trials to test clinical effectiveness have begun.

“(B) Information pertaining to experimental treatments for serious or life-threatening diseases and conditions that may be available—

“(i) under a treatment investigational new drug application that has been submitted to the Food and Drug Administration under section 551(c) of the Federal Food, Drug, and Cosmetic Act; or

“(ii) as a Group C cancer drug (as defined by the National Cancer Institute).

The data bank may also include information pertaining to the results of clinical trials of such treatments, with the consent of the sponsor, including information concerning potential toxicities or adverse effects associated with the use or administration of such experimental treatments.

“(4) The data bank shall not include information relating to an investigation if the sponsor has provided a detailed certification to the Secretary that disclosure of such information would substantially interfere with the timely enrollment of subjects in the investigation, unless the Secretary, after the receipt of the certification, provides the sponsor with a detailed written determination that such disclosure would not substantially interfere with such enrollment.

“(5) For the purpose of carrying out this subsection, there are authorized to be appropriated such sums as may be necessary. Fees collected under section 736 of the Federal Food, Drug, and Cosmetic Act shall not be used in carrying out this subsection.”

(b) COLLABORATION AND REPORT.—

(1) IN GENERAL.—The Secretary of Health and Human Services, the Director of the National Institutes of Health, and the Commissioner of Food and Drugs shall collaborate to determine the feasibility of including device investigations within the scope of the registry requirements set forth in section 402(j) of the Public Health Service Act.

(2) REPORT.—Not later than 2 years after the date of enactment of this section, the Secretary of Health and Human Services shall prepare and submit to the Committee on Labor and Human Resources of the Senate and the Committee on Commerce of the House of Representatives a report—

(A) of the public health need, if any, for inclusion of device investigations within the scope of the registry requirements set forth in section 402(j) of the Public Health Service Act;

(B) on the adverse impact, if any, on device innovation and research in the United States if information relating to such device investigation is required to be publicly disclosed; and

(C) on such other issues relating to such section 402(j) as the Secretary may deem appropriate.

SEC. 7. DISSEMINATION OF INFORMATION ON NEW USES.

(a) IN GENERAL.—Chapter VII (21 U.S.C. 371 et seq.), as amended by section 4, is amended by adding at the end the following:

“SUBCHAPTER E—DISSEMINATION OF TREATMENT INFORMATION

“SEC. 745. REQUIREMENTS FOR DISSEMINATION OF TREATMENT INFORMATION ON DRUGS.

“(a) IN GENERAL.—Notwithstanding sections 301(d), 502(f), and 505 and section 351 of the Public Health Service Act (42 U.S.C. 262), a manufacturer may disseminate to—

- “(1) a health care practitioner,
- “(2) a pharmacy benefit manager,
- “(3) a health insurance issuer,
- “(4) a group health plan, or
- “(5) a Federal or State governmental agency,

written information concerning the safety, effectiveness, or benefit of a use not described in the approved labeling of a drug if the manufacturer meets the requirements of subsection (b).

“(b) SPECIFIC REQUIREMENTS.—A manufacturer may disseminate information about a new use of a drug under subsection (a) only if—

- “(1) there is in effect for such drug an application filed under section 505(b) or a biologics license issued under section 351 of the Public Health Service Act;
- “(2) the information meets the requirements of section 746;
- “(3) the information to be disseminated is not derived from clinical research conducted by another manufacturer or if it was derived from research conducted by another manufacturer, the manufacturer disseminating the information has the permission of such other manufacturer to make the dissemination;
- “(4) the manufacturer has, 60 days before such dissemination, submitted to the Secretary—

- “(A) a copy of the information disseminated; and
- “(B) any clinical trial information the manufacturer has relating to the safety or effectiveness of the new use, any reports of clinical experience pertinent to the safety of the new use, and a summary of such information;
- “(5) the manufacturer has complied with the requirements of section 748 (relating to certification that the manufacturer will submit a supplemental application with respect to such use);
- “(6) the manufacturer agrees to include along with the information disseminated under this subsection—

- “(A) a prominently displayed statement that discloses—
 - “(i) that the information concerns a use of a drug that has not been approved by the Food and Drug Administration;
 - “(ii) if applicable, that the information is being disseminated at the expense of the manufacturer;
 - “(iii) if applicable, the name of any authors of the information who are employees of, consultants to, or have received compensation from, the manufacturer, or who have a significant financial interest in the manufacturer;
 - “(iv) the official labeling for the drug and all updates with respect to the labeling;
 - “(v) if applicable, a statement that there are products or treatments that have been approved for the use that is the subject of the information being disseminated pursuant to subsection (a)(1); and
 - “(vi) the identification of any person that has provided funding for the conduct of a study relating to the new use of a drug for which such information is being disseminated; and
- “(B) a bibliography of other articles from a scientific reference publication or scientific or medical journal that have been previously published about the such use of the drug covered by the information disseminated (unless the information already includes such bibliography).

“(c) ADDITIONAL INFORMATION.—If the Secretary determines, after providing notice of such determination and an opportunity for a meeting with respect to such determination, that the information submitted by a manufacturer under subsection (b)(3)(B), with respect to the use of a drug for which the manufacturer is disseminating information, fails to provide data, analyses, or other written matter that is objective and balanced, the Secretary may require the manufacturer to disseminate—

- “(1) additional objective and scientifically sound information that pertains to the safety or effectiveness of the use and is necessary to provide objectivity and balance, including any information that the manufacturer has submitted to the Secretary or, where appropriate, a summary of such information or any other information that the Secretary has authority to make available to the public; and

“(2) an objective statement of the Secretary, based on data or other scientifically sound information available to the Secretary, that bears on the safety or effectiveness of the new use of the drug.

“SEC. 746. INFORMATION AUTHORIZED TO BE DISSEMINATED.

“(a) AUTHORIZED INFORMATION.—A manufacturer may disseminate the information on the new use of a drug under section 745 only if the information—

“(1) is in the form of an unabridged—

“(A) reprint or copy of an article, peer-reviewed by experts qualified by scientific training or experience to evaluate the safety or effectiveness of the drug, which was published in a scientific or medical journal (as defined in section 750(6)), which is about a clinical investigation with respect to the drug, and which would be considered to be scientifically sound by such experts; or

“(B) reference publication, described in subsection (b), that includes information about a clinical investigation with respect to the drug that would be considered to be scientifically sound by experts qualified by scientific training or experience to evaluate the safety or effectiveness of the drug that is the subject of such a clinical investigation; and

“(2) is not false or misleading and would not pose a significant risk to the public health.

“(b) REFERENCE PUBLICATION.—A reference publication referred to in subsection (a)(1)(B) is a publication that—

“(1) has not been written, edited, excerpted, or published specifically for, or at the request of, a manufacturer of a drug;

“(2) has not been edited or significantly influenced by a such a manufacturer;

“(3) is not solely distributed through such a manufacturer but is generally available in bookstores or other distribution channels where medical textbooks are sold;

“(4) does not focus on any particular drug of a manufacturer that disseminates information under section 745 and does not have a primary focus on new uses of drugs that are marketed or under investigation by a manufacturer supporting the dissemination of information; and

“(5) presents materials that are not false or misleading.

“SEC. 747. ESTABLISHMENT OF LIST OF ARTICLES AND PUBLICATIONS DISSEMINATED AND LIST OF PROVIDERS THAT RECEIVED ARTICLES AND REFERENCE PUBLICATIONS.

“(a) IN GENERAL.—A manufacturer may disseminate information under section 745 only if the manufacturer prepares and submits to the Secretary biannually—

“(1) a list containing the titles of the articles and reference publications relating to the new use of drugs that were disseminated by the manufacturer to a person described in section 745(a) for the 6-month period preceding the date on which the manufacturer submits the list to the Secretary; and

“(2) a list that identifies the categories of providers (as described in section 745(a)) that received the articles and reference publications for the 6-month period described in paragraph (1).

“(b) RECORDS.—A manufacturer that disseminates information under section 745 shall keep records that may be used by the manufacturer when, pursuant to section 749, such manufacturer is required to take corrective action and shall be made available to the Secretary, upon request, for purposes of ensuring or taking corrective action pursuant to such section. Such records, at the Secretary’s discretion, may identify the recipient of information provided pursuant to section 745 or the categories of such recipients.

“SEC. 748. REQUIREMENT REGARDING SUBMISSION OF SUPPLEMENTAL APPLICATION FOR NEW USE; EXEMPTION FROM REQUIREMENT.

“(a) IN GENERAL.—A manufacturer may disseminate information under section 745 on a new use only if—

“(1) the manufacturer meets the condition described in subsection (b) or in subsection (c); or

“(2) there is in effect for the manufacturer an exemption under subsection (d) from the requirement of paragraph (1).

“(b) SUPPLEMENTAL APPLICATION; CONDITION IN CASE OF COMPLETED STUDIES.—For purposes of subsection (a)(1), a manufacturer may disseminate information on a new use if the manufacturer has submitted to the Secretary an application containing a certification that—

“(1) the studies needed for the submission of a supplemental application for the new use have been completed; and

“(2) the supplemental application will be submitted to the Secretary not later than 6 months after the date of the initial dissemination of information under section 745.

“(c) SUPPLEMENTAL APPLICATION; CONDITION IN CASE OF PLANNED STUDIES.—

“(1) IN GENERAL.—For purposes of subsection (a)(1), a manufacturer may disseminate information on a new use if—

“(A) the manufacturer has submitted to the Secretary an application containing—

“(i) a proposed protocol and schedule for conducting the studies needed for the submission of a supplemental application for the new use; and

“(ii) a certification that the supplemental application will be submitted to the Secretary not later than 36 months after the date of the initial dissemination of information under section 745 (or, as applicable, not later than such date as the Secretary may specify pursuant to an extension under this paragraph or paragraph (3)); and

“(B) the Secretary has determined that the proposed protocol is adequate and that the schedule for completing such studies is reasonable.

The Secretary may grant a longer period of time for a manufacturer to submit a supplemental application if the Secretary determines that the studies needed to submit such an application cannot be completed and submitted within 36 months.

“(2) PROGRESS REPORTS ON STUDIES.—A manufacturer that submits to the Secretary an application under paragraph (1) shall submit to the Secretary periodic reports describing the status of the studies involved.

“(3) EXTENSION OF TIME REGARDING PLANNED STUDIES.—The period of 36 months authorized in paragraph (1)(A)(ii) for the completion of studies may be extended by the Secretary if the manufacturer involved submits to the Secretary a written request for the extension and the Secretary determines that the manufacturer has acted with due diligence to conduct the studies in a timely manner. Such extension may not provide more than 24 additional months.

“(d) EXEMPTION FROM REQUIREMENT OF SUPPLEMENTAL APPLICATION.—

“(1) IN GENERAL.—For purposes of subsection (a)(2), a manufacturer may disseminate information on a new use if—

“(A) the manufacturer has submitted to the Secretary an application for an exemption from meeting the requirement of subsection (a)(1); and

“(B)(i) the Secretary has approved the application in accordance with paragraph (2); or

“(ii) the application is deemed under paragraph (3)(A) to have been approved (unless such approval is terminated pursuant to paragraph (3)(B)).

“(2) CONDITIONS FOR APPROVAL.—The Secretary may approve an application under paragraph (1) for an exemption only if the Secretary determines that—

“(A) it would be economically prohibitive with respect to such drug for the manufacturer to incur the costs necessary for the submission of a supplemental application for reasons, as defined by the Secretary, such as the lack of availability under law of any period during which the manufacturer would have exclusive marketing rights with respect to the new use involved or that the population expected to benefit from approval of the supplemental application is small; or

“(B) it would be unethical to conduct the studies necessary for the supplemental application for a reason such as the new use involved is the standard of medical care for a health condition.

“(3) TIME FOR CONSIDERATION OF APPLICATION; DEEMED APPROVAL.—

“(A) IN GENERAL.—The Secretary shall approve or deny an application under paragraph (1) for an exemption not later than 60 days after the receipt of the application. If the Secretary does not comply with the preceding sentence, the application is deemed to be approved.

“(B) TERMINATION OF DEEMED APPROVAL.—If pursuant to a deemed approval under subparagraph (A) a manufacturer disseminates written information under section 745 on a new use, the Secretary may at any time terminate such approval and under section 749(b)(3) order the manufacturer to cease disseminating the information.

“(e) REQUIREMENTS REGARDING APPLICATIONS.—Applications under this section shall be submitted in the form and manner prescribed by the Secretary.

“(f) TRANSITION RULE.—For purposes of this section, in any case in which a manufacturer has submitted to the Secretary a supplemental application for which action by the Secretary is pending as of the date of the enactment of the Prescription Drug User Fee Reauthorization and Drug and Biological Products Regulatory Moderniza-

tion Act of 1997, the application is deemed to be a supplemental application submitted under subsection (b).

“SEC. 749. CORRECTIVE ACTIONS; CESSATION OF DISSEMINATION.

“(a) POSTDISSEMINATION DATA REGARDING SAFETY AND EFFECTIVENESS.—

“(1) CORRECTIVE ACTIONS.—With respect to data received by the Secretary after the dissemination of information under section 745 by a manufacturer has begun (whether received pursuant to paragraph (2) or otherwise), if the Secretary determines that the data indicate that the new use involved may not be effective or may present a significant risk to public health, the Secretary shall, in consultation with the manufacturer, take such action regarding the dissemination of the information as the Secretary determines to be appropriate for the protection of the public health, which may include ordering that the manufacturer cease the dissemination of the information.

“(2) RESPONSIBILITIES OF MANUFACTURERS TO SUBMIT DATA.—After a manufacturer disseminates information pursuant to section 745, the manufacturer shall submit to the Secretary a notification of any additional knowledge of the manufacturer on clinical research or other data that relate to the safety or effectiveness of the new use involved. If the manufacturer is in possession of the data, the notification shall include the data. The Secretary shall by regulation establish the scope of the responsibilities of manufacturers under this paragraph, including such limits on the responsibilities as the Secretary determines to be appropriate.

“(b) CESSATION OF DISSEMINATION.—

“(1) FAILURE OF MANUFACTURER TO COMPLY WITH REQUIREMENTS.—The Secretary may order a manufacturer to cease the dissemination of information pursuant to section 745 if the Secretary determines that the information being disseminated does not comply with the requirements established in this subchapter. Such an order may be issued only after the Secretary has provided notice to the manufacturer of the intent of the Secretary to issue the order and has provided an opportunity for a meeting with respect to such intent unless paragraph (2)(B) applies. If the failure of the manufacturer constitutes a minor violation of this subchapter, the Secretary shall delay issuing the order and provide to the manufacturer an opportunity to correct the violation.

“(2) SUPPLEMENTAL APPLICATIONS.—The Secretary may order a manufacturer to cease the dissemination of information pursuant to section 745 if the Secretary determines that—

“(A) in the case of a manufacturer to which section 748(b) applies, the Secretary determines that the supplemental application received under such section does not contain adequate information for approval of the new use with respect to which the application was submitted; or

“(B) in the case of a manufacturer to which section 748(c) applies, the Secretary determines, after an informal hearing, that the manufacturer is not acting with due diligence to complete the studies involved.

“(3) TERMINATION OF DEEMED APPROVAL OF EXEMPTION REGARDING SUPPLEMENTAL APPLICATIONS.—If under section 748(d)(3) the Secretary terminates a deemed approval of an exemption, the Secretary may order the manufacturer involved to cease disseminating the information. A manufacturer shall comply with an order under the preceding sentence not later than 60 days after the receipt of the order.

“(c) CORRECTIVE ACTIONS BY MANUFACTURERS.—

“(1) IN GENERAL.—In any case in which under this section the Secretary orders a manufacturer to cease disseminating information, the Secretary may order the manufacturer to take action to correct the information that has been disseminated, except as provided in paragraph (2).

“(2) TERMINATION OF DEEMED APPROVAL OF EXEMPTION REGARDING SUPPLEMENTAL APPLICATIONS.—In the case of an order under subsection (b)(3) to cease disseminating information, the Secretary may not order the manufacturer involved to take action to correct the information that has been disseminated unless the Secretary determines that the new use described in the information would pose a significant risk to the public health.

“SEC. 750. DEFINITIONS.

“For purposes of this subchapter:

“(1) The term ‘health care practitioner’ means a physician, or other individual who is a provider of health care, who is licensed under the law of a State to prescribe drugs.

“(2) The terms ‘health insurance issuer’ and ‘group health plan’ have the meaning given such terms under section 2791 of the Public Health Service Act.

“(3) The term ‘manufacturer’ means a person who manufactures a drug, or who is licensed by such person to distribute or market the drug.

“(4) The term ‘new use’, with respect to a drug, means a use that is not included in the approved labeling of the drug.

“(5) The term ‘pharmacy benefit manager’ means an organization that—

“(A) manages pharmaceutical costs through—

“(i) pharmacy benefit administration, including claims processing adjudication, pharmacy networks, mail service, and data reporting;

“(ii) formulary management and contracting, including evaluating drugs for formulary status, negotiations of contracts with manufacturers, and disbursement of rebates; and

“(iii) utilization management, including communicating and enforcing therapy guidelines and drug use principles to physicians, pharmacists, and patients; and

“(B) serves 2 principal types of customers which are—

“(i) employers, both private- and public-sector, who use either self-funded health benefits through a third party administrator’s insurance carrier or use traditional indemnity coverage, using providers from a preferred provider network or in a fee-for-service capacity; and

“(ii) health maintenance organizations.

“(6) The term ‘scientific or medical journal’ means a scientific or medical publication—

“(A) that is published by an organization—

“(i) that has an editorial board;

“(ii) that utilizes experts, who have demonstrated expertise in the subject of an article under review by the organization and who are independent of the organization, to review and objectively select, reject, or provide comments about proposed articles; and

“(iii) that has a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interest or biases for all authors or contributors involved with the journal or organization;

“(B) whose articles are peer-reviewed and published in accordance with the regular peer-review procedures of the organization;

“(C) that is generally recognized to be of national scope and reputation;

“(D) that is indexed in the Index Medicus of the National Library of Medicine of the National Institutes of Health; and

“(E) that is not in the form of a special supplement that has been funded in whole or in part by 1 or more manufacturers.

“SEC. 751. RULES OF CONSTRUCTION.

“(a) UNSOLICITED REQUEST.—Nothing in section 745 shall be construed as prohibiting a manufacturer from disseminating information in response to an unsolicited request from a health care practitioner.

“(b) DISSEMINATION OF INFORMATION ON DRUGS NOT EVIDENCE OF INTENDED USE.—Notwithstanding subsection (a), (f), or (o) of section 502, or any other provision of law, the dissemination of information relating to a new use of a drug, in accordance with section 745, shall not be construed by the Secretary as evidence of a new intended use of the drug that is different from the intended use of the drug set forth in the official labeling of the drug. Such dissemination shall not be considered by the Secretary as labeling, adulteration, or misbranding of the drug.

“(c) PATENT PROTECTION.—Nothing in section 745 shall affect patent rights in any manner.

“(d) AUTHORIZATION FOR DISSEMINATION OF ARTICLES AND FEES FOR REPRINTS OF ARTICLES.—Nothing in section 745 shall be construed as prohibiting an entity that publishes a scientific journal (as defined in section 750(6)) from requiring authorization from the entity to disseminate an article published by such entity or charging fees for the purchase of reprints of published articles from such entity.”.

(b) PROHIBITED ACT.—Section 301 (21 U.S.C. 331) is amended by adding at the end the following:

“(x) The dissemination of information in violation of section 745.”.

(c) REGULATIONS.—Not later than 1 year after the date of enactment of this Act, the Secretary of Health and Human Services shall promulgate regulations to implement the amendments made by this section.

(d) EFFECTIVE DATE.—The amendments made by this section shall take effect 1 year after the date of enactment of this Act, or upon the Secretary’s issuance of final regulations pursuant to subsection (c), whichever is sooner.

(e) SUNSET.—The amendments made by this section cease to be effective September 30, 2006, or 7 years after the date on which the Secretary promulgates the regulations described in subsection (c), whichever is later.

SEC. 8. STUDIES AND REPORTS.

(a) IN GENERAL.—The Comptroller General of the United States shall conduct a study—

(1) to determine the impact of the amendments made by section 7 on the resources of the Department of Health and Human Services; and

(2) of the scientific issues raised as a result of the amendments made by section 7, including issues relating to—

(A) the effectiveness of such amendments with respect to the provision of useful scientific information to health care practitioners;

(B) the quality of the information being disseminated pursuant to such amendments;

(C) the quality and usefulness of the information provided, in accordance with such amendments, by the Secretary or by a manufacturer at the request of the Secretary; and

(D) the impact of such amendments on research in the area of new uses of drugs, indications for new uses, or dosages of drugs for new uses, particularly the impact on pediatric indications and rare diseases.

(b) REPORT.—Not later than January 1, 2002, the Comptroller General of the United States shall prepare and submit to the Committee on Labor and Human Resources of the Senate and the Committee on Commerce of the House of Representatives a report of the results of the study under subsection (a).

SEC. 9. APPROVAL OF SUPPLEMENTAL APPLICATIONS FOR APPROVED PRODUCTS.

(a) PERFORMANCE STANDARDS.—Not later than 180 days after the date of enactment of this Act, the Secretary shall publish in the Federal Register performance standards for the prompt review of supplemental applications submitted for approved drugs under the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321 et seq.) or section 351 of the Public Health Service Act (42 U.S.C. 262).

(b) GUIDANCE TO INDUSTRY.—Not later than 180 days after the date of enactment of this Act, the Secretary shall issue final guidances to clarify the requirements for, and facilitate the submission of data to support, the approval of supplemental applications for the approved articles described in subsection (a). The guidances shall—

(1) clarify circumstances in which published matter may be the basis for approval of a supplemental application;

(2) specify data requirements that will avoid duplication of previously submitted data by recognizing the availability of data previously submitted in support of an original application; and

(3) define supplemental applications that are eligible for priority review.

(c) RESPONSIBILITIES OF CENTERS.—The Secretary shall designate an individual in each center within the Food and Drug Administration which is responsible for the review of applications for approval of drugs for—

(1) encouraging the prompt review of supplemental applications for approved articles; and

(2) working with sponsors to facilitate the development and submission of data to support supplemental applications.

(d) COLLABORATION.—The Secretary shall implement programs and policies that will foster collaboration between the Food and Drug Administration, the National Institutes of Health, professional medical and scientific societies, and other persons, to identify published and unpublished studies that may support a supplemental application, and to encourage sponsors to make supplemental applications or conduct further research in support of a supplemental application based, in whole or in part, on such studies.

SEC. 10. HEALTH CARE ECONOMIC INFORMATION.

Section 502(a) (21 U.S.C. 352(a)) is amended by adding at the end the following: “Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading if the health care economic information directly relates to an indication approved under section 505 or 507 or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 505(a), 507, or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the sub-

stantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term 'health care economic information' means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention."

SEC. 11. CLINICAL INVESTIGATIONS.

(a) **CLARIFICATION OF THE NUMBER OF REQUIRED CLINICAL INVESTIGATIONS FOR APPROVAL.**—Section 505(d) (21 U.S.C. 355(d)) is amended by adding at the end the following: "If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence."

(b) **WOMEN AND MINORITIES.**—Section 505(b)(1) (21 U.S.C. 355(b)(1)) is amended by adding at the end the following: "The Secretary shall, in consultation with the Director of the National Institutes of Health, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A)."

SEC. 12. MANUFACTURING CHANGES FOR DRUGS.

(a) **IN GENERAL.**—Chapter VII (21 U.S.C. 371 et seq.), as amended by section 7, is amended by adding at the end the following subchapter:

"SUBCHAPTER F—MANUFACTURING CHANGES

"SEC. 755. MANUFACTURING CHANGES.

"(a) **IN GENERAL.**—With respect to a drug for which there is in effect an approved application under section 505 or 512 or a license under section 351 of the Public Health Service Act, a change from the manufacturing process approved pursuant to such application or license may be made, and the drug as made with the change may be distributed, if—

"(1) the holder of the approved application or license (referred to in this section as a 'holder') has validated the effects of the change in accordance with subsection (b); and

"(2)(A) in the case of a major manufacturing change, the holder has complied with the requirements of subsection (c); or

"(B) in the case of a change that is not a major manufacturing change, the holder complies with the applicable requirements of subsection (d).

"(b) **VALIDATION OF EFFECTS OF CHANGES.**—For purposes of subsection (a)(1), a drug made with a manufacturing change (whether a major manufacturing change or otherwise) may be distributed only if, before distribution of the drug as so made, the holder involved validates the effects of the change on the identity, strength, quality, purity, and potency of the drug as the identity, strength, quality, purity, and potency may relate to the safety, bioequivalence, bioavailability, or effectiveness of the drug.

"(c) **MAJOR MANUFACTURING CHANGES.**—

"(1) **REQUIREMENT OF SUPPLEMENTAL APPLICATION.**—For purposes of subsection (a)(2)(A), a drug made with a major manufacturing change may be distributed only if, before the distribution of the drug as so made, the holder involved submits to the Secretary a supplemental application for such change and the Secretary approves the application. The application shall contain such information as the Secretary determines to be appropriate, and shall include the information developed under subsection (b) by the holder in validating the effects of the change.

"(2) **CHANGES QUALIFYING AS MAJOR CHANGES.**—For purposes of subsection (a)(2)(A), a major manufacturing change is a manufacturing change that—

"(A) is determined by the Secretary to have substantial potential to adversely affect the identity, strength, quality, purity, or potency of the drug as they may relate to the safety, bioequivalence, bioavailability, or effectiveness of a drug; and

"(B)(i) is made in the qualitative or quantitative formulation of the drug involved or in the specifications in the approved application or license referred to in subsection (a) for the drug (unless exempted by the Secretary from the requirements of this subsection);

"(ii) is determined by the Secretary by regulation or guidance to require completion of an appropriate clinical study demonstrating equivalence of the drug to the drug as manufactured without the change; or

“(iii) is determined by the Secretary by regulation or guidance to have a substantial potential to adversely affect the safety or effectiveness of the drug.

“(d) OTHER MANUFACTURING CHANGES.—

“(1) IN GENERAL.—For purposes of subsection (a)(2)(B), the Secretary may regulate drugs made with manufacturing changes that are not major manufacturing changes as follows:

“(A) The Secretary may authorize holders to distribute such drugs without prior approval by the Secretary.

“(B) The Secretary may require that, prior to the distribution of such drugs, holders submit to the Secretary supplemental applications for such changes.

“(C) The Secretary may establish categories of such changes and designate categories to which subparagraph (A) applies and categories to which subparagraph (B) applies.

“(2) CHANGES NOT REQUIRING SUPPLEMENTAL APPLICATION.—

“(A) SUBMISSION OF REPORT.—A holder making a manufacturing change to which paragraph (1)(A) applies shall submit to the Secretary a report on the change, which shall contain such information as the Secretary determines to be appropriate, and which shall include the information developed under subsection (b) by the holder in validating the effects of the change. The report shall be submitted by such date as the Secretary may specify.

“(B) AUTHORITY REGARDING ANNUAL REPORTS.—In the case of a holder that during a single year makes more than one manufacturing change to which paragraph (1)(A) applies, the Secretary may in carrying out subparagraph (A) authorize the holder to comply with such subparagraph by submitting a single report for the year that provides the information required in such subparagraph for all the changes made by the holder during the year.

“(3) CHANGES REQUIRING SUPPLEMENTAL APPLICATION.—

“(A) SUBMISSION OF SUPPLEMENTAL APPLICATION.—The supplemental application required under paragraph (1)(B) for a manufacturing change shall contain such information as the Secretary determines to be appropriate, which shall include the information developed under subsection (b) by the holder in validating the effects of the change.

“(B) AUTHORITY FOR DISTRIBUTION.—In the case of a manufacturing change to which paragraph (1)(B) applies:

“(i) The holder involved may commence distribution of the drug involved 30 days after the Secretary receives the supplemental application under such paragraph, unless the Secretary notifies the holder within such 30-day period that prior approval of the application is required before distribution may be commenced.

“(ii) The Secretary may designate a category of such changes for the purpose of providing that, in the case of a change that is in such category, the holder involved may commence distribution of the drug involved upon the receipt by the Secretary of a supplemental application for the change.

“(iii) If the Secretary disapproves the supplemental application, the Secretary may order the manufacturer to cease the distribution of the drugs that have been made with the manufacturing change.”

(b) TRANSITION RULE.—The amendment made by subsection (a) takes effect upon the effective date of regulations promulgated by the Secretary of Health and Human Services to implement such amendment, or upon the expiration of the 24-month period beginning on the date of the enactment of this Act, which occurs first.

SEC. 13. STREAMLINING CLINICAL RESEARCH ON DRUGS.

Section 505(i) (21 U.S.C. 355(i)) is amended by adding “(1)” before “The Secretary”, by redesignating paragraphs (1), (2), and (3) as subparagraphs (A), (B), and (C), respectively, by striking the last two sentences, and by adding the following new paragraphs:

“(2) Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including—

“(A) information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and

“(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

“(3)(A) At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a ‘clinical hold’) if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information available to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

“(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that—

“(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subject of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

“(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before the date of the enactment of the Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997).

Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

“(C) Any request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.”

SEC. 14. DATA REQUIREMENTS FOR DRUGS.

Within 12 months after the date of enactment of this Act, the Secretary of the Health and Human Services, acting through the Commissioner of Food and Drugs, shall issue guidance that describes, for certain types of studies, when abbreviated study reports may be submitted, in lieu of full reports, with a new drug application under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and with a biologics license application under section 351 of the Public Health Service Act (42 U.S.C. 262). Such guidance shall describe the kinds of studies for which abbreviated reports are appropriate and the appropriate abbreviated report formats.

SEC. 15. CONTENT AND REVIEW OF APPLICATIONS.

(a) SECTION 505(b).—Section 505(b) (21 U.S.C. 355(b)) is amended by adding at the end the following:

“(4)(A) The Secretary shall issue guidance for the review of applications submitted under paragraph (1) relating to promptness, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards which shall apply equally to all individuals who review such applications.

“(B) The Secretary shall meet with a sponsor of an investigation or an applicant for approval under this section or section 351 of the Public Health Service Act if the sponsor or applicant makes a reasonable request for a meeting, for the purpose of reaching agreement on the design and size of clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.

“(C) Agreement regarding the parameters of the design and size of clinical trials of a new drug that are reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

“(i) with the written agreement of the sponsor or applicant; or

“(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the division in which the drug is reviewed, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

“(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting

at which the director and the sponsor or applicant will be present and at which the director documents the scientific issue involved.

“(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified. For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug (including all scientific and medical matters, chemistry, manufacturing, and controls).

“(F) No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.”

(b) SECTION 505(j).—

(1) AMENDMENT.—Section 505(j) (21 U.S.C 355(j)) is amended by redesignating paragraphs (3) through (8) as paragraphs (4) through (9), respectively, and by adding after paragraph (2) the following:

“(3)(A) The Secretary shall issue guidance for the review of applications submitted under paragraph (1) relating to promptness, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards which shall apply equally to all individuals who review such applications.

“(B) The Secretary shall meet with an applicant for approval of a drug under this subsection if the applicant makes a reasonable request for a meeting for the purpose of reaching agreement on the design and size of studies needed for approval of such application. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

“(C) Agreements regarding the parameters of design and size of bioavailability and bioequivalence trials of a drug under this subsection that are reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

“(i) with the written agreement of the sponsor or applicant; or

“(ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the division in which the drug is reviewed, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

“(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director documents the scientific issue involved.

“(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified. For purposes of this paragraph, the reviewing division is the division responsible for the review of an application under this subsection (including scientific matters, chemistry, manufacturing, and controls).

“(F) No action by the reviewing division may at any time be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.”

(2) CONFORMING AMENDMENTS.—Section 505(j) (21 U.S.C. 355(j)), as amended by paragraph (1), is amended—

(A) in paragraph (2)(A)(i), by striking “(6)” and inserting “(7)”;

(B) in paragraph (4), by striking “(4)” and inserting “(5)”;

(C) in paragraph (4)(I), by striking “(5)” and inserting “(6)”; and

(D) in paragraph (7)(C), by striking “(5)” each place it occurs and inserting “(6)”.

SEC. 16. SCIENTIFIC ADVISORY PANELS.

Section 505 (21 U.S.C. 355) is amended by adding at the end the following:

“(n)(1) For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under section 505 or section 351 of the Public Health Service Act, the Secretary shall establish panels of experts or use panels of experts established before the date of the enactment of this subsection, or both.

“(2) The Secretary may delegate the appointment and oversight authority granted under section 904 to a director of a center or successor entity within the Food and Drug Administration.

“(3) The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of—

“(A) members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;

“(B) members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoconomics, biological and physical sciences, and other related professions;

“(C) a representative of consumer interests and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

“(D) 2 or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this Act may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

“(4) Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member’s own scientific work is involved.

“(5) The Secretary shall provide education and training to each new panel member before such member participates in a panel’s activities, including education regarding requirements under this Act and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

“(6) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including travel-time, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS-15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, United States Code, for persons in the Government service employed intermittently.

“(7) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meeting.

“(8) Within 60 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

“(9) A scientific advisory panel under this subsection shall not be subject to the annual chartering and annual report requirements of the Federal Advisory Committee Act.”.

SEC. 17. DISPUTE RESOLUTION.

Chapter V (21 U.S.C. 351 et seq.), as amended by section 3, is amended by inserting after section 505A the following:

“DISPUTE RESOLUTION

“SEC. 506. If, regarding an obligation under this Act, there is a scientific controversy between the Secretary and a person who is a sponsor, applicant, or manufacturer and no specific provision of this Act or regulation promulgated under this Act provides a right of review of the matter in controversy, the Secretary shall, by

regulation, establish a procedure under which such sponsor, applicant, or manufacturer may request a review of such controversy by an appropriate scientific advisory panel under section 505(n). Such review shall take place in a timely manner. The Secretary shall promulgate such regulations within 180 days of the date of the enactment of the Prescription Drug User Fee Reauthorization and Medical Device Regulatory Modernization Act of 1997.”

SEC. 18. INFORMAL AGENCY STATEMENTS.

Section 701 (21 U.S.C. 371) is amended by adding at the end the following:

“(h)(1)(A) The Secretary shall develop guidance documents with public participation and ensure that the existence of such documents and the documents themselves are made available to the public both in written form and through electronic means. Such documents shall not create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the Food and Drug Administration.

“(B) Although guidance documents shall not be binding on the Secretary, the Secretary shall ensure that employees of the Food and Drug Administration do not deviate from such guidances without appropriate justification and supervisory concurrence.

“(C) For guidance documents that set forth initial interpretations of statute or regulation, changes in interpretation or policy that are of more than a minor nature, complex scientific issues, or highly controversial issues, the Secretary shall ensure public participation prior to implementation of any guidance documents, unless the Secretary determines that for reasons of the public health need, such prior public participation is not feasible. In such cases, the Secretary shall provide for public comment upon implementation, and take such comment into account.

“(D) For guidance documents that set forth existing practices or minor changes in policy, the Secretary shall provide for public comment upon implementation.

“(2) In developing guidance documents, the Secretary shall ensure uniform nomenclature and uniform internal procedures for approval of such documents. The Secretary shall ensure that guidance documents and revisions of such documents are properly dated and indicate the nonbinding nature of the documents.

“(3) The Secretary, through the Food and Drug Administration, shall maintain electronically and publish periodically in the Federal Register a list of guidance documents. Such list shall be updated quarterly. All such documents shall be made available to the public.

“(4) The Secretary shall report to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate no later than July 1, 2000, on the implementation of these practices.”

SEC. 19. POSITRON EMISSION TOMOGRAPHY.

(a) REGULATION OF COMPOUNDED POSITRON EMISSION TOMOGRAPHY DRUGS.—

(1) DEFINITION.—Section 201 (21 U.S.C. 321) is amended by adding at the end the following:

“(ii) The term ‘compounded positron emission tomography drug’—

“(1) means a drug that—

“(A) exhibits spontaneous disintegration of unstable nuclei by the emission of positrons and is used for the purpose of providing dual photon positron emission tomographic diagnostic images; and

“(B) has been compounded by or on the order of a practitioner who is licensed by a State to compound or order compounding for a drug described in subparagraph (A), and is compounded in accordance with that State’s law, for a patient or for research, teaching, or quality control; and

“(2) includes any nonradioactive reagent, reagent kit, ingredient, nuclide generator, accelerator, target material, electronic synthesizer, or other apparatus or computer program to be used in the preparation of such a drug.”

(b) ADULTERATION.—

(1) IN GENERAL.—Section 501(a)(2) (21 U.S.C. 351(a)(2)) is amended by striking “; or (3)” and inserting the following: “; or (C) if it is a compounded positron emission tomography drug and the methods used in, or the facilities and controls used for, its compounding, processing, packing, or holding do not conform to or are not operated or administered in conformity with the positron emission tomography compounding standards and the official monographs of the United States Pharmacopeia to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, that it purports or is represented to possess; or (3)”.

(2) SUNSET.—Section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(C)) shall not apply 4 years after the date of enactment of this Act or 2 years after the date on which the Secretary of Health and

Human Services establishes the requirements described in subsection (c)(1)(B), whichever is later.

(c) REQUIREMENTS FOR REVIEW OF APPROVAL PROCEDURES AND CURRENT GOOD MANUFACTURING PRACTICES FOR POSITRON EMISSION TOMOGRAPHY.—

(1) PROCEDURES AND REQUIREMENTS.—

(A) IN GENERAL.—In order to take account of the special characteristics of compounded positron emission tomography drugs and the special techniques and processes required to produce these drugs, not later than 2 years after the date of enactment of this Act, the Secretary of Health and Human Services shall establish—

(i) appropriate procedures for the approval of compounded positron emission tomography drugs pursuant to section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355); and

(ii) appropriate current good manufacturing practice requirements for such drugs.

(B) CONSIDERATIONS AND CONSULTATION.—In establishing the procedures and requirements required by subparagraph (A), the Secretary of Health and Human Services shall take due account of any relevant differences between not-for-profit institutions that compound the drugs for their patients and commercial manufacturers of the drugs. Prior to establishing the procedures and requirements, the Secretary of Health and Human Services shall consult with patient advocacy groups, professional associations, manufacturers, and physicians and scientists licensed to make or use compounded positron emission tomography drugs.

(2) SUBMISSION OF NEW DRUG APPLICATIONS AND ABBREVIATED NEW DRUG APPLICATIONS.—

(A) IN GENERAL.—Except as provided in subparagraph (B), the Secretary of Health and Human Services shall not require the submission of new drug applications or abbreviated new drug applications under subsection (b) or (j) of section 505 (21 U.S.C. 355), for compounded positron emission tomography drugs that are not adulterated drugs described in section 501(a)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351(a)(2)(C)) (as amended by subsection (b)), for a period of 4 years after the date of enactment of this Act, or for 2 years after the date on which the Secretary establishes procedures and requirements under paragraph (1), whichever is later.

(B) EXCEPTION.—Nothing in this Act shall prohibit the voluntary submission of such applications or the review of such applications by the Secretary of Health and Human Services. Nothing in this Act shall constitute an exemption for a compounded positron emission tomography drug from the requirements of regulations issued under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) for such drugs.

(d) REVOCATION OF CERTAIN INCONSISTENT DOCUMENTS.—Within 30 days after the date of enactment of this Act, the Secretary of Health and Human Services shall publish in the Federal Register a notice terminating the application of the following notices and rule, to the extent the notices and rule relate to compounded positron emission tomography drugs:

(1) A notice entitled “Regulation of Positron Emission Tomographic Drug Products: Guidance; Public Workshop”, published in the Federal Register on February 27, 1995.

(2) A notice entitled “Guidance for Industry: Current Good Manufacturing Practices for Positron Emission Tomographic (PET) Drug Products; Availability”, published in the Federal Register on April 22, 1997.

(3) A final rule entitled “Current Good Manufacturing Practice for Finished Pharmaceuticals; Positron Emission Tomography”, published in the Federal Register on April 22, 1997.

(e) DEFINITION.—As used in this section, the term “compounded positron emission tomography drug” has the meaning given the term in section 201 of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 321).

SEC. 20. REQUIREMENTS FOR RADIOPHARMACEUTICALS.

(a) REQUIREMENTS.—

(1) REGULATIONS.—

(A) PROPOSED REGULATIONS.—Not later than 180 days after the date of enactment of this Act, the Secretary of Health and Human Services, after consultation with patient advocacy groups, associations, physicians licensed to use radiopharmaceuticals, and the regulated industry, shall issue proposed regulations governing the approval of radiopharmaceuticals designed

for diagnosis and monitoring of diseases and conditions. The regulations shall provide that the determination of the safety and effectiveness of such a radiopharmaceutical under section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) or section 351 of the Public Health Service Act (42 U.S.C. 262) shall include consideration of the proposed use of the radiopharmaceutical in the practice of medicine, the pharmacological and toxicological activity of the radiopharmaceutical (including any carrier or ligand component of the radiopharmaceutical), and the estimated absorbed radiation dose of the radiopharmaceutical.

(B) FINAL REGULATIONS.—Not later than 18 months after the date of enactment of this Act, the Secretary shall promulgate final regulations governing the approval of the radiopharmaceuticals.

(2) SPECIAL RULE.—In the case of a radiopharmaceutical intended to be used for diagnostic or monitoring purposes, the indications for which such radiopharmaceutical is approved for marketing may, in appropriate cases, refer to manifestations of disease (such as biochemical, physiological, anatomic, or pathological processes) common to, or present in, one or more disease states.

(b) DEFINITION.—In this section, the term “radiopharmaceutical” means—

(1) an article—

(A) that is intended for use in the diagnosis or monitoring of a disease or a manifestation of a disease in humans; and

(B) that exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons; or

(2) any nonradioactive reagent kit or nuclide generator that is intended to be used in the preparation of any such article.

SEC. 21. MODERNIZATION OF REGULATION.

(a) LICENSES.—

(1) IN GENERAL.—Section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) is amended to read as follows:

“(a)(1) No person shall introduce or deliver for introduction into interstate commerce any biological product unless—

“(A) a biologics license is in effect for the biological product; and

“(B) each package of the biological product is plainly marked with—

“(i) the proper name of the biological product contained in the package;

“(ii) the name, address, and applicable license number of the manufacturer of the biological product; and

“(iii) the expiration date of the biological product.

“(2)(A) The Secretary shall establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.

“(B) The Secretary shall approve a biologics license application—

“(i) on the basis of a demonstration that—

“(I) the biological product that is the subject of the application is safe, pure, and potent; and

“(II) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and

“(ii) if the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

“(3) The Secretary shall prescribe requirements under which a biological product undergoing investigation shall be exempt from the requirements of paragraph (1).”.

(2) ELIMINATION OF EXISTING LICENSE REQUIREMENT.—Section 351(d) of the Public Health Service Act (42 U.S.C. 262(d)) is amended—

(A) by striking “(d)(1)” and all that follows through “of this section.”;

(B) in paragraph (2)—

(i) by striking “(2)(A) Upon” and inserting “(d)(1) Upon” and

(ii) by redesignating subparagraph (B) as paragraph (2); and

(C) in paragraph (2) (as so redesignated by subparagraph (B)(ii))—

(i) by striking “subparagraph (A)” and inserting “paragraph (1)”; and

(ii) by striking “this subparagraph” each place it appears and inserting “this paragraph”.

(b) LABELING.—Section 351(b) of the Public Health Service Act (42 U.S.C. 262(b)) is amended to read as follows:

“(b) No person shall falsely label or mark any package or container of any biological product or alter any label or mark on the package or container of the biological product so as to falsify the label or mark.”.

(c) INSPECTION.—Section 351(c) of the Public Health Service Act (42 U.S.C. 262(c)) is amended by striking “virus, serum,” and all that follows and inserting “biological product.”

(d) DEFINITION; APPLICATION.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended by adding at the end the following:

“(i) In this section, the term ‘biological product’ means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.”

(e) CONFORMING AMENDMENT.—Section 503(g)(4) (21 U.S.C. 353(g)(4)) is amended—

(1) in subparagraph (A)—

(A) by striking “section 351(a)” and inserting “section 351(i)”; and

(B) by striking “262(a)” and inserting “262(i)”; and

(2) in subparagraph (B)(iii), by striking “product or establishment license under subsection (a) or (d)” and inserting “biologics license application under subsection (a)”.

(f) SPECIAL RULE.—The Secretary of Health and Human Services shall take measures to minimize differences in the review and approval of products required to have approved biologics license applications under section 351 of the Public Health Service Act (42 U.S.C. 262) and products required to have approved new drug applications under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(b)(1)).

(g) EXAMINATIONS AND PROCEDURES.—Paragraph (3) of section 353(d) of the Public Health Service Act (42 U.S.C. 263a(d)) is amended to read as follows:

“(3) EXAMINATIONS AND PROCEDURES.—The examinations and procedures identified in paragraph (2) are laboratory examinations and procedures which have been approved by the Food and Drug Administration for home use or which, as determined by the Secretary, are simple laboratory examinations and procedures which have an insignificant risk of an erroneous result, including those which—

“(A) employ methodologies that are so simple and accurate as to render the likelihood of erroneous results by the user negligible, or

“(B) the Secretary has determined pose no reasonable risk of harm to the patient if performed incorrectly.”

SEC. 22. PILOT AND SMALL SCALE MANUFACTURE.

(a) HUMAN DRUGS.—Section 505(c) (21 U.S.C. 355(c)) is amended by adding at the end thereof the following:

“(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval prior to scaling up to a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.”

(b) ANIMAL DRUGS.—Section 512(c) (21 U.S.C. 360b(c)) is amended by adding at the end the following:

“(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval prior to scaling up to a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.”

SEC. 23. INSULIN AND ANTIBIOTICS.

(a) CERTIFICATION OF DRUGS CONTAINING INSULIN.—

(1) AMENDMENT.—Section 506 (21 U.S.C. 356), as in effect before the date of the enactment of this Act, is repealed.

(2) CONFORMING AMENDMENTS.—

(A) Section 301(j) (21 U.S.C. 331(j)) is amended by striking “506, 507.”

(B) Subsection (k) of section 502 (21 U.S.C. 352) is repealed.

(C) Sections 301(i)(1), 510(j)(1)(A), and 510(j)(1)(D) (21 U.S.C. 331(i)(1), 360(j)(1)(A), 360(j)(1)(D)) are each amended by striking “, 506, 507.”

(D) Section 801(d)(1) (21 U.S.C. 381(d)(1)) is amended by inserting after “503(b)” the following: “or composed wholly or partly of insulin”.

(E) Section 8126(h)(2) of title 38, United States Code, is amended by inserting “or” at the end of subparagraph (B), by striking “; or” at the end of subparagraph (C) and inserting a period, and by striking subparagraph (D).

(b) CERTIFICATION OF ANTIBIOTICS.—

(1) AMENDMENT.—Section 507 (21 U.S.C. 357) is repealed.

(2) CONFORMING AMENDMENTS.—

(A) Section 201(aa) (21 U.S.C. 321(aa)) is amended by striking out “or 507”, section 201(dd) (21 U.S.C. 321(dd)) is amended by striking “507,”, and section 201(ff)(3)(A) (21 U.S.C. 321(ff)(3)(A)) is amended by striking “, certified as an antibiotic under section 507,”.

(B) Section 301(e) (21 U.S.C. 331(e)) is amended by striking “507(d) or (g),”.

(C) Section 306(d)(4)(B)(ii) (21 U.S.C. 335a(d)(4)(B)(ii)) is amended by striking “or 507”.

(D) Section 502 (21 U.S.C. 352) is amended by striking subsection (l).

(E) Section 520(l) (21 U.S.C. 360j(l)) is amended by striking paragraph (4) and by striking “or Antibiotic Drugs” in the subsection heading.

(F) Section 525(a) (21 U.S.C. 360aa(a)) is amended by inserting “or” at the end of paragraph (1), by striking paragraph (2), and by redesignating paragraph (3) as paragraph (2).

(G) Section 525(a) (21 U.S.C. 360aa(a)) is amended by striking “, certification of such drug for such disease or condition under section 507,”.

(H) Section 526(a)(1) (21 U.S.C. 360bb) is amended by striking “the submission of an application for certification of the drug under section 507,”, by inserting “or” at the end of subparagraph (A), by striking subparagraph (B), and by redesignating subparagraph (C) as subparagraph (B).

(I) Section 526(b) (21 U.S.C. 360bb(b)) is amended—

(i) in paragraph (1), by striking “, a certificate was issued for the drug under section 507,”; and

(ii) in paragraph (2) by striking “, a certificate has not been issued for the drug under section 507,” and by striking “, approval of an application for certification under section 507,”.

(J) Section 527(a) (21 U.S.C. 360cc(a)) is amended by inserting “or” at the end of paragraph (1), by striking paragraph (2), by redesignating paragraph (3) as paragraph (2), and by striking “, issue another certificate under section 507,”.

(K) Section 527(b) (21 U.S.C. 360cc(b)) is amended by striking “, if a certification is issued under section 507 for such a drug, or”, “of the issuance of the certification under section 507,”, and “issue another certification under section 507, or”.

(L) Section 704(a)(1) (21 U.S.C. 374(a)(1)) is amended by striking “, section 507 (d) or (g)”.

(M) Section 735(1) (21 U.S.C. 379g(1)(C)) is amended by inserting “or” at the end of subparagraph (B), by striking subparagraph (C), and by redesignating subparagraph (D) as subparagraph (C).

(N) Subparagraphs (A)(ii) and (B) of sections 5(b)(1) of the Orphan Drug Act (21 U.S.C. 360ee(b)(1)(A), 360ee(b)(1)(B)) are each amended by striking “or 507”.

(O) Section 45C(b)(2)(A)(ii)(II) of the Internal Revenue Code of 1986 is amended by striking “or 507”.

(P) Section 156(f)(4)(B) of title 35, United States Code, is amended by striking “507,” each place it occurs.

(c) EXPORTATION.—Section 802 (21 U.S.C. 382) is amended by adding at the end thereof the following:

“(i) Insulin and antibiotics may be exported without regard to the requirements in this section if the insulin and antibiotics meet the requirements of section 801(e)(1).”.

(d) APPLICATION.—An antibiotic drug which was certified or exempted from certification under section 507 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 357) before the date of the enactment of this Act shall, after such date, be considered to be a drug for which an application was filed under section 505(b) of such Act (21 U.S.C. 355(b)), and approved for safety and effectiveness under section 505(c) of such Act (21 U.S.C. 355(c)), except that if such antibiotic drug was approved under an abbreviated application under such section 507, such drug shall be considered to have been approved under section 505(j) of such Act.

(e) EFFECT.—In the application of section 505 of the Federal Food, Drug, and Cosmetic Act after the date of enactment of this Act to a drug that contains an active ingredient (including any ester or salt of the active ingredient) that was an antibiotic drug within the meaning of section 507 of such Act and was the subject of an approved or pending application for marketing approval (exemption from certification) before the date of the enactment of such Act, none of the patent or market exclusivity provisions of section 505 shall apply to such a drug.

SEC. 24. FDA MISSION AND ANNUAL REPORT.

(a) MISSION.—Section 903 (21 U.S.C. 393) is amended by redesignating subsections (b) and (c) as subsections (c) and (d), respectively, and by adding after subsection (a) the following:

“(b) MISSION.—The Food and Drug Administration shall promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner, and with respect to such products shall protect the public health by ensuring that—

“(1) foods are safe, wholesome, sanitary, and properly labeled;

“(2) human and veterinary drugs are safe and effective;

“(3) there is reasonable assurance of safety and effectiveness of devices intended for human use;

“(4) cosmetics are safe and properly labeled; and

“(5) public health and safety are protected from electronic product radiation.

The Food and Drug Administration shall participate with other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements.”

(b) ANNUAL REPORT.—Section 903 (21 U.S.C. 393), as amended by subsection (a), is amended by adding at the end the following:

“(e) ANNUAL REPORT.—The Secretary shall, simultaneously with the submission each year of the budget for the Food and Drug Administration, submit to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate an annual report which shall—

“(1) review the performance of the Food and Drug Administration in meeting its mission and the development of Food and Drug Administration policies to implement such mission;

“(2) review the performance of the Food and Drug Administration in meeting its own performance standards, including its own outcome measurements, and statutory deadlines for the approval of products or for other purposes contained in this Act;

“(3) describe the staffing and resources of the Food and Drug Administration; and

“(4)(A) list each bilateral and multinational meeting held by the Food and Drug Administration to address methods and approaches to reduce the burden of regulation, to harmonize regulation, and to seek appropriate reciprocal arrangements, (B) describe the goals, activities, and accomplishments of the Food and Drug Administration in such meetings, and (C) list issues that the Food and Drug Administration is considering or has presented for each such meeting.”

SEC. 25. INFORMATION SYSTEM.

Chapter IX is amended by adding at the end the following section:

“SEC. 906. INFORMATION SYSTEM.

“The Secretary shall establish and maintain an information system to track the status and progress of each application or submission (including a petition, notification, or other similar form of request) submitted to the Food and Drug Administration requesting agency action.”

SEC. 26. EDUCATION AND TRAINING.

Chapter IX, as amended by section 25, is amended by adding at the end the following sections:

“SEC. 907. EDUCATION.

“The Secretary shall conduct training and education programs for the employees of the Food and Drug Administration relating to the regulatory responsibilities and policies established by this Act, including programs for scientific training and training in administrative process and procedure and integrity issues.”

SEC. 27. CENTERS FOR EDUCATION AND RESEARCH ON DRUGS.

Chapter IX, as amended by section 26, is amended by adding at the end the following section:

“SEC. 908. DEMONSTRATION PROGRAM REGARDING CENTERS FOR EDUCATION AND RESEARCH ON DRUGS.

“(a) IN GENERAL.—The Secretary, acting through the Commissioner of Food and Drugs, shall establish a demonstration program for the purpose of making one or more grants for the establishment and operation of one or more centers to carry out the activities specified in subsection (b).

“(b) REQUIRED ACTIVITIES.—The activities referred to in subsection (a) are the following:

“(1) The conduct of state-of-the-art clinical and laboratory research for the following purposes:

“(A) To increase awareness of new uses of drugs and the unforeseen risks of new uses of drugs.

“(B) To provide objective clinical information to the following entities:

“(i) Health care practitioners or other providers of health care goods or services.

“(ii) Pharmacy benefit managers.

“(iii) Health maintenance organizations or other managed health care organizations.

“(iv) Health care insurers or governmental agencies.

“(C) To improve the quality of health care while reducing the cost of health care through the prevention of adverse effects of drugs and the consequences of such effects, such as unnecessary hospitalizations.

“(2) The conduct of research on the comparative effectiveness and safety of drugs.

“(3) Such other activities as the Secretary determines to be appropriate, except that the grant may not be expended to assist the Secretary in the review of new drugs.

“(c) APPLICATION FOR GRANT.—A grant under subsection (a) may be made only if an application for the grant is submitted to the Secretary and the application is in such form, is made in such manner, and contains such agreements, assurances, and information as the Secretary determines to be necessary to carry out this section.

“(d) PEER REVIEW.—A grant under subsection (a) may be made only if the application for the grant has undergone appropriate technical and scientific peer review.

“(e) AUTHORIZATION OF APPROPRIATIONS.—For the purpose of carrying out this section, there are authorized to be appropriated \$2,000,000 for fiscal year 1998, and \$3,000,000 for fiscal year 1999.”.

SEC. 28. HARMONIZATION.

Section 803 (21 U.S.C. 383) is amended by adding at the end the following:

“(c) The Secretary shall participate in meetings with representatives of other countries to discuss methods and approaches to reduce the burden of regulation and harmonize regulatory requirements if the Secretary determines that such harmonization continues consumer protections consistent with the purposes of this Act. The Secretary shall report to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate at least 60 days before executing any bilateral or multilateral agreement under subsection (b).”.

SEC. 29. ENVIRONMENTAL IMPACT REVIEW.

Chapter VII, as amended by section 12, is amended by adding at the end the following:

“SUBCHAPTER G—ENVIRONMENTAL IMPACT REVIEW

“SEC. 761. ENVIRONMENTAL IMPACT REVIEW.

“Notwithstanding any other provision of law, an environmental impact statement prepared in accordance with the regulations published at part 25 of 21 C.F.R. (as in effect on August 31, 1997) in connection with an action carried out under (or a recommendation or report relating to) this Act, shall be considered to meet the requirements for a detailed statement under section 102(2)(C) of the National Environmental Policy Act.”.

SEC. 30. NATIONAL UNIFORMITY.

(a) NONPRESCRIPTION DRUGS.—Chapter VII (21 U.S.C. 371 et seq.), as amended by section 29, is further amended by adding at the end the following:

“SUBCHAPTER H—NATIONAL UNIFORMITY FOR NONPRESCRIPTION DRUGS FOR HUMAN USE AND PREEMPTION FOR LABELING OR PACKAGING OF COSMETICS

“SEC. 771. NATIONAL UNIFORMITY FOR NONPRESCRIPTION DRUGS FOR HUMAN USE.

“(a) IN GENERAL.—Except as provided in subsection (b), (c)(1), (d), (e), or (f), no State or political subdivision of a State may establish or continue in effect any requirement—

“(1) that relates to the regulation of a drug intended for human use that is not subject to the requirements of section 503(b)(1); and

“(2) that is different from or in addition to, or that is otherwise not identical with, a requirement under this Act, the Poison Prevention Packaging Act of 1970 (15 U.S.C. 1471 et seq.), or the Fair Packaging and Labeling Act (15 U.S.C. 1451 et seq.).

“(b) EXEMPTION.—Upon application of a State or political subdivision thereof, the Secretary may by regulation, after notice and opportunity for written and oral presentation of views, exempt from subsection (a), under such conditions as may be prescribed in such regulation, a State or political subdivision requirement that—

“(1) protects an important public interest that would otherwise be unprotected;

“(2) would not cause any drug to be in violation of any applicable requirement or prohibition under Federal law; and

“(3) would not unduly burden interstate commerce.

“(c) SCOPE.—

“(1) IN GENERAL.—This section shall not apply to—

“(A) any State or political subdivision requirement that relates to the practice of pharmacy; or

“(B) any State or political subdivision requirement that a drug be dispensed only upon the prescription of a practitioner licensed by law to administer such drug.

“(2) SAFETY OR EFFECTIVENESS.—For purposes of subsection (a), a requirement that relates to the regulation of a drug shall be deemed to include any requirement relating to public information or any other form of public communication relating to a warning of any kind for a drug.

“(d) EXCEPTIONS.—

“(1) IN GENERAL.—In the case of a drug described in subsection (a)(1) that is not the subject of an application approved under section 505 or 507 or a final regulation promulgated by the Secretary establishing conditions under which the drug is generally recognized as safe and effective and not misbranded, subsection (a) shall apply only with respect to a requirement of a State or political subdivision of a State that relates to the same subject as, but is different from or in addition to, or that is otherwise not identical with—

“(A) a regulation in effect with respect to the drug pursuant to a statute described in subsection (a)(2); or

“(B) any other requirement in effect with respect to the drug pursuant to an amendment to such a statute made on or after the date of enactment of this section.

“(2) STATE INITIATIVES.—This section shall not apply to a State public initiative enacted prior to the date of enactment of this section.

“(e) NO EFFECT ON PRODUCT LIABILITY LAW.—Nothing in this section shall be construed to modify or otherwise affect any action or the liability of any person under the product liability law of any State.

“(f) STATE ENFORCEMENT AUTHORITY.—Nothing in this section shall prevent a State or political subdivision thereof from enforcing, under any relevant civil or other enforcement authority, a requirement that is identical to a requirement of this Act.”

(b) INSPECTIONS.—Section 704(a)(1) (21 U.S.C. 374(a)(1)) is amended by striking “prescription drugs” each place it appears and inserting “prescription drugs, nonprescription drugs intended for human use.”

(c) MISBRANDING.—Paragraph (1) of section 502(e) (21 U.S.C. 352(e)(1)) is amended to read as follows:

“(1)(A) If it is a drug, unless its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula)—

“(i) the established name (as defined in subparagraph (3)) of the drug, if there is such a name;

“(ii) the established name and quantity or, if deemed appropriate by the Secretary, the proportion of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including whether active or not the established name and quantity or if deemed appropriate by the Secretary, the proportion of any bromides, ether, chloroform, acetanilide, acetophenetidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein, except that the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this subclause, shall not apply to nonprescription drugs not intended for human use; and

“(iii) the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package and, if deemed appropriate by the Secretary, on the immediate container, as prescribed in regulation promulgated by the Secretary, but nothing in this clause shall be deemed to require that any trade secret be divulged, except that the requirements of this subclause with respect to alphabetical order shall apply only to nonprescription drugs that are not also cosmetics and this subclause shall not apply to non-prescription drugs not intended for human use.

“(B) For any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) shall be printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient, except that to the extent that compliance with the requirements of clause (A)(ii) or (iii) or this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary.”

(d) COSMETICS.—Subchapter H of chapter VII, as amended by subsection (a), is further amended by adding at the end the following:

“SEC. 772. PREEMPTION FOR LABELING OR PACKAGING OF COSMETICS.

“(a) IN GENERAL.—Except as provided in subsection (b), (d), or (e), a State or political subdivision of a State shall not impose or continue in effect any requirement for labeling or packaging of a cosmetic that is different from or in addition to, or that is otherwise not identical with a requirement that is specifically applicable to a particular cosmetic or class of cosmetics under this Act, the Poison Prevention Packaging Act of 1970 (15 U.S.C. 1471 et seq.), or the Fair Packaging and Labeling Act (15 U.S.C. 1451 et seq.).

“(b) EXEMPTION.—Upon application of a State or political subdivision thereof, the Secretary may by regulation after notice and opportunity for written and oral presentation of views, exempt from subsection (a), under such conditions as may be prescribed in such regulation, a State or political subdivision requirement for labeling and packaging that—

“(1) protects an important public interest that would otherwise be unprotected;

“(2) would not cause a cosmetic to be in violation of any applicable requirements or prohibition under Federal law; and

“(3) would not unduly burden interstate commerce.

“(c) SCOPE.—For purposes of subsection (a), a reference to a State requirement that relates to the packaging or labeling of a cosmetic means any specific requirement relating to the same aspect of such cosmetic as a requirement specifically applicable to that particular cosmetic or class of cosmetics under this Act for packaging or labeling, including any State requirement relating to public information or any other form of public communication.

“(d) NO EFFECT ON PRODUCT LIABILITY LAW.—Nothing in this section shall be construed to modify or otherwise affect any action or the liability of any person under the product liability law of any State.

“(e) STATE INITIATIVE.—This section shall not apply to a State requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997.”

SEC. 31. FDA STUDY OF MERCURY COMPOUNDS IN DRUGS AND FOOD.

(a) LIST AND ANALYSIS.—The Secretary of Health and Human Services shall, through the Food and Drug Administration—

(1) compile a list of drugs and foods that contain intentionally introduced mercury compounds, and

(2) provide a quantitative and qualitative analysis of the mercury compounds in the list under paragraph (1).

The Secretary shall compile the list required by paragraph (1) within 2 years after the date of the enactment of this section and shall provide the analysis required by paragraph (2) within 2 years of such date of enactment.

(b) STUDY.—The Secretary of Health and Human Services, acting through the Food and Drug Administration, shall conduct a study of the effect on humans of the use of mercury compounds in nasal sprays. Such study shall include data from other studies that have been made of such use.

(c) STUDY OF MERCURY SALES.—

(1) STUDY.—The Secretary of Health and Human Services, acting through the Food and Drug Administration and subject to appropriations, shall conduct, or shall contract with the Institute of Medicine of the National Academy of Sciences to conduct, a study of the effect on humans of the use of elemental, organic or inorganic mercury when offered for sale as a drug or dietary supplement. Such study shall, among other things, evaluate—

- (A) the scope of mercury use as a drug or dietary supplement; and
- (B) the adverse effects on health of children and other sensitive populations resulting from exposure to, or ingestion or inhalation of, mercury when so used.

In conducting such study, the Secretary shall consult with the Administrator of the Environmental Protection Agency, the Chair of the Consumer Product Safety Commission, and the Administrator of the Agency for Toxic Substances and Disease Registry, and, to the extent the Secretary believes necessary or appropriate, with any other Federal or private entity.

(2) REGULATIONS.—If, in the opinion of the Secretary, the use of elemental, organic or inorganic mercury offered for sale as a drug or dietary supplement poses a threat to human health, the Secretary shall promulgate regulations restricting the sale of mercury intended for such use. At a minimum, such regulations shall be designed to protect the health of children and other sensitive populations from adverse effects resulting from exposure to, or ingestion or inhalation of, mercury. Such regulations, to the extent feasible, should not unnecessarily interfere with the availability of mercury for use in religious ceremonies.

SEC. 32. NOTIFICATION OF DISCONTINUANCE OF A LIFE SAVING PRODUCT.

Chapter VII (21 U.S.C. 371 et seq.), as amended by section 30, is further amended by adding at the end the following:

“Subchapter I—Notification of the Discontinuance of a Life Saving Product

“SEC. 781. DISCONTINUANCE OF A LIFE SAVING PRODUCT.

“(a) IN GENERAL.—A manufacturer that is the sole manufacturer of a drug (including a biological product) or device—

“(1) that is—

“(A) life supporting;

“(B) life sustaining; or

“(C) intended for use in the prevention of a debilitating disease or condition; and

“(2) for which an application has been approved under section 505(b), 505(j), or 515(d),

shall notify the Secretary of a discontinuance of the manufacture of the drug or device at least 6 months prior to the date of the discontinuance.

“(b) REDUCTION IN NOTIFICATION PERIOD.—On application of a manufacturer, the Secretary may reduce the notification period required under subsection (a) for the manufacturer if good cause exists for the reduction, such as a situation in which—

“(1) a public health problem may result from continuation of the manufacturing for the 6-month period;

“(2) a biomaterials shortage prevents the continuation of the manufacturing for the 6-month period;

“(3) a liability problem may exist for the manufacturer if the manufacturing is continued for the 6-month period;

“(4) continuation of the manufacturing for the 6-month period may cause substantial economic hardship for the manufacturer; or

“(5) the manufacturer has filed for bankruptcy under chapter 7 or 11 of title 11, United States Code.

“(6) the Secretary determines that there would be no adverse impact from the discontinuance of a drug or device.

“(c) DISTRIBUTION.—To the maximum extent practicable, the Secretary shall distribute information on the discontinuation of the drugs and devices described in subsection (a) to appropriate physician and patient organizations.”.

PURPOSE AND SUMMARY

H.R. 1411, the Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997, is a comprehensive proposal to revise the Nation’s laws governing the review of drug and biological products. It reauthorizes the Prescription Drug User Fee Act (PDUFA) for five years and amends the Federal Food, Drug, and Cosmetic Act (FFDCA) in an effort to change several of the Food and Drug Administration’s (FDA’s) current policies and practices regarding product review and approval. The legislation

seeks to encourage pharmaceutical research and accelerate the availability of new products.

BACKGROUND AND NEED FOR LEGISLATION

A. REAUTHORIZATION OF PDUFA

In 1992, Congress enacted the Prescription Drug User Fee Act (PDUFA), which required companies to pay user fees to the FDA to improve the agency's review of drug and biologic applications. The law expired on September 30, 1997, although the FDA has sufficient resources to maintain current levels of operations for an additional 90 days following that date.

Reauthorization of PDUFA is widely viewed as necessary to continue the progress that has been made toward reducing the FDA's review time for new pharmaceutical products. At present, the PDUFA landscape is as follows:

User fees paid by drug companies to FDA, 1993–1997: \$327 million.

Additional reviewers hired by FDA with user fee funds: 600.

Reduction in drug review times due to user fees: 13.7 months (from an average of 29.2 months in 1992 to an average of 15.5 months in 1996).

Increase in annual number of drugs approved since user fees began: 27 (there were 53 new medicines approved in 1996, up from 26 in 1992).

Number of new medicines in development “pipeline”: At least 1,000, including more than 317 for cancer, 122 for AIDS, 96 for heart disease and stroke, 146 for diseases that affect children, 118 for neurologic disorders such as Alzheimer's and Lou Gehrig's disease, 125 for infectious diseases, and 64 for mental illness.

While pharmaceutical manufacturers have benefited from speedier drug approvals, the primary beneficiaries are patients and providers who have gained access to the medicines they need sooner. For example, in 1996, the FDA approved a new medicine for multiple sclerosis (MS) after a review time of 14.3 months. This will benefit many of the 300,000 Americans with MS. A new medicine for asthma was approved in 15 months, a positive development for the 12 million Americans with this disease. And a new medicine that could help some of the 4 million Americans suffering from Alzheimer's was approved in 7.7 months. As described above, the net result of PDUFA is that new drugs have moved from the laboratory to the patient 13.7 months faster. For some patients, that 13.7 months could mean the difference between life and death.

B. THE NEED TO ADDRESS STRUCTURAL AGENCY PROBLEMS

As important as the reauthorization of PDUFA is, the manner in which the FDA approves and regulates pharmaceuticals and biologics remains an issue of concern impacting millions of patients and providers alike. Currently, it takes nearly 15 years to develop a new drug—twice the time required in the 1960s. New scientific knowledge can produce effective new treatments for uncured diseases, but a drug development process slowed by outmoded regulation may mean that cures come too late for many patients.

Although the United States has long led the world in drug discovery, too many medicines are introduced in other countries before they are made available to American patients. In fact, the majority of drugs approved by the FDA since 1990 were approved first in another country. Of additional concern is the fact that lengthy drug development times in the United States have served as a barrier to pharmaceutical innovation. A 1996 Tufts University study found that the percentage of drug tests in humans initiated in the United States by American firms dropped from 61 percent in the 1970s to 36 percent in the 1990s, as companies moved testing programs to other nations.

Although medical progress has relegated many diseases to the history books, other diseases remain undiagnosed, untreated, or uncured. As the American population ages, diseases such as Alzheimer's, arthritis, cancer, and Parkinson's will take an increasing human and financial toll. AIDS continues to ravage, antibiotic resistance is on the rise, and new and deadly infectious diseases are emerging.

Armed with new knowledge of the mechanisms of disease and new tools, researchers are taking up the challenge of uncured diseases. Unfortunately, many patients do not have the time to wait the nearly 15 years it now takes to bring a new drug or biologic from the laboratory to the pharmacy shelf. According to recent testimony before the Subcommittee on Health and Environment, drug development times have steadily increased—from 8.1 years in the 1960s to 11.6 years in the 1970s to 14.2 years in the 1980s to approximately 15 years for drugs approved in the 1990s.

Part of the reason for this growing development time is the increasing complexity of the diseases researchers are targeting. But an undeniable part of the delay in getting medicines to patients lies in the rules and regulations imposed by the FDA—requirements that add to development and approval time without enhancing the safety and effectiveness of new drugs and biologics.

In order to address these concerns, H.R. 1411, the Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997, achieves two important objectives: (1) it reauthorizes the Prescription Drug User Fee Act, and (2) it includes commonsense provisions enabling the FDA not only to better ensure the safety and efficacy of new biomedical technologies but also to better ensure that individuals and the Nation as a whole have timely access to those technologies, now and in the future.

HEARINGS

In preparation for action on modernization of the Food and Drug Administration, the Committee held 17 hearings over the last 30 months, including an April 23, 1997, hearing entitled, "Reauthorization of the Prescription Drug User Fee Act and FDA Reform." The Subcommittee on Health and Environment received testimony from the following witnesses: Dr. Michael A. Friedman, Lead Deputy Commissioner, Food and Drug Administration; Dr. Raymond L. Woosley, Professor and Chairman, Department of Pharmacology, Georgetown University Medical Center; Dr. Joseph A. DiMasi, Director of Economic Analysis, Tufts Center for the Study of Drug Development, Tufts University; Dr. Samuel Broder, Senior Vice

President for Research and Development and Chief Scientific Officer, IVAX Corporation; Mr. Gordon M. Binder, Chairman & CEO, Amgen, Inc., representing the Pharmaceutical Research & Manufacturers of America and the Biotechnology Industry Organization; Mr. Bruce Downey, Chairman & CEO, Barr Laboratories, Inc., representing the Generic Pharmaceutical Industry Association and the National Pharmaceutical Alliance; Mr. David Holveck, President & CEO, Centocor, Inc.; The Honorable Martha Keys, Senior Public Policy Advisor, National Multiple Sclerosis Society; Ms. Susan L. Weiner, Executive Director, Children's Brain Tumor Foundation; Mr. Jeff Bloom, representing The Patients' Coalition; and Dr. Sanford Cohen, Pediatrician, representing the American Academy of Pediatrics.

COMMITTEE CONSIDERATION

On September 17, 1997, the Subcommittee on Health and Environment met in an open markup session and approved H.R. 1411 for Full Committee consideration, amended, by a voice vote. On September 25, 1997, the Full Committee met in an open markup session and ordered H.R. 1411, reported to the House, amended, by a rollcall vote of 43 yeas to 0 nays.

ROLLCALL VOTES

Clause 2(1)(2)(B) of rule XI of the Rules of the House requires the Committee to list the recorded votes on the motion to report legislation and amendments thereto. The following are the recorded votes on the motion to report H.R. 1411 and on amendments offered to the measure, including the names of those Members voting for and against.

**COMMITTEE ON COMMERCE -- 105TH CONGRESS
ROLL CALL VOTE #43**

BILL: H.R. 1411, Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Deutsch re: timeframes for completing pediatric studies.

DISPOSITION: NOT AGREED TO, by a roll call vote of 9 yeas to 32 nays.

REPRESENTATIVE	YEAS	NAYS	PRESENT	REPRESENTATIVE	YEAS	NAYS	PRESENT
Mr. Bilely		X		Mr. Dingell		X	
Mr. Tauzin		X		Mr. Waxman	X		
Mr. Oxley		X		Mr. Markey	X		
Mr. Bilirakis		X		Mr. Hall		X	
Mr. Schaefer		X		Mr. Boucher			
Mr. Barton		X		Mr. Manton		X	
Mr. Hastert		X		Mr. Towns		X	
Mr. Upton				Mr. Pallone	X		
Mr. Stearns				Mr. Brown	X		
Mr. Paxon		X		Mr. Gordon		X	
Mr. Gillmor		X		Ms. Furse			
Mr. Klug				Mr. Deutsch	X		
Mr. Greenwood		X		Mr. Rush			
Mr. Crapo		X		Ms. Eshoo		X	
Mr. Cox		X		Mr. Klink		X	
Mr. Deal		X		Mr. Stupak	X		
Mr. Largent				Mr. Engel		X	
Mr. Burr		X		Mr. Sawyer		X	
Mr. Bilbray		X		Mr. Wynn	X		
Mr. Whitfield				Mr. Green		X	
Mr. Ganske		X		Ms. McCarthy		X	
Mr. Norwood		X		Mr. Strickland	X		
Mr. White		X		Ms. DeGette	X		
Mr. Coburn		X					
Mr. Lazio							
Mrs. Cubin		X					
Mr. Rogan							
Mr. Shimkus		X					

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**COMMITTEE ON COMMERCE -- 105TH CONGRESS
ROLL CALL VOTE #44**

BILL: H.R. 1411, Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Pallone re: notice of discontinuance of lifesaving product.

DISPOSITION: AGREED TO, by a roll call vote of 21 yeas to 20 nays.

REPRESENTATIVE	YEAS	NAYS	PRESENT	REPRESENTATIVE	YEAS	NAYS	PRESENT
Mr. Bliley		X		Mr. Dingell	X		
Mr. Tauzin		X		Mr. Waxman	X		
Mr. Oxley				Mr. Markey			
Mr. Bilirakis		X		Mr. Hall	X		
Mr. Schaefer		X		Mr. Boucher			
Mr. Barton		X		Mr. Manton	X		
Mr. Hastert				Mr. Towns			
Mr. Upton		X		Mr. Pallone	X		
Mr. Stearns				Mr. Brown	X		
Mr. Paxon		X		Mr. Gordon	X		
Mr. Gillmor		X		Ms. Furse	X		
Mr. Klug		X		Mr. Deutsch	X		
Mr. Greenwood		X		Mr. Rush	X		
Mr. Crapo		X		Ms. Eshoo	X		
Mr. Cox		X		Mr. Klink	X		
Mr. Deal		X		Mr. Stupak	X		
Mr. Largent		X		Mr. Engel			
Mr. Burr		X		Mr. Sawyer	X		
Mr. Bilbray				Mr. Wynn	X		
Mr. Whitfield		X		Mr. Green	X		
Mr. Ganske		X		Ms. McCarthy	X		
Mr. Norwood		X		Mr. Strickland	X		
Mr. White		X		Ms. DeGette	X		
Mr. Coburn	X						
Mr. Lazio							
Mrs. Cubin		X					
Mr. Rogan							
Mr. Shimkus	X						

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**COMMITTEE ON COMMERCE – 105TH CONGRESS
ROLL CALL VOTE #45**

BILL: H.R. 1411, Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Brown re: appropriations for dissemination of treatment information.

DISPOSITION: NOT AGREED TO, by a roll call vote of 7 yeas to 36 nays.

REPRESENTATIVE	YEAS	NAYS	PRESENT	REPRESENTATIVE	YEAS	NAYS	PRESENT
Mr. Bliley		X		Mr. Dingell	X		
Mr. Tauzin		X		Mr. Waxman	X		
Mr. Oxley				Mr. Markey			
Mr. Bilirakis		X		Mr. Hall		X	
Mr. Schaefer		X		Mr. Boucher			
Mr. Barton		X		Mr. Manton	X		
Mr. Hastert				Mr. Towns			
Mr. Upton		X		Mr. Pallone	X		
Mr. Stearns				Mr. Brown	X		
Mr. Paxon		X		Mr. Gordon		X	
Mr. Gillmor		X		Ms. Furse		X	
Mr. Klug		X		Mr. Deutsch		X	
Mr. Greenwood		X		Mr. Rush		X	
Mr. Crapo		X		Ms. Eshoo		X	
Mr. Cox		X		Mr. Klink		X	
Mr. Deal		X		Mr. Stupak		X	
Mr. Largent		X		Mr. Engel		X	
Mr. Burr		X		Mr. Sawyer	X		
Mr. Bilbray		X		Mr. Wynn		X	
Mr. Whitfield		X		Mr. Green	X		
Mr. Ganske		X		Ms. McCarthy		X	
Mr. Norwood		X		Mr. Strickland		X	
Mr. White		X		Ms. DeGette		X	
Mr. Coburn		X					
Mr. Lazio							
Mrs. Cubin		X					
Mr. Rogan							
Mr. Shimkus		X					

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**COMMITTEE ON COMMERCE -- 105TH CONGRESS
ROLL CALL VOTE #46**

BILL: H.R. 1411, Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997

MOTION: Motion by Mr. Bliley to order H.R. 1411, reported to the House, amended.

DISPOSITION: **AGREED TO**, by a roll call vote of 43 yeas to 0 nays.

REPRESENTATIVE	YEAS	NAYS	PRESENT	REPRESENTATIVE	YEAS	NAYS	PRESENT
Mr. Bliley	X			Mr. Dingell	X		
Mr. Tauzin	X			Mr. Waxman	X		
Mr. Oxley	X			Mr. Markey	X		
Mr. Bilirakis	X			Mr. Hall	X		
Mr. Schaefer	X			Mr. Boucher			
Mr. Barton	X			Mr. Manton	X		
Mr. Hastert	X			Mr. Towns	X		
Mr. Upton	X			Mr. Pallone	X		
Mr. Stearns				Mr. Brown	X		
Mr. Paxon	X			Mr. Gordon			
Mr. Gillmor				Ms. Furse	X		
Mr. Klug	X			Mr. Deutsch	X		
Mr. Greenwood	X			Mr. Rush	X		
Mr. Crapo	X			Ms. Eshoo	X		
Mr. Cox				Mr. Klink	X		
Mr. Deal	X			Mr. Stupak	X		
Mr. Largent	X			Mr. Engel	X		
Mr. Burr	X			Mr. Sawyer	X		
Mr. Bilbray	X			Mr. Wynn	X		
Mr. Whitfield	X			Mr. Green			
Mr. Ganske	X			Ms. McCarthy	X		
Mr. Norwood	X			Mr. Strickland	X		
Mr. White	X			Ms. DeGette	X		
Mr. Coburn	X						
Mr. Lazio							
Mrs. Cubin	X						
Mr. Rogan							
Mr. Shimkus	X						

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COMMITTEE ON COMMERCE -- 105TH CONGRESS
VOICE VOTES
9/25/97

BILL: H.R. 1411, Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997

AMENDMENT: Amendment in the Nature of a Substitute by Mr. Burr.

DISPOSITION: **AGREED TO**, amended, by a voice vote.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Stearns re: chlorofluorocarbons in metered-dose inhalers.

DISPOSITION: **WITHDRAWN**, by unanimous consent.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Rush re: inclusion of women and minorities in clinical research studies.

DISPOSITION: **AGREED TO**, by a voice vote.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Burr re: applicability of exclusivity incentives for antibiotic drugs.

DISPOSITION: **AGREED TO**, by a voice vote.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Brown re: restrictions on citizens' petitions.

DISPOSITION: **WITHDRAWN**, by unanimous consent.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Deutsch re: applicability of exclusivity incentives for antibiotic drugs.

DISPOSITION: **WITHDRAWN**, by unanimous consent.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Waxman re: exemption from filing supplemental application for off-label use.

DISPOSITION: **WITHDRAWN**, by unanimous consent.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Deutsch re: report on economic impact of pediatric studies.

DISPOSITION: **AGREED TO**, by a voice vote.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Pallone re: study of mercury sales.

DISPOSITION: **AGREED TO**, by a voice vote.

AMENDMENT: Amendment to the Burr Amendment in the Nature of a Substitute by Mr. Pallone re: State initiatives relating to national uniformity for nonprescription drugs and cosmetics.

DISPOSITION: **NOT AGREED TO**, by a voice vote.

COMMITTEE OVERSIGHT FINDINGS

Pursuant to clause 2(1)(3)(A) of rule XI of the Rules of the House of Representatives, the Committee has held an oversight hearing on issues addressed in this legislation.

COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT

Pursuant to clause 2(1)(3)(D) of rule XI of the Rules of the House of Representatives, no oversight findings have been submitted to the Committee by the Committee on Government Reform and Oversight.

NEW BUDGET AUTHORITY AND TAX EXPENDITURES

In compliance with clause 2(1)(3)(B) of rule XI of the Rules of the House of Representatives, the Committee finds that H.R. 1411 would result in no new or increased budget authority or tax expenditures or revenues.

COMMITTEE COST ESTIMATE

The Committee adopts as its own the cost estimate prepared by the Director of the Congressional Budget Office pursuant to section 403 of the Congressional Budget Act of 1974.

CONGRESSIONAL BUDGET OFFICE ESTIMATE

Pursuant to clause 2(1)(3)(C) of rule XI of the Rules of the House of Representatives, the following is the cost estimate provided by the Congressional Budget Office pursuant to section 403 of the Congressional Budget Act of 1974:

U.S. CONGRESS,
CONGRESSIONAL BUDGET OFFICE,
Washington, DC, October 1, 1997.

Hon. TOM BLILEY,
*Chairman, Committee on Commerce,
House of Representatives, Washington, DC.*

DEAR MR. CHAIRMAN: The Congressional Budget Office has prepared the enclosed cost estimate for H.R. 1411, the Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997.

If you wish further details on this estimate, we will be pleased to provide them. The CBO staff contact is Anne Hunt.

Sincerely,

JUNE E. O'NEILL, *Director.*

Enclosure.

H.R. 1411—Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997

Summary: H.R. 1411 would reauthorize the Prescription Drug User Fee Act (PDUFA) of 1992, which empowers the Food and Drug Administration (FDA) to collect user fees from the pharmaceutical industry. The user fee program would be reauthorized, with some modifications, for an additional five years. The bill

would also amend the Food, Drug and Cosmetic Act (FD&CA) and the Public Health Service Act to reform the FDA's regulatory and approval processes for drugs, biologics, and antibiotics. One provision would grant a six-month extension of market exclusivity for pharmaceutical manufacturers who conduct pediatric studies on select prescription drugs. Another would make certain antibiotics eligible for patent extensions under the 1984 Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Act).

CBO estimates that enacting H.R. 1411 would result in net additional discretionary spending of \$9 million in 1998 and \$214 million over the 1998–2002 period, assuming appropriation of the authorized amounts. Reauthorizing the user fee program would yield \$601 million in offsetting collections over five years; these amounts would also be authorized to be spent, subject to appropriation. Extending market exclusivity for certain drugs would increase direct spending by \$65 million and reduce revenues by \$61 million over the 1998–2002 period. The direct cost implications of the provision extending eligibility for Hatch-Waxman extensions to some antibiotics cannot be estimated at this time.

By preempting state and local laws that regulate nonprescription drugs and labeling of cosmetics differently than federal law, H.R. 1411 would impose an intergovernmental mandate as defined in the Unfunded Mandates Reform Act (UMRA). CBO estimates that compliance with this mandate would result in no significant costs for state and local governments.

Estimated cost to the Federal Government: The estimated budgetary impact of H.R. 1411 is shown in the following table. For the purposes of this estimate, CBO assumes that all amounts authorized in the bill would be appropriated by the start of each fiscal year and that outlays would follow the historical spending patterns for the FDA. The costs of this legislation fall within budget function 550 (Health).

	By fiscal years, in millions of dollars—					
	1997	1998	1999	2000	2001	2002
SPENDING SUBJECT TO APPROPRIATION						
Spending Under Current Law:						
Estimated Authorizations:						
Authorization Level	887	919	949	982	1,106	1,050
Estimated Outlays	880	905	937	971	1,005	1,038
Collection of User Fees:						
Authorization Level	–88	0	0	0	0	0
Estimated Outlays	–88	0	0	0	0	0
Spending of User Fees:						
Authorization Level	88	0	0	0	0	0
Estimated Outlays	87	22	4	0	0	0
Proposed Changes:						
Estimated Authorizations:						
Authorization Level	0	26	64	68	70	70
Estimated Outlays	0	9	31	46	60	68
Collection of User Fees:						
Authorization Level	0	–110	–116	–119	–128	–128
Estimated Outlays	0	–110	–116	–119	–128	–128
Spending of User Fees:						
Authorization Level	0	110	116	119	128	128
Estimated Outlays	0	82	109	118	126	127

	By fiscal years, in millions of dollars—					
	1997	1998	1999	2000	2001	2002
Spending Under H.R. 1411:						
Estimated Authorizations:						
Authorization Level ¹	887	945	1,103	1,050	1,086	1,120
Estimated Outlays	895	923	968	1,017	1,065	1,106
Collection of User Fees:						
Authorization Level ¹	-88	-110	-116	-119	-128	-128
Estimated Outlays	-88	-110	-116	-119	-128	-128
Spending of User Fees:						
Authorization Level ¹	88	110	116	119	128	128
Estimated Outlays	87	104	113	118	126	127
DIRECT SPENDING AND REVENUES						
Direct Spending:						
Estimated Budget Authority	0	0	7	18	28	11
Estimated Outlays	0	0	7	18	28	11
Revenues:						
Estimated Revenues	0	0	-6	-15	-25	-15

¹The 1997 level is the amount appropriated for that year.

Basis of estimate

Estimated authorizations

The bill would reform the FDA's approval and regulatory processes with the intent of accelerating product approvals and reducing regulatory requirements. H.R. 1411 would require the FDA, in coordination with the National Institutes of Health (NIH) and the Centers for Disease Control (CDC), to establish a program to provide information on treatment, detection, and prevention of serious diseases and on clinical trials currently studying these conditions. Other provisions would result in small budgetary savings.

Information Program on Clinical Trials. H.R. 1411 would require the Director of the NIH in coordination with the FDA and the CDC to establish a program to provide information in treatment, detection, and prevention of serious diseases and on clinical trials currently studying these conditions. This program would include establishing a database of all federally and private funded clinical trials and a toll-free telephone information line available to health care providers, researchers, individuals with serious diseases, and all other members of the public.

The NIH already has such a program for clinical trials that it funds for cancer, AIDS, and rare diseases. Privately-funded clinical trials are also included in these databases on a voluntary basis. The FDA would be able to disclose information in clinical trials, and NIH would be required to expand its current database significantly to accommodate the increase in volume of trials and information. After the system was set up, additional maintenance costs would be incurred to keep up with the status and results of clinical trials, and with new protocols on treatment and prevention of serious diseases and conditions. Costs would also arise to operate the telephone information line, which would be staffed by health professionals.

CBO based its estimate on the cost of maintaining the current data banks and information networks, the estimated portion of clinical trials currently contained in NIH's databases, and on conversations with professionals experienced in this area. CBO as-

sumes that it would take two years to create a system that would meet the minimum requirements specified in the bill, at a cost of \$20 million in 1998 and \$45 million in 1999. For each year thereafter, CBO estimated a cost of \$50 million for maintenance and quality improvement. Costs would total \$215 million over the 1998–2002 period.

Dissemination of Off-Label Use Information. H.R. 1411 would permit manufacturers, within one year of enactment, to disseminate to select professional audiences information on a product use not described in the approved labeling of the drug. The only information that could be disseminated would be copies of articles in a peer-reviewed journal or in a reference publication. The manufacturer must also certify that a supplemental application for the product will be submitted to the Secretary within a specified time. The manufacturer must submit to the Secretary biannually a list of the titles of the articles disseminated and a list of the categories of health care providers receiving this information. CBO estimates that this provision would have no federal costs in 1998 but would cost \$59 million through 2002.

Regulation of Positron Emission Tomography (PET) and Radiopharmaceuticals. H.R. 1411 would require the FDA to establish an approval process and good manufacturing practice requirements for PET. The agency also could not require the submission of new drug applications or abbreviated new drug applications for PET products that are not adulterated for four years after enactment of the bill. Three FDA notices and rulings regarding the regulation of PET products would also be revoked. Finally, the bill would direct the FDA to issue regulations for the approval of radiopharmaceuticals used for diagnostic or monitoring purposes. The cost of fulfilling these requirements would be \$300,000 in 1998 and approximately \$1 million over five years.

Information Systems. The FDAS would be required to establish and maintain an information system that would allow the agency to track product applications and systems. Fulfilling these requirements would cost \$4 million in 1998 and \$13 million over five years.

User fees

The bill would reauthorize current prescription drug user fees through September 30, 2002. The current authorization expired at the end of fiscal year 1997. Proceeds from these fees would be available for spending, subject to appropriation.

Reauthorization of the Prescription Drug User Fee Act of 1992. As with prior law, the reauthorized program would levy three types of user fees on pharmaceutical manufacturers: application and supplement fees, establishment fees, and product fees. Aggregate amounts of such fees are specified in the bill for each fiscal year through 2002; these amounts would be adjusted to reflect cumulative inflation since 1997. CBO's estimate assumes that the inflation adjustment would apply to the specified authorization, not to the prior year's actual authorization. The amounts collected are authorized to be spent, subject to appropriation. CBO estimates that the FDA would collect \$110 million in 1998 and \$601 million over five years.

Any fees collected in excess of the amount specified in the appropriations act for a given year would be credited to the FDA appropriations account and subtracted from the amount of fees authorized for the following year. The FDA could not assess the user fees unless appropriations for FDA salaries and expenses, excluding any user fees, were at least equal to appropriations for 1997, adjusted for inflation.

Direct spending

The bill would grant an additional six months of market exclusivity to pharmaceutical manufacturers that conduct pediatric studies on select drugs. This provision would affect direct spending because it would increase costs of the Medicaid rebate program and the Federal Employees Health Benefit Program (FEHBP). This provision would apply to pediatric studies commenced before January 1, 2002.

The Secretary of Health and Human Services, through the Commissioner of the FDA, would issue a list of drugs for which additional pediatric information may yield a health benefit. The Secretary of Health and Human Services, through the Commissioner of the FDA, would issue a list of drugs for which additional, pediatric information may yield a health benefit. If manufacturers of targeted drugs submitted pediatric studies to the FDA, their product would receive an additional six months of market exclusivity. This benefit would accrue to both approved drugs and those awaiting approval. Manufacturers of an approved drug that received an extension under this provision could, if eligible, receive an additional six months of exclusivity for a supplemental application.

By extending the market exclusivity of certain drugs, this proposal would increase prescription drug costs for Medicaid, FEHBP, Veterans Affairs (VA) facilities, the Department of Defense, and the Public Health Service for the six months of the extension. In the absence of this provision, these programs may have had access to less expensive generic products. In the case of Medicaid and FEHBP, the additional costs of this provision would represent direct spending. At this time, the costs to the VA, the Department of Defense and the Public Health Service cannot be determined. CBO estimates that this provision would have no net budgetary effect in 1998 but would increase federal outlays for Medicaid and FEHBP by \$68 million over the 1998–2002 period. This provision would also reduce revenues to the federal government. Private insurers would raise premiums in response to higher pharmaceutical prices. Because individuals would have to pay higher insurance premiums, their taxable income would decrease. Total revenue reductions over five years are estimated at \$61 million.

Finally, section 23 of the bill would make certain antibiotics eligible for a patent extension under the Hatch-Waxman Act. Although this provision would increase costs to Medicaid, FEHBP, and other federal programs and would reduce federal revenues, these changes cannot be estimated at this time.

Pay-as-you-go considerations: The Balanced Budget and Emergency Deficit Control Act of 1985 sets up pay-as-you-go procedures for legislation affecting direct spending or receipts. Because the bill would affect direct spending and receipts, pay-as-you-go procedures

would apply. The projected changes in direct spending and receipts are summarized in the following table for fiscal years 1998–2007. For purposes of enforcing pay-as-you-go procedures, only the effects in the budget year and the succeeding four years are counted.

SUMMARY OF PAY-AS-YOU-GO EFFECTS

	By fiscal years, in millions of dollars—									
	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Change in outlays	0	7	18	28	11	0	0	0	0	0
Change in receipts	0	–6	–15	–25	–15	0	0	0	0	0

Estimated impact on State, local, and tribal governments: By preempting state and local laws that regulate nonprescription drugs and cosmetics differently than federal law, H.R. 1411 would impose an intergovernmental mandate as defined in UMRA. CBO estimates that compliance with this mandate would result in no significant costs for state and local governments. Consequently, the threshold established in UMRA (\$50 million in 1996, adjusted annually for inflation) would not be exceeded. This mandate would not affect tribal governments.

By granting certain drug manufacturers a six-month extension of market exclusivity for their products, the bill would make prescription drugs provided under Medicaid more expensive. CBO estimates that states' share of these costs would total about \$28 million over the next five years. Another provision in the bill would make certain antibiotics eligible for patent extension under the Hatch-Waxman Act. This provision also would result in increased costs for Medicaid; however, CBO is unable at this time to estimate the magnitude of these costs. In any event, these provisions would not constitute mandates under UMRA because prescription drugs under Medicaid are provided at a state's option.

Estimated impact on the private sector: H.R. 1411 would impose some new private-sector mandates, and in several instances would replace existing mandates with new, less burdensome requirements. In addition, the bill would reauthorize application fees and certain other fees paid by pharmaceutical companies. However, since these fees do not become effective until Congress appropriates them, they do not constitute a private-sector mandate. Thus, the direct costs of all private-sector mandates in this bill that could be estimated are minimal and the total effect could be a net reduction in mandate costs imposed on the private sector.

Sections 6 and 32 would impose new mandates on the private sector. Section 6 would direct the Secretary of Health and Human Services to establish “a data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions.” This provision would impose a new mandate on sponsors of such clinical trials by requiring them to forward to the data bank information about eligibility criteria for participation in the trial, the location of the trial, and a point of contact within 21 days after the clinical trials have begun. Section 32 would require manufacturers of drugs, biological products and class III medical devices that are life supporting or prevent a debilitating disease to notify the Secretary of any discontinuation in the manufacture of the product, 6

months in advance. CBO estimates that the costs of these mandates would be minimal.

Section 31 would require the Secretary to promulgate regulations restricting the sale of mercury for use as a drug or dietary supplement if the Secretary believes that the use of the product poses a threat to human health. Because such regulations are contingent on an analysis that has not yet been performed, the FDA was unable to provide any information that would clarify whether the restriction on the sale of mercury would be needed. Thus, CBO is unable to estimate the impact of this section on the private sector.

Several new mandates would cost no more and perhaps less than the current regulatory requirements that they would replace. Section 19 would set new quality standards for positron emission tomography drugs but relieve them of the new drug application process and certain other requirements. Section 21 would establish a single licensing requirement for biological products that would replace current licensing requirements.

Estimate prepared by: Federal Cost: Anne Hunt (FDA) and Cyndi Dudzinski (NIH). Impact on State, Local, and Tribal Governments: Leo Lex. Impact on the Private Sector: Anna Cook.

Estimate approved by: Paul N. Van de Water, Assistant Director for Budget Analysis.

FEDERAL MANDATES STATEMENT

The Committee adopts as its own the estimate of Federal mandates prepared by the Director of the Congressional Budget Office pursuant to section 423 of the Unfunded Mandates Reform Act.

ADVISORY COMMITTEE STATEMENT

No new advisory committees within the meaning of section 5(b) of the Federal Advisory Committee Act were created by this legislation. The bill, however, statutorily establishes existing scientific advisory panels and states that such panels shall not be subject to annual chartering and annual reporting requirements under the Federal Advisory Committee Act.

CONSTITUTIONAL AUTHORITY STATEMENT

Pursuant to clause 2(1)(4) of rule XI of the Rules of the House of Representatives, the Committee finds that the Constitutional authority for this legislation is provided in article I, section 8, clause 3, which grants Congress the power to regulate commerce with foreign nations, among the several States, and with the Indian tribes.

APPLICABILITY TO LEGISLATIVE BRANCH

The Committee finds that the legislation does not relate to the terms and conditions of employment or access to public services or accommodations within the meaning of section 102(b)(3) of the Congressional Accountability Act.

SECTION-BY-SECTION ANALYSIS OF THE LEGISLATION

Section 1. Short title; references; table of contents

Section 1 provides that the Act may be cited as the Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997, and unless otherwise specified, all references are to sections or provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA: 21 U.S.C. 321 et seq.). It also contains the table of contents.

Sec. 2. Fees relating to drugs

Section 2(a) sets forth four Congressional findings: (1) the prompt approval of safe and effective new drugs and other therapies is critical to improve public health; (2) the public health is served by making additional funds available for the purpose of augmenting resources of the FDA that are devoted to the process for human drug application review; (3) the provisions added by PDUFA have substantially reduced drug review times, should be reauthorized for an additional 5 years, and should be carried out by the FDA with new commitments to implement more ambitious and comprehensive improvements in the agency's regulatory processes; and (4) fees authorized by these amendments will be used to expedite the drug development and application review process through goals identified in letters from the Secretary of Health and Human Services to the Chairman of the House Committee on Commerce and the Chairman of the Senate Committee on Labor and Human Resources, to be set forth in the Congressional Record.

Section 2(b) augments several definitions in section 735 (21 U.S.C. 379(g)). Currently, section 735 defines what applications, products, and establishments will be assessed user fees. New section 735 defines certain applications and products that will not be assessed user fees, including biological license applications for products that will only be used for further manufacturing, and applications submitted by State or Federal governmental entities for products that will not be distributed commercially. User fees would be assessed on applications for large volume biological products used for single dose intravenous injection or infusion.

Section 735(5) is amended to define the term "prescription drug establishment" to mean a foreign or domestic place of business which is at one general physical location consisting of one or more buildings all of which are within 5 miles of each other and at which one or more prescription drug products are manufactured in final dosage form. Section 735(7)(A) is amended to allow expenses of contractors of FDA to be paid with PDUFA funds even if the contractors are not working in FDA facilities. Section 735(8) is amended by replacing August 1992 with April 1997 and updating from Fiscal Year 1992 to Fiscal Year 1997 when defining how the "adjustment factor" will now be calculated. It will now be the lower of either the Consumer Price Index for all urban consumers for April of the preceding fiscal year divided by such Index for April 1997, or the total discretionary domestic spending budget authority for the preceding fiscal year divided by such budget authority for Fiscal Year 1997.

Section 2(c) contains the authority to assess and use the drug user fees. It amends section 736(a) (21 U.S.C. 379h(a)) establishing

types of fees. PDUFA reauthorization will begin in Fiscal Year 1998. It will require payment of fees on submission of an application or supplement, instead of in two parts, one-half when the application is submitted and the second half when an action is taken on the application. This section also contains other conforming changes necessitated by this change.

New section 736(a)(1)(E) exempts from application fees applications or supplements for orphan drugs designated under section 526 for treatment of a rare disease or condition. To qualify for an exemption, an application cannot include any uses other than for rare diseases or conditions. Supplements qualify for an exemption if the drug has been designated under section 526 for the indication proposed in the supplement. Section 736(a)(1)(F) adds an exemption for a supplement to an application that provides for use of the drug product in the pediatric population.

New section 736(a)(2)(B) provides exceptions to the establishment fee. If, during the fiscal year, the establishment begins manufacturing a drug that it did not manufacture in the previous year, and if the establishment paid the full establishment fee before the manufacturing of this new drug began, the applicant initiating the manufacture will not be assessed a share of the establishment fee for that fiscal year.

Section 2(c)(1)(D) amends section 736(a)(3)(B) of the FFDCA, the prescription drug product fee, to make minor technical changes to the payment procedures and to correct an anomaly regarding antibiotics contained in PDUFA as enacted in 1992. Under the amended section, a fee will be paid for the fiscal year in which the product is first submitted for listing under section 510 of the FFDCA or for relisting if the product had been withdrawn. After the fee is paid in the first year, it must be paid on or before January 31 of each year thereafter.

Under PDUFA as enacted in 1992, innovator products approved under section 505 that were the same generic drugs approved under section 505(b)(2) or 505(j) of the FFDCA did not pay user fees. However, antibiotic drugs, which were approved under section 507, continued to pay fees even after a generic product was approved, and even though the generic product was not assessed fees. Under section 2(c)(1)(D), innovator antibiotic products approved under section 507 would not be required to pay user fees once a comparable generic product was approved. Thus, innovator antibiotics would be treated like other types of drugs with respect to user fees.

Section 2(c)(2)(b) amends section 736(b) relating to fee amounts with a new application fee schedule (\$205,704 in FY 1998; \$256,338 in each of FY 1999 and FY 2000; \$267,606 in FY 2001; and \$258,451 in FY 2002), and new target establishment fee revenues for each of five fiscal years (\$35.6 million in FY 1998; \$36.4 million in each of FY 1999 and FY 2000; \$38 million in FY 2001; and \$36.7 million in FY 2002). The supplement fee is set at approximately one-half of the application fee.

Section 2(c)(3) amends section 736 of the FFDCA to provide for annual workload and inflation adjustments. Under the provision as amended, beginning in FY 1998, the Secretary may adjust the fees each year cumulatively for inflation since FY 1997 and also may

adjust the establishment and product fees so that the amount of revenue collected in each category will equal the amount the FDA expects to collect as application fees. This amendment is designed to allow the Secretary to adjust the fees to account for changes in workload. Section 2(c)(3) provides that these adjustments are compounded annually.

Section 2(c)(4)(A) amends section 736(d) on fee waivers and reductions to change the way the small business exception is administered. Under PDUFA as enacted in 1992, a small business qualifying for the exception was assessed one-half the application user fee for the first application it submitted and was permitted to defer payment of the fee until one year after the date the application was submitted. Under the new section (E)(1), a small business qualifying for the exception will not be assessed any fee on the first application it submits, although supplements to the application and other applications will be assessed fees.

Section 2(c)(5) updates section 736(f)(1) (21 U.S.C. 379g(f)(1)) to FY 1997. Section 2(c)(6)(A) amends section 736(g) (21 U.S.C. 379h(g)) of the FFDCFA to allow the transfer of appropriated funds from the salaries and expenses account without fiscal year limitation to the appropriations account with fiscal year limitation, if the funds are available solely for reviewing human drug applications. It also amends the statute to allow funds to be collected in each fiscal year in an amount specified in appropriation Acts or otherwise be made available for obligation. Section 2(c)(6)(B) specifies that fees shall only be collected and be available to defray increases in the costs of the resources allocated for the review process for human drugs over such costs, excluding costs paid for fees collected under this section, for FY 1997 and multiplied by the adjustment factor.

Section 2(c)(6)(C) amends section 736(g)(3) of the FFDCFA and authorizes to be appropriated for fees: \$106,800,000 for FY 1998; and \$109,200,000 for each of FY 1999 and FY 2000; \$114,000,000 for FY 2001; and \$110,100,000 for FY 2002. These amounts may be further adjusted for workload and inflation.

This section also adds a new section 736(g)(4) to require that any collected fees over the appropriated amount be credited to the appropriation account of the FDA and be subtracted from the subsequent fiscal year authorization to collect fees.

Section 2(c)(7) amends section 736 (21 U.S.C. 379h) to create a new requirement for written requests for waivers, reductions, or refunds of fees. It redesignates subsection (i) as subsection (j) and provides in subsection (i) that, to qualify for consideration of a waiver or fee reduction or refund, a person must submit a written request to the Secretary for this action within 180 days after the fee is due.

Section 2(c)(8) amends section 736 (21 U.S.C. 379h) to create a subsection providing for a special rule for waivers, refunds, and exceptions. It requires that any requests for waivers, refunds, or exceptions for fees paid prior to the date of enactment be submitted in writing to the Secretary within one year after enactment of this Act.

Section 2(d) requires two annual reports to be submitted by the Secretary of Health and Human Services to the House Committee

on Commerce and the Senate Committee on Labor and Human Resources. The first will report, within 60 days after the end of the fiscal year, on the progress the FDA achieved in meeting the performance goals identified in the letters described in subsection 2(a)(4). The second will report within 120 days on the implementation of the authority for such fees during the fiscal year and FDA's use of the fees.

Section 2(e) states that the amendments made by this section shall take effect October 1, 1997.

Section 2(f) sunsets the amendments made by section 2(b) and (2)(c) on October 1, 2002, and the amendments made by section 2(d) requiring annual reports 120 days thereafter.

Sec. 3. Pediatric studies of drugs

Section 3 amends Chapter V (21 U.S.C. 351 et seq.) of the FDCA by creating a new section 505A, "Pediatric Studies of Drugs." Subsection 505A(a) provides that if, prior to the approval of a new drug, the Secretary determines that information about the drug will produce health benefits in a pediatric population, and makes a written request for pediatric studies (including a time frame for completing the studies), and the studies are completed and accepted by the Secretary, then the sponsor or manufacturer can qualify for up to 6 months of extra market exclusivity. The Committee has authorized the Secretary to determine the time frame for completing the studies, although the Committee emphasizes that such studies should be sought, conducted, and completed at the earliest possible opportunity. The Committee does not intend that such studies be artificially timed for market advantage.

Subsection (b) directs the Secretary to develop a list of already-approved drugs for which additional pediatric information may produce health benefits. In doing so, the Secretary is to set priorities among these drugs and to publish this list and the priorities. The list is to be updated annually.

Subsection (c) creates the authority for the Secretary to award exclusivity to drugs that are on the list developed under subsection (b). After the list has been published, the Secretary may make a request for pediatric studies of drugs on the list. This request must include a time frame for the completion of such studies. As with new drugs under subsection (a), if the manufacturer completes such studies in accordance with other provisions of Section 3, the manufacturer may be awarded six additional months of market exclusivity. The additional exclusivity would be over and above the period of exclusivity currently provided to the drug, whether it is derived from patent or Waxman-Hatch exclusivity.

Subsection (d) specifies two possible means of conducting studies requested under subsections (a) or (c). If the sponsor and the Secretary agree on written protocols, the requirement is satisfied if the studies are conducted according to those protocols. If, however, the sponsor and the Secretary do not agree on written protocols, the Secretary is to evaluate whether the studies conducted fairly respond to the request, have been conducted according to commonly accepted scientific principles and protocols, and have been adequately reported.

Subsection (e) deals with the circumstances in which a study report has been submitted before the expiration of a patent (or other form of exclusivity), but has not been accepted or rejected by the Secretary at the time of such expiration. In that case, the Secretary is to delay the approval of another drug until the Secretary determines whether the study is accepted, although this delay may not exceed 90 days. If the study is subsequently accepted and exclusivity granted, the period of additional exclusivity will be considered to have begun on the date of the expiration of the previous exclusivity. The Committee has made this provision for exceptional circumstances.

Subsection (f) requires the Secretary to publish a notice of acceptance of studies under subsection (d).

Subsection (g) defines the term “pediatric studies” to mean “at least one clinical investigation” in appropriate age groups. This definition has been chosen to ensure that the studies requested will be those requiring some substantial work, and not merely a review of existing data.

Subsection (h) limits the availability of exclusivity to one award per product except in the case of a drug supplemental application for a new use. In that case, the Secretary may award yet another six months of exclusivity to be added to any exclusivity for the use of the drug that is available under Waxman-Hatch authorities. Such additional exclusivity is not awarded in any other case.

Subsection (i) provides that if, under regulations promulgated under other authorities of law, the Secretary requires pediatric studies, those studies are to be deemed to satisfy the requirements of section 3 and to be the basis for the award of exclusivity.

Subsection (j) terminates the authority of section 3 on January 1, 2002. Moreover, the subsection requires that a study be conducted on the program and be submitted by January 1, 2001. That study is to include all aspects of the program, as well as the impact of the program on the price and availability of drugs. The Committee expects the Secretary to include in this report a specific assessment of the impact of this program on the availability of generic drugs.

Sec. 4. Expediting study and approval of fast track drugs

This section creates a new 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 and life-threatening conditions. This new mechanism, known as the fast track program, builds upon existing FDA programs for orphan drugs and accelerated approval products.

All drugs and biological products, including fast track products, must be shown to be safe and effective prior to receiving marketing approval. Ordinarily, a drug must have an effect on a clinical endpoint, such as morbidity or mortality, or on a validated surrogate endpoint, such as blood pressure or cholesterol levels, to demonstrate effectiveness. A fast track product that meets this standard would ordinarily receive a regular approval and would not be subject to the requirements or limitations (i.e., post-approval study requirement, pre-approval of promotional materials, and expedited withdrawal of approval) included in new FFDCA subsection 741(b).

New FDCA subsection 741(b) provides an alternative basis for approving fast track products that essentially codifies FDA's accelerated approval regulation. Under this regulation, a product may be approved if it has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. Such surrogate endpoints are considered not to be validated because, while suggestive of clinical benefit, their relationship to clinical outcomes, such as morbidity or mortality, is not proven. For example, if a drug can be shown to reduce the amount of human immunodeficiency virus (HIV) detectable in the blood of an acquired immunodeficiency syndrome (AIDS) patient, it can be approved on the basis of its effect on this surrogate endpoint, even though the drug's ultimate effect on health and survival requires more study to determine.

Accelerated approval based on surrogate endpoints, therefore, results in much quicker patient access to important new drugs, often reducing the pre-approval clinical trial process by several years. The FDA has approved 22 products, mostly for AIDS and cancer, under the accelerated approval regulation since it was adopted in 1992. This legislation makes it clear that surrogate endpoints that are reasonably likely to predict clinical benefit may serve as the basis for approval of drugs for any serious or life-threatening condition.

The Committee is aware that there are occasions when the evidence of a drug's effect on a clinical endpoint strongly suggests effectiveness, but is not sufficiently conclusive with respect to the ultimate outcome to warrant ordinary approval. The legislation authorizes the Secretary to approve such products under subsection 741(b), so that ultimate clinical benefit can be verified on the same post-approval basis as for accelerated approval products. This would allow the Secretary to facilitate patient access to promising drugs while retaining the right to require confirmation of the clinical benefit through an appropriate post-approval study, preapprove any promotional materials, and expeditiously withdraw approval if the post-approval study fails to confirm clinical benefit.

The Committee intends that the Secretary, in using the authority of this new subsection, apply the definition of "serious and life-threatening condition" that was published in the preamble to the final rule on the accelerated approval of new drugs and biologics for serious and life threatening diseases (57 Federal Register 58942 (December 11, 1992)). The definition is as follows:

The seriousness of a disease is a matter of judgement, 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 Federal Register 13235).

Drug sponsors may request that the Secretary designate drugs for fast track consideration, and the designation may be made concurrently with, or at any time after, the submission of the investigational application. Within 30 days of the request, the Secretary will determine if the drug meets the fast track criteria, and, if so, will designate the drug as a fast track product and take action to expedite its development and review.

Currently, under FDA's accelerated approval regulation, sponsors are required to conduct post-approval studies and to submit copies of promotional materials prior to dissemination. Subsection 741(b) provides the Secretary with the authority to impose such requirements but does not require this. However, the Committee expects that post-approval studies will routinely be required. With respect to prior approval of promotional materials, the Committee believes that the requirement should be imposed 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. Preapproval of promotional materials may terminate, even if post-approval studies have not been completed, as soon as the Secretary determines that the sponsor is compliant with the agency's requirements.

The approval of a fast track drug may be withdrawn using expedited procedures, including an informal hearing, if the sponsor fails to exercise diligence in conducting the post-approval studies; a post-approval study fails to verify a clinical benefit; other evidence demonstrates that the drug is not safe or effective for its intended use; or the manufacturer disseminates false or misleading promotional materials.

This provision also provides for the Secretary to initiate review of an application before the application is complete. If early evaluation of clinical data for a fast track drug shows evidence of effectiveness, the Secretary will evaluate for filing and may commence review of portions of an application, if the sponsor provides a schedule for submitting the information necessary for a complete application and pays any required user fee. In situations where the fast track drug's application is incomplete, the time periods for review of human drug applications agreed to in the letters referred to in Section (2)(a)(4) will not apply until a completed application is submitted.

The Secretary must develop and widely distribute to physicians, patient organizations, and pharmaceutical and biotechnology companies a comprehensive description of the provisions applicable to fast track drugs, and establish an ongoing program to encourage the development of surrogate endpoints that are reasonably likely to predict clinical benefit. Within 1 year of enactment, the Secretary must issue guidance that describes FDA's policies and procedures required for implementing this provision.

Sec. 5. Expanded access to investigational therapies

New FDCA Section 551(a) provides that in emergency situations the Secretary may authorize the shipment of investigational

drugs (as defined in regulations prescribed by the Secretary) for the diagnosis or treatment of a serious disease or condition.

New FFDC section 551(b) would permit any person, acting through a licensed physician, to request an investigational drug from a manufacturer or distributor, and permit a manufacturer or distributor to provide to such physician an investigational drug for the diagnosis or treatment of a serious disease or condition. Access is conditional on (1) a licensed physician determining that the person has no comparable or satisfactory alternative therapy and that the risk to the patient from the investigational product is not greater than that of the risk from the disease or condition; (2) the Secretary determining that there is sufficient evidence of the investigational drug's safety and effectiveness; (3) the Secretary determining that provision of the investigational drug will not interfere with the initiation, conduct, or completion of clinical investigation to support marketing approval; and (4) the sponsor or clinical investigator submitting to the Secretary a clinical protocol consistent with regulations promulgated describing the use of investigational drugs in a single patient or a small group of patients.

New FFDC section 551(c) authorizes the Secretary, upon submission by a sponsor or a physician of a protocol intended to provide widespread access to an investigational drug, to permit the drug to be made available for expanded access if it is determined that under the treatment investigational new drug application, the investigational drug is intended for use in the diagnosis or treatment of a serious or immediately life-threatening disease or condition, and there is no comparable alternative therapy available to diagnose or treat that stage of disease or condition in the intended patient population.

The Secretary must also determine that the investigational drug is under investigation in a controlled clinical trial or that all clinical trials necessary for approval of the use of the drug have been completed; the sponsor of the clinical trial is actively pursuing marketing approval; the availability of the investigational drug would not interfere with the enrollment of patients in ongoing clinical investigations; in the case of a serious disease, there is sufficient safety and effectiveness evidence to support the drug's use; and, in the case of immediately life-threatening diseases, whether there is scientific evidence available to provide a reasonable basis to conclude that the product may be effective for its intended use and would not expose patients to significant risk or injury. The protocol is also subject to the provisions of Section 505(i) and implementing regulations. The Secretary is authorized to inform National, State, and local medical associations and societies and voluntary health organizations about the availability of the investigational drug under the expanded protocol.

Under new FFDC section 551(d), the Secretary may, at any time, terminate expanded access for investigational drugs if the requirements of this section are no longer met.

Sec. 6. Information program on clinical trials for serious or life-threatening diseases

This section amends the Public Health Service Act (PHSA) by adding a new section 402(j) that directs the Secretary, acting

through the Director of the National Institutes of Health (NIH), to establish, maintain, and operate a program providing information on research relating to the treatment, detection, and prevention of serious and life-threatening diseases and conditions. The program is to be coordinated with other data banks containing similar information. After consultation with the Commissioner of the Food and Drug Administration, the directors of the appropriate components of the National Institutes of Health (including the National Library of Medicine), and the Director of the Centers for Disease Control and Prevention (CDC), the Secretary is required to establish a data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions. The Secretary must disseminate this data bank information through information systems, including toll-free telephone communications, made available to individuals with serious or life-threatening diseases, members of the public, health care providers, and researchers.

The data bank must include a registry of clinical trials that describes the purpose of the experimental drug, either with the consent of the protocol sponsor or when a trial to test effectiveness begins. The information provided must include eligibility criteria, location of the trial sites, and points of contact for those wanting to enroll. The information must be provided in a form that is readily understood by the general public, and it must be forwarded to the data bank by the sponsor of the trials not later than 21 days after the trials for clinical effectiveness begin.

The data bank must also include information pertaining to experimental treatments for life-threatening diseases that may be available under a treatment investigational new drug application or as a Group C cancer drug. The data bank may also include information pertaining to results of clinical trials of such treatments, with the consent of the sponsor, including information concerning potential toxicities or adverse effects. The data bank may not include information relating to an investigation if the sponsor has provided a detailed certification to the Secretary that the disclosure of the information would interfere with the enrollment of subjects, unless the Secretary, after receiving such a certification, provides the sponsor with a written determination that the disclosure would not interfere with the enrollment.

To carry out the provisions of this section there are authorized to be appropriated such sums as may be necessary. However, fees collected under the drug user fee section of the FFDCA may not be used to carry out this subsection. Further, the Secretary, the Director of NIH, and the Commissioner of the FDA must collaborate to determine the feasibility of including device investigations within the scope of the registry requirements. In addition, no later than 2 years after enactment, the Secretary must prepare and submit to Congress a report of the need for inclusion of device investigations; the adverse impact (if any) on device innovation in the U.S. if information relating to such device investigations is required to be disclosed publicly; and such other issues as the Secretary may deem appropriate.

Sec. 7. Dissemination of information on new uses

Section 7 amends Chapter VII of the FFDCA (21 U.S.C. 371 et seq.) by adding a new subchapter E, which lays out the requirements for the dissemination of treatment information on off-label uses of drugs. New FFDCA section 745(a) provides that a drug manufacturer may disseminate to health care practitioners, pharmacy benefit managers, health insurance issuers, group health plans, or Federal or State governmental agencies, written information concerning the safety, effectiveness, or benefit of a use not described in a product's FDA approved labeling, if the manufacturer meets the requirements of 745(b), which are:

(1) a new drug application filed under section 505(b), or a biologics license issued under section 351 of the PHSA is in effect;

(2) the information meets the requirements of section 746;

(3) the disseminated information is not derived from clinical research conducted by another manufacturer or, if it was derived from such research, the manufacturer disseminating the information has the permission of the other manufacturer to make the dissemination;

(4) 60 days before dissemination, the manufacturer has submitted to the Secretary a copy of the information to be disseminated, any clinical trial information relating to the safety and effectiveness of the unapproved use, any reports of clinical experience pertinent to the safety of the unapproved use, and a summary of such use;

(5) the manufacturer has complied with section 748 relating to the certification that the manufacturer will file a supplemental application with respect to the unapproved use; and

(6) the manufacturer agrees to include, along with the disseminated information, a prominently displayed statement that the information concerns a use of a drug that has not been approved by the FDA; if applicable, that the information being disseminated is being paid for by the manufacturer; if applicable, the names of authors of the information who have received financial compensation from the manufacturer; the drug's official label (with updates); if applicable, a statement that there are other products or treatments that have been approved for the use for which the information is being disseminated; and identification of any person that has provided funding for a study relating to the unapproved new use. The manufacturer also must provide a bibliography of other articles from scientific or medical journals that have been published previously about the unapproved use.

Section 745(c) provides that if the Secretary determines, after providing a notice and an opportunity for a meeting, that the off-label use information being disseminated fails to provide data, analyses, or other written matter that is objective and balanced, the Secretary may require the manufacturer to disseminate additional objective and scientifically sound information that pertains to the safety or effectiveness of the unapproved use and is necessary to provide objectivity and balance. Further, the Secretary may require the manufacturer to disseminate an objective statement of the Secretary, based on data or scientifically sound infor-

mation, that bears on the safety and effectiveness of the drug's unapproved use.

The principal policy considerations that underlie this provision are the facilitation of greater access to timely and accurate information by health care providers. Coupled with this goal is a recognition that the FDA has a responsibility to protect the public health. Thus, these provisions preserve the discretionary authority of the Secretary to offer objective statements on the proposed dissemination and to require the manufacturer to disseminate additional information to achieve objectivity and balance.

The Committee emphasizes that it has been the long held view of Congress that the FDA should not regulate the practice of medicine. In general, the FDA has no authority to regulate how physicians prescribe approved drugs in the context of their medical practice. Physicians prescribing off-label uses of approved drugs is not within the jurisdiction of the FDA. However, in the case where a physician is receiving information from a drug sponsor (whose activities are within the jurisdiction of the FDA), the FDA has a role to play with respect to assuring balance and objectivity and to protecting the public health. Nevertheless, health care providers retain the responsibility of making decisions about treatment of individual patients, and the FDA's role with respect to such individual treatment decisions based on information derived from peer-reviewed articles and textbooks, is advisory. In that advisory capacity, the FDA will take steps to make sure that the amount of information given to the provider is useful, useable, sufficient, and otherwise in compliance with this section. This does not mean that the FDA must comment on every proposed dissemination. Rather, the Committee expects that the authority of the Secretary to include an objective statement likely will be used in limited circumstances in which balance cannot be fully met by appending other journal articles, or data or analyses. The intent is that such a statement by the Secretary be limited to objective and scientific information. The Committee does not intend this to be an opportunity for the Secretary to editorialize based on independently derived scientific information. Any statement of the Secretary should provide significant scientific information to health care providers.

Section 746(a) provides that a manufacturer may disseminate information about an unapproved new use if the information is in the form of an unabridged reprint or copy of an article peer-reviewed by experts or in a reference publication, is not false or misleading, and would not pose a significant risk to the public health. The information must have been published in a scientific or medical journal and be about a clinical investigation which would be considered by the experts to be scientifically sound. The information can also be from an unabridged reference publication that includes information about a scientifically sound clinical investigation. A reference publication is a publication that:

- (1) has not been written, edited, or published specifically for a manufacturer;
- (2) has not been edited or significantly influenced by a manufacturer;

(3) is not solely distributed through a manufacturer, but is generally available in bookstores or distribution channels where medical texts are sold;

(4) does not focus on any particular drug of a manufacturer and does not have primary focus on unapproved uses of drugs that are marketed or under investigation by a manufacturer supporting the dissemination; and

(5) presents materials that are not false or misleading.

Section 747 establishes that a manufacturer may disseminate information under section 745 only if the manufacturer prepares and submits to the Secretary biannually a list containing the titles of the articles and reference publications relating to the unapproved use of drugs that were disseminated by the manufacturer for the 6-month period preceding the date on which the manufacturer submits the list to the Secretary. Additionally, the manufacturer must submit a list that identifies the categories of providers that received the articles and reference publications for the same 6-month period. A manufacturer that disseminates information under section 745 must keep records that may be used should the manufacturer be required to take corrective action. These records must be made available to the Secretary upon request, and at the Secretary's discretion, the records may identify the recipient of the information.

Section 748 establishes that a manufacturer may disseminate information under section 745 only if the manufacturer submits an application to the Secretary, containing a certification that a supplemental application will be filed for the unapproved use or the manufacturer is granted an exemption from this requirement. The application may contain a certification that the studies needed for the submission of a supplemental application for the unapproved use have been completed and that the supplement will be filed with the Secretary no later than 6 months after the date of the initial dissemination.

Alternatively, if the studies have not been completed but are planned, a manufacturer may disseminate information on an unapproved use if the manufacturer has submitted to the Secretary an application containing: a proposed protocol and schedule for conducting the studies needed for the supplemental application; and a certification that the supplemental application will be submitted to the Secretary no later than 3 years after the date of the initial dissemination of information (or, as applicable, not later than a date the Secretary may specify pursuant to an extension). The Secretary must determine that the proposed protocol is adequate and that the completion schedule is reasonable. A longer time for submitting a supplemental application may be granted if the Secretary determines that the studies needed cannot be completed and submitted within 3 years. Manufacturers must submit periodic reports describing the status of their studies. The proposal authorizes an extension of the 3-year period for the completion of studies if the Secretary determines that the manufacturer has shown due diligence in conducting the studies. Such extensions may not be longer than 2 years.

The proposal also provides for exemptions from the requirement for supplemental applications if the Secretary determines that con-

ducting the studies necessary for the supplemental application would be economically prohibitive, or unethical.

The Committee recognizes that there may be cases where the size of a patient population may be cause for the Secretary to determine that a supplemental application should not be filed. However, this is intended to be the exception, rather than the rule, in the case of populations suffering from orphan or rare disorders. For many years, this Committee has sought to encourage research into orphan diseases and the approval of innovative drugs for their treatment. The Secretary should examine very carefully whether an exemption from filing a supplemental application might hinder such research and recognize the vital importance of encouraging application for new drugs and new drug uses intended to treat rare disorders.

Manufacturers may disseminate information if they have filed an application for an exemption and the Secretary has approved the application, or the application is deemed to have been approved.

If the Secretary does not act on an application for an exemption within 60 days, the application will be deemed approved. Under a situation where the application is deemed approved and the manufacturer disseminates information on an unapproved use, the Secretary may at any time terminate approval and order the manufacturer to cease disseminating the information. A transition rule provides that for supplemental applications pending on the date of enactment, the application is deemed to be a supplemental application submitted under this provision.

Section 749 provides for circumstances where corrective action is necessary when the Secretary determines that the unapproved use may not be effective or may present a significant risk to the public health. The proposal specifies when manufacturers, after disseminating information, are responsible for reporting additional knowledge of clinical research related to the safety and effectiveness of the unapproved use. The Secretary may order a manufacturer to cease the dissemination of information if the Secretary determines that the information does not comply with the provisions of this subchapter. In addition, the Secretary may order a manufacturer to cease the dissemination of information if the Secretary determines that a supplemental application does not contain adequate information for approval of the unapproved use. In certain situations where the Secretary orders a manufacturer to cease disseminating information, the Secretary may order the manufacturer to take action to correct the information disseminated. In the case of an order to cease dissemination which was based on the termination of a deemed approval of an application for an exemption from the requirement to file a supplemental application, the Secretary may not order the manufacturer to take corrective action unless the unapproved use would pose a significant risk to public health.

New section 751(a) provides that nothing in section 745 shall be construed as prohibiting a manufacturer from disseminating information in response to an unsolicited request from a health care practitioner. The Committee wants to emphasize that current FDA policies that encourage scientific exchange are not being modified by section 745. At the same time, insofar as the Secretary may cur-

rently have authority under other sections of the FFDCa to restrict a manufacturer's dissemination of information in response to an unsolicited request from a health care practitioner, nothing in section 745 is intended to change or limit that authority.

New FFDCa section 751(e) provides that the amendments by this section shall cease to be effective September 30, 2006, or 7 years after the date on which the Secretary promulgates the regulations to implement the provisions, whichever is later.

Sec. 8. Studies and reports

This section directs the General Accounting Office (GAO) to study the impact of the amendments made by section 7 on the resources of the Department of Health and Human Services (HHS), and of the scientific issues raised by the amendments of section 7. Issues to be addressed include the effectiveness of the amendments in getting useful information to health care practitioners; the quality of the information being disseminated; the quality and usefulness of the information provided; and the impact the amendments have had on research on new uses of drugs, indications for new uses, dosages for new uses, and the impact on pediatric indications and rare diseases. The GAO report will be submitted no later than January 1, 2002, to the House Committee on Commerce and the Senate Committee on Labor and Human Resources.

Sec. 9. Approval of supplemental applications for approved products

Once a new drug or biological product is approved for marketing by the FDA, the medical profession immediately begins to determine its proper place in the pharmaceutical armamentarium through clinical use and investigation. New uses of approved products often become known and widely followed. Although the use of an approved product for an unapproved use does not violate the law, it is important to encourage the addition of new uses to the FDA-approved product labeling in order to keep that labeling current with medical practice.

New uses of approved products can be added to the product label if the sponsor submits a supplemental new drug application (NDA) to the FDA, and the FDA approves that application. In many instances, however, there is no incentive for the submission of a supplemental application, and in fact there may be disincentives. The cost of clinical studies to support a supplemental NDA can be substantial. When the patent and market exclusivity periods are short or expired, no one company is prepared to make the investment necessary to obtain FDA approval of a supplemental NDA. Market exclusivity for a new use provides little protection where generic products already exist. Administrative requirements and regulatory delays at the FDA have also contributed to this problem. As a result, a significant number of drugs in the United States are prescribed in a manner which differs in some respect from the labeling approved by the FDA. Studies have shown that most cancer drugs and AIDS drugs are used in this manner.

Recognizing that current policy has resulted in the labeling for most prescription drugs to become obsolete, the FDA has begun to address this matter. Recent draft guidance from the agency has

identified ways to approve a supplemental NDA on the basis of evidence different from the adequate and well controlled clinical trial usually required to support initial approval of an NDA. The Committee agrees that a supplemental NDA, in appropriate circumstances, may be approved on the basis of literature reports without duplication of previously submitted data. This legislation requires the FDA to issue final guidance that will clarify the circumstances under which such evidence will be sufficient for approval of a supplemental application in order to encourage the regulated industry to submit supplemental applications whenever feasible.

This provision directs the FDA to determine new policy in order to reduce the disincentives to the submissions of these applications, by reducing the cost and increasing the efficiency of handling these matters within the agency. By reducing the overall burden of submitting supplemental applications and obtaining their approval, the legislation will increase the incentive for industry to increase the appropriate use of important prescription drugs and reduce the risks of unsafe or inappropriate use.

The legislation will accomplish these important purposes in three ways. First, the FDA is required to issue final guidance that will reduce the administrative and regulatory requirements for supplemental applications. Second, the FDA must designate an individual, and establish a procedure, that will facilitate the development and submission of supplemental NDAs and encourage their prompt review. Third, the FDA must establish programs and policies in collaboration with NIH and professional medical and scientific societies to identify existing data, foster further research, and encourage sponsors to submit supplemental applications. Thus, the legislation establishes a comprehensive approach that will reduce the gap between the approved labeling and the actual use of prescription drugs.

Specifically, Section 9(a) requires that, within 180 days of enactment, the Secretary must publish in the Federal Register performance standards for the prompt review of supplemental applications for previously approved drugs. Section 9(b) provides that within this same time frame, the Secretary also must issue final guidance to industry to clarify requirements and facilitate the submission of data to support the approval of supplemental applications. The guidance must: (1) clarify the circumstances that will permit published material to qualify as the basis for approval; (2) specify data requirements that will avoid duplication by recognizing the availability of data previously submitted; and (3) define supplemental applications that are eligible for priority review.

Section 9(c) requires the Secretary to designate someone in each FDA Center (except the Center for Food Safety and Applied Nutrition) who will be responsible for encouraging prompt review of supplemental applications, and who will work with sponsors to facilitate the development and submission of data to support supplemental applications. Section 9(d) requires that in addition, the Secretary must implement programs and policies that will foster collaboration among the FDA, the NIH, professional medical and scientific societies, and others to identify published and unpublished studies that could support a supplemental application. Moreover,

the Secretary must encourage sponsors to submit supplemental applications or conduct further research based on these studies.

Sec. 10. Health care economic information

This section amends section 502(a) (21 U.S.C. 352(a)) of the FDCA to specify that health care economic information will not be considered false and misleading if the information directly relates to an approved indication for such drug and is based on competent and reliable information. It establishes that a health care economic statement may be submitted to a formulary committee, managed care organization, or similar entity with drug selection responsibilities.

The proposal defines “health care economic statement as” an analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.”

The purpose of section 10 is to make it possible for drug companies to provide information about the economic consequences of the use of their products to parties that are charged with making medical product selection decisions for managed care or similar organizations. Such parties include formulary committees, drug information centers, and other multidisciplinary committees within health care organizations that review scientific studies and technology assessments and recommend drug acquisition and treatment guidelines. The provision is limited to analyses provided to such entities because such entities are constituted to consider this type of information through a deliberative process and are expected to have the appropriate range of expertise to interpret health care economic information presented to them to inform their decision-making process, and to distinguish facts from assumptions. This limitation is important because it will ensure that the information is presented only to parties who have established procedures and skills to interpret the methods and limitations of economic studies. The provision is not intended to permit manufacturers to provide such health care economic information to medical practitioners who are making individual patient prescribing decisions nor is it intended to permit the provision of such information in the context of medical education.

Health care economic information is defined as an analysis that identifies, measures, or compares the economic consequences of the use of the drug to the use of another drug, another health care intervention, or no intervention. Incorporated into economic consequences are the costs of health outcomes. Data about health outcomes associated with the use of a drug, other treatments, or no treatment are therefore incorporated into the economic analysis. This provision limits such incorporation to health outcomes that are directly related to the approved use of the drug and are determined based on competent and reliable scientific evidence. The provision presumes that the current standard practice of including full disclosure of all assumptions and health outcomes used in the economic analysis will continue.

The type of health care economic information that can be provided pursuant to this section is that which is directly related to

an approved labeled indication. To illustrate this point, economic claims based on preventing disease progression would ordinarily not be considered to be directly related to an approved indication for the treatment of symptoms of a disease, for a drug for which the use in prevention of disease progression has not been approved. For example, rheumatoid arthritis drugs are approved for the treatment of symptoms and not for the prevention of deformity. Therefore, economic claims based in part on an assumption of prevention of deformity would not be considered directly related to the approved indications for these drugs.

Similarly, economic claims based on prolonging patient survival would not be considered directly related and would not, therefore, be permitted under this subsection, for agents approved for the symptomatic treatment of heart failure, but not approved for prolonging survival in heart failure patients. This provision also is not intended to provide manufacturers a path for promoting off-label indications or claiming clinical advantages of one drug over another when such claims do not satisfy FDA's evidentiary standards for such claims.

However, the provision would permit health care economic information that includes reasonable assumptions about health care economic consequences derived from, but not explicitly cited in, the approved indication that are supported by competent and reliable scientific evidence. The nature of the evidence needed will depend on how closely related the assumptions are to the approved indication and to the health significance of the assumptions. For example, modeling the resource savings of insulin therapy to achieve tight control of blood sugar in Type 1 diabetes could include cost savings associated with the prevention of retinopathy (an eye disease) and nephropathy (kidney disease), based on well-controlled study(ies) that demonstrate that control of blood sugar levels with insulin leads to a reduction of such consequences. Because prevention of retinopathy and nephropathy could not simply be assumed to be a result of blood sugar control, these prevention claims would have to be shown by well-controlled study(ies) before inclusion as health care outcome assumptions.

In contrast, economic claims that model, based on observational studies in a population of women, the economic consequences of prevention of fractures due to osteoporosis would be permitted for drugs already approved for prevention of fractures due to osteoporosis. This is possible because observational data may be considered competent and reliable for making an assumption about the secondary consequences of an osteoporotic fracture once the primary prevention has been established. Similarly, the long-term economic consequences of the prevention of meningitis by haemophilus b influenza vaccine could be modeled using population-based data once the primary prevention claim is established.

The standard of competent and reliable scientific evidence (49 Federal Register 30, 999, (August 2, 1984)) supporting health care economic information provided under this subsection takes into account the current scientific standards for assessing the various types of data and analyses that underlie such information. Thus, the nature of the evidence required to support various components of health care economic analyses depends on which component of

the analysis is involved. For example, the methods for establishing the economic costs and consequences used to construct the health care economic information would be assessed using standards widely accepted by economic experts. The methods used in establishing the clinical outcome assumptions used to construct the health care economic analysis would be evaluated using standards widely accepted by experts familiar with evaluating the merits of clinical assessments. In addition, the evidence needed could be affected by other pertinent factors. The competent and reliable standard is not intended to supplant the current FFDCA definition of “false and misleading.”

Under the FDA’s current postmarketing reporting regulations, health care economic information as defined in this section must be submitted to the FDA at the time it is initially provided to a formulary committee or other similar entity. In addition, pursuant to this provision, the FDA will have access, upon request, to any data or other information related to the substantiation of the health care economic information. Such information will be evaluated by the Secretary to determine if the health care economic information meets the requirements of this section. This includes, for example, health outcome data, health resource utilization data, and other information related to the economic consequences of the use of the drug. It would not include, for example, confidential corporate financial data, including confidential pricing data.

Sec. 11. Clinical investigations

In 1962, Congress amended the new drug provisions of the law to require that the FDA approve the marketing of a new drug on the basis of substantial evidence of effectiveness. The statutory definition of substantial evidence requires adequate and well-controlled investigations, including clinical investigations, on the basis of which experts qualified by training and experience may fairly and responsibly conclude that the drug will have the effect it is represented to have under the conditions of use set forth in the labeling. On some occasions in the past, the FDA has stated that this always requires at least two well-controlled investigations. On other occasions, the FDA has stated that it requires only one well-controlled investigation in appropriate circumstances. In practice, the agency has approved many new drugs on the basis of one well-controlled investigation, where other evidence was available to confirm the effectiveness of the drug.

This legislation amends the law to codify current FDA practice. It authorizes the FDA, in its discretion, to approve an NDA on the basis of one adequate and well-controlled clinical investigation and confirmatory evidence obtained prior to or after that investigation, where the FDA concludes that such data and evidence are sufficient to constitute substantial evidence of effectiveness. The FDA will also retain its inherent administrative discretion to waive this requirement completely, as it has done in the past, where it would be unethical or unnecessary.

The FDA has itself recognized in recent guidance that substantial evidence of effectiveness may consist of one adequate and well-controlled investigation and confirmatory evidence consisting of earlier clinical trials, pharmacokinetic data, or other appropriate

scientific studies. The Committee agrees that the quality of the data and information available about a drug, rather than the number of studies performed, should determine the standard for FDA approval of a new drug. Authorizing the FDA to approve a drug on the basis of one well-controlled investigation will reduce the number of patients required to undergo clinical trials and the possibility of receiving a placebo; reduce the cost of drug development, and thus, the ultimate cost of a new drug to the public; reduce the total time needed to obtain FDA approval of a new drug; increase the number of new drugs that can be investigated; and thus speed the development and availability of important new drugs to help improve the public health.

The codification applies to all drugs, including those that are and are not for serious and life-threatening disease. Each disease is important to those who suffer from it, and every disease has a debilitating effect both on the patient and on the family and caretakers. This statutory standard will assure that the rights of all patients are recognized in the development of new drugs intended to alleviate their suffering. There is no scientific or public health basis for imposing different standards for approval of drugs for different categories of diseases.

This section amends section 505(d) of the FFDCA by clarifying that if the Secretary determines, based on relevant science, that the data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence of effectiveness.

The Committee considers confirmatory evidence to comprise scientifically sound data (as defined by the Secretary) from any investigation in the new drug application that provides substantiation as to the safety and effectiveness of the new drug.

This section also amends section 505(b)(1) to require that the Secretary, in consultation with the Director of the National Institutes of Health, review and develop guidance as appropriate on the inclusion of women and minorities in clinical trials.

Sec. 12. Manufacturing changes for drugs

Section 12 amends Chapter VII (21 U.S.C. 371) of the FFDCA, by establishing a new section 755 under new Subchapter F, "Manufacturing Changes." It describes the types of manufacturing changes the manufacturer of a new drug or biologic may make under section 505 or 512 of the FFDCA or section 351 of the PHSA. Section 755(b) requires that before distributing a new drug or biologic made after a manufacturing change (whether a major manufacturing change or otherwise), the holder involved must validate the effect of the change on the product's identity, strength, quality, purity, and potency as they relate to its safety, bioequivalence, bioavailability, or effectiveness.

Under section 755(c)(1), a drug made with a major manufacturing change may be distributed only if, before distribution, the holder submits to the Secretary a supplemental application for the change and the Secretary approves the application. The application must contain such information as the Secretary determines is ap-

appropriate, and shall include the information developed under subsection (b). Drugs made after these changes may not be distributed until the Secretary approves the supplement.

Section 755(c)(2) specifies the types of manufacturing changes that qualify as major changes. Such changes would be those determined to have substantial potential to adversely affect the identity, strength, quality, purity, or potency of the drug as they relate to the drug's safety, bioequivalence, bioavailability, or effectiveness (section 755(c)(2)(A)). Major manufacturing changes also are changes in the qualitative or quantitative formulation of the drug or in specifications in the approved application or license, changes the Secretary determines require an appropriate clinical study, and changes which the Secretary determines would have an adverse effect on the drug's safety or effectiveness (Sections 755(c)(2)(B)).

Manufacturing changes other than major changes, as determined by the Secretary must be reported annually with supporting data, or in a supplemental application. Drugs for which a minor manufacturing change has been made may be distributed 30 days after the Secretary receives a supplemental application, unless the applicant is notified that prior approval of the supplement is required (section 755(d)). After notification to the applicant, the Secretary must approve or disapprove each supplement. Section 755(d) allows the Secretary to determine the types of manufacturing changes after which distribution of the drug may begin when the supplement is submitted. A period for transition from prior requirements is defined.

Sec. 13. Streamlining clinical research on drugs

This section amends section 505(i) of the FFDCA to revise the clinical research process in several ways. It provides flexibility to reduce the amount of information required by the FDA from the drug sponsor before clinical research can begin. The section also establishes what information is needed for a clinical investigation submission to the FDA, and the terms and conditions under which the agency may request additional information to protect the health or safety of research subjects. New section 505(i)(2) establishes that a clinical investigation may begin 30 days after the FDA receives a submission containing information about the drug and the clinical investigation which includes:

(A) information about the design of the investigation and adequate reports of basic information, certified by the applicant to be accurate, necessary to assess the drug's safety in a clinical trial; and

(B) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

New section 505(i)(3) establishes that the Secretary may halt the conduct of a clinical research trial at any time by issuing a clinical hold, confirmed in writing, prohibiting the sponsor from conducting the investigation. The clinical hold may be issued based on a determination by the FDA that the drug represents an unreasonable risk to the safety of the persons who are in the clinical study, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation,

the condition for which the drug is to be investigated, and the health status of the subjects involved. Clinical holds also could be issued for such other reasons as the Secretary may establish by regulation, including reasons included in regulations that already have been promulgated. The FDA would be required to decide in 30 days on a request from the sponsor for the removal of a clinical hold, specifying in writing the reasons for continuing the hold.

Sec. 14. Data requirements for drugs

Before a new drug may lawfully be marketed, the sponsor must submit a NDA to the FDA, the FDA must review the NDA to verify that it demonstrates the safety and effectiveness of the drug, and the FDA must then approve the NDA. Under current FDA regulations and policy, a NDA consists of hundreds of volumes of detailed materials that are painstakingly reviewed by the FDA staff. Individual FDA reviewers have substantial discretion to impose on sponsors either more detailed or less detailed submissions. Some reviewers require that every report of a clinical or preclinical study be submitted with individual case report forms or other detailed back-up data. Other reviewers impose these requirements only for pivotal studies and permit data from confirmatory studies to be submitted in abbreviated or summary form.

The FDA and the regulated industry agree that much of the data that is submitted with a NDA can be presented in a more streamlined and efficient format. The elimination of extra or unnecessary data will result in a consistent and uniform approach throughout the agency, reduce the cost of NDAs, speed up the submission of these applications, reduce wasted time in FDA review of applications, and, thus, result in more efficient and effective development and review of product applications.

The Committee intends that studies that are pivotal in supporting label claims must be provided to the FDA in sufficient detail for agency reviewers to properly evaluate the study. Other information should be submitted in abbreviated or summary form. Under the legislation, the FDA is required to establish guidance for the industry in determining the kinds of studies for which abbreviated or summary reports are appropriate and the format that those summary reports should follow. This will adopt the best practices currently used within the agency and provide consistent and efficient policy for industry to follow in the future.

Section 14 requires the Secretary, acting through the Commissioner of the FDA, within 1 year of enactment, to issue guidance that describes when manufacturers will be permitted to submit certain abbreviated study reports instead of traditional full reports with their new drug applications (NDAs). The guidance must describe when abbreviated reports are appropriate and what their format should be.

Sec. 15. Content and review of applications

This section amends section 505(b) (21 U.S.C. 355(b)) of the FDCA to require the Secretary to issue guidance, for the review of applications, relating to promptness, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards which must apply to all individuals who review

applications. The Committee intends that this guidance should apply to all applications for investigational new drug exemptions, new drug approvals, and biologics licenses.

New section 505(b)(4)(B) requires that the Secretary meet with sponsor of an investigation or an applicant for approval if the sponsor or applicant makes a reasonable request for a meeting for the purpose of reaching agreement on the design and size of clinical trials. Minutes of such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request. Section 505(b)(4)(C) requires that any agreement between the Secretary and the sponsor or applicant regarding the parameters of the design and size of clinical trails of a new drug shall be made part of the written administrative record by the Secretary. This agreement cannot be changed after the testing begins, except with the written agreement of the sponsor or applicant; or pursuant to a decision made by the director of the division in which the drug is reviewed, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun. In the case when a substantial scientific issue has been identified the directors's decision shall be in writing, and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director documents the scientific issue involved.

New section 505(b)(4)(E) provides that written decision of the reviewing division shall be binding upon the field and compliance division personnel unless such personnel demonstrate to the reviewing division why such decision should be modified. Section 505(b)(4)(F) prohibits a delay in an action by a reviewing division, based on lack of availability of information from field personnel, unless the reviewing division determines that a delay is needed to assure safety and effectiveness of a product.

New section 505(j)(3) requires that the Secretary meet with an applicant for approval of a generic drug if the applicant makes a reasonable request for a meeting to reach agreement on the design and size of studies needed for approval of an abbreviated new drug application (ANDA). Any agreements regarding the parameters of design and size of bioavailability and bioequivalence trials of a drug shall be made part of the written administrative record. Such agreement shall not be changed after the testing begins, except with the written agreement of the sponsor or applicant; or pursuant to a decision made by the director of the division, that a substantial scientific issue essential to the determination of the safety or effectiveness of the drug has been identified. Such a decision shall be in writing and the Secretary shall provide to the sponsor or applicant the opportunity for a meeting where the director shall document the scientific issue.

The written decision of the reviewing division shall be binding upon the field or compliance office personnel unless such field or compliance personnel demonstrate to the reviewing division why such decision should be modified. Further, no action by the reviewing division may be delayed by lack of availability of the information from the field personnel, unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

This section is intended by the Committee to provide for a predictable and dependable structure through which the FDA and sponsors of applications for marketing of new products can communicate effectively regarding requirements that must be met to secure marketing clearance or approval. The Committee believes that meetings between the appropriate FDA experts and their industry counterparts may provide the avenue to successful communication that may result in agreements that can expedite a manufacturer's understanding of what information, data, or investigations may be needed for any particular product. The legislation requires that such meetings be held upon the reasonable request of a sponsor or applicant, within a specified time frame after such request. By "reasonable request," the Committee means that the person requesting the meeting must be adequately prepared so that the meeting can be productive. Specifically, the person requesting the meeting must provide to the FDA a detailed description of the person's proposal (whether for clinical protocols for other studies), and any other available information about the product that will assist FDA experts in providing useful advice and guidance.

The provisions of this section also make clear that the FDA, when it has been provided with sufficient information by the sponsor or applicant, must respond to meeting requests promptly and be prepared to participate in such meetings with a view toward reaching the desired conclusion—an agreement between that agency and the sponsor or applicant about the data, information, or studies needed before marketing approval or clearance can be achieved. The Committee intends that when FDA officials, including reviewers, provide advice during such meetings, and such advice results in an agreement between the FDA and the sponsor or applicant, the agreement should be communicated in writing by the FDA to the sponsor or applicant, and should be made part of the agency's administrative record related to the particular application or product.

Although the Committee believes that such agreements should be binding on both parties, the Committee also recognizes that changes in medical or scientific information which have a direct impact on issues that may have been part of the agreement may occur after the agreement has been reached. In addition, the Committee recognizes that, despite everyone's best efforts to provide all available information at the time of the meeting, there may have been information not known to the FDA (or to the sponsor or applicant) which has direct bearing on a decision or agreement made at the meeting. This is why the legislation allows for changes in any such agreements, based on the fact that a substantial scientific issue has come to light after an agreement has been reached, which has a direct bearing on the safety or effectiveness of the product. In general, changes also can be made if there is agreement between the agency and the sponsor or applicant.

Sec. 16. Scientific advisory panels

This section amends section 505 for the purpose of enhancing the way expert scientific advice and recommendations may be provided to the Secretary regarding clinical investigation of a drug or the ap-

proval for marketing of a drug under section 505 of the FFDCA or section 351 of the PHSA.

The Committee has laid out some important requirements regarding advisory committee membership, expertise, and operations. The intent of these provisions is not merely to create additional administrative requirements for either the FDA or its scientific advisors, but to make the advisory committee system more responsive to the needs of the FDA, sponsors and manufacturers, and patients.

The bill also provides that a scientific advisory panel under this section shall not be subject to the annual chartering and annual report requirements of the Federal Advisory Committee Act.

Sec. 17. Dispute resolution

Neither the current law nor existing regulations provides an adequate basis for resolving scientific and medical disputes that arise in the course of FDA implementation of the law. Such disputes are inevitable, considering the breadth of the FDA jurisdiction and the depth of FDA authority to regulate products subject to its jurisdiction. It is important that these matters receive appropriate attention, and be resolved efficiently and quickly in order to expedite agency action on important matters.

Current practice, and some regulations, establish at least an informal FDA recommendation that any disputed matter be appealed through the chain of command to the highest agency official responsible for the matter. The Committee agrees that this is a reasonable approach. Nonetheless, it must be recognized that some matters will not readily be resolved in this manner. Where there is a scientific controversy between the FDA and a person or company, and it cannot be resolved internally, the Secretary shall establish a process by which a person or company may request review of the matter by an appropriate scientific advisory committee. Any review by an advisory committee should take place in a timely manner. This process may provide that important scientific issues will receive appropriate attention from independent scientists who can bring a fresh perspective to assure that the regulated industry receives a fair and impartial hearing and that the FDA receives sound recommendations and advice.

This section amends chapter V (21 U.S.C. 351 et seq.) of FFDCA by establishing a new section 506, to require that the Secretary establish, by regulation, a mechanism for resolving scientific disputes between the Secretary and a person who is a sponsor, applicant, or manufacturer, and there is no specific provision or regulation under the FFDCA that provides a right of review of the matter in controversy. In particular, the regulations must provide an opportunity for advisory panel review of the issue.

Sec. 18. Informal agency statements

Section 701(h) would require the Secretary to follow predictable and consistent procedures in developing, issuing, and using guidance documents. The Committee believes providing consistent and predictable guidance to sponsors and applicants is critical for a rational and efficient process relating to the “processing, content, and evaluation/approval of applications and relating to the design, pro-

duction, manufacturing, and testing of regulated products; and (2) documents prepared for FDA personnel and/or the public that establish policies intended to achieve consistency in the agency's regulatory approach and establish inspection and enforcement procedure." (62 Fed. Reg., 39, 8961 (February 27, 1997)).

Subsection (h)(1) requires the Secretary to develop guidance documents with public participation and to ensure that the documents are made available to the public. These guidance documents are not binding on the agency or the public; rather, they present the current views of the Secretary on matters under the jurisdiction of the FDA. Although these documents do not create any rights for, or on, any persons and do not bind the Secretary or the public, the Secretary must ensure that employees of the FDA do not deviate from such guidance without appropriate justification from supervisory personnel. The Committee strongly endorses the view that the value of guidance documents is to provide consistency and predictability and emphasizes the importance of ensuring that the staff of the FDA will apply the statute and regulations in a consistent manner.

Subsection (h)(1)(C) requires the Secretary to ensure public participation prior to the implementation of any guidance document that sets forth initial interpretations of statutes or regulation, changes in interpretation of policy that are of more than a minor nature, or presents complex scientific issues or highly controversial issues. The Secretary can waive this requirement upon a determination that, for reasons such as public health, such prior participation is not feasible. In those cases, the Secretary shall provide for public comment upon implementation of the guidance. The Committee intends that the Secretary will waive this requirement for prior public participation only in rare and extraordinary circumstances where there is a compelling rationale.

Subsection (h)(1)(D) requires, for guidance documents that set forth existing practices or minor changes in policy, that the Secretary shall provide for public comment upon implementation.

Subsection (h)(2) requires the Secretary to ensure uniform nomenclature and uniform internal procedures for approval of guidance documents. Subsection (h)(3) requires the FDA to maintain electronically and publish periodically in the Federal Register a list of guidance documents. Subsection (h)(4) requires the Secretary to report to the House Committee on Commerce and the Senate Committee on Labor and Human Resources by no later than July 1, 2000, on the implementation of these practices.

Sec. 19. Positron emission tomography

Section 19 amends the FFDCFA to include the regulation of compounded positron emission tomography (PET) drugs. The provision defines compounded PET drugs to mean drugs that exhibit spontaneous disintegration of unstable nuclei; include nonradioactive reagents, nuclide generators, accelerators, electronic synthesizers, or associated software used to prepare any such drug. The Act is further amended to provide that neither a New Drug Application (NDA) nor an Abbreviated New Drug Application (ANDA) is required by a licensed practitioner to produce a compounded PET product in accordance with United States Phar-

macopeia (USP) standards. Within 30 days of enactment, the Secretary must publish in the Federal Register a notice revoking all previously published efforts by the FDA to provide industry guidance and regulatory standards for PET products.

The provisions require the Secretary, in 2 years, to establish procedures for approving compounded PET products and good manufacturing practices for the product, taking account of relevant differences between commercial manufacturers and non-profit organizations and in consultation with patient groups, physicians, and others. The Secretary may not require NDAs or ANDAs for these products for 4 years (or 2 years after these procedures mentioned above are established) The Secretary is required to terminate application of certain notices and a final rule of April 22, 1997, related to PET products.

Sec. 20. Requirements for radiopharmaceuticals

Section 20 requires the Secretary, within 180 days of enactment, and after consultation with patient advocacy groups, associations, physicians licensed to use radiopharmaceuticals, and the regulated industry, to issue proposed regulations governing the approval of radiopharmaceuticals designed for diagnosis and monitoring of diseases and conditions. The regulations must provide that the product's safety and effectiveness, governed under section 505 of the FDCA and section 351 of the Public Health Service Act, must include (but not be limited to) consideration of the product's proposed use in the practice of medicine, the product's pharmacological and toxicological activity (including any carrier or ligand of the radiopharmaceutical), and the product's estimated absorbed radiation dose.

Within 18 months of enactment, the Secretary must issue final regulations governing the approval of radiopharmaceuticals. This section establishes a "Special Rule" stating that in the case of a radiopharmaceutical intended to be used for diagnostic or monitoring purposes, its approved marketing indications may, in appropriate situations, refer to manifestations of disease (such as biochemical, physiological, anatomic, or pathological processes) common to, or present in, one or more disease states. The term "radiopharmaceutical" is defined to mean:

(A) an article intended for use in the diagnosis or monitoring of a disease or a manifestation of a disease in humans, and which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons; or

(B) any nonradioactive reagent kit or nuclide generator which is intended to be used in its preparation.

Sec. 21. Modernization of regulation

Section 21 amends section 351(a) of the Public Health Service Act (PHSA) (42 U.S.C. 262(a)) to modify the regulation of biological products. This section provides that a biological product may not be introduced into interstate commerce unless (A) the product has a biologics license; and (B) the package is marked with the product's name, the manufacturer's name, address, and license number, and the product's expiration date. By regulation, the Secretary must establish requirements for the approval, suspension, and revocation

of biologics licenses. A license will be approved based on a demonstration that the biological product is safe, pure, and potent, and that the facility where the product is manufactured, processed, packed, or held meets standards to assure the product's continued safety, purity, and potency. Also, the application will be approved only on the condition that the licensee agrees to permit inspection of its production facility. The Secretary must prescribe certain licensing and labeling exemptions for products undergoing investigation.

This section also amends section 351 to prohibit any person from falsely labeling or marking or altering any label or mark to falsify the label or mark of any package or container of a biological product and to eliminate the requirement that biologics manufacturers obtain establishment licenses. In addition, a biological product is redefined as: "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivatives of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings."

Section 21(f) establishes a "Special Rule" directing the Secretary to take steps necessary to minimize differences in the review and approval of products required to have both a biologic license application under section 351 of the PHS Act and a new drug application (NDA) under section 505(b)(1) of the FDCA.

Section 21(g) provides a technical correction to minimize any duplication between the Centers for Disease Control and Prevention (CDC) and the FDA determinations related to the accuracy of test systems. In re-writing Paragraph (3) of section 353(d) of the Public Health Service Act, the Committee intends to clarify that approval of a test for a home use by the FDA is an automatic route to waived status under the Clinical Laboratories Improvement Act (CLIA). The Committee is aware that the CDC, because of a misunderstanding of the statutory language, has denied waived status for at least one test approved for home use by prescription. The bill clarifies that, when the FDA already has determined that a diagnostic product can be used safely and effectively by a layperson at home, such a product should not require additional review or action by the Secretary to determine whether CLIA requirements can be waived for this product. This is the case whether the product is available over the counter or by prescription.

In addition to waiving CLIA requirements for tests approved by the FDA for home use, current law also provides that the Secretary may determine that other products are simple and have an insignificant risk of erroneous results. Subparagraphs (A) and (B) provide examples of product types that could satisfy this criteria. The bill clarifies, in subparagraph (A) that this criteria should focus on test performance "by the user" and the potential for operator error in performing the test. The purpose of CLIA quality control, proficiency testing, and personnel requirements is to ensure consistent, reliable, and appropriate use of a test system by users of the test. Without the clarifying "by the user," interpretations of "erroneous result" and "accurate" could include the inherent clinical sensitivity/specificity of a test system, parameters that are properly re-

viewed by the FDA in its process of determining whether to approve or clear product for marketing. CLIA controls would not meaningfully affect a product's inherent sensitivity/specificity profile, and would provide no assurances of proper test performance by users. This "by the user" clarification is intended only to specify the focus of subparagraph (A) and is not meant in any way to change the acceptable level of user error.

Sec. 22. Pilot and small scale manufacture

Section 22 amends Section 505(c) (21 U.S.C. 355(c)) of the FDCA to establish that a new human drug manufactured in a pilot or small facility may be used to demonstrate the drug's safety and effectiveness and to obtain its approval prior to scaling up to a larger facility. The Secretary retains the authority to determine whether a full scale production facility is necessary to ensure the drug's safety and effectiveness. Section 512(c) of the FDCA is similarly amended for animal drugs.

Sec. 23. Insulin and antibiotics

This section repeals sections 506 and 507 of the FDCA, thereby eliminating certain requirements for batch certification of insulin and certain antibiotic products. The section would also preserve the current provisions for the export of insulin and antibiotics.

The repeal of section 507 also results in applications for new antibiotic products being submitted to the FDA under all the requirements and benefits of section 505, including the granting of market exclusivity to all new drugs under the so-called Waxman-Hatch provisions. The Committee intends that the granting of market exclusivity be limited to products that achieve the policy objective of increasing research toward the development of new antibiotics. Thus, the granting of market exclusivity to new antibiotic drugs is limited to those products that are New Chemical Entities and to products for which a New Drug Application has not been submitted prior to the date of enactment.

Sec. 24. FDA mission and annual report

Section 24 amends FDCA Section 903 (21 U.S.C. 393) by redesignating subsections (b) and (c) as subsections (c) and (d) and adding a new section (b), "Mission," consisting of two parts: (1) the FDA shall promote public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner; and (2) the FDA shall protect the public health by ensuring that foods are safe, wholesome, and sanitary; human and veterinary drugs are safe and effective; there is a reasonable assurance of safety and effectiveness of devices intended for human use; cosmetics are safe and properly labeled; and the public health and safety are protected from electronic product radiation. Further, the FDA shall participate with other countries to reduce the burden of regulation, to harmonize regulatory requirements, and to achieve appropriate reciprocal arrangements.

Section 24 also requires the Secretary to submit an annual report to Congress, at the time of submission of its budget, which reviews FDA's performance in meeting its mission and assesses the agen-

cy's policies to implement its mission. The report must address the agency's efforts to meet its own performance standards, outcome measurements, and statutory deadlines for new product approvals. The report also must include a description of agency staffing and resources. In addition, the report must describe the FDA's goals, activities, and accomplishments in bilateral and multinational meetings that address reducing the burden of regulation, harmonizing regulations, and seeking reciprocal arrangements.

Sec. 25. Information system

This provision requires the Secretary to establish and maintain an information system to track the status and progress of each application or submission (e.g., petition, notification, or other form of request) submitted to the FDA.

Sec. 26. Education and training

This section requires the Secretary to conduct training and education programs for FDA employees related to the regulatory responsibilities and policies established by this Act (including scientific and administrative process training programs and programs related to integrity issues).

Sec. 27. Centers for education and research on drugs

This section amends chapter IX of the FFDCDA to create new section 908, "Demonstration Program Regarding Centers For Education and Research On Drugs, Devices, And Biological Products," which would require the Secretary to establish a demonstration program to make at least one grant for the establishment and operation of one center that would conduct clinical and laboratory research to increase awareness of new uses and unforeseen risks of new uses of drugs. The clinical information gained in the project would be provided to health care practitioners, pharmacy benefit managers, health maintenance or managed health care organizations, and health care insurers or government agencies. The purpose of the research also would be to improve health care quality while reducing costs through the prevention of adverse effects of these products such as unnecessary hospitalizations. Research would also be conducted on the comparative effectiveness and safety of drugs. The grant has one limitation: it cannot be used to assist the Secretary in the review of new drugs. Applications for grants must contain all agreements, assurances, and information that would be needed to carry out program activities. The grant application must undergo appropriate technical and scientific peer review. The bill authorizes \$2 million in Fiscal Year 1998 and \$3 million in Fiscal Year 1999 to be spent on this demonstration program.

Sec. 28. Harmonization

Section 28 requires the Secretary to participate in meetings with foreign governments to reduce the burden of regulation and harmonize regulatory requirements if the Secretary finds that harmonization would further consumer protections consistent with the purposes of this Act. The Secretary must report to the House Committee on Commerce and the Senate Committee on Labor and

Human Resources at least 60 days before executing a bilateral or multilateral agreement.

Sec. 29. Environmental impact review

Section 29 amends Chapter VII of the FFDCA, as amended, adding new section 761 dealing with environmental impact reviews. An environmental impact statement prepared in accordance with regulations published under part 25 of 21 C.F.R. in connection with an action carried out under this Act will be considered to meet the requirements under section 102(2)(C) of the National Environmental Policy Act.

Sec. 30. National uniformity

Section 30 amends Chapter VII (21 U.S.C. 371 et seq.) of the FFDCA, as amended by section 29 of the bill, by adding a new subchapter H entitled "National Uniformity for Nonprescription Drugs for Human Use and Preemption for Labeling or Packaging of Cosmetics." New section 771(a) provides that, with certain exceptions, no State or political subdivision of a State may establish or continue in effect any requirement: (1) that relates to the regulation of a drug intended for human use that is not subject to the requirements of section 503(b)(1); and (2) that is different from, or in addition to, a requirement of this Act, the Poison Prevention Packaging Act of 1970, or the Fair Packaging and Labeling Act. This section "grandfathers" California's Proposition 65.

However, upon application by a State or political subdivision, the Secretary may, by regulation, after notice and opportunity for written and oral views, exempt a State requirement that protects an important public interest that would otherwise be unprotected; would not cause any drug to be in violation of any applicable requirement or prohibition under Federal law; and would not unduly burden interstate commerce. This provision does not apply to any requirement that relates to the practice of pharmacy or any requirement that a drug be dispensed only upon the prescription of a practitioner licensed by law to administer the drug. Furthermore, with regard to scope, this provision shall include any requirement relating to public information or any public communication relating to a warning for a drug or cosmetic. And, nothing in this section shall be construed to modify or otherwise affect any action or the liability of any person under the product liability law of any State.

With respect to drugs that are not the subject of an application approved under section 505 or 507 or a final regulation established by the Secretary, this section applies only to State requirements that relate to the same subject as, but are different from, or in addition to, or that is otherwise not identical with a regulation or other requirement under Federal law. Nothing in this section prevents any State from enforcing, under relevant civil or other enforcement authority, a requirement that is identical to a requirement of this Act.

Section 772 applies to uniformity for labeling or packaging of cosmetics and is intended to apply to any State requirement, whether imposed by statute, regulation, common law, or otherwise. The Committee believes that uniformity of Federal and State require-

ments is important for cosmetics, which are manufactured and distributed in national markets.

Under section 772, with stated exceptions, a state requirement applicable to an aspect or aspects of the packaging or labeling of a cosmetic or class of cosmetics is preempted for such cosmetics or class of cosmetic, if there is a federal requirement related to that aspect or aspects of the cosmetic, and the state requirement is not identical with the federal requirement. A requirement may be a “requirement for labeling or packaging of a cosmetic” even if it also applies to other kinds of products. A requirement that is “specifically applicable” to a particular cosmetic or class of cosmetics is one that applies to a cosmetic or class of cosmetics, whether or not it also applies to other kinds of products.

Under the concept of the “same aspect” if the FDA has required disclosure of a particular risk on the label of a cosmetic and has specified the text of the disclosure or criteria that it must meet, a state would be preempted from applying to that cosmetic a disclosure or other requirement that relates to the same risk that differs from the FDA requirement in any aspect, including the form or location of the disclosure.

Sec. 31. FDA study of mercury compounds in drugs and food

Section 31(a) requires that within 2 years, the FDA compile a list of drugs and foods that contain intentionally introduced mercury compounds and provide a quantitative and qualitative analysis of these mercury compounds. Section 31(b) also requires the FDA to study the effect on humans of the use of mercury compounds in nasal sprays. Section 31(c) requires that the FDA or, under a contract, the Institute of Medicine, conduct a study on the effect on humans of the use of elemental, organic, or inorganic mercury when offered for sale as a drug or dietary supplement. The study will evaluate the scope of mercury use as a drug or dietary supplement and evaluate the adverse effects on health of children and other sensitive populations resulting from exposure to, or ingestion or inhalation of, mercury when so used. In conducting the study, the FDA shall consult with the Administrator of the Environmental Protection Agency, the Chair of the Consumer Product Safety Commission, and the Administrator of the Agency for Toxic Substances and Disease Registry. The conduct of this study is subject to available appropriations.

Sec. 32. Notification of discontinuance of a life saving product

Section 32 amends Chapter VII (21 U.S.C. 371 et seq.), as amended by section 30, by adding a new subchapter I entitled “Notification of the Discontinuance of a Life Saving Product.” This section provides that a manufacturer that is the sole manufacturer of a drug or device that is life supporting, life sustaining, or intended for use in the prevention of a debilitating disease or condition, and for which an application has been approved under section 505(b), 505(j), or 515(d), shall notify the Secretary of a discontinuance of the manufacture of the drug or device at least 6-months prior to the date of the discontinuance.

On the application of the manufacturer, this 6 month period for notification may be reduced by the Secretary if good cause exists

for the reduction of the period such as the following situations: (1) a public health problem may result from continuation of the manufacturing for the 6-month period; (2) a biomaterial shortage prevents the continuation of the manufacturing for the 6-month period; (3) a liability problem may exist for the manufacturer if the manufacturing is continued for the 6-month period; (4) continuation of the manufacturing for the 6-month period may cause substantial economic hardship for the manufacturer; (5) the manufacturer has filed for bankruptcy; or (6) the Secretary determines that there would be no adverse impact from the discontinuance of a drug or device.

The Secretary shall distribute information on the discontinuance of the drugs and devices to appropriate physician and patient groups to the maximum extent practicable.

CHANGES IN EXISTING LAW MADE BY THE BILL, AS REPORTED

In compliance with clause 3 of rule XIII of the Rules of the House of Representatives, changes in existing law made by the bill, as reported, are shown as follows (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italic, existing law in which no change is proposed is shown in roman):

FEDERAL FOOD, DRUG, AND COSMETIC ACT

* * * * *

CHAPTER II—DEFINITIONS

* * * * *

SEC. 201. For the purposes of this Act—

(a) * * *

* * * * *

(aa) The term “abbreviated drug application” means an application submitted under section 505(j) [or 507] for the approval of a drug that relies on the approved application of another drug with the same active ingredient to establish safety and efficacy, and—

(1) * * *

* * * * *

(dd) For purposes of sections 306 and 307, the term “drug product” means a drug subject to regulation under section 505, [507,] 512, or 802 of this Act or under section 351 of the Public Health Service Act.

* * * * *

(ff) The term “dietary supplement”—

(1) * * *

* * * * *

(3) does—

(A) include an article that is approved as a new drug under section 505[, certified as an antibiotic under section 507,] or licensed as a biologic under section 351 of the Public Health Service Act (42 U.S.C. 262) and was, prior to such approval, certification, or license, marketed as a dietary supplement or as a food unless the Secretary has is-

sued a regulation, after notice and comment, finding that the article, when used as or in a dietary supplement under the conditions of use and dosages set forth in the labeling for such dietary supplement, is unlawful under section 402(f); and

* * * * *
(ii) The term “*compounded positron emission tomography drug*”—
(1) means a drug that—

(A) exhibits spontaneous disintegration of unstable nuclei by the emission of positrons and is used for the purpose of providing dual photon positron emission tomographic diagnostic images; and

(B) has been compounded by or on the order of a practitioner who is licensed by a State to compound or order compounding for a drug described in subparagraph (A), and is compounded in accordance with that State’s law, for a patient or for research, teaching, or quality control; and

(2) includes any nonradioactive reagent, reagent kit, ingredient, nuclide generator, accelerator, target material, electronic synthesizer, or other apparatus or computer program to be used in the preparation of such a drug.

CHAPTER III—PROHIBITED ACTS AND PENALTIES

PROHIBITED ACTS

SEC. 301. The following acts and the causing thereof are hereby prohibited:

(a) * * *

* * * * *
(e) The refusal to permit access to or copying of any record as required by section 412, 504, or 703; or the failure to establish or maintain any record, or make any report, required under section 412, 504, 505 (i) or (k), [507(d) or (g),] 512(a)(4)(C), 512 (j), (l) or (m), 515(f), or 519 or the refusal to permit access to or verification or copying of any such required record.

* * * * *
(i)(1) Forging, counterfeiting, simulating, or falsely representing, or without proper authority using any mark, stamp, tag, label, or other identification device authorized or required by regulations promulgated under the provisions of section 404[, 506, 507,] or 721.

* * * * *
(j) The using by any person to his own advantage, or revealing, other than to the Secretary or officers or employees of the Department, or to the courts when relevant in any judicial proceeding under this Act, any information acquired under authority of section 404, 409, 412, 505, [506, 507,] 510, 512, 513, 514, 515, 516, 518, 519, 520, 704, 708, or 721 concerning any method or process which as a trade secret is entitled to protection; or the violating of section 408(i)(2) or any regulation issued under that section. This paragraph does not authorize the withholding of information from either House of Congress or from, to the extent of matter within its

jurisdiction, any committee or subcommittee of such committee or any joint committee of Congress or any subcommittee of such joint committee.

* * * * *
 (x) *The dissemination of information in violation of section 745.*
 * * * * *

DEBARMENT, TEMPORARY DENIAL OF APPROVAL, AND SUSPENSION

SEC. 306. (a) * * *

* * * * *

(d) TERMINATION OF DEBARMENT.—

(1) * * *

* * * * *

(4) SPECIAL TERMINATION.—

(A) * * *

(B) CORPORATIONS.—Upon an application submitted under subparagraph (A), the Secretary may take the action described in subparagraph (D) if the Secretary, after an informal hearing, finds that—

(i) * * *

(ii) all individuals who were involved in the commission of the offense or who knew or should have known of the offense have been removed from employment involving the development or approval of any drug subject to section 505 [or 507],

* * * * *

CHAPTER V—DRUGS AND DEVICES

SUBCHAPTER A—DRUGS AND DEVICES

ADULTERATED DRUGS AND DEVICES

SEC. 501. A drug or device shall be deemed to be adulterated—

(a)(1) If it consists in whole or in part of any filthy, putrid, or decomposed substance; or (2)(A) if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health; or (B) if it is a drug and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess[; or (3)]; or (C) if it is a compounded positron emission tomography drug and the methods used in, or the facilities and controls used for, its compounding, processing, packing, or holding do not conform to or are not operated or administered in conformity with the positron emission tomography compounding standards and the official monographs of the United States Pharmacopeia to assure that such drug meets the requirements of this Act as to safety and has

the identity and strength, and meets the quality and purity characteristics, that it purports or is represented to possess; or (3) if its container is composed, in whole or in part, of any poisonous or deleterious substance which may render the contents injurious to health; or (4) if (A) it bears or contains, for purposes of coloring only, a color additive which is unsafe within the meaning of section 721(a), or (B) it is a color additive the intended use of which in or on drugs or devices is for purposes of coloring only and is unsafe within the meaning of section 721(a); or (5) if it is a new animal drug which is unsafe within the meaning of section 512; or (6) if it is an animal feed bearing or containing a new animal drug, and such animal feed is unsafe within the meaning of section 512.

* * * * *

MISBRANDED DRUGS AND DEVICES

SEC. 502. A drug or device shall be deemed to be misbranded—

(a) If its labeling is false or misleading in any particular. *Health care economic information provided to a formulary committee, or other similar entity, in the course of the committee or the entity carrying out its responsibilities for the selection of drugs for managed care or other similar organizations, shall not be considered to be false or misleading if the health care economic information directly relates to an indication approved under section 505 or 507 or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) for such drug and is based on competent and reliable scientific evidence. The requirements set forth in section 505(a), 507, or section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) shall not apply to health care economic information provided to such a committee or entity in accordance with this paragraph. Information that is relevant to the substantiation of the health care economic information presented pursuant to this paragraph shall be made available to the Secretary upon request. In this paragraph, the term "health care economic information" means any analysis that identifies, measures, or compares the economic consequences, including the costs of the represented health outcomes, of the use of a drug to the use of another drug, to another health care intervention, or to no intervention.*

* * * * *

(e) (1) If it is a drug, unless (A) its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula), (i) the established name (as defined in subparagraph (3)) of the drug, if such there be, and (ii) in case it is fabricated from two or more ingredients, the established name and quantity of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including whether active or not, the established name and quantity or proportion of any bromides, ether, chloroform, acetanilide, acetophenetidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein. *Provided*, That the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this paragraph,

shall apply only to prescription drugs; and (B) for any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) is printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient: and *Provided*, That to the extent that compliance with the requirements of clause (A)(ii) or clause (B) of this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary. **】**
(1)(A) If it is a drug, unless its label bears, to the exclusion of any other nonproprietary name (except the applicable systematic chemical name or the chemical formula)—

(i) the established name (as defined in subparagraph (3)) of the drug, if there is such a name;

(ii) the established name and quantity or, if deemed appropriate by the Secretary, the proportion of each active ingredient, including the quantity, kind, and proportion of any alcohol, and also including whether active or not the established name and quantity or if deemed appropriate by the Secretary, the proportion of any bromides, ether, chloroform, acetanilide, acetophenetidin, amidopyrine, antipyrine, atropine, hyoscine, hyoscyamine, arsenic, digitalis, digitalis glucosides, mercury, ouabain, strophanthin, strychnine, thyroid, or any derivative or preparation of any such substances, contained therein, except that the requirement for stating the quantity of the active ingredients, other than the quantity of those specifically named in this subclause, shall not apply to nonprescription drugs not intended for human use; and

(iii) the established name of each inactive ingredient listed in alphabetical order on the outside container of the retail package and, if deemed appropriate by the Secretary, on the immediate container, as prescribed in regulation promulgated by the Secretary, but nothing in this clause shall be deemed to require that any trade secret be divulged, except that the requirements of this subclause with respect to alphabetical order shall apply only to nonprescription drugs that are not also cosmetics and this subclause shall not apply to nonprescription drugs not intended for human use.

(B) For any prescription drug the established name of such drug or ingredient, as the case may be, on such label (and on any labeling on which a name for such drug or ingredient is used) shall be printed prominently and in type at least half as large as that used thereon for any proprietary name or designation for such drug or ingredient, except that to the extent that compliance with the requirements of clause (A)(ii) or (iii) or this subparagraph is impracticable, exemptions shall be established by regulations promulgated by the Secretary.

* * * * *

【(k) If it is, or purports to be, or is represented as a drug composed wholly or partly of insulin, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 506, and (2) such certificate or release is in effect with respect to such drug.

[(1) If it is, or purports to be, or is represented as a drug (except a drug for use in animals other than man) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug, or any derivative thereof, unless (1) it is from a batch with respect to which a certificate or release has been issued pursuant to section 507, and (2) such certificate or release is in effect with respect to such drug: *Provided*, That this paragraph shall not apply to any drug or class of drugs exempted by regulations promulgated under section 507 (c) or (d).]

* * * * *

EXEMPTIONS AND CONSIDERATION FOR CERTAIN DRUGS, DEVICES, AND BIOLOGICAL PRODUCTS

SEC. 503. (a) * * *

* * * * *

(g)(1) * * *

* * * * *

(4) As used in this subsection:

(A) The term "biological product" has the meaning given the term in section [351(a)] 351(i) of the Public Health Service Act (42 U.S.C. [262(a)] 262(i)).

(B) The term "market clearance" includes—

(i) * * *

* * * * *

(iii) approval of a [product or establishment license under subsection (a) or (d)] *biologics license application under subsection (a)* of section 351 of the Public Health Service Act (42 U.S.C. 262).

* * * * *

NEW DRUGS

SEC. 505. (a) * * *

(b)(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a). Such persons shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and (F) specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture use, or sale of the drug. If

an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences. *The Secretary shall, in consultation with the Director of the National Institutes of Health, review and develop guidance, as appropriate, on the inclusion of women and minorities in clinical trials required by clause (A).*

* * * * *

(4)(A) *The Secretary shall issue guidance for the review of applications submitted under paragraph (1) relating to promptness, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards which shall apply equally to all individuals who review such applications.*

(B) *The Secretary shall meet with a sponsor of an investigation or an applicant for approval under this section or section 351 of the Public Health Service Act if the sponsor or applicant makes a reasonable request for a meeting, for the purpose of reaching agreement on the design and size of clinical trials. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant upon request.*

(C) *Agreement regarding the parameters of the design and size of clinical trials of a new drug that are reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—*

- (i) *with the written agreement of the sponsor or applicant; or*
- (ii) *pursuant to a decision, made in accordance with subparagraph (D) by the director of the division in which the drug is reviewed, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.*

(D) *A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director documents the scientific issue involved.*

(E) *The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance division personnel unless such field or compliance division personnel demonstrate to the reviewing division why such decision should be modified. For purposes of this paragraph, the reviewing division is the division responsible for the review of an application for approval of a drug (including all scientific and medical matters, chemistry, manufacturing, and controls).*

(F) *No action by the reviewing division may be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.*

(c)(1) * * *

* * * * *

(4) A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval prior to scaling up to a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.

(d) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b), do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b); or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e), the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. *If the Secretary determines, based on relevant science, that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) are sufficient to establish effectiveness, the Secretary may consider such data and evidence to constitute substantial evidence for purposes of the preceding sentence.*

* * * * *

(i)(I) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of

the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon—

【(1)】 (A) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, or preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

【(2)】 (B) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings; and

【(3)】 (C) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b).

【Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.】

(2) *Subject to paragraph (3), a clinical investigation of a new drug may begin 30 days after the Secretary has received from the manufacturer or sponsor of the investigation a submission containing such information about the drug and the clinical investigation, including —*

(A) *information on design of the investigation and adequate reports of basic information, certified by the applicant to be accurate reports, necessary to assess the safety of the drug for use in clinical investigation; and*

(B) *adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.*

(3)(A) *At any time, the Secretary may prohibit the sponsor of an investigation from conducting the investigation (referred to in this paragraph as a “clinical hold”) if the Secretary makes a determination described in subparagraph (B). The Secretary shall specify the basis for the clinical hold, including the specific information avail-*

able to the Secretary which served as the basis for such clinical hold, and confirm such determination in writing.

(B) For purposes of subparagraph (A), a determination described in this subparagraph with respect to a clinical hold is that—

(i) the drug involved represents an unreasonable risk to the safety of the persons who are the subject of the clinical investigation, taking into account the qualifications of the clinical investigators, information about the drug, the design of the clinical investigation, the condition for which the drug is to be investigated, and the health status of the subjects involved; or

(ii) the clinical hold should be issued for such other reasons as the Secretary may by regulation establish (including reasons established by regulation before the date of the enactment of the Prescription Drug User Fee Reauthorization and Drug Regulatory Modernization Act of 1997).

Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

(C) Any request to the Secretary from the sponsor of an investigation that a clinical hold be removed shall receive a decision, in writing and specifying the reasons therefor, within 30 days after receipt of such request. Any such request shall include sufficient information to support the removal of such clinical hold.

(j)(1) * * *

(2)(A) An abbreviated application for a new drug shall contain—

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph [(6)] (7) (hereinafter in this subsection referred to as a “listed drug”);

* * * * *

(3)(A) The Secretary shall issue guidance for the review of applications submitted under paragraph (1) relating to promptness, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards which shall apply equally to all individuals who review such applications.

(B) The Secretary shall meet with an applicant for approval of a drug under this subsection if the applicant makes a reasonable request for a meeting for the purpose of reaching agreement on the design and size of studies needed for approval of such application. Minutes of any such meeting shall be prepared by the Secretary and made available to the sponsor or applicant.

(C) Agreements regarding the parameters of design and size of bioavailability and bioequivalence trials of a drug under this sub-

section that are reached between the Secretary and a sponsor or applicant shall be reduced to writing and made part of the administrative record by the Secretary. Such agreement shall not be changed after the testing begins, except—

- (i) with the written agreement of the sponsor or applicant; or
- (ii) pursuant to a decision, made in accordance with subparagraph (D) by the director of the division in which the drug is reviewed, that a substantial scientific issue essential to determining the safety or effectiveness of the drug has been identified after the testing has begun.

(D) A decision under subparagraph (C)(ii) by the director shall be in writing and the Secretary shall provide to the sponsor or applicant an opportunity for a meeting at which the director and the sponsor or applicant will be present and at which the director documents the scientific issue involved.

(E) The written decisions of the reviewing division shall be binding upon, and may not directly or indirectly be changed by, the field or compliance office personnel unless such field or compliance office personnel demonstrate to the reviewing division why such decision should be modified. For purposes of this paragraph, the reviewing division is the division responsible for the review of an application under this subsection (including scientific matters, chemistry, manufacturing, and controls).

(F) No action by the reviewing division may at any time be delayed because of the unavailability of information from or action by field personnel unless the reviewing division determines that a delay is necessary to assure the marketing of a safe and effective drug.

[(3)] (4) Subject to paragraph [(4)] (5), the Secretary shall approve an application for a drug unless the Secretary finds—

(A) * * *

* * * * *

(I) the approval under subsection (c) of the listed drug referred to in the application under this subsection has been withdrawn or suspended for grounds described in the first sentence of subsection (e), the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) for grounds described in the first sentence of subsection (e), the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph [(5)] (6), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

* * * * *

[(4)] (5)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

* * * * *

[(5)] (6) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under this para-

graph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended—

(A) * * *

* * * * *

[(6)] (7)(A)(i) Within sixty days of the date of the enactment of this subsection, the Secretary shall publish and make available to the public—

(I) * * *

* * * * *

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) or was withdrawn or suspended under paragraph [(5)] (6) or if the Secretary determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list—

(i) for the same period as the withdrawal or suspension under subsection (e) or paragraph [(5)] (6), or

* * * * *

[(7)] (8) For purposes of this subsection:

(A) The term “bioavailability” means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

* * * * *

[(8)] (9) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of—

(A) * * *

* * * * *

(n)(1) *For the purpose of providing expert scientific advice and recommendations to the Secretary regarding a clinical investigation of a drug or the approval for marketing of a drug under section 505 or section 351 of the Public Health Service Act, the Secretary shall establish panels of experts or use panels of experts established before the date of the enactment of this subsection, or both.*

(2) *The Secretary may delegate the appointment and oversight authority granted under section 904 to a director of a center or successor entity within the Food and Drug Administration.*

(3) *The Secretary shall make appointments to each panel established under paragraph (1) so that each panel shall consist of—*

(A) *members who are qualified by training and experience to evaluate the safety and effectiveness of the drugs to be referred to the panel and who, to the extent feasible, possess skill and experience in the development, manufacture, or utilization of such drugs;*

(B) *members with diverse expertise in such fields as clinical and administrative medicine, pharmacy, pharmacology, pharmacoconomics, biological and physical sciences, and other related professions;*

(C) a representative of consumer interests and a representative of interests of the drug manufacturing industry not directly affected by the matter to be brought before the panel; and

(D) 2 or more members who are specialists or have other expertise in the particular disease or condition for which the drug under review is proposed to be indicated.

Scientific, trade, and consumer organizations shall be afforded an opportunity to nominate individuals for appointment to the panels. No individual who is in the regular full-time employ of the United States and engaged in the administration of this Act may be a voting member of any panel. The Secretary shall designate one of the members of each panel to serve as chairman thereof.

(4) Each member of a panel shall publicly disclose all conflicts of interest that member may have with the work to be undertaken by the panel. No member of a panel may vote on any matter where the member or the immediate family of such member could gain financially from the advice given to the Secretary. The Secretary may grant a waiver of any conflict of interest upon public disclosure of such conflict of interest if such waiver is necessary to afford the panel essential expertise, except that the Secretary may not grant a waiver for a member of a panel when the member's own scientific work is involved.

(5) The Secretary shall provide education and training to each new panel member before such member participates in a panel's activities, including education regarding requirements under this Act and related regulations of the Secretary, and the administrative processes and procedures related to panel meetings.

(6) Panel members (other than officers or employees of the United States), while attending meetings or conferences of a panel or otherwise engaged in its business, shall be entitled to receive compensation for each day so engaged, including traveltime, at rates to be fixed by the Secretary, but not to exceed the daily equivalent of the rate in effect for positions classified above grade GS-15 of the General Schedule. While serving away from their homes or regular places of business, panel members may be allowed travel expenses (including per diem in lieu of subsistence) as authorized by section 5703 of title 5, United States Code, for persons in the Government service employed intermittently.

(7) The Secretary shall ensure that scientific advisory panels meet regularly and at appropriate intervals so that any matter to be reviewed by such panel can be presented to the panel not more than 60 days after the matter is ready for such review. Meetings of the panel may be held using electronic communication to convene the meeting.

(8) Within 60 days after a scientific advisory panel makes recommendations on any matter under its review, the Food and Drug Administration official responsible for the matter shall review the conclusions and recommendations of the panel, and notify the affected persons of the final decision on the matter, or of the reasons that no such decision has been reached. Each such final decision shall be documented including the rationale for the decision.

(9) A scientific advisory panel under this subsection shall not be subject to the annual chartering and annual report requirements of the Federal Advisory Committee Act.

PEDIATRIC STUDIES OF DRUGS

SEC. 505A. (a) MARKET EXCLUSIVITY FOR NEW DRUGS.—If, prior to approval of an application that is submitted under section 505(b)(1), the Secretary determines that information relating to the use of a drug in the pediatric population may produce health benefits in that population, the Secretary makes a written request for pediatric studies (which shall include a timeframe for completing such studies), and such studies are completed within any such timeframe and the reports thereof submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)—

(1)(A) the period during which an application may not be submitted under subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of section 505 shall be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of section 505 to four years, to forty-eight months, and to seven and one-half years shall be deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(B) the period of market exclusivity under subsections (c)(3)(D)(iii) and (iv) and (j)(4)(D)(iii) and (iv) of section 505 shall be three years and six months rather than three years; and

(2)(A) if the drug is the subject of—

(i) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(ii) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(b) **SECRETARY TO DEVELOP LIST OF DRUGS FOR WHICH ADDITIONAL PEDIATRIC INFORMATION MAY BE BENEFICIAL.**—Not later than 180 days after the date of enactment of this section, the Secretary, after consultation with experts in pediatric research shall develop, prioritize, and publish an initial list of approved drugs for which additional pediatric information may produce health benefits in the pediatric population. The Secretary shall annually update the list.

(c) *MARKET EXCLUSIVITY FOR ALREADY-MARKETED DRUGS.*—If the Secretary makes a written request to the holder of an approved application under section 505(b)(1) for pediatric studies (which shall include a timeframe for completing such studies) concerning a drug identified in the list described in subsection (b), the holder agrees to the request, the studies are completed within any such timeframe and the reports thereof are submitted in accordance with subsection (d)(2) or accepted in accordance with subsection (d)(3)—

(1)(A) the period during which an application may not be submitted under subsection (c)(3)(D)(ii) or (j)(4)(D)(ii) of section 505 shall be five years and six months rather than five years, and the references in subsections (c)(3)(D)(ii) and (j)(4)(D)(ii) of section 505 to four years, to forty-eight months, and to seven and one-half years shall be deemed to be four and one-half years, fifty-four months, and eight years, respectively; or

(B) the period of market exclusivity under subsections (c)(3)(D)(iii) and (iv) and (j)(4)(D)(iii) and (iv) of section 505 shall be three years and six months rather than three years; and

(2)(A) if the drug is the subject of—

(i) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 505 and for which pediatric studies were submitted prior to the expiration of the patent (including any patent extensions); or

(ii) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 505,

the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions); or

(B) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 505, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 505(c)(3) or section 505(j)(4)(B) shall be extended by a period of six months after the date the patent expires (including any patent extensions).

(d) *CONDUCT OF PEDIATRIC STUDIES.*—

(1) *AGREEMENT FOR STUDIES.*—The Secretary may, pursuant to a written request for studies, after consultation with—

(A) the sponsor of an application for an investigational new drug under section 505(i);

(B) the sponsor of an application for a drug under section 505(b)(1); or

(C) the holder of an approved application for a drug under section 505(b)(1),
agree with the sponsor or holder for the conduct of pediatric studies for such drug.

(2) *WRITTEN PROTOCOLS TO MEET THE STUDIES REQUIREMENT.*—If the sponsor or holder and the Secretary agree upon

written protocols for the studies, the studies requirement of subsection (a) or (c) is satisfied upon the completion of the studies and submission of the reports thereof in accordance with the original written request and the written agreement referred to in paragraph (1). Not later than 60 days after the submission of the report of the studies, the Secretary shall determine if such studies were or were not conducted in accordance with the original written request and the written agreement and reported in accordance with the requirements of the Secretary for filing and so notify the sponsor or holder.

(3) *OTHER METHODS TO MEET THE STUDIES REQUIREMENT.*—If the sponsor or holder and the Secretary have not agreed in writing on the protocols for the studies, the studies requirement of subsection (a) or (c) is satisfied when such studies have been completed and the reports accepted by the Secretary. Not later than 90 days after the submission of the reports of the studies, the Secretary shall accept or reject such reports and so notify the sponsor or holder. The Secretary's only responsibility in accepting or rejecting the reports shall be to determine, within the 90 days, whether the studies fairly respond to the written request, whether such studies have been conducted in accordance with commonly accepted scientific principles and protocols, and whether such studies have been reported in accordance with the requirements of the Secretary for filing.

(e) *DELAY OF EFFECTIVE DATE FOR CERTAIN APPLICATIONS; PERIOD OF MARKET EXCLUSIVITY.*—If the Secretary determines that the acceptance or approval of an application under section 505(b)(2) or 505(j) for a drug may occur after submission of reports of pediatric studies under this section, which were submitted prior to the expiration of the patent (including any patent extension) or market exclusivity protection, but before the Secretary has determined whether the requirements of subsection (d) have been satisfied, the Secretary shall delay the acceptance or approval under section 505(b)(2) or 505(j), respectively, until the determination under subsection (d) is made, but such delay shall not exceed 90 days. In the event that requirements of this section are satisfied, the applicable period of market exclusivity referred to in subsection (a) or (c) shall be deemed to have been running during the period of delay.

(f) *NOTICE OF DETERMINATIONS ON STUDIES REQUIREMENT.*—The Secretary shall publish a notice of any determination that the requirements of subsection (d) have been met and that submissions and approvals under section 505(b)(2) or (j) for a drug will be subject to the provisions of this section.

(g) *DEFINITIONS.*—As used in this section, the term “pediatric studies” or “studies” means at least one clinical investigation (that, at the Secretary's discretion, may include pharmacokinetic studies) in pediatric age groups in which a drug is anticipated to be used.

(h) *LIMITATION.*—The holder of an approved application for a new drug that has already received six months of market exclusivity under subsection (a) or (c) may, if otherwise eligible, obtain six months of market exclusivity under subsection (c)(1)(B) for a supplemental application, except that the holder is not eligible for exclusivity under subsection (c)(2).

(i) *RELATIONSHIP TO REGULATIONS.*—Notwithstanding any other provision of law, if any pediatric study is required pursuant to regulations promulgated by the Secretary, such study shall be deemed to satisfy the requirement for market exclusivity pursuant to this section.

(j) *SUNSET.*—No period of market exclusivity shall be granted under this section based on studies commenced after January 1, 2002. The Secretary shall conduct a study and report to Congress not later than January 1, 2001, based on the experience under the program. The study and report shall examine all relevant issues, including—

- (1) the effectiveness of the program in improving information about important pediatric uses for approved drugs;
- (2) the adequacy of the incentive provided under this section;
- (3) the economic impact of the program on taxpayers and consumers, including the impact of the lack of lower cost generic drugs on lower income patients; and
- (4) any suggestions for modification that the Secretary deems appropriate.

【CERTIFICATION OF DRUGS CONTAINING INSULIN

【SEC. 506. (a) The Secretary, pursuant to regulations promulgated by him, shall provide for the certification of batches of drugs composed wholly or partly of insulin. A batch of any such drug shall be certified if such drug has such characteristics of identity and such batch has such characteristics of strength, quality, and purity, as the Secretary prescribes in such regulations as necessary to adequately insure safety and efficacy of use, but shall not otherwise be certified. Prior to the effective date of such regulations the Secretary, in lieu of certification, shall issue a release for any batch which, in his judgment, may be released without risk as to the safety and efficacy of its use. Such release shall prescribe the date of its expiration and other conditions under which it shall cease to be effective as to such batch and as to portions thereof.

【(b) Regulations providing for such certification shall contain such provisions as are necessary to carry out the purposes of this section, including provisions prescribing (1) standards of identity and of strength, quality, and purity; (2) tests and methods of assay to determine compliance with such standards; (3) effective periods for certificates, and other conditions under which they shall cease to be effective as to certified batches and as to portions thereof; (4) administration and procedure; and (5) such fees, specified in such regulations, as are necessary to provide, equip, and maintain an adequate certification service. Such regulations shall prescribe no standard of identity or of strength, quality, or purity for any drug different from the standard of identity, strength, quality, or purity set forth for such drug in an official compendium.

【(c) Such regulations, insofar as they prescribe tests or methods of assay to determine strength, quality, or purity of any drug, different from the tests or methods of assay set forth for such drug in an official compendium, shall be prescribed, after notice and opportunity for revision of such compendium, in the manner provided in the second sentence of section 501(b). The provisions of subsections (e), (f), and (g) of section 701 shall be applicable to such

portion of any regulation as prescribes any such different test or method, but shall not be applicable to any other portion of any such regulation.

【CERTIFICATION OF ANTIBIOTICS

【SEC. 507. (a) The Secretary, pursuant to regulations promulgated by him, shall provide for the certification of batches of drugs (except drugs for use in animals other than man) composed wholly or partly of any kind of penicillin, streptomycin, chlortetracycline, chloramphenicol, bacitracin, or any other antibiotic drug, or any derivative thereof. A batch of any such drug shall be certified if such drug has such characteristics of identity and such batch has such characteristics of strength, quality, and purity, as the Secretary prescribes in such regulations as necessary to adequately insure safety and efficacy of use, but shall not otherwise be certified. Prior to the effective date of such regulations the Secretary, in lieu of certification, shall issue a release for any batch which, in his judgment, may be released without risk as to the safety and efficacy of its use. Such release shall prescribe the date of its expiration and other conditions under which it shall cease to be effective as to such batch and as to portions thereof. For purposes of this section and of section 502(1), the term "antibiotic drug" means any drug intended for use by man containing any quantity of any chemical substance which is produced by a micro-organism and which has the capacity to inhibit or destroy micro-organisms in dilute solution (including the chemically synthesized equivalent of any such substance).

【(b) Regulations providing for such certifications shall contain such provisions as are necessary to carry out the purposes of this section, including provisions prescribing (1) standards of identity and of strength, quality, and purity; (2) tests and methods of assay to determine compliance with such standards; (3) effective periods for certificates, and other conditions under which they shall cease to be effective as to certified batches and as to portions thereof; (4) administration and procedure; and (5) such fees, specified in such regulations, as are necessary to provide, equip, and maintain an adequate certification service. Such regulations shall prescribe only such tests and methods of assay as will provide for certification or rejection within the shortest time consistent with the purposes of this section.

【(c) Whenever in the judgment of the Administrator, the requirements of this section and of section 502(1) with respect to any drug or class of drugs are not necessary to insure safety and efficacy of use, the Administrator shall promulgate regulations exempting such drug or class of drugs from such requirements. In deciding whether an antibiotic drug, or class of antibiotic drugs, is to be exempted from the requirement of certification the Secretary shall give consideration, among other relevant factors, to—

【(1) whether such drug or class of drugs is manufactured by a person who has, or hereafter shall have, produced fifty consecutive batches of such drug or class of drugs in compliance with the regulations for the certification thereof within a period of not more than eighteen calendar months, upon the application by such person to the Secretary; or

[(2) whether such drug or class of drugs is manufactured by any person who has otherwise demonstrated such consistency in the production of such drug or class of drugs, in compliance with the regulations for the certification thereof, as in the judgment of the Secretary is adequate to insure the safety and efficacy of use thereof.

When an antibiotic drug or a drug manufacturer has been exempted from the requirement of certification, the manufacturer may still obtain certification of a batch or batches of that drug if he applies for and meets the requirements for certification. Nothing in this Act shall be deemed to prevent a manufacturer or distributor of an antibiotic drug from making a truthful statement in labeling or advertising of the product as to whether it has been certified or exempted from the requirement of certification.

[(d) The Administrator shall promulgate regulations exempting from any requirement of this section and of section 502(l), (1) drugs which are to be stored, processed, labeled, or repacked at establishments other than those where manufactured, on condition that such drugs comply with all such requirements upon removal from such establishments; (2) drugs which conform to applicable standards of identity, strength, quality, and purity prescribed by these regulations and are intended for use in manufacturing other drugs; and (3) drugs which are intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and efficacy of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning the exemption under clause (3) upon—

[(1) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of pre-clinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

[(2) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings; and

[(3) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application for certification or release pursuant to subsection (a).

Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform

any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

[(e) No drug which is subject to this section shall be deemed to be subject to any provision of section 505 except a new drug exempted from the requirements of this section and of section 502(l) pursuant to regulations promulgated by the Secretary. For purposes of section 505, the initial request for certification, as thereafter duly amended, pursuant to this section, of a new drug so exempted shall be considered a part of the application filed pursuant to section 505(b) with respect to the person filing such request and to such drug as of the date of the exemption. Compliance of any drug subject to section 502(l) or this section with section 501(b) and 502(g) shall be determined by the application of the standards of strength, quality, and purity, the tests and methods of assay, and the requirements of packaging, and labeling, respectively, prescribed by regulations promulgated under this section.

[(f) Any interested person may file with the Administrator a petition proposing the issuance, amendment, or repeal of any regulation contemplated by this section. The petition shall set forth the proposal in general terms and shall state reasonable grounds therefor. The Administrator shall give public notice of the proposal and an opportunity for all interested persons to present their views thereon, orally or in writing, and as soon as practicable thereafter shall make public his action upon such proposal. At any time prior to the thirtieth day after such action is made public any interested person may file objections to such action, specifying with particularity the changes desired, stating reasonable grounds therefor, and requesting a public hearing upon such objections. The Administrator shall thereupon, after due notice, hold such public hearing. As soon as practicable after completion of the hearing, the Administrator shall by order make public his action on such objections. The Administrator shall base his order only on substantial evidence of record at the hearing and shall set forth as part of the order detailed findings of fact on which the order is based. The order shall be subject to the provision of section 701 (f) and (g).

[(g)(1) Every person engaged in manufacturing, compounding, or processing any drug within the purview of this section with respect to which a certificate or release has been issued pursuant to this section shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such person with respect to such drug, as the Secretary may by general regulation, or by order with respect to such certification or release, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to make, or to facilitate, a determination as to whether such certification or release should be rescinded or whether any regulation issued under this

section should be amended or repealed. Regulations and orders issued under this subsection and under clause (3) of subsection (d) shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, of similar information received or otherwise obtained by the Secretary.

[(2) Every person required under this section to maintain records, and every person having charge or custody thereof, shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

[(h) In the case of a drug for which, on the day immediately preceding the effective date of this subsection, a prior approval of an application under section 505 had not been withdrawn under section 505(e), the initial issuance of regulations providing for certification or exemption of such drug under this section shall, with respect to the conditions of use prescribed, recommended, or suggested in the labeling covered by such application, not be conditioned upon an affirmative finding of the efficacy of such drug. Any subsequent amendment or repeal of such regulations so as no longer to provide for such certification or exemption on the ground of a lack of efficacy of such drug for use under such conditions of use may be effected only on or after that effective date of clause (3) of the first sentence of section 505(e) which would be applicable to such drug under such conditions of use if such drug were subject to section 505(e), and then only if (1) such amendment or repeal is made in accordance with the procedure specified in subsection (f) of this section (except that such amendment or repeal may be initiated either by a proposal of the Secretary or by a petition of any interested person) and (2) the Secretary finds, on the basis of new information with respect to such drug evaluated together with the information before him when the application under section 505 became effective or was approved, that there is a lack of substantial evidence (as defined in section 505(d)) that the drug has the effect it purports or is represented to have under such conditions of use.]

DISPUTE RESOLUTION

SEC. 506. If, regarding an obligation under this Act, there is a scientific controversy between the Secretary and a person who is a sponsor, applicant, or manufacturer and no specific provision of this Act or regulation promulgated under this Act provides a right of review of the matter in controversy, the Secretary shall, by regulation, establish a procedure under which such sponsor, applicant, or manufacturer may request a review of such controversy by an appropriate scientific advisory panel under section 505(n). Such review shall take place in a timely manner. The Secretary shall promulgate such regulations within 180 days of the date of the enactment of the Prescription Drug User Fee Reauthorization and Medical Device Regulatory Modernization Act of 1997.

* * * * *

REGISTRATION OF PRODUCERS OF DRUGS AND DEVICES

SEC. 510. (a) * * *

* * * * *

(j)(1) Every person who registers with the Secretary under subsection (b), (c), or (d) shall, at the time of registration under any such subsection, file with the Secretary a list of all drugs and a list of all devices and a brief statement of the basis for believing that each device included in the list is a device rather than a drug (with each drug and device in each list listed by its established name (as defined in section 502(e)) and by any proprietary name) which are being manufactured, prepared, propagated, compounded, or processed by him for commercial distribution and which he has not included in any list of drugs or devices filed by him with the Secretary under this paragraph or paragraph (2) before such time of registration. Such list shall be prepared in such form and manner as the Secretary may prescribe and shall be accompanied by—

(A) in the case of a drug contained in the applicable list and subject to section 505[, 506, 507,] or 512, or a device intended for human use contained in the applicable list with respect to which a performance standard has been established under section 514 or which is subject to section 515, a reference to the authority for the marketing of such drug or device and a copy of all labeling for such drug or device;

* * * * *

(D) if the registrant filing a list has determined that a particular drug product or device contained in such list is not subject to section 505[, 506, 507,] or 512, or the particular device contained in such list is not subject to a performance standard established under section 514 or to section 515 or is not a restricted device, a brief statement of the basis upon which the registrant made such determination if the Secretary requests such a statement with respect to that particular drug product or device.

* * * * *

NEW ANIMAL DRUGS

SEC. 512. (a) * * *

* * * * *

(c)(1) * * *

* * * * *

(4) *A drug manufactured in a pilot or other small facility may be used to demonstrate the safety and effectiveness of the drug and to obtain approval prior to scaling up to a larger facility, unless the Secretary makes a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug.*

* * * * *

GENERAL PROVISIONS RESPECTING CONTROL OF DEVICES INTENDED FOR HUMAN USE

General Rule

SEC. 520. (a) * * *

* * * * *

Transitional Provisions for Devices Considered as New Drugs [or Antibiotic Drugs]

(1)(1) * * *

* * * * *

[(4) Any device intended for human use which on the enactment date was subject to the requirements of section 507 shall be subject to such requirements as follows:

[(A) In the case of such a device which is classified into class I, such requirements shall apply to such device until the effective date of the regulation classifying the device into such class.

[(B) In the case of such a device which is classified into class II, such requirements shall apply to such device until the effective date of a performance standard applicable to the device under section 514.

[(C) In the case of such a device which is classified into class III, such requirements shall apply to such device until the date on which the device is required to have in effect an approved application under section 515.]

* * * * *

SUBCHAPTER B—DRUGS FOR RARE DISEASES OR CONDITIONS

RECOMMENDATIONS FOR INVESTIGATIONS OF DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 525. (a) The sponsor of a drug for a disease or condition which is rare in the States may request the Secretary to provide written recommendations for the nonclinical and clinical investigations which must be conducted with the drug before—

(1) it may be approved for such disease or condition under section 505, or

[(2) if the drug is an antibiotic, it may be certified for such disease or condition under section 507, or]

[(3)] (2) if the drug is a biological product, it may be licensed for such disease or condition under section 351 of the Public Health Service Act.

If the Secretary has reason to believe that a drug for which a request is made under this section is a drug for a disease or condition which is rare in the States, the Secretary shall provide the person making the request written recommendations for the nonclinical and clinical investigations which the Secretary believes, on the basis of information available to the Secretary at the time of the request under this section, would be necessary for approval of such drug for such disease or condition under section 505[, certification

of such drug for such disease or condition under section 507,] or licensing of such drug for such disease or condition under section 351 of the Public Health Service Act.

* * * * *

DESIGNATION OF DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 526. (a)(1) The manufacturer or the sponsor of a drug may request the Secretary to designate the drug as a drug for a rare disease or condition. A request for designation of a drug shall be made before the submission of an application under section 505(b) for the drug, [the submission of an application for certification of the drug under section 507,] or the submission of an application for licensing of the drug under section 351 of the Public Health Service Act. If the Secretary finds that a drug for which a request is submitted under this subsection is being or will be investigated for a rare disease or condition and—

(A) if an application for such drug is approved under section 505, or

[(B) if a certification for such drug is issued under section 507, or]

[(C)] (B) if a license for such drug is issued under section 351 of the Public Health Service Act,

the approval, certification, or license would be for use for such disease or condition, the Secretary shall designate the drug as a drug for such disease or condition. A request for a designation of a drug under this subsection shall contain the consent of the applicant to notice being given by the Secretary under subsection (b) respecting the designation of the drug.

* * * * *

(b) A designation of a drug under subsection (a) shall be subject to the condition that—

(1) if an application was approved for the drug under section 505(b)[, a certificate was issued for the drug under section 507,] or a license was issued for the drug under section 351 of the Public Health Service Act, the manufacturer of the drug will notify the Secretary of any discontinuance of the production of the drug at least one year before discontinuance, and

(2) if an application has not been approved for the drug under section 505(b)[, a certificate has not been issued for the drug under section 507,] or a license has not been issued for the drug under section 351 of the Public Health Service Act and if preclinical investigations or investigations under section 505(i) are being conducted with the drug, the manufacturer or sponsor of the drug will notify the Secretary of any decision to discontinue active pursuit of approval of an application under section 505(b)[, approval of an application for certification under section 507,] or approval of a license under section 351 of the Public Health Service Act.

* * * * *

PROTECTION FOR DRUGS FOR RARE DISEASES OR CONDITIONS

SEC. 527. (a) Except as provided in subsection (b), if the Secretary—

- (1) approves an application filed pursuant to section 505, or
- [(2) issues a certification under section 507, or]
- [(3)] (2) issues a license under section 351 of the Public Health Service Act

for a drug designated under section 526 for a rare disease or condition, the Secretary may not approve another application under section 505[, issue another certification under section 507,] or issue another license under section 351 of the Public Health Service Act for such drug for such disease or condition for a person who is not the holder of such approved application, of such certification, or of such license until the expiration of seven years from the date of the approval of the approved application, the issuance of the certification, or the issuance of the license. Section 505(c)(2) does not apply to the refusal to approve an application under the preceding sentence.

(b) If an application filed pursuant to section 505 is approved for a drug designated under section 526 for a rare disease or condition[, if a certification is issued under section 507 for such a drug, or] if a license is issued under section 351 of the Public Health Service Act for such a drug, the Secretary may, during the seven-year period beginning on the date of the application approval, [of the issuance of the certification under section 507,] or of the issuance of the license, approve another application under section 505, [issue another certification under section 507, or] issue a license under section 351 of the Public Health Service Act, for such drug for such disease or condition for a person who is not the holder of such approved application, of such certification, or of such license if—

- (1) * * *

* * * * *

SUBCHAPTER D—UNAPPROVED THERAPIES AND DIAGNOSTICS

SEC. 551. EXPANDED ACCESS TO UNAPPROVED THERAPIES AND DIAGNOSTICS.

(a) EMERGENCY SITUATIONS.—*The Secretary may, under appropriate conditions determined by the Secretary, authorize the shipment of investigational drugs (as defined in regulations prescribed by the Secretary) for the diagnosis or treatment of a serious disease or condition in emergency situations.*

(b) INDIVIDUAL PATIENT ACCESS TO INVESTIGATIONAL PRODUCTS INTENDED FOR SERIOUS DISEASES.—*Any person, acting through a physician licensed in accordance with State law, may request from a manufacturer or distributor, and any manufacturer or distributor may provide to such physician after compliance with the provisions of this subsection, an investigational drug (as defined in regulations prescribed by the Secretary) for the diagnosis or treatment of a serious disease or condition if—*

- (1) *the licensed physician determines that the person has no comparable or satisfactory alternative therapy available to diagnose or treat the disease or condition involved, and that the*

risk to the person from the investigational drug is not greater than the risk from the disease or condition;

(2) the Secretary determines that there is sufficient evidence of safety and effectiveness to support the use of the investigational drug in the case described in paragraph (1);

(3) the Secretary determines that provision of the investigational drug will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval; and

(4) the sponsor, or clinical investigator, of the investigational drug submits to the Secretary a clinical protocol consistent with the provisions of section 505(i) and any regulations promulgated under section 505(i) describing the use of investigational drugs in a single patient or a small group of patients.

(c) TREATMENT INDS.—Upon submission by a sponsor or a physician of a protocol intended to provide widespread access to an investigational drug for eligible patients, the Secretary shall permit such investigational drug to be made available for expanded access under a treatment investigational new drug application if the Secretary determines that—

(1) under the treatment investigational new drug application, the investigational drug is intended for use in the diagnosis or treatment of a serious or immediately life-threatening disease or condition;

(2) there is no comparable or satisfactory alternative therapy available to diagnose or treat that stage of disease or condition in the population of patients to which the investigational drug is intended to be administered;

(3)(A) the investigational drug is under investigation in a controlled clinical trial for the use described in paragraph (1) under an effective investigational new drug application; or

(B) all clinical trials necessary for approval of that use of the investigational drug have been completed;

(4) the sponsor of the controlled clinical trials is actively pursuing marketing approval of the investigational drug for the use described in paragraph (1) with due diligence;

(5) the provision of the investigational drug will not interfere with the enrollment of patients in ongoing clinical investigations under section 505(i);

(6) in the case of serious diseases, there is sufficient evidence of safety and effectiveness to support the use described in paragraph (1); and

(7) in the case of immediately life-threatening diseases, the available scientific evidence, taken as a whole, provides a reasonable basis to conclude that the product may be effective for its intended use and would not expose patients to an unreasonable and significant risk of illness or injury.

A protocol submitted under this subsection shall be subject to the provisions of section 505(i) and regulations promulgated under section 505(i). The Secretary may inform national, State, and local medical associations and societies, voluntary health associations, and other appropriate persons about the availability of an investigational drug under expanded access protocols submitted under this subsection. The information provided by the Secretary, in accord-

ance with the preceding sentence, shall be of the same type of information that is required by section 402(j)(3) of the Public Health Service Act.

(d) *TERMINATION.*—The Secretary may, at any time, with respect to a sponsor, physician, manufacturer, or distributor described in this section, terminate expanded access provided under this section for an investigational drug if the requirements under this section are no longer met.

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CHAPTER VII—GENERAL AUTHORITY

SUBCHAPTER A—GENERAL ADMINISTRATIVE PROVISIONS

REGULATIONS AND HEARINGS

SEC. 701. (a) * * *

* * * * *

(h)(1)(A) *The Secretary shall develop guidance documents with public participation and ensure that the existence of such documents and the documents themselves are made available to the public both in written form and through electronic means. Such documents shall not create or confer any rights for or on any person, although they present the views of the Secretary on matters under the jurisdiction of the Food and Drug Administration.*

(B) *Although guidance documents shall not be binding on the Secretary, the Secretary shall ensure that employees of the Food and Drug Administration do not deviate from such guidances without appropriate justification and supervisory concurrence.*

(C) *For guidance documents that set forth initial interpretations of statute or regulation, changes in interpretation or policy that are of more than a minor nature, complex scientific issues, or highly controversial issues, the Secretary shall ensure public participation prior to implementation of any guidance documents, unless the Secretary determines that for reasons of the public health need, such prior public participation is not feasible. In such cases, the Secretary shall provide for public comment upon implementation, and take such comment into account.*

(D) *For guidance documents that set forth existing practices or minor changes in policy, the Secretary shall provide for public comment upon implementation.*

(2) *In developing guidance documents, the Secretary shall ensure uniform nomenclature and uniform internal procedures for approval of such documents. The Secretary shall ensure that guidance documents and revisions of such documents are properly dated and indicate the nonbinding nature of the documents.*

(3) *The Secretary, through the Food and Drug Administration, shall maintain electronically and publish periodically in the Federal Register a list of guidance documents. Such list shall be updated quarterly. All such documents shall be made available to the public.*

(4) *The Secretary shall report to the Committee on Commerce of the House of Representatives and the Committee on Labor and*

Human Resources of the Senate no later than July 1, 2000, on the implementation of these practices.

* * * * *

FACTORY INSPECTION

SEC. 704. (a)(1) For purposes of enforcement of this Act, officers or employees duly designated by the Secretary, upon presenting appropriate credentials and a written notice to the owner, operator, or agent in charge, are authorized (A) to enter, at reasonable times, any factory, warehouse, or establishment in which food, drugs, devices, or cosmetics are manufactured, processed, packed, or held, for introduction into interstate commerce or after such introduction, or to enter any vehicle, being used to transport or hold such food, drugs, devices, or cosmetics in interstate commerce; and (B) to inspect, at reasonable times and within reasonable limits and in a reasonable manner, such factory, warehouse, establishment, or vehicle and all pertinent equipment, finished and unfinished materials, containers, and labeling therein. In the case of any factory, warehouse, establishment, or consulting laboratory in which **【prescription drugs】** *prescription drugs, nonprescription drugs intended for human use*, or restricted devices are manufactured, processed, packed, or held, inspection shall extend to all things therein (including records, files, papers, processes, controls, and facilities) bearing on whether **【prescription drugs】** *prescription drugs, nonprescription drugs intended for human use*, or restricted devices which are adulterated or misbranded within the meaning of this Act, or which may not be manufactured, introduced into interstate commerce, or sold, or offered for sale by reason of any provision of this Act, have been or are being manufactured, processed, packed, transported, or held in any such place, or otherwise bearing on violation of this Act. No inspection authorized by the preceding sentence or by paragraph (3) shall extend to financial data, sales data other than shipment data, pricing data, personnel data (other than data as to qualifications of technical and professional personnel performing functions subject to this Act), and research data (other than data relating to new drugs, antibiotic drugs, and devices and subject to reporting and inspection under regulations lawfully issued pursuant to section 505 (i) or (k)**【**section 507 (d) or (g)**】**, section 519, or 520(g), and data relating to other drugs or devices which in the case of a new drug would be subject to reporting or inspection under lawful regulations issued pursuant to section 505(j)). A separate notice shall be given for each such inspection, but a notice shall not be required for each entry made during the period covered by the inspection. Each such inspection shall be commenced and completed with reasonable promptness.

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SUBCHAPTER C—FEES

* * * * *

PART 2—FEES RELATING TO DRUGS

SEC. 735. DEFINITIONS.

For purposes of this subchapter:

(1) The term “human drug application” means an application for—

(A) approval of a new drug submitted under section 505(b)(1),

(B) approval of a new drug submitted under section 505(b)(2) after September 30, 1992, which requests approval of—

(i) a molecular entity which is an active ingredient (including any salt or ester of an active ingredient), or

(ii) an indication for a use, that had not been approved under an application submitted under section 505(b), or

[(C) initial certification or initial approval of an antibiotic drug under section 507, or]

[(D)] (C) licensure of a biological product under section 351 of the Public Health Service Act.

Such term does not include a supplement to such an application, does not include an application with respect to whole blood or a blood component for transfusion, does not include an application with respect to a bovine blood product for topical application licensed before September 1, 1992, an allergenic extract product, or an in vitro diagnostic biologic product licensed under section 351 of the Public Health [Service Act, and] *Service Act*, does not include an application with respect to a large volume parenteral drug product approved before [September 1, 1992.] *September 1, 1992, does not include an application for a licensure of a biological product for further manufacturing use only, and does not include an application or supplement submitted by a State or Federal Government entity for a drug that is not distributed commercially. Such term does include an application for licensure, as described in subparagraph (D), of a large volume biological product intended for single dose injection for intravenous use or infusion.*

* * * * *

(3) The term “prescription drug product” means a specific strength or potency of a drug in final dosage form—

(A) for which a human drug application has been approved, and

(B) which may be dispensed only under prescription pursuant to section 503(b).

Such term does not include whole blood or a blood component for transfusion, does not include a bovine blood product for topical application licensed before September 1, 1992, an allergenic extract product, or an in vitro diagnostic biologic product licensed under section 351 of the Public Health [Service Act, and] *Service Act*, does not include a large volume parenteral drug product approved before [September 1, 1992.] *September 1, 1992, does not include a biological product that is licensed for further manufacturing use only, and does not include a*

drug that is not distributed commercially and is the subject of an application or supplement submitted by a State or Federal Government entity. Such term does include a large volume biological product intended for single dose injection for intravenous use or infusion.

(4) The term “final dosage form” means, with respect to a prescription drug product, a finished dosage form which is approved for administration to a patient **[without]** *without substantial* further manufacturing.

[(5) The term “prescription drug establishment” means a foreign or domestic place of business which is—

[(A) at one general physical location consisting of one or more buildings all of which are within 5 miles of each other, at which one or more prescription drug products are manufactured in final dosage form, and

[(B) under the management of a person that is listed as the applicant in a human drug application for a prescription drug product with respect to at least one such product.

For purposes of this paragraph, the term “manufactured” does not include packaging.]

(5) The term “prescription drug establishment” means a foreign or domestic place of business which is at one general physical location consisting of one or more buildings all of which are within 5 miles of each other and at which one or more prescription drug products are manufactured in final dosage form.

* * * * *

(7) The term “costs of resources allocated for the process for the review of human drug applications” means the expenses incurred in connection with the process for the review of human drug applications for—

(A) officers and employees of the Food and Drug Administration, **[employees under contract with the Food and Drug Administration who work in facilities owned or leased for the Food and Drug Administration,]** *contractors of the Food and Drug Administration,* advisory committees, and costs related to such officers, employees, **[and committees,]** *and committees and to contracts with such contractors,*

* * * * *

(8) The term “adjustment factor” applicable to a fiscal year is the lower of—

(A) the Consumer Price Index for all urban consumers (all items; United States city average) for **[August of]** *April of* the preceding fiscal year divided by such Index for **[August 1992]** *April 1997,* or

(B) the total of discretionary budget authority provided for programs in the domestic category for the immediately preceding fiscal year (as reported in the Office of Management and Budget sequestration preview report, if available, required under section 254(d) of the Balanced Budget and Emergency Deficit Control Act of 1985) divided by such budget authority for fiscal year **[1992]** *1997* (as re-

ported in the Office of Management and Budget final sequestration report submitted after the end of the 102d Congress, 2d Session).

【The terms “budget authority” and “category” in subparagraph (B) are as defined in the Balanced Budget and Emergency Deficit Control Act of 1985, as in effect as of September 1, 1992.】

(9) The term “affiliate” means a business entity that has a relationship with a second business entity if, directly or indirectly—

(A) one business entity controls, or has the power to control, the other business entity; or

(B) a third party controls, or has power to control, both of the business entities.

SEC. 736. AUTHORITY TO ASSESS AND USE DRUG FEES.

(a) **TYPES OF FEES.**—**【Beginning in fiscal year 1993】** *Beginning in fiscal year 1998*, the Secretary shall assess and collect fees in accordance with this section as follows:

(1) **HUMAN DRUG APPLICATION AND SUPPLEMENT FEE.**—

(A) * * *

【(B) PAYMENT SCHEDULE.—

【(i) FIRST PAYMENT.—50 percent of the fee required by subparagraph (A) shall be due upon submission of the application or supplement.

【(ii) FINAL PAYMENT.—The remaining 50 percent of the fee required by subparagraph (A) shall be due upon—

【(I) the expiration of 30 days from the date the Secretary sends to the applicant a letter designated by the Secretary as an action letter described in section 735(6)(B), or

【(II) the withdrawal of the application or supplement after it is filed unless the Secretary waives the fee or a portion of the fee because no substantial work was performed on such application or supplement after it was filed.

The designation under subclause (I) or the waiver under subclause (II) shall be solely in the discretion of the Secretary and shall not be reviewable.】

(B) PAYMENT.—*The fee required by subparagraph (A) shall be due upon submission of the application or supplement.*

* * * * *

(D) REFUND OF FEE IF APPLICATION 【NOT ACCEPTED】 REFUSED FOR FILING.—The Secretary shall refund **【50】 75** percent of the fee paid under **【subparagraph (B)(i)】 subparagraph (B)** for any application or supplement which is **【not accepted】 refused** for filing.

(E) EXCEPTION FOR DESIGNATED ORPHAN DRUG OR INDICATION.—*A human drug application for a prescription drug product that has been designated as a drug for a rare disease or condition pursuant to section 526 shall not be subject to a fee under subparagraph (A), unless the human drug application includes indications for other than rare*

diseases or conditions. A supplement proposing to include a new indication for a rare disease or condition in a human drug application shall not be subject to a fee under subparagraph (A), if the drug has been designated pursuant to section 526 as a drug for a rare disease or condition with regard to the indication proposed in such supplement.

(F) *EXCEPTION FOR SUPPLEMENTS FOR PEDIATRIC INDICATIONS.*—A supplement to a human drug application for an indication for use in pediatric populations shall not be assessed a fee under subparagraph (A).

(G) *REFUND OF FEE IF APPLICATION WITHDRAWN.*—If an application or supplement is withdrawn after the application or supplement is filed, the Secretary may waive and refund the fee or a portion of the fee if no substantial work was performed on the application or supplement after the application or supplement was filed. The Secretary shall have the sole discretion to waive and refund a fee or a portion of the fee under this subparagraph. A determination by the Secretary concerning a waiver or refund under this paragraph shall not be reviewable.

[(2) *PRESCRIPTION DRUG ESTABLISHMENT FEE.*—Each person that—

[(A) owns a prescription drug establishment, at which is manufactured at least 1 prescription drug product which is not the, or not the same as a, product approved under an application filed under section 505(b)(2) or 505(j), and

[(B) after September 1, 1992, had pending before the Secretary a human drug application or supplement, shall be subject to the annual fee established in subsection (b) for each such establishment, payable on or before January 31 of each year.]

(2) *PRESCRIPTION DRUG ESTABLISHMENT FEE.*—

(A) *IN GENERAL.*—Except as provided in subparagraph (B), each person that is named as the applicant in a human drug application, and after September 1, 1992, had pending before the Secretary a human drug application or supplement, shall be assessed an annual fee established in subsection (b) for each prescription drug establishment listed in its approved human drug application as an establishment that manufactures the prescription drug product named in the application. The annual establishment fee shall be assessed in each fiscal year in which the prescription drug product named in the application is assessed a fee under paragraph (3) unless the prescription drug establishment listed in the application does not engage in the manufacture of the prescription drug product during the fiscal year. The establishment fee shall be payable on or before January 31 of each year. Each such establishment shall be assessed only one fee per establishment, notwithstanding the number of prescription drug products manufactured at the establishment. In the event an establishment is listed in a human drug application by more than 1 applicant, the establishment fee for the fiscal year shall be divided equally and assessed among the applicants

whose prescription drug products are manufactured by the establishment during the fiscal year and assessed product fees under paragraph (3).

(B) EXCEPTION.—If, during the fiscal year, an applicant initiates or causes to be initiated the manufacture of a prescription drug product at an establishment listed in its human drug application—

(i) that did not manufacture the product in the previous fiscal year; and

(ii) for which the full establishment fee has been assessed in the fiscal year at a time before manufacture of the prescription drug product was begun;

the applicant will not be assessed a share of the establishment fee for the fiscal year in which the manufacture of the product began.

(3) PRESCRIPTION DRUG PRODUCT FEE.—

(A) IN GENERAL.—Except as provided in subparagraph (B), each person—

(i) who is named as the applicant in a human drug application for a prescription drug product which **is listed** *has been submitted for listing* under section 510, and

(ii) who, after September 1, 1992, had pending before the Secretary a human drug application or supplement,

shall pay for each such prescription drug product the annual fee established in subsection (b). **Such fee shall be payable at the time of the first such listing of such product in each calendar year. Such fee shall be paid only once each year for each listed prescription drug product irrespective of the number of times such product is listed under section 510.** *Such fee shall be payable for the fiscal year in which the product is first submitted for listing under section 510, or for relisting under section 510 if the product has been withdrawn from listing and relisted. After such fee is paid for that fiscal year, such fee shall be payable on or before January 31 of each year. Such fee shall be paid only once for each product for a fiscal year in which the fee is payable.*

(B) EXCEPTION.—The listing of a prescription drug product under section 510 shall not require the person who listed such product to pay the fee prescribed by subparagraph (A) if such product is the same product as a product approved under an application filed under section 505(b)(2) or **505(j).** *505(j), under an abbreviated application filed under section 507, or under an abbreviated new drug application pursuant to regulations in effect prior to the implementation of the Drug Price Competition and Patent Term Restoration Act of 1984.*

[(b) FEE AMOUNTS.—

[(1) SCHEDULE.—Except as provided in paragraph (2) and subsections (c), (d), (f), and (g), the fees required under subsection (a) shall be paid in accordance with the following schedule:

	Fiscal Year 1993	Fiscal Year 1994	Fiscal Year 1995	Fiscal Year 1996	Fiscal Year 1997
Drug application fee:					
Subsection (a)(1)(A)(i) fee	\$100,000	\$150,000	\$208,000	\$217,000	\$233,000
Subsection (a)(1)(A)(ii) fee	\$50,000	\$75,000	\$104,000	\$108,000	\$116,000
Fee revenue	\$12,000,000	\$18,000,000	\$25,000,000	\$26,000,000	\$28,000,000
Annual establishment fee:					
Fee per establishment	\$60,000	\$88,000	\$126,000	\$131,000	\$138,000
Fee revenue	\$12,000,000	\$18,000,000	\$25,000,000	\$26,000,000	\$28,000,000
Annual product fee:					
Fee per product	\$6,000	\$9,000	\$12,500	\$13,000	\$14,000
Fee revenue	\$12,000,000	\$18,000,000	\$25,000,000	\$26,000,000	\$28,000,000
Total fee revenues	\$36,000,000	\$54,000,000	\$75,000,000	\$78,000,000	\$84,000,000

[(2) SMALL BUSINESS EXCEPTION.—Any business which has fewer than 500 employees, including employees of affiliates, and which does not have a prescription drug product introduced or delivered for introduction into interstate commerce shall pay one-half the amount of the fee for human drug applications it submits and shall pay the entire amount of the fee for supplements it submits. Such a business shall not be required to pay any portion of any fee required under subsection (a)(1)(A) until 1 year after the date of the submission of the application involved. For purposes of this paragraph, one business is an affiliate of another business when, directly or indirectly, one business controls, or has the power to control, the other business or a third party controls, or has the power to control, both businesses.]

(b) FEE AMOUNTS.—*Except as provided in subsections (c), (d), (f), and (g), the fees required under subsection (a) shall be determined and assessed as follows:*

(1) APPLICATION AND SUPPLEMENT FEES.—

(A) FULL FEES.—*The application fee under subsection (a)(1)(A)(i) shall be \$250,704 in fiscal year 1998, \$256,338 in each of fiscal years 1999 and 2000, \$267,606 in fiscal year 2001, and \$258,451 in fiscal year 2002.*

(B) OTHER FEES.—*The fee under subsection (a)(1)(A)(ii) shall be \$125,352 in fiscal year 1998, \$128,169 in each of fiscal years 1999 and 2000, \$133,803 in fiscal year 2001, and \$129,226 in fiscal year 2002.*

(2) FEE REVENUES FOR ESTABLISHMENT FEES.—*The total fee revenues to be collected in establishment fees under subsection (a)(2) shall be \$35,600,000 in fiscal year 1998, \$36,400,000 in each of fiscal years 1999 and 2000, \$38,000,000 in fiscal year 2001, and \$36,700,000 in fiscal year 2002.*

(3) TOTAL FEE REVENUES FOR PRODUCT FEES.—*The total fee revenues to be collected in product fees under subsection (a)(3) in a fiscal year shall be equal to the total fee revenues collected in establishment fees under subsection (a)(2) in that fiscal year.*

(c) **【INCREASES AND】** ADJUSTMENTS.—

【(1) REVENUE INCREASE.—The total fee revenues established by the schedule in subsection (b)(1) shall be increased by the Secretary **】** *(1) INFLATION ADJUSTMENT.—The fees and total fee revenues established in subsection (b) shall be adjusted by the Secretary by notice, published in the Federal Register, for a fiscal year to reflect the greater of—*

(A) the total percentage **【increase】** *change* that occurred during the preceding fiscal year in the Consumer Price Index for all urban consumers (all items; U.S. city average), or

(B) the total percentage **【increase】** *change* for such fiscal year in basic pay under the General Schedule in accordance with section 5332 of title 5, United States Code, as adjusted by any locality-based comparability payment pursuant to section 5304 of such title for Federal employees stationed in the District of Columbia.

The adjustment made each fiscal year by this subsection will be added on a compounded basis to the sum of all adjustments made each fiscal year after fiscal year 1997 under this subsection.

(2) ANNUAL FEE ADJUSTMENT.—Subject to the amount appropriated for a fiscal year under subsection (g), the Secretary shall, within 60 days after the end of each fiscal year beginning after **【October 1, 1992, adjust the fees established by the schedule in subsection (b)(1) for the following fiscal year to achieve the total fee revenues, as may be increased under paragraph (1). Such fees shall be adjusted under this paragraph to maintain the proportions established in such schedule.】** *September 30, 1997, adjust the establishment and product fees described in subsection (b) for the fiscal year in which the adjustment occurs so that the revenues collected from each of the categories of fees described in paragraphs (2) and (3) of subsection (b) shall be set to be equal to the revenues collected from the category of application and supplement fees described in paragraph (1) of subsection (b).*

(3) LIMIT.—The total amount of fees charged, as adjusted under **【paragraph (2)】** *this subsection*, for a fiscal year may not exceed the total costs for such fiscal year for the resources allocated for the process for the review of human drug applications.

(d) FEE WAIVER OR REDUCTION.—【The Secretary shall grant a waiver from or a reduction of 1 or more fees under subsection (a) where the Secretary finds that—**】**

(1) IN GENERAL.—The Secretary shall grant a waiver from or a reduction of one or more fees assessed under subsection (a) where the Secretary finds that—

【(1)】 (A) such waiver or reduction is necessary to protect the public health,

【(2)】 (B) the assessment of the fee would present a significant barrier to innovation because of limited resources available to such person or other circumstances,

【(3)】 (C) the fees to be paid by such person will exceed the anticipated present and future costs incurred by the

Secretary in conducting the process for the review of human drug applications for such person [, or],

[(4)] (D) assessment of the fee for an application or a supplement filed under section 505(b)(1) pertaining to a drug containing an active ingredient would be inequitable because an application for a product containing the same active ingredient filed by another person under section 505(b)(2) could not be assessed fees under subsection (a)(1) [,], or

(E) the applicant is a small business submitting its first human drug application to the Secretary for review.

[In making the finding in paragraph (3), the Secretary may use standard costs.]

(2) USE OF STANDARD COSTS.—In making the finding in paragraph (1)(C), the Secretary may use standard costs.

(3) RULES RELATING TO SMALL BUSINESSES.—

(A) DEFINITION.—In paragraph (1)(E), the term “small business” means an entity that has fewer than 500 employees, including employees of affiliates.

(B) WAIVER OF APPLICATION FEE.—The Secretary shall waive under paragraph (1)(E) the application fee for the first human drug application that a small business or its affiliate submits to the Secretary for review. After a small business or its affiliate is granted such a waiver, the small business or its affiliate shall pay—

(i) application fees for all subsequent human drug applications submitted to the Secretary for review in the same manner as an entity that does not qualify as a small business; and

(ii) all supplement fees for all supplements to human drug applications submitted to the Secretary for review in the same manner as an entity that does not qualify as a small business.

* * * * *

(f) ASSESSMENT OF FEES.—

(1) LIMITATION.—Fees may not be assessed under subsection (a) for a fiscal year beginning after fiscal year [1993] 1997 unless appropriations for salaries and expenses of the Food and Drug Administration for such fiscal year (excluding the amount of fees appropriated for such fiscal year) are equal to or greater than the amount of appropriations for the salaries and expenses of the Food and Drug Administration for the [fiscal year 1992] fiscal year 1997 (excluding the amount of fees appropriated for such fiscal year) multiplied by the adjustment factor applicable to the fiscal year involved.

* * * * *

(g) CREDITING AND AVAILABILITY OF FEES.—

(1) IN GENERAL.—Fees collected for a fiscal year pursuant to subsection (a) shall be credited to the appropriation account for salaries and expenses of the Food and Drug Administration and shall be available in accordance with appropriation Acts until expended without fiscal year limitation. Such sums as may be necessary may be transferred from the Food and Drug

Administration salaries and expenses appropriation account without fiscal year limitation to such appropriation account for salaries and expenses with such fiscal year limitation. The sums transferred shall be available solely for the process for the review of human drug applications within the meaning of section 735(6).

(2) COLLECTIONS AND APPROPRIATION ACTS.—The fees authorized by this section—

(A) shall be collected in each fiscal year in an amount equal to the amount specified in appropriation ~~Acts~~ *Acts*, or otherwise made available for obligation, for such fiscal year, and

(B) shall only be collected and available to defray increases in the costs of the resources allocated for the process for the review of human drug applications (including increases in such costs for an additional number of full-time equivalent positions in the Department of Health and Human Services to be engaged in such process) ~~over such costs for fiscal year 1992~~ *over such costs, excluding costs paid from fees collected under this section, for fiscal year 1997* multiplied by the adjustment factor.

~~[(3) AUTHORIZATION OF APPROPRIATIONS.—There are authorized to be appropriated for fees under this section—~~

~~[(A) \$36,000,000 for fiscal year 1993,~~

~~[(B) \$54,000,000 for fiscal year 1994,~~

~~[(C) \$75,000,000 for fiscal year 1995,~~

~~[(D) \$78,000,000 for fiscal year 1996, and~~

~~[(E) \$84,000,000 for fiscal year 1997,~~

~~as adjusted to reflect increases in the total fee revenues made under subsection (c)(1).]~~

~~(3) AUTHORIZATION OF APPROPRIATIONS.—There is authorized to be appropriated for fees under this section—~~

~~(A) \$106,800,000 for fiscal year 1998;~~

~~(B) \$109,200,000 for fiscal year 1999;~~

~~(C) \$109,200,000 for fiscal year 2000;~~

~~(D) \$114,000,000 for fiscal year 2001; and~~

~~(E) \$110,100,000 for fiscal year 2002,~~

~~as adjusted to reflect adjustments in the total fee revenues made under this section and changes in the total amounts collected by application, supplement, establishment, and product fees.~~

~~(4) OFFSET.—Any amount of fees collected for a fiscal year which exceeds the amount of fees specified in appropriation Acts for such fiscal year shall be credited to the appropriation account of the Food and Drug Administration as provided in paragraph (1), and shall be subtracted from the amount of fees that would otherwise be authorized to be collected under appropriation Acts for a subsequent fiscal year.~~

* * * * *

(i) WRITTEN REQUESTS FOR WAIVERS, REDUCTIONS, AND REFUNDS.—To qualify for consideration for a waiver or reduction under subsection (d), or for a refund of any fee collected in accordance with subsection (a), a person shall submit to the Secretary a written request for such waiver, reduction, or refund not later than 180 days after such fee is due.

[(i)] (j) CONSTRUCTION.—This section may not be construed to require that the number of full-time equivalent positions in the Department of Health and Human Services, for officers, employers, and advisory committees not engaged in the process of the review of human drug applications, be reduced to offset the number of officers, employees, and advisory committees so engaged.

SUBCHAPTER D—FAST TRACK PRODUCTS

SEC. 741. FAST TRACK PRODUCTS.

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

(1) IN GENERAL.—The Secretary shall facilitate the development and expedite the review of new drugs that are intended for the treatment of serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs for such conditions. In this section, such products shall be known as “fast track products”.

(2) REQUEST FOR DESIGNATION.—The sponsor of a 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)(4) of the Public Health Service Act.

(3) DESIGNATION.—Within 30 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) APPROVAL OF APPLICATION FOR A FAST TRACK PRODUCT.—

(1) IN GENERAL.—The Secretary may approve an application for approval of a fast track product under section 505(b) or section 351 of the Public Health Service Act (21 U.S.C. 262) upon a determination that the product has an effect on a clinical endpoint or a surrogate endpoint that is reasonably likely to predict clinical benefit.

(2) LIMITATION.—Approval of a fast track product under this subsection may be subject to the requirements—

(A) that the sponsor conduct appropriate post-approval studies to validate the surrogate endpoint or otherwise confirm the effect on the clinical endpoint; and

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

(3) EXPEDITED WITHDRAWAL OF APPROVAL.—The Secretary may withdraw approval of a fast track product 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 fast track drug with due diligence;

(B) a post-approval study of the fast track product fails to verify clinical benefit of the product;

(C) other evidence demonstrates that the fast track 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 Secretary 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 applicable to fast track products established under this section; and

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

SUBCHAPTER E—DISSEMINATION OF TREATMENT INFORMATION

SEC. 745. REQUIREMENTS FOR DISSEMINATION OF TREATMENT INFORMATION ON DRUGS.

(a) **IN GENERAL.**—Notwithstanding sections 301(d), 502(f), and 505 and section 351 of the Public Health Service Act (42 U.S.C. 262), a manufacturer may disseminate to—

(1) a health care practitioner,

(2) a pharmacy benefit manager,

(3) a health insurance issuer,

(4) a group health plan, or

(5) a Federal or State governmental agency,

written information concerning the safety, effectiveness, or benefit of a use not described in the approved labeling of a drug if the manufacturer meets the requirements of subsection (b).

(b) **SPECIFIC REQUIREMENTS.**—A manufacturer may disseminate information about a new use of a drug under subsection (a) only if—

(1) *there is in effect for such drug an application filed under section 505(b) or a biologics license issued under section 351 of the Public Health Service Act;*

(2) *the information meets the requirements of section 746;*

(3) *the information to be disseminated is not derived from clinical research conducted by another manufacturer or if it was derived from research conducted by another manufacturer, the manufacturer disseminating the information has the permission of such other manufacturer to make the dissemination;*

(4) *the manufacturer has, 60 days before such dissemination, submitted to the Secretary—*

(A) *a copy of the information disseminated; and*

(B) *any clinical trial information the manufacturer has relating to the safety or effectiveness of the new use, any reports of clinical experience pertinent to the safety of the new use, and a summary of such information;*

(5) *the manufacturer has complied with the requirements of section 748 (relating to certification that the manufacturer will submit a supplemental application with respect to such use);*

(6) *the manufacturer agrees to include along with the information disseminated under this subsection—*

(A) *a prominently displayed statement that discloses—*

(i) *that the information concerns a use of a drug that has not been approved by the Food and Drug Administration;*

(ii) *if applicable, that the information is being disseminated at the expense of the manufacturer;*

(iii) *if applicable, the name of any authors of the information who are employees of, consultants to, or have received compensation from, the manufacturer, or who have a significant financial interest in the manufacturer;*

(iv) *the official labeling for the drug and all updates with respect to the labeling;*

(v) *if applicable, a statement that there are products or treatments that have been approved for the use that is the subject of the information being disseminated pursuant to subsection (a)(1); and*

(vi) *the identification of any person that has provided funding for the conduct of a study relating to the new use of a drug for which such information is being disseminated; and*

(B) *a bibliography of other articles from a scientific reference publication or scientific or medical journal that have been previously published about the such use of the drug covered by the information disseminated (unless the information already includes such bibliography).*

(c) **ADDITIONAL INFORMATION.**—*If the Secretary determines, after providing notice of such determination and an opportunity for a meeting with respect to such determination, that the information submitted by a manufacturer under subsection (b)(3)(B), with respect to the use of a drug for which the manufacturer is disseminating information, fails to provide data, analyses, or other written*

matter that is objective and balanced, the Secretary may require the manufacturer to disseminate—

(1) additional objective and scientifically sound information that pertains to the safety or effectiveness of the use and is necessary to provide objectivity and balance, including any information that the manufacturer has submitted to the Secretary or, where appropriate, a summary of such information or any other information that the Secretary has authority to make available to the public; and

(2) an objective statement of the Secretary, based on data or other scientifically sound information available to the Secretary, that bears on the safety or effectiveness of the new use of the drug.

SEC. 746. INFORMATION AUTHORIZED TO BE DISSEMINATED.

(a) **AUTHORIZED INFORMATION.**—A manufacturer may disseminate the information on the new use of a drug under section 745 only if the information—

(1) is in the form of an unabridged—

(A) reprint or copy of an article, peer-reviewed by experts qualified by scientific training or experience to evaluate the safety or effectiveness of the drug, which was published in a scientific or medical journal (as defined in section 750(6)), which is about a clinical investigation with respect to the drug, and which would be considered to be scientifically sound by such experts; or

(B) reference publication, described in subsection (b), that includes information about a clinical investigation with respect to the drug that would be considered to be scientifically sound by experts qualified by scientific training or experience to evaluate the safety or effectiveness of the drug that is the subject of such a clinical investigation; and

(2) is not false or misleading and would not pose a significant risk to the public health.

(b) **REFERENCE PUBLICATION.**—A reference publication referred to in subsection (a)(1)(B) is a publication that—

(1) has not been written, edited, excerpted, or published specifically for, or at the request of, a manufacturer of a drug;

(2) has not been edited or significantly influenced by a such a manufacturer;

(3) is not solely distributed through such a manufacturer but is generally available in bookstores or other distribution channels where medical textbooks are sold;

(4) does not focus on any particular drug of a manufacturer that disseminates information under section 745 and does not have a primary focus on new uses of drugs that are marketed or under investigation by a manufacturer supporting the dissemination of information; and

(5) presents materials that are not false or misleading.

SEC. 747. ESTABLISHMENT OF LIST OF ARTICLES AND PUBLICATIONS DISSEMINATED AND LIST OF PROVIDERS THAT RECEIVED ARTICLES AND REFERENCE PUBLICATIONS.

(a) **IN GENERAL.**—A manufacturer may disseminate information under section 745 only if the manufacturer prepares and submits to the Secretary biannually—

(1) a list containing the titles of the articles and reference publications relating to the new use of drugs that were disseminated by the manufacturer to a person described in section 745(a) for the 6-month period preceding the date on which the manufacturer submits the list to the Secretary; and

(2) a list that identifies the categories of providers (as described in section 745(a)) that received the articles and reference publications for the 6-month period described in paragraph (1).

(b) **RECORDS.**—A manufacturer that disseminates information under section 745 shall keep records that may be used by the manufacturer when, pursuant to section 749, such manufacturer is required to take corrective action and shall be made available to the Secretary, upon request, for purposes of ensuring or taking corrective action pursuant to such section. Such records, at the Secretary's discretion, may identify the recipient of information provided pursuant to section 745 or the categories of such recipients.

SEC. 748. REQUIREMENT REGARDING SUBMISSION OF SUPPLEMENTAL APPLICATION FOR NEW USE; EXEMPTION FROM REQUIREMENT.

(a) **IN GENERAL.**—A manufacturer may disseminate information under section 745 on a new use only if—

(1) the manufacturer meets the condition described in subsection (b) or in subsection (c); or

(2) there is in effect for the manufacturer an exemption under subsection (d) from the requirement of paragraph (1).

(b) **SUPPLEMENTAL APPLICATION; CONDITION IN CASE OF COMPLETED STUDIES.**—For purposes of subsection (a)(1), a manufacturer may disseminate information on a new use if the manufacturer has submitted to the Secretary an application containing a certification that—

(1) the studies needed for the submission of a supplemental application for the new use have been completed; and

(2) the supplemental application will be submitted to the Secretary not later than 6 months after the date of the initial dissemination of information under section 745.

(c) **SUPPLEMENTAL APPLICATION; CONDITION IN CASE OF PLANNED STUDIES.**—

(1) **IN GENERAL.**—For purposes of subsection (a)(1), a manufacturer may disseminate information on a new use if—

(A) the manufacturer has submitted to the Secretary an application containing—

(i) a proposed protocol and schedule for conducting the studies needed for the submission of a supplemental application for the new use; and

(ii) a certification that the supplemental application will be submitted to the Secretary not later than 36 months after the date of the initial dissemination of information under section 745 (or, as applicable, not later than such date as the Secretary may specify pursuant to an extension under this paragraph or paragraph (3)); and

(B) the Secretary has determined that the proposed protocol is adequate and that the schedule for completing such studies is reasonable.

The Secretary may grant a longer period of time for a manufacturer to submit a supplemental application if the Secretary determines that the studies needed to submit such an application cannot be completed and submitted within 36 months.

(2) *PROGRESS REPORTS ON STUDIES.*—A manufacturer that submits to the Secretary an application under paragraph (1) shall submit to the Secretary periodic reports describing the status of the studies involved.

(3) *EXTENSION OF TIME REGARDING PLANNED STUDIES.*—The period of 36 months authorized in paragraph (1)(A)(ii) for the completion of studies may be extended by the Secretary if the manufacturer involved submits to the Secretary a written request for the extension and the Secretary determines that the manufacturer has acted with due diligence to conduct the studies in a timely manner. Such extension may not provide more than 24 additional months.

(d) *EXEMPTION FROM REQUIREMENT OF SUPPLEMENTAL APPLICATION.*—

(1) *IN GENERAL.*—For purposes of subsection (a)(2), a manufacturer may disseminate information on a new use if—

(A) the manufacturer has submitted to the Secretary an application for an exemption from meeting the requirement of subsection (a)(1); and

(B)(i) the Secretary has approved the application in accordance with paragraph (2); or

(ii) the application is deemed under paragraph (3)(A) to have been approved (unless such approval is terminated pursuant to paragraph (3)(B)).

(2) *CONDITIONS FOR APPROVAL.*—The Secretary may approve an application under paragraph (1) for an exemption only if the Secretary determines that—

(A) it would be economically prohibitive with respect to such drug for the manufacturer to incur the costs necessary for the submission of a supplemental application for reasons, as defined by the Secretary, such as the lack of availability under law of any period during which the manufacturer would have exclusive marketing rights with respect to the new use involved or that the population expected to benefit from approval of the supplemental application is small; or

(B) it would be unethical to conduct the studies necessary for the supplemental application for a reason such as the new use involved is the standard of medical care for a health condition.

(3) *TIME FOR CONSIDERATION OF APPLICATION; DEEMED APPROVAL.*—

(A) *IN GENERAL.*—The Secretary shall approve or deny an application under paragraph (1) for an exemption not later than 60 days after the receipt of the application. If the Secretary does not comply with the preceding sentence, the application is deemed to be approved.

(B) *TERMINATION OF DEEMED APPROVAL.*—If pursuant to a deemed approval under subparagraph (A) a manufacturer disseminates written information under section 745

on a new use, the Secretary may at any time terminate such approval and under section 749(b)(3) order the manufacturer to cease disseminating the information.

(e) **REQUIREMENTS REGARDING APPLICATIONS.**—*Applications under this section shall be submitted in the form and manner prescribed by the Secretary.*

(f) **TRANSITION RULE.**—*For purposes of this section, in any case in which a manufacturer has submitted to the Secretary a supplemental application for which action by the Secretary is pending as of the date of the enactment of the Prescription Drug User Fee Reauthorization and Drug and Biological Products Regulatory Modernization Act of 1997, the application is deemed to be a supplemental application submitted under subsection (b).*

SEC. 749. CORRECTIVE ACTIONS; CESSATION OF DISSEMINATION.

(a) **POSTDISSEMINATION DATA REGARDING SAFETY AND EFFECTIVENESS.**—

(1) **CORRECTIVE ACTIONS.**—*With respect to data received by the Secretary after the dissemination of information under section 745 by a manufacturer has begun (whether received pursuant to paragraph (2) or otherwise), if the Secretary determines that the data indicate that the new use involved may not be effective or may present a significant risk to public health, the Secretary shall, in consultation with the manufacturer, take such action regarding the dissemination of the information as the Secretary determines to be appropriate for the protection of the public health, which may include ordering that the manufacturer cease the dissemination of the information.*

(2) **RESPONSIBILITIES OF MANUFACTURERS TO SUBMIT DATA.**—*After a manufacturer disseminates information pursuant to section 745, the manufacturer shall submit to the Secretary a notification of any additional knowledge of the manufacturer on clinical research or other data that relate to the safety or effectiveness of the new use involved. If the manufacturer is in possession of the data, the notification shall include the data. The Secretary shall by regulation establish the scope of the responsibilities of manufacturers under this paragraph, including such limits on the responsibilities as the Secretary determines to be appropriate.*

(b) **CESSATION OF DISSEMINATION.**—

(1) **FAILURE OF MANUFACTURER TO COMPLY WITH REQUIREMENTS.**—*The Secretary may order a manufacturer to cease the dissemination of information pursuant to section 745 if the Secretary determines that the information being disseminated does not comply with the requirements established in this subchapter. Such an order may be issued only after the Secretary has provided notice to the manufacturer of the intent of the Secretary to issue the order and has provided an opportunity for a meeting with respect to such intent unless paragraph (2)(B) applies. If the failure of the manufacturer constitutes a minor violation of this subchapter, the Secretary shall delay issuing the order and provide to the manufacturer an opportunity to correct the violation.*

(2) *SUPPLEMENTAL APPLICATIONS.*—*The Secretary may order a manufacturer to cease the dissemination of information pursuant to section 745 if the Secretary determines that—*

(A) *in the case of a manufacturer to which section 748(b) applies, the Secretary determines that the supplemental application received under such section does not contain adequate information for approval of the new use with respect to which the application was submitted; or*

(B) *in the case of a manufacturer to which section 748(c) applies, the Secretary determines, after an informal hearing, that the manufacturer is not acting with due diligence to complete the studies involved.*

(3) *TERMINATION OF DEEMED APPROVAL OF EXEMPTION REGARDING SUPPLEMENTAL APPLICATIONS.*—*If under section 748(d)(3) the Secretary terminates a deemed approval of an exemption, the Secretary may order the manufacturer involved to cease disseminating the information. A manufacturer shall comply with an order under the preceding sentence not later than 60 days after the receipt of the order.*

(c) *CORRECTIVE ACTIONS BY MANUFACTURERS.*—

(1) *IN GENERAL.*—*In any case in which under this section the Secretary orders a manufacturer to cease disseminating information, the Secretary may order the manufacturer to take action to correct the information that has been disseminated, except as provided in paragraph (2).*

(2) *TERMINATION OF DEEMED APPROVAL OF EXEMPTION REGARDING SUPPLEMENTAL APPLICATIONS.*—*In the case of an order under subsection (b)(3) to cease disseminating information, the Secretary may not order the manufacturer involved to take action to correct the information that has been disseminated unless the Secretary determines that the new use described in the information would pose a significant risk to the public health.*

SEC. 750. DEFINITIONS.

For purposes of this subchapter:

(1) *The term “health care practitioner” means a physician, or other individual who is a provider of health care, who is licensed under the law of a State to prescribe drugs.*

(2) *The terms “health insurance issuer” and “group health plan” have the meaning given such terms under section 2791 of the Public Health Service Act.*

(3) *The term “manufacturer” means a person who manufactures a drug, or who is licensed by such person to distribute or market the drug.*

(4) *The term “new use”, with respect to a drug, means a use that is not included in the approved labeling of the drug.*

(5) *The term “pharmacy benefit manager” means an organization that—*

(A) *manages pharmaceutical costs through—*

(i) *pharmacy benefit administration, including claims processing adjudication, pharmacy networks, mail service, and data reporting;*

(ii) *formulary management and contracting, including evaluating drugs for formulary status, negotiations*

of contracts with manufacturers, and disbursement of rebates; and

(iii) utilization management, including communicating and enforcing therapy guidelines and drug use principles to physicians, pharmacists, and patients; and

(B) serves 2 principal types of customers which are—

(i) employers, both private- and public-sector, who use either self-funded health benefits through a third party administrator's insurance carrier or use traditional indemnity coverage, using providers from a preferred provider network or in a fee-for-service capacity; and

(ii) health maintenance organizations.

(6) The term "scientific or medical journal" means a scientific or medical publication—

(A) that is published by an organization—

(i) that has an editorial board;

(ii) that utilizes experts, who have demonstrated expertise in the subject of an article under review by the organization and who are independent of the organization, to review and objectively select, reject, or provide comments about proposed articles; and

(iii) that has a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interest or biases for all authors or contributors involved with the journal or organization;

(B) whose articles are peer-reviewed and published in accordance with the regular peer-review procedures of the organization;

(C) that is generally recognized to be of national scope and reputation;

(D) that is indexed in the Index Medicus of the National Library of Medicine of the National Institutes of Health; and

(E) that is not in the form of a special supplement that has been funded in whole or in part by 1 or more manufacturers.

SEC. 751. RULES OF CONSTRUCTION.

(a) **UNSOLICITED REQUEST.**—Nothing in section 745 shall be construed as prohibiting a manufacturer from disseminating information in response to an unsolicited request from a health care practitioner.

(b) **DISSEMINATION OF INFORMATION ON DRUGS NOT EVIDENCE OF INTENDED USE.**—Notwithstanding subsection (a), (f), or (o) of section 502, or any other provision of law, the dissemination of information relating to a new use of a drug, in accordance with section 745, shall not be construed by the Secretary as evidence of a new intended use of the drug that is different from the intended use of the drug set forth in the official labeling of the drug. Such dissemination shall not be considered by the Secretary as labeling, adulteration, or misbranding of the drug.

(c) **PATENT PROTECTION.**—Nothing in section 745 shall affect patent rights in any manner.

(d) *AUTHORIZATION FOR DISSEMINATION OF ARTICLES AND FEES FOR REPRINTS OF ARTICLES.*—Nothing in section 745 shall be construed as prohibiting an entity that publishes a scientific journal (as defined in section 750(6)) from requiring authorization from the entity to disseminate an article published by such entity or charging fees for the purchase of reprints of published articles from such entity.

SUBCHAPTER F—MANUFACTURING CHANGES

SEC. 755. MANUFACTURING CHANGES.

(a) *IN GENERAL.*—With respect to a drug for which there is in effect an approved application under section 505 or 512 or a license under section 351 of the Public Health Service Act, a change from the manufacturing process approved pursuant to such application or license may be made, and the drug as made with the change may be distributed, if—

(1) the holder of the approved application or license (referred to in this section as a “holder”) has validated the effects of the change in accordance with subsection (b); and

(2)(A) in the case of a major manufacturing change, the holder has complied with the requirements of subsection (c); or

(B) in the case of a change that is not a major manufacturing change, the holder complies with the applicable requirements of subsection (d).

(b) *VALIDATION OF EFFECTS OF CHANGES.*—For purposes of subsection (a)(1), a drug made with a manufacturing change (whether a major manufacturing change or otherwise) may be distributed only if, before distribution of the drug as so made, the holder involved validates the effects of the change on the identity, strength, quality, purity, and potency of the drug as the identity, strength, quality, purity, and potency may relate to the safety, bioequivalence, bioavailability, or effectiveness of the drug.

(c) *MAJOR MANUFACTURING CHANGES.*—

(1) *REQUIREMENT OF SUPPLEMENTAL APPLICATION.*—For purposes of subsection (a)(2)(A), a drug made with a major manufacturing change may be distributed only if, before the distribution of the drug as so made, the holder involved submits to the Secretary a supplemental application for such change and the Secretary approves the application. The application shall contain such information as the Secretary determines to be appropriate, and shall include the information developed under subsection (b) by the holder in validating the effects of the change.

(2) *CHANGES QUALIFYING AS MAJOR CHANGES.*—For purposes of subsection (a)(2)(A), a major manufacturing change is a manufacturing change that—

(A) is determined by the Secretary to have substantial potential to adversely affect the identity, strength, quality, purity, or potency of the drug as they may relate to the safety, bioequivalence, bioavailability, or effectiveness of a drug; and

(B)(i) is made in the qualitative or quantitative formulation of the drug involved or in the specifications in the approved application or license referred to in subsection (a)

for the drug (unless exempted by the Secretary from the requirements of this subsection);

(ii) is determined by the Secretary by regulation or guidance to require completion of an appropriate clinical study demonstrating equivalence of the drug to the drug as manufactured without the change; or

(iii) is determined by the Secretary by regulation or guidance to have a substantial potential to adversely affect the safety or effectiveness of the drug.

(d) OTHER MANUFACTURING CHANGES.—

(1) IN GENERAL.—For purposes of subsection (a)(2)(B), the Secretary may regulate drugs made with manufacturing changes that are not major manufacturing changes as follows:

(A) The Secretary may authorize holders to distribute such drugs without prior approval by the Secretary.

(B) The Secretary may require that, prior to the distribution of such drugs, holders submit to the Secretary supplemental applications for such changes.

(C) The Secretary may establish categories of such changes and designate categories to which subparagraph (A) applies and categories to which subparagraph (B) applies.

(2) CHANGES NOT REQUIRING SUPPLEMENTAL APPLICATION.—

(A) SUBMISSION OF REPORT.—A holder making a manufacturing change to which paragraph (1)(A) applies shall submit to the Secretary a report on the change, which shall contain such information as the Secretary determines to be appropriate, and which shall include the information developed under subsection (b) by the holder in validating the effects of the change. The report shall be submitted by such date as the Secretary may specify.

(B) AUTHORITY REGARDING ANNUAL REPORTS.—In the case of a holder that during a single year makes more than one manufacturing change to which paragraph (1)(A) applies, the Secretary may in carrying out subparagraph (A) authorize the holder to comply with such subparagraph by submitting a single report for the year that provides the information required in such subparagraph for all the changes made by the holder during the year.

(3) CHANGES REQUIRING SUPPLEMENTAL APPLICATION.—

(A) SUBMISSION OF SUPPLEMENTAL APPLICATION.—The supplemental application required under paragraph (1)(B) for a manufacturing change shall contain such information as the Secretary determines to be appropriate, which shall include the information developed under subsection (b) by the holder in validating the effects of the change.

(B) AUTHORITY FOR DISTRIBUTION.—In the case of a manufacturing change to which paragraph (1)(B) applies:

(i) The holder involved may commence distribution of the drug involved 30 days after the Secretary receives the supplemental application under such paragraph, unless the Secretary notifies the holder within such 30-day period that prior approval of the application is required before distribution may be commenced.

(ii) *The Secretary may designate a category of such changes for the purpose of providing that, in the case of a change that is in such category, the holder involved may commence distribution of the drug involved upon the receipt by the Secretary of a supplemental application for the change.*

(iii) *If the Secretary disapproves the supplemental application, the Secretary may order the manufacturer to cease the distribution of the drugs that have been made with the manufacturing change.*

SUBCHAPTER G—ENVIRONMENTAL IMPACT REVIEW

SEC. 761. ENVIRONMENTAL IMPACT REVIEW.

Notwithstanding any other provision of law, an environmental impact statement prepared in accordance with the regulations published at part 25 of 21 C.F.R. (as in effect on August 31, 1997) in connection with an action carried out under (or a recommendation or report relating to) this Act, shall be considered to meet the requirements for a detailed statement under section 102(2)(C) of the National Environmental Policy Act.

SUBCHAPTER H—NATIONAL UNIFORMITY FOR NONPRESCRIPTION DRUGS FOR HUMAN USE AND PREEMPTION FOR LABELING OR PACKAGING OF COSMETICS

SEC. 771. NATIONAL UNIFORMITY FOR NONPRESCRIPTION DRUGS FOR HUMAN USE.

(a) *IN GENERAL.—Except as provided in subsection (b), (c)(1), (d), (e), or (f), no State or political subdivision of a State may establish or continue in effect any requirement—*

(1) that relates to the regulation of a drug intended for human use that is not subject to the requirements of section 503(b)(1); and

(2) that is different from or in addition to, or that is otherwise not identical with, a requirement under this Act, the Poison Prevention Packaging Act of 1970 (15 U.S.C. 1471 et seq.), or the Fair Packaging and Labeling Act (15 U.S.C. 1451 et seq.).

(b) *EXEMPTION.—Upon application of a State or political subdivision thereof, the Secretary may by regulation, after notice and opportunity for written and oral presentation of views, exempt from subsection (a), under such conditions as may be prescribed in such regulation, a State or political subdivision requirement that—*

(1) protects an important public interest that would otherwise be unprotected;

(2) would not cause any drug to be in violation of any applicable requirement or prohibition under Federal law; and

(3) would not unduly burden interstate commerce.

(c) *SCOPE.—*

(1) IN GENERAL.—This section shall not apply to—

(A) any State or political subdivision requirement that relates to the practice of pharmacy; or

(B) any State or political subdivision requirement that a drug be dispensed only upon the prescription of a practitioner licensed by law to administer such drug.

(2) *SAFETY OR EFFECTIVENESS.*—For purposes of subsection (a), a requirement that relates to the regulation of a drug shall be deemed to include any requirement relating to public information or any other form of public communication relating to a warning of any kind for a drug.

(d) *EXCEPTIONS.*—

(1) *IN GENERAL.*—In the case of a drug described in subsection (a)(1) that is not the subject of an application approved under section 505 or 507 or a final regulation promulgated by the Secretary establishing conditions under which the drug is generally recognized as safe and effective and not misbranded, subsection (a) shall apply only with respect to a requirement of a State or political subdivision of a State that relates to the same subject as, but is different from or in addition to, or that is otherwise not identical with—

(A) a regulation in effect with respect to the drug pursuant to a statute described in subsection (a)(2); or

(B) any other requirement in effect with respect to the drug pursuant to an amendment to such a statute made on or after the date of enactment of this section.

(2) *STATE INITIATIVES.*—This section shall not apply to a State public initiative enacted prior to the date of enactment of this section.

(e) *NO EFFECT ON PRODUCT LIABILITY LAW.*—Nothing in this section shall be construed to modify or otherwise affect any action or the liability of any person under the product liability law of any State.

(f) *STATE ENFORCEMENT AUTHORITY.*—Nothing in this section shall prevent a State or political subdivision thereof from enforcing, under any relevant civil or other enforcement authority, a requirement that is identical to a requirement of this Act.

SEC. 772. PREEMPTION FOR LABELING OR PACKAGING OF COSMETICS.

(a) *IN GENERAL.*—Except as provided in subsection (b), (d), or (e), a State or political subdivision of a State shall not impose or continue in effect any requirement for labeling or packaging of a cosmetic that is different from or in addition to, or that is otherwise not identical with a requirement that is specifically applicable to a particular cosmetic or class of cosmetics under this Act, the Poison Prevention Packaging Act of 1970 (15 U.S.C. 1471 et seq.), or the Fair Packaging and Labeling Act (15 U.S.C. 1451 et seq.).

(b) *EXEMPTION.*—Upon application of a State or political subdivision thereof, the Secretary may by regulation after notice and opportunity for written and oral presentation of views, exempt from subsection (a), under such conditions as may be prescribed in such regulation, a State or political subdivision requirement for labeling and packaging that—

(1) protects an important public interest that would otherwise be unprotected;

(2) would not cause a cosmetic to be in violation of any applicable requirements or prohibition under Federal law; and

(3) would not unduly burden interstate commerce.

(c) *SCOPE.*—For purposes of subsection (a), a reference to a State requirement that relates to the packaging or labeling of a cosmetic means any specific requirement relating to the same aspect of such cosmetic as a requirement specifically applicable to that particular cosmetic or class of cosmetics under this Act for packaging or labeling, including any State requirement relating to public information or any other form of public communication.

(d) *NO EFFECT ON PRODUCT LIABILITY LAW.*—Nothing in this section shall be construed to modify or otherwise affect any action or the liability of any person under the product liability law of any State.

(e) *STATE INITIATIVE.*—This section shall not apply to a State requirement adopted by a State public initiative or referendum enacted prior to September 1, 1997.

SUBCHAPTER I—NOTIFICATION OF THE DISCONTINUANCE OF A LIFE SAVING PRODUCT

SEC. 781. DISCONTINUANCE OF A LIFE SAVING PRODUCT.

(a) *IN GENERAL.*—A manufacturer that is the sole manufacturer of a drug or device—

(1) that is—

(A) life supporting;

(B) life sustaining; or

(C) intended for use in the prevention of a debilitating disease or condition; and

(2) for which an application has been approved under section 505(b), 505(j), or 515(d),

shall notify the Secretary of a discontinuance of the manufacture of the drug or device at least 6 months prior to the date of the discontinuance.

(b) *REDUCTION IN NOTIFICATION PERIOD.*—On application of a manufacturer, the Secretary may reduce the notification period required under subsection (a) for the manufacturer if good cause exists for the reduction, such as a situation in which—

(1) a public health problem may result from continuation of the manufacturing for the 6-month period;

(2) a biomaterials shortage prevents the continuation of the manufacturing for the 6-month period;

(3) a liability problem may exist for the manufacturer if the manufacturing is continued for the 6-month period;

(4) continuation of the manufacturing for the 6-month period may cause substantial economic hardship for the manufacturer;

(5) the manufacturer has filed for bankruptcy under chapter 7 or 11 of title 11, United States Code; or

(6) the Secretary determines that there would be no adverse impact from the discontinuance of a drug or device.

(c) *DISTRIBUTION.*—To the maximum extent practicable, the Secretary shall distribute information on the discontinuation of the drugs and devices described in subsection (a) to appropriate physician and patient organizations.

CHAPTER VIII—IMPORTS AND EXPORTS

IMPORTS AND EXPORTS

SEC. 801. (a) * * *

* * * * *

(d)(1) Except as provided in paragraph (2), no drug subject to section 503(b) or composed wholly or partly of insulin which is manufactured in a State and exported may be imported into the United States unless the drug is imported by the manufacturer of the drug.

* * * * *

EXPORTS OF CERTAIN UNAPPROVED PRODUCTS

SEC. 802. (a) * * *

* * * * *

(i) Insulin and antibiotics may be exported without regard to the requirements in this section if the insulin and antibiotics meet the requirements of section 801(e)(1).

OFFICE OF INTERNATIONAL RELATIONS

SEC. 803. (a) * * *

* * * * *

(c) The Secretary shall participate in meetings with representatives of other countries to discuss methods and approaches to reduce the burden of regulation and harmonize regulatory requirements if the Secretary determines that such harmonization continues consumer protections consistent with the purposes of this Act. The Secretary shall report to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate at least 60 days before executing any bilateral or multilateral agreement under subsection (b).

CHAPTER IX—MISCELLANEOUS

* * * * *

SEC. 903. FOOD AND DRUG ADMINISTRATION.

(a) * * *

(b) MISSION.—The Food and Drug Administration shall promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner, and with respect to such products shall protect the public health by ensuring that—

- (1) foods are safe, wholesome, sanitary, and properly labeled;
- (2) human and veterinary drugs are safe and effective;
- (3) there is reasonable assurance of safety and effectiveness of devices intended for human use;
- (4) cosmetics are safe and properly labeled; and
- (5) public health and safety are protected from electronic product radiation.

The Food and Drug Administration shall participate with other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements.

[(b)] (c) COMMISSIONER.—

(1) * * *

* * * * *

[(c)] (d) TECHNICAL AND SCIENTIFIC REVIEW GROUPS.—The Secretary through the Commissioner of Food and Drugs may, without regard to the provisions of title 5, United States Code, governing appointments in the competitive service and without regard to the provisions of chapter 51 and subchapter III of chapter 53 of such title relating to classification and General Schedule pay rates, establish such technical and scientific review groups as are needed to carry out the functions of the Administration, including functions under the Federal Food, Drug, and Cosmetic Act, and appoint and pay the members of such groups, except that officers and employees of the United States shall not receive additional compensation for service as members of such groups.

(e) ANNUAL REPORT.—*The Secretary shall, simultaneously with the submission each year of the budget for the Food and Drug Administration, submit to the Committee on Commerce of the House of Representatives and the Committee on Labor and Human Resources of the Senate an annual report which shall—*

(1) *review the performance of the Food and Drug Administration in meeting its mission and the development of Food and Drug Administration policies to implement such mission;*

(2) *review the performance of the Food and Drug Administration in meeting its own performance standards, including its own outcome measurements, and statutory deadlines for the approval of products or for other purposes contained in this Act;*

(3) *describe the staffing and resources of the Food and Drug Administration; and*

(4)(A) *list each bilateral and multinational meeting held by the Food and Drug Administration to address methods and approaches to reduce the burden of regulation, to harmonize regulation, and to seek appropriate reciprocal arrangements, (B) describe the goals, activities, and accomplishments of the Food and Drug Administration in such meetings, and (C) list issues that the Food and Drug Administration is considering or has presented for each such meeting.*

* * * * *

SEC. 906. INFORMATION SYSTEM.

The Secretary shall establish and maintain an information system to track the status and progress of each application or submission (including a petition, notification, or other similar form of request) submitted to the Food and Drug Administration requesting agency action.

SEC. 907. EDUCATION.

The Secretary shall conduct training and education programs for the employees of the Food and Drug Administration relating to the regulatory responsibilities and policies established by this Act, in-

cluding programs for scientific training and training in administrative process and procedure and integrity issues.

SEC. 908. DEMONSTRATION PROGRAM REGARDING CENTERS FOR EDUCATION AND RESEARCH ON DRUGS.

(a) *IN GENERAL.*—The Secretary, acting through the Commissioner of Food and Drugs, shall establish a demonstration program for the purpose of making one or more grants for the establishment and operation of one or more centers to carry out the activities specified in subsection (b).

(b) *REQUIRED ACTIVITIES.*—The activities referred to in subsection (a) are the following:

(1) *The conduct of state-of-the-art clinical and laboratory research for the following purposes:*

(A) *To increase awareness of new uses of drugs and the unforeseen risks of new uses of drugs.*

(B) *To provide objective clinical information to the following entities:*

(i) *Health care practitioners or other providers of health care goods or services.*

(ii) *Pharmacy benefit managers.*

(iii) *Health maintenance organizations or other managed health care organizations.*

(iv) *Health care insurers or governmental agencies.*

(C) *To improve the quality of health care while reducing the cost of health care through the prevention of adverse effects of drugs and the consequences of such effects, such as unnecessary hospitalizations.*

(2) *The conduct of research on the comparative effectiveness and safety of drugs.*

(3) *Such other activities as the Secretary determines to be appropriate, except that the grant may not be expended to assist the Secretary in the review of new drugs.*

(c) *APPLICATION FOR GRANT.*—A grant under subsection (a) may be made only if an application for the grant is submitted to the Secretary and the application is in such form, is made in such manner, and contains such agreements, assurances, and information as the Secretary determines to be necessary to carry out this section.

(d) *PEER REVIEW.*—A grant under subsection (a) may be made only if the application for the grant has undergone appropriate technical and scientific peer review.

(e) *AUTHORIZATION OF APPROPRIATIONS.*—For the purpose of carrying out this section, there are authorized to be appropriated \$2,000,000 for fiscal year 1998, and \$3,000,000 for fiscal year 1999.

PUBLIC HEALTH SERVICE ACT

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TITLE III—GENERAL POWERS AND DUTIES OF PUBLIC HEALTH SERVICE

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PART F—LICENSING—BIOLOGICAL PRODUCTS AND CLINICAL
LABORATORIES

Subpart 1—Biological Products

REGULATION OF BIOLOGICAL PRODUCTS

SEC. 351. [(a) No person shall sell, barter, or exchange, or offer for sale, barter, or exchange in the District of Columbia, or send, carry, or bring for sale, barter, or exchange from any State or possession into any other State or possession or into any foreign country, or from any foreign country into any State or possession, any virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or its derivatives (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of diseases or injuries of man, unless (1) such virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product has been propagated or manufactured and prepared at an establishment holding an unsuspended and unrevoked license, issued by the Secretary as hereinafter authorized, to propagate or manufacture, and prepare such virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product for sale in the District of Columbia, or for sending, bringing, or carrying from place to place aforesaid; and (2) each package of such virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product is plainly marked with the proper name of the article contained therein, the name, address, and license number of the manufacturer, and the date beyond which the contents cannot be expected beyond reasonable doubt to yield their specific results. The suspension or revocation of any license shall not prevent the sale, barter, or exchange of any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid which has been sold and delivered by the licensee prior to such suspension or revocation, unless the owner or custodian of such virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid has been notified by the Secretary not to sell, barter, or exchange the same.

[(b) No person shall falsely label or mark any package or container or any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid; nor alter any label or mark on any package or container of any virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid so as to falsify such label or mark.]

(a)(1) No person shall introduce or deliver for introduction into interstate commerce any biological product unless—

(A) a biologics license is in effect for the biological product;
and

(B) each package of the biological product is plainly marked with—

(i) the proper name of the biological product contained in the package;

- (ii) the name, address, and applicable license number of the manufacturer of the biological product; and
- (iii) the expiration date of the biological product.
- (2)(A) The Secretary shall establish, by regulation, requirements for the approval, suspension, and revocation of biologics licenses.
- (B) The Secretary shall approve a biologics license application—
- (i) on the basis of a demonstration that—
- (I) the biological product that is the subject of the application is safe, pure, and potent; and
- (II) the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and
- (ii) if the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).
- (3) The Secretary shall prescribe requirements under which a biological product undergoing investigation shall be exempt from the requirements of paragraph (1).

(b) No person shall falsely label or mark any package or container of any biological product or alter any label or mark on the package or container of the biological product so as to falsify the label or mark.

(c) Any officer, agent, or employee of the Department of Health and Human Services, authorized by the Secretary for the purpose, may during all reasonable hours enter and inspect any establishment for the propagation or manufacture and preparation of any [virus, serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or other product aforesaid for sale, barter, or exchange in the District of Columbia, or to be sent, carried, or brought from any State or possession into any other State or possession or into any foreign country, or from any foreign country into any State or possession.] *biological product.*

[(d)(1) Licenses for the maintenance of establishments for the propagation or manufacture and preparation of products described in subsection (a) of this section may be issued only upon a showing that the establishment and the products for which a license is desired meet standards, designed to insure the continued safety, purity, and potency of such products, prescribed in regulations, and licenses for new products may be issued only upon a showing that they meet such standards. All such licenses shall be issued, suspended, and revoked as prescribed by regulations and all licenses issued for the maintenance of establishment for the propagation or manufacture and preparation, in any foreign country, of any such products for sale, barter, or exchange in any State or possession shall be issued upon condition that the licensees will permit the inspection of their establishments in accordance with subsection (c) of this section.]

[(2)(A) Upon] (d)(1) Upon a determination that a batch, lot, or other quantity of a product licensed under this section presents an imminent or substantial hazard to the public health, the Secretary shall issue an order immediately ordering the recall of such batch, lot, or other quantity of such product. An order under this para-

graph shall be issued in accordance with section 554 of title 5, United States Code.

[(B)] (2) Any violation of [subparagraph (A)] *paragraph (1)* shall subject the violator to a civil penalty of up to \$100,000 per day of violation. The amount of a civil penalty under [this subparagraph] *this paragraph* shall, effective December 1 of each year beginning 1 year after the effective date of [this subparagraph] *this paragraph*, be increased by the percent change in the Consumer Price Index for the base quarter of such year over the Consumer Price Index for the base quarter of the preceding year, adjusted to the nearest $\frac{1}{10}$ of 1 percent. For purposes of [this subparagraph] *this paragraph*, the term “base quarter”, as used with respect to a year, means the calendar quarter ending on September 30 of such year and the price index for a base quarter is the arithmetical mean of such index for the 3 months comprising such quarter.

* * * * *

(i) *In this section, the term “biological product” means a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, or analogous product, or arsphenamine or derivative of arsphenamine (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of a disease or condition of human beings.*

* * * * *

Subpart 2—Clinical Laboratories

CERTIFICATION OF LABORATORIES

SEC. 353. (a) * * *

* * * * *

(d) REQUIREMENTS FOR CERTIFICATES.—

(1) * * *

* * * * *

[(3) EXAMINATIONS AND PROCEDURES.—The examinations and procedures identified in paragraph (2) are simple laboratory examinations and procedures which, as determined by the Secretary, have an insignificant risk of an erroneous result, including those which—

[(A) have been approved by the Food and Drug Administration for home use,

[(B) employ methodologies that are so simple and accurate as to render the likelihood of erroneous results negligible, or

[(C) the Secretary has determined pose no reasonable risk of harm to the patient if performed incorrectly.]

(3) *EXAMINATIONS AND PROCEDURES.—The examinations and procedures identified in paragraph (2) are laboratory examinations and procedures which have been approved by the Food and Drug Administration for home use or which, as determined by the Secretary, are simple laboratory examinations and procedures which have an insignificant risk of an erroneous result, including those which—*

(A) employ methodologies that are so simple and accurate as to render the likelihood of erroneous results by the user negligible, or

(B) the Secretary has determined pose no reasonable risk of harm to the patient if performed incorrectly.

* * * * *

TITLE IV—NATIONAL RESEARCH INSTITUTES

PART A—NATIONAL INSTITUTES OF HEALTH

* * * * *

APPOINTMENT AND AUTHORITY OF DIRECTOR OF NIH

SEC. 402. (a) * * *

* * * * *

(j)(1) The Secretary, acting through the Director of the National Institutes of Health, shall establish, maintain, and operate a program with respect to information on research relating to the treatment, detection, and prevention of serious or life-threatening diseases and conditions. The program shall, with respect to the agencies of the Department of Health and Human Services, be integrated and coordinated, and, to the extent practicable, coordinated with other data banks containing similar information.

(2)(A) After consultation with the Commissioner of Food and Drugs, the directors of the appropriate agencies of the National Institutes of Health (including the National Library of Medicine), and the Director of the Centers for Disease Control and Prevention, the Secretary shall, in carrying out paragraph (1), establish a data bank of information on clinical trials for drugs for serious or life-threatening diseases and conditions.

(B) In carrying out subparagraph (A), the Secretary shall collect, catalog, store, and disseminate the information described in such subparagraph. The Secretary shall disseminate such information through information systems, which shall include toll-free telephone communications, available to individuals with serious or life-threatening diseases and conditions, to other members of the public, to health care providers, and to researchers.

(3) The data bank shall include the following:

(A) A registry of clinical trials (whether federally or privately funded) of experimental treatments for serious or life-threatening diseases and conditions under regulations promulgated pursuant to sections 505 of the Federal Food, Drug, and Cosmetic Act that provides a description of the purpose of each experimental drug, either with the consent of the protocol sponsor, or when a trial to test effectiveness begins. Information provided shall consist of eligibility criteria, a description of the location of trial sites, and a point of contact for those wanting to enroll in the trial, and shall be in a form that can be readily understood by members of the public. Such information must be forwarded to the data bank by the sponsor of the trial not later than 21 days after trials to test clinical effectiveness have begun.

(B) Information pertaining to experimental treatments for serious or life-threatening diseases and conditions that may be available—

(i) under a treatment investigational new drug application that has been submitted to the Food and Drug Administration under section 551(c) of the Federal Food, Drug, and Cosmetic Act; or

(ii) as a Group C cancer drug (as defined by the National Cancer Institute).

The data bank may also include information pertaining to the results of clinical trials of such treatments, with the consent of the sponsor, including information concerning potential toxicities or adverse effects associated with the use or administration of such experimental treatments.

(4) The data bank shall not include information relating to an investigation if the sponsor has provided a detailed certification to the Secretary that disclosure of such information would substantially interfere with the timely enrollment of subjects in the investigation, unless the Secretary, after the receipt of the certification, provides the sponsor with a detailed written determination that such disclosure would not substantially interfere with such enrollment.

(5) For the purpose of carrying out this subsection, there are authorized to be appropriated such sums as may be necessary. Fees collected under section 736 of the Federal Food, Drug, and Cosmetic Act shall not be used in carrying out this subsection.

[(j)] (k)(1) The Director of NIH may establish a program to provide day care services for the employees of the National Institutes of Health similar to those services provided by other Federal agencies (including the availability of day care service on a 24-hour-a-day basis).

* * * * *

[(k)] (l) The Director of NIH shall carry out the program established in part F of title XII (relating to interagency research on trauma).

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SECTION 8126 OF TITLE 38, UNITED STATES CODE

§ 8126. Limitation on prices of drugs procured by Department and certain other Federal agencies

(a) * * *

* * * * *

(h) In this section:

(1) * * *

(D) Section 8126(h)(2) of title 38, United States Code, is amended by inserting “or” at the end of subparagraph (B), by striking “; or” at the end of subparagraph (C) and inserting a period, and by striking subparagraph (D).

(2) The term “covered drug” means—

(A) * * *

(B) a drug described in section 1927(k)(7)(A)(iv) of the Social Security Act, or that would be described in such sec-

tion but for the application of the first sentence of section 1927(k)(3) of such Act; or

(C) any biological product identified under section 600.3 of title 21, Code of Federal Regulations; or

[(D) insulin certified under section 506 of the Federal Food, Drug, and Cosmetic Act.]

* * * * *

SECTION 5 OF THE ORPHAN DRUG ACT

GRANTS AND CONTRACTS FOR DEVELOPMENT OF DRUGS FOR RARE DISEASES AND CONDITIONS

SEC. 5. (a) * * *

(b) For purposes of subsection (a):

(1) The term “qualified testing” means—

(A) human clinical testing—

(i) * * *

(ii) which occurs after the date such drug is designated under section 526 of such Act and before the date on which an application with respect to such drug is submitted under section 505(b) [or 507] of such Act or under section 351 of the Public Health Service Act; and

(B) preclinical testing involving a drug for a rare disease or condition which occurs after the date such drug is designated under section 526 of such Act and before the date on which an application with respect to such drug is submitted under section 505(b) [or 507] of such Act or under section 351 of the Public Health Service Act.

* * * * *

SECTION 45C OF THE INTERNAL REVENUE CODE OF 1986

§ 45C. Clinical testing expenses for certain drugs for rare diseases or conditions

(a) GENERAL RULE.—For purposes of section 38, the credit determined under this section for the taxable year is an amount equal to 50 percent of the qualified clinical testing expenses for the taxable year.

(b) QUALIFIED CLINICAL TESTING EXPENSES.—For purposes of this section—

(1) * * *

(2) CLINICAL TESTING.—

(A) IN GENERAL.—The term “clinical testing” means any human clinical testing—

(i) * * *

(ii) which occurs—

(I) after the date such drug is designated under section 526 of such Act, and

(II) before the date on which an application with respect to such drug is approved under section 505(b) [or 507] of such Act or, if the drug is a biological product, before the date on which a license for such drug is issued under section 351 of the Public Health Service Act, and

* * * * *

SECTION 156 OF TITLE 35, UNITED STATES CODE

§ 156. Extension of patent term

(a) * * *

* * * * *

(f) For purposes of this section:

(1) * * *

* * * * *

(4)(A) * * *

(B) Any reference to section 503, 505, [507,] 512, or 515 is a reference to section 503, 505, [507,] 512, or 515 of the Federal Food, Drug, and Cosmetic Act.

* * * * *

ADDITIONAL VIEWS OF HON. EDWARD J. MARKEY

The United States has the safest foods and drugs in the world because American consumers and patients demand that the Food and Drug Administration be given full authority to reign in the renegades and require food and drug manufacturers to maintain the highest possible safety and effectiveness standards before allowing products to come to market. We must be vigilant in our defense of those high standards, and of a strong FDA.

The drug bill will reauthorize the Prescription Drug User Fee Act, a program universally regarded as a success. Since the inception of PDUFA, the FDA has made the review and approval process for new drug applications an efficient and expeditious exercise. The bill will permit the Secretary to require companies to perform studies on the benefits of new drugs in pediatric populations. And the bill will expedite the study, approval and access to “fast track” drugs, investigational therapies and clinical trials for serious or life-threatening diseases. In the areas of food and devices, some of the reforms will result in increased streamlining and less unwanted and unneeded bureaucracy.

But, we are also being asked to take the bad with the good. The drug bill contains a dangerous and precedent-setting provision regarding dissemination of information. The “Off-label” provision could be better described as the “under the table” provision, allowing companies to market a product for unsupported uses that could seriously send thousands of consumers “off the cliff.” In putting profits over patient care, this bill opens the door for aggressive promotion of unproven uses of drugs, while giving companies three to five years to produce scientific evidence that these off-label uses are safe and effective. Much has been said recently about the Fen-Phen tragedy—clearly this drug combination was overprescribed and undermonitored, putting thousands of Americans, mainly women, at risk of heart-valve irregularities and pulmonary hypertension—and these prescriptions were written without an aggressive off-label marketing campaign.

I realize that the bill as written applies to journal and text articles, that the FDA may review this material, and that the provision sunsets in 7 years—but there is no excuse for approving an ill-considered and dangerous off-label experiment on the grounds that it is only temporary. The sun could set on the health of thousands of consumers long before it sets on this provision.

I am hopeful that stronger consumer and patient protections in the “off-label” section of this bill are included before the final version of H.R. 1411 comes to the House floor.

EDWARD J. MARKEY.

ADDITIONAL VIEWS OF HON. BOBBY L. RUSH

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL TRIALS

During the markup of H.R. 1411, The Drug and Biological Products Modernization Act of 1997, I offered an amendment to the bill to ensure that women and members of minority and ethnic groups would be adequately represented in clinical trials of new drugs that are submitted to the Food and Drug Administration [FDA] for approval. This amendment specifically directs the Secretary of Health and Human Services to consult with the National Institute of Health (NIH) to review and develop guidelines on the inclusion of women and minorities in clinical trials.

This important amendment was unanimously adopted by the Committee by voice vote.

This amendment is long overdue. Medical research in the last 15 years points to the rapid development of a new field—pharmacogenetics. We are quickly learning that women and members of racial and ethnic groups may respond differently to certain drugs than white males. Dr. Richard Levy has highlighted these key findings in his 1993 study “Ethnic and Racial Differences in Response to Medicine.”

In passing H.R. 1411, the Committee engaged in a vigorous debate about the respective roles of government and the industry. We have heard a lot about how we must not sacrifice the public health and consumer safety by allowing faster approval of new drugs. In the same spirit, we must not lose sight of equity issues.

We know too much not to pass this amendment. Historically, women and members of minority groups have faced barriers to participation in many areas of American life—higher education, business, and government. Congress has recognized these inequities and enacted legislation and federal programs that target participation of these groups in our economic and political life.

My amendment calls for development of guidance by FDA. It does not ask the FDA to require industry to demonstrate that they have adequately included women and minorities in clinical drug trials. However, in 1993, Congress, passed the National Institutes of Health [NIH] Revitalization Act. The Act requires the NIH include women and members of minority groups as subjects in each clinical research project supported by NIH. It has been argued that the FDA does not conduct studies and, therefore, should not have to adopt the same requirements. Nevertheless, the agency has a responsibility to make sure that new drugs they do approve have been adequately tested on the populations they are intend to help. If, for example, we know that African-American males suffer higher rates of hypertension than white males, then companies seeking approval for these drugs should be required to demonstrate that they have been adequately tested on African-American men.

The FDA has indicated a desire to move in this direction. The Agency has issued guidelines on the inclusion of women in clinical trials. However, there is no similar guidance on inclusion of minorities. If FDA recognizes the differential impact of drugs on certain groups, then the agency must assume responsibility for assuring that they have access to this information from the industry. This inevitably means that clinical trials must be designed and carried out with participation of persons from different age groups, genders, and racial subgroups.

There appears to be evidence that an increasing number of drug manufacturers do test new drugs on more ethnic and racial minority groups. A study reported by the Pharmaceutical Manufacturers Association in 1991 showed that a majority of drug companies include racial minorities (67 percent) and women (76 percent) in their clinical trials. This represents progress. However, FDA must take the next step to make sure that women and/or members of minority groups are sufficiently represented, based on what we know about the incidence of particular diseases among these groups.

My amendment was offered with the intent of urging the Administration to seriously move in this direction. As we move into the 21st century and become a more culturally diverse society, the FDA and the industry should begin to work toward developing a process to ensure that clinical drug trials reflect this diversity. This public policy is vital to guaranteeing that all Americans, regardless of their background, have access to the most lifesaving therapies.

BOBBY L. RUSH.

