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Food and Drug Administration Modernization Act of 1997 — The Provisions

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Abstract

This report presents a detailed summary of the provisions of the Food and Drug Administration Modernization Act of 1997, P.L. 105-115, signed into law on November 21, 1997. This Act is the first comprehensive revision of the Nation's food, drug, and medical device laws in 30 years and amended the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §§ 301 et. seq.) and the Public Health Service Act (42 U.S.C. §§ 201 et. seq.). For each section of the Act, a brief summary of previous policy or law is presented followed by a detailed description of the new law. An appendix is included that provides a list and description of all of the deadlines for actions set in the Act. The discussion is intended to provide the reader with a narrative of the provisions in the Act. It is not intended to serve as a basis for legal actions. For that purpose, the language of the Act itself must be used. This report will not be updated.

Food and Drug Administration Modernization Act of 1997 — The Provisions

Summary

The Food and Drug Administration Modernization Act of 1997, P.L. 105-115, is the first comprehensive revision of the Nation's food, drug, and medical device laws in 30 years. This statute establishes new standards for product review and regulatory approval under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act. Several of the changes made by the new law codify regulatory initiatives undertaken previously by the Food and Drug Administration.

Title I deals with various drug regulatory concerns. Key provisions include a five-year reauthorization of the Prescription Drug User Fee Act allowing the agency to charge manufacturers fees to facilitate the review of new drugs and biological products. Manufacturers who conduct additional studies to enhance pediatric labeling for products will qualify for six months additional marketing exclusivity, and drugs to treat life-threatening conditions will be given fast track consideration. In addition, drug approval norms will be eased by reducing the number of clinical investigations needed and granting manufacturers the latitude to submit abbreviated study reports. Agency guidance documents will be issued to streamline the drug review process and provide a means for resolving controversial scientific issues.

Requirements for medical device approval and postmarket surveillance are addressed in Title II. The measure seeks to improve the premarket review process by requiring clarity, timeliness, and better communication between the FDA and regulated industry. Regulatory issues addressed include investigational device exemptions, premarket notification, special review, humanitarian uses of devices, device standards, data requirements, classification, and development protocols. Moreover, a third-party review program is established to expedite the review of certain Class I and II devices. Regulatory requirements are reduced for such postmarket activities as tracking, surveillance, and reporting.

Title III addresses several food regulation issues. It allows expedited procedures for the use of new nutrient content and health claims and specifies timely action on claims petitions. It also allows nutrient content and health claims to be made based on authoritative statements issued as current policy of relevant scientific agencies. The Act amends the food irradiation provisions to prohibit labeling requirements that are more prominent than the ingredient listing, and it requires a timely decision on review of the pending red meat irradiation petition. Further, the law establishes a notification system for food contact substances.

Title IV permits the dissemination of information about "off-label" uses of drugs or devices not yet approved by the FDA. Other provisions allow patients expanded access to investigational therapies, encourage international harmonization agreements, and establish national uniformity in the regulation of nonprescription drugs and cosmetics. For the first time, the FDA must conduct its regulatory functions under a mission statement that will obligate it to maintain a public health protection role while seeking to expedite the marketing of regulated products.

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Food and Drug Administration Modernization Act of 1997 — The Provisions

Introduction

On November 17, 1997, the President signed into law the Food and Drug Administration Modernization Act of 1997 (FDAMA97), P.L. 105-115. This law is the first comprehensive revision of the Nation's food, drug, and medical device laws in 30 years and amended the Federal Food, Drug, and Cosmetic Act (21 U.S.C. §§ 301 et. seq.) and the Public Health Service Act (42 U.S.C. §§ 201 et. seq.).

The purpose of this report is to describe that law in detail. The report is arranged by title and section of the statute. For each section, a brief description of previous law or policy precedes a more detailed description of the new law. An appendix provides a list describing the intent and target date of all of the deadlines set by the law. The discussion is intended to provide the reader with a narrative of the provisions enacted by the law. It is not intended to serve as a basis for legal actions. For that purpose, the language of the law itself must be used.

The report was prepared by the following CRS analysts. Unless otherwise noted, all are from the Science, Technology, and Medicine Division. Title I, Subtitle A — Donna Vogt; Title I, Subtitle B — B. Randall. Title II — (name redacted); Title III — Donna Porter; Title IV, Sections 401-413 — B. Randall; Title IV, Sections 414-422 and Title V — Dianne Duffy, American Law Division; Appendix — Donna Vogt; and Summary — B. Randall. The report was coordinated by Richard Rowberg.

Title I — Improving Regulation of Drugs

Subtitle A — Fees Relating to Drugs

Sec. 101. Findings

Previous Law or Policy. There are no findings in the 1992 Prescription Drug User Fee Act (1992 PDUFA).

FDAMA97. Congress finds that (1) prompt approval of drugs and therapies is critical to improve public health; (2) public health is served by making funds available to review human drug applications; (3) the PDUFA program has been successful, should be reauthorized for five years, and the agency should improve its regulatory processes; and (4) the fees authorized by this amendment should be used to expedite both human drug development and application review processes. Congress also require the FDA to publish in the *Congressional Record* goals to approve or act upon certain numbers of human drug applications within constrained times. The goals will be set forth in letters from the Secretary of Health and Human Services to the chairmen of the House Committee on Commerce and the Senate Committee on Labor and Human Resources.

Sec. 102. Definitions

Previous Law or Policy. Section 735 of the 1992 PDUFA defines the applications, products, and establishments that will be used to assess fees and the review process, cost, and adjustment factors that were to be used in the program.

FDAMA97. The Act amends the criteria used to judge whether a new product is exempt from fees, and clarifies and updates other key factors. Biological product applications are exempt from user fee assessments if they will be used only for further manufacturing. Drugs that are not distributed commercially and are the subject of an application from a state or federal government entity are also exempt. Fees can be assessed on large volume biological products intended for single dose injection for intravenous use or infusion. Fees can now be used to pay the salaries of “contractors of the FDA.” The new “adjustment factor” for calculating user fee rates will be based on the greater percentage change of either the Consumer Price Index for all urban consumers for April of the preceding fiscal year (FY) divided by the April 1997 index, or the total percentage pay change for that FY for Federal employees, as adjusted for any locality based payment for employees of the District of Columbia. The term “business affiliate” means a business that has a direct or indirect relationship with another in which one controls the other or a third party controls both.

Sec. 103. Authority to Assess and Use Drug Fees

Previous Law or Policy. The five-year authorization of the 1992 PDUFA program expired on Sept. 30, 1997. It required payment of one-half of the fee when the human drug application or supplemental application was submitted for review to the FDA and payment of the other half when the agency acted on the application. The Secretary was required to refund 50% of the fee if the application was not accepted for filing. In addition to an application fee, drug sponsors also paid annual prescription drug establishment fees and drug product fees once an application was approved. The statute contained a schedule of the total amount that could be collected each year but exempted from payment small businesses of fewer than 500 employees. A small business that qualified for an exemption, however, was assessed one-half the standard application fee on the first application it submitted, but could defer payment for one year. The 1992 PDUFA statute also allowed the FDA to increase total revenue from fees to reflect the greater percentage increase of either the Consumer Price Index or the civil service base pay for Federal employees in the District of Columbia to keep the value of total fee collections on par with inflation. The total amount of collected fees was adjusted annually to reflect the total costs of reviewing drugs, and the adjustment was to be cumulative and compounded annually starting in 1997. The fees could be waived if certain conditions were met. An application would be considered incomplete unless the fees were paid. The Act prohibited the FDA from collecting fees unless its appropriations were equal to or greater than the salaries and expenses for FY 1992 multiplied by an adjustment factor. The fees were to be available without fiscal year limitation and were to be used only to defray the expenses allocated for the review of human drug applications.

FDAMA97. The Act authorizes the collection and use of drug fees for five years beginning in FY1998. It requires 100% payment of the fee when the application or supplement is first submitted for approval to the agency. The Act requires the Secretary to refund 75% of the fee if the FDA does not accept an application for filing. It provides that fees would be waived if the application is for approval of an orphan drug to be used for a rare disease or condition, or for a new indication for use in pediatric populations. If an application or supplement is withdrawn, the Secretary can refund the fee if no substantial work was performed on the application or supplement before it was withdrawn.

Each applicant listed must pay an annual fee for each establishment that manufactures a drug and is listed in the drug application. This establishment fee, due on January 31 of each year, is assessed for each fiscal year that the establishment manufactures the drug. Establishments are required to pay only one fee each year. If more than one applicant lists an establishment, the fee can be divided equally among the applicants whose products the establishment manufactures during the fiscal year. The amount of establishment fees collected cannot exceed the total costs of applications review for any fiscal year. If, during the fiscal year, an applicant begins manufacturing a drug at a listed establishment that did not manufacture it during the previous year, but the full establishment fee was paid before it began manufacturing the new drug, the applicant will not be assessed a share of the fee for that fiscal year.

Prescription drug product fees are payable not only on listed products but also when the product application is first submitted for listing or relisting. Exceptions from fee payments are expanded to include generic and antibiotic products. Annual fiscal year drug product fees must be paid on or before January 31 of each year.

For each applicant, the fee amounts vary according to the fiscal year. The full application fee shall be \$250,704 in FY 1998, \$256,338 in FY 1999, \$256,338 in FY2000, \$267,606 in FY 2001, and \$258,451 in FY 2002. The supplement fee, which equals about one-half the application fee, shall be \$125,352 in FY 1998, \$128,169 in FY 1999 and FY 2000, \$133,803 in FY 2001, and \$129,226 in FY 2002. The annual revenue from establishment fees will be \$35.6 million in FY 1998, \$36.4 million in FY 1999 and FY 2000, \$38 million in FY 2001, and \$36.7 million in FY 2002. The same totals apply to total product fee revenues for each fiscal year. The Secretary must adjust the annual establishment and product fees so that the total amount collected will equal that collected from application and supplement fees.

Each fiscal year, the Secretary must adjust fees and total fee revenues to reflect the percentage change of either the average urban Consumer Price Index or the civil service base pay for Federal Employees in the District of Columbia, whichever is greater. The adjustment made for a given year will be added on a compounded basis to the sum of all adjustments made for each prior fiscal year, starting with FY 1997.

The Secretary shall waive the fee if a small business or its affiliate submits for the first time an application for approval of a human drug. After the waiver is granted, the business or affiliate must pay fees on all subsequent applications or supplements filed to an application.

The Secretary may use "standard costs" in deciding if future applicant fees will exceed the anticipated present and future costs incurred by the Secretary in conducting the review process for human drug applications.

The Act sets FY 1997 as a baseline date. For the authorization to collect PDUFA user fees to take place, total FDA appropriations must be equal to or greater than the total appropriation for FY 1997. Such a trigger level ensures that the fees collected under PDUFA are in addition to and do not replace appropriated funds.

The Act continues to allow transfer of collected fees to the FDA salaries and expenses account without fiscal year limitations even when the account itself has a fiscal year limitation. Fees shall be collected and available to defray costs for the review of new drug applications only if those costs are more than amount appropriated for human drug application review activities in FY1997. The total appropriated amounts authorized to be collected are \$106,800,000 for FY 1998; \$109,200,000 for FY 1999 and for FY 2000; \$114,000,000 for FY 2001; and \$110,100,000 for FY 2002. Any collected fees that exceed the authorized amount must be credited to the FDA appropriation account and subtracted from fee authorizations for subsequent fiscal years.

To qualify for consideration of a waiver, fee reduction, or refund, an applicant must submit a written request to the Secretary for such a fee waiver, reduction, or refund within 180 days after the date the fee is due. If the request for a fee waiver,

reduction or refund was made before FDAMA97 was enacted (November 21, 1997), this request must be submitted in writing to the Secretary within one year of the enactment date. Any request for waivers or refunds pertaining to a fee on a human drug application or supplement that had been accepted for filing before October 1, 1997, or request for waivers or refunds of FY 1997 fees on any product or establishment, will be evaluated according to the 1992 PDUFA payment criteria.

Sec. 104. Annual Reports

Previous Law or Policy. The 1992 PDUFA required that the FDA submit two annual reports to Congress for each fiscal year during which fees were collected: a performance report due within 60 days of the end of the fiscal year, and a financial report due within 120 days of the end of the fiscal year. It also stated that the reports were to be submitted to the House Committee on Energy and Commerce and the Senate Committee on Labor and Human Resources.

FDAMA97. The Act requires two reports to be prepared by the Secretary and submitted to the House Committee on Commerce and the Senate Committee on Labor and Human Resources. The first report, to be submitted within 60 days after the end of the fiscal year, will report on the FDA's progress in meeting the performance goals identified in the letters to the Committee chairmen and the agency's plan for meeting those goals. The second report will be submitted to the same committees within 120 days of the end of the previous FY and will report on how the FDA implemented the authority to collect the fees.

Sec. 105. Savings

Previous Law or Policy. No provision existed on savings.

FDAMA97. The Act authorizes the Secretary to retain the authority to assess and collect any fee on an application or supplement accepted for filing prior to October 1, 1997, or any establishment or product fee required by the FFDCFA for FY 1997 or earlier.

Sec. 106. Effective Date

Previous Law or Policy. The 1992 PDUFA was authorized from October 1, 1992 through September 30, 1997.

FDAMA97. October 1, 1997 is established as the effective date of this Subtitle.

Sec. 107. Termination of Effectiveness

Previous Law and Policy. Section 105 of the 1992 PDUFA provided that the amendments made by section 103 shall not be in effect after October 1, 1997, and section 104 provided that the required annual financial report shall not be in effect beyond 120 days after that date.

FDAMA97. The Act provides a “sunset” date so that the authority to assess and use drug fees shall cease on October 1, 2002, and the required annual reports will be due no later than 120 days thereafter.

Title I — Improving Regulation of Drugs

Subtitle B — Fees Relating to Drugs

Sec. 111. Pediatric Studies of Drugs

Previous Law or Policy. Drugs for pediatric use require specific labeling requirements providing information about the use of drugs in this age group. Drug manufacturers are required to examine existing data and determine whether the pediatric use section on the labels of their products can be modified on the basis of results of well-controlled studies in adults. In August of 1997, the Administration proposed new rules (62 FR 43900, Aug. 15, 1997) to further address the problem of certain drugs and biological products not having sufficient pediatric use information on their labels.

FDAMA97. The Act provides additional incentives for drug manufacturers to explore pediatric applications of their drugs. Prior to the approval of a new drug, if 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, then the sponsor or manufacturer can qualify for up to six months of extended market exclusivity. If the Secretary makes a written request for pediatric studies of an already marketed drug, and those studies are completed, then the manufacturer may be granted up to six months of extended market exclusivity as well. Sponsors of so-called orphan drugs who complete pediatric studies can have their marketing exclusivity extended by six months.

Within 180 days of enactment, the Secretary, after consultation with experts, must develop and publish a list of approved drugs for which additional pediatric information may produce health benefits. When the Secretary has formally requested pediatric studies, those studies must be conducted by a written protocol agreed to by the sponsor, the patent holder, and the Secretary. No more than 60 days after the pediatric studies have been submitted, the Secretary must determine whether the studies were done properly and must notify the sponsor or patent holder. If a written protocol agreement is not reached, the Secretary may still accept the study as long as it responds to the study request and follows good scientific principles.

This provision contains a sunset clause that states that a drug may not receive any additional marketing exclusivity unless its new drug application is submitted on or before January 1, 2002. In addition, the Secretary must complete a study and report to Congress no later than January 1, 2001, about the program's effectiveness and the adequacy of its incentives. The study must also address the economic impact of the program on taxpayers and consumers, including the impact of the lack of lower cost generic drugs on patients, including those with lower income levels. The report must include any suggestions for the program's modification.

Sec. 112. Expediting Study and Approval of Fast Track Drugs

Previous Law or Policy. Over the past decade, the FDA has initiated several regulatory policies to address the issue of earlier patient access to investigational

therapies. Currently, there are regulations pertaining to “treatment investigational drugs,” allowing patients with serious and life-threatening conditions to obtain experimental drugs for treatment purposes; “parallel track,” allowing patients simultaneous access to certain therapies undergoing clinical trials; and “accelerated approval,” speeding the approval of drugs or biologics that promise a significant benefit over existing therapies. The FDA has maintained that under these collective policies it has generally granted the highest approval priority to so-called breakthrough drugs that offer significant therapeutic advantages.

FDAMA97. The Act grants statutory authority to the Secretary, at the request of a new drug sponsor, to facilitate the development and expedite the review of a new drug if it is intended for treating a serious or life-threatening condition and demonstrates the potential to address an unmet medical need. 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 drug’s investigational application. Within 60 calendar days of the request, the Secretary must determine if the drug meets the fast track criteria, and if so, designate the drug as a fast track drug and take action to expedite its development and review.

The Secretary may approve a fast track drug based on a determination that the product has an effect on a clinical or surrogate endpoint that is likely to be beneficial. Such an approval may obligate the manufacturer to conduct post-approval studies for validation. In addition, sponsors may be asked to submit copies of all promotional materials about the fast track drug during the preapproval review period and, following approval for as long as the Secretary finds appropriate, at least 30 days prior to the dissemination of the materials.

The approval of a fast track drug may be withdrawn using expedited procedures, including an informal hearing, if the sponsor fails to diligently conduct 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.

The Act also provides for the review of incomplete applications for the approval of fast track drugs. If early evaluation of clinical data for a fast track drug shows evidence of effectiveness, the Secretary will evaluate an application for product approval for filing before the complete application is submitted. The Secretary may also start review of portions of that product approval applications. The review will begin only if the sponsor provides a schedule for submitting the information necessary for a complete application and any required user fee. In situations where the application is incomplete, the review period agreed to under the drug user fee authority 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 be beneficial. Within one year of enactment, the Secretary must issue guidance on the FDA’s policies and procedures required to implement this provision.

Sec. 113. Information Program on Clinical Trials for Serious or Life-Threatening Diseases

Previous Law or Policy. The National Institutes of Health (NIH), primarily through its National Cancer Institute (NCI), currently provides access to databases that can provide physicians and patients with information about cancer drugs being used in clinical trials around the country. Examples include the Physicians Data Query database and CancerNet, an internet site dedicated to up-to-date, peer-reviewed information on virtually every common type of cancer. Similar information is available via CancerFax. In addition, NCI provides toll-free telephone numbers to offer patients or their physicians additional referral information.

FDAMA97. The Act codifies programs to provide information about clinical trials for drugs to treat serious or life-threatening diseases. The Secretary, acting through the Director of NIH, is directed to establish, maintain, and operate a database on such clinical trials. The program is to be coordinated with other databases containing similar information and developed after consultation with the FDA Commissioner, the NIH (including the National Library of Medicine), and the Director of the Centers for Disease Control and Prevention. The Secretary must disseminate this database through information systems, including toll-free telephone numbers, made available to individuals with serious or life-threatening diseases, members of the public, health care providers, and researchers.

The database must include a registry of clinical trials that describes the purpose of the experimental drug, either with the consent of the trial's sponsor or when an effectiveness test 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 can be understood by the general public, and it must be forwarded to the database not later than 21 days after the trials for clinical effectiveness begin.

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

To carry out this section, there are authorized to be appropriated such sums as may be necessary. However, fees collected under section 736 (drug user fees) of the FFDCFA are not to be used to implement this subsection. Further, the Secretary, the NIH Director of NIH, and the FDA Commissioner must collaborate to determine the feasibility of including investigations of medical devices within the scope of the data bank. In addition, no later than two years after enactment, the Secretary must prepare and submit to Congress a report about inclusion of device investigations; the adverse impact (if any) on device innovation in the U.S. if information relating to

such device investigation is required to be publicly disclosed; and such other issues as the Secretary may deem appropriate.

Sec. 114. Health Care Economic Information

Previous Law or Policy. The FDA was in the process of developing a policy on economic claims of drugs when FDAMA97 was being considered by Congress.

FDAMA97. The Act codifies criteria for judging the validity of healthcare economic claims made about a drug. Health care economic information provided in the course of selecting drugs for managed care or other similar organizations, by a formulary committee or similar entity, is not be considered false or misleading if the information directly relates to a use of the drug as approved under provisions of the FFDCA and PHSA. The information must also be based on competent and reliable scientific evidence. Information that helps substantiate the health care economic information presented in accordance with this section must be made available to the Secretary upon request.

Health care economic information is defined to mean “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.” The General Accounting Office is to conduct a study of the implementation of this section’s provisions and submit a report to Congress not later than four and one-half years after enactment.

Sec. 115. Clinical Investigations

Previous Law or Policy. Under current law, evidence of a drug’s effectiveness is based on “substantial evidence” consisting of data derived from adequate and well-controlled investigations, including clinical investigations. Although the number of clinical investigations required is not specified by statute, the FDA has historically interpreted the language to mean that effectiveness should be confirmed and verified by at least two well-controlled clinical trials.

In 1993, the FDA issued a guideline (58 FR 39406, July 22, 1993) regarding its expectation that drug manufacturers should include both males and females clinical testing undertaken in drug development. The agency further stated that drug manufacturers should analyze their clinical data by gender, assess pharmacokinetic differences between genders, and conduct specific additional studies in women if appropriate. In 1997, the FDA issued a proposal rule (62 FR 49946) stating that the agency is considering placing a “clinical hold” on studies of drugs intended to treat a life-threatening disease if men or women with reproductive potential who have the disease—and are otherwise eligible—are excluded from participation in the clinical trial. The guideline and the proposal do not make specific references to minorities.

FDAMA97. The Act addresses issues about the number and makeup of clinical studies needed for drug approval. If the Secretary determines that data from one adequate and well-controlled clinical investigation and confirmatory evidence (obtained prior to or after such investigation) establish the drug’s effectiveness, the Secretary may consider such data and evidence sufficient for drug approval.

Additionally, the Secretary, in consultation with the NIH Director and representatives of the pharmaceutical industry, is directed to review and develop guidance on the inclusion of women and minorities in clinical trials.

Sec. 116. Manufacturing Changes For Drugs

Previous Law or Policy. Since 1995, the FDA has instituted new policies to reduce the number of manufacturing changes that would require prior approval. Subsequently, the agency issued several guidance documents specifying when drug manufacturers need not submit supplemental applications, and instead file only periodic reports. A year later, the FDA proposed extending those regulatory changes to biological products.

FDAMA97. The Act codifies guidelines for accounting for changes in manufacturing processes. It characterizes when certain types of manufacturing changes, made by drug manufacturers regulated under the FDCA or the PHS Act, require supplemental applications, when product distribution can occur after changes are made, and the circumstances where manufacturing changes require report filing.

In situations where a change is made from the manufacturing process approved in the product's original application, an approved drug or licensed biologic may be distributed if the holder of the approved application or license properly validates the effects of the change, or in the case of a major manufacturing change, files a supplemental application. Before distributing a new drug or biologic made after a manufacturing change (whether a major manufacturing change or otherwise), the holder must validate the effects of the change on the product's identity, strength, quality, purity, and potency as related to the drug's safety or effectiveness.

Major manufacturing changes are characterized as changes the Secretary determines have substantial potential for adversely affecting the identity, strength, quality, purity, or potency of the drug. Such changes include qualitative or quantitative changes in the drug's formulation or changes in the specifications from the original approved application. Other major changes include those, as determined by the Secretary, that require a clinical study to demonstrate that the drug manufactured after the change is equivalent to the drug manufactured before the change, and changes that might adversely affect the drug's safety or effectiveness.

The Secretary may regulate, in any one of several ways, drugs made with manufacturing changes that are not major. The Secretary may authorize distribution of such drugs with or without a supplemental application, and may establish categories of changes and designate when a supplement will or will not be needed.

For manufacturing changes that are not major, sponsors must submit a report to the Secretary containing appropriate information on the change. If drug sponsors or licensees make more than one such manufacturing change, the Secretary may authorize submission of a single report on all the changes made for the year.

Supplemental applications filed for a manufacturing change that is not major must include information that the Secretary determines to be appropriate and that has

been developed in validating the change's effects. Manufacturers making such changes may begin distribution of the drug 30 days after the Secretary receives the application unless they are issued a notification that prior approval is required. The Secretary may designate a category of changes that will permit a manufacturer to distribute the drug when the Secretary receives the supplemental application for the change. If the Secretary disapproves the application, the manufacturer can be ordered to cease such distribution.

This provision contains a "transition rule" that states that the amendment made by this section takes effect upon the effective date of regulations promulgated by the Secretary, or two years after the date of enactment of this Act, whichever occurs first.

Sec. 117. Streamlining Clinical Research on Drugs

Previous Law or Policy. Currently, there is no statutory requirement that the Secretary review an investigational new drug (IND) application within 30 days. However, by regulation, drug sponsors can begin their clinical trial 30 days after filing an IND unless the FDA objects. The FDA currently has the authority to issue clinical holds, halting a clinical research trial. In 1995, the agency introduced a new policy of reviewing and responding to IND submissions within 30 days.

FDAMA97. The Act revises and clarifies certain procedures and requirements of the clinical research process used in the drug development process. It provides flexibility to reduce the amount of information required by the FDA from the drug sponsor before clinical investigations can begin, and 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 of research subjects. A clinical investigation may begin 30 days after the FDA receives a submission containing information about the drug and the clinical investigation. The submission must contain the following: (1) 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 (2) adequate information on the chemistry and manufacturing of the drug, controls available for the drug, and primary data tabulations from animal or human studies.

The Secretary may issue a "clinical hold," confirmed in writing, prohibiting the sponsor from continuing with the research trial. The hold may be based on a determination by the agency 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. A clinical hold may also be issued for reasons established by regulation before enactment of this Act. 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 reasons for continuing the hold.

An exemption, under the FFDCA, from filing a new drug application that is granted to drugs intended solely for clinical investigation requires that the manufacturer, or the sponsor of the investigation, require of the experts using the investigational drug that they inform any human beings to whom the drug is

administered, or their representatives, that it is for experimental purposes. Moreover, manufacturers or sponsors must obtain informed consent, except where it is not feasible or it is contrary to the best interests of the subjects involved. Clinical investigators will not be required to submit directly to the Secretary reports on the investigational use of the drugs.

Sec. 118. Data Requirements for Drugs and Biologics

Previous Law or Policy. Current law requires drug manufacturers, when submitting new drug applications for marketing approval to provide the FDA with “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.”

FDAMA97. The Act establishes procedures for reducing data reporting requirements for clinical investigations. The Secretary, acting through the Commissioner of the FDA, within one year of enactment, is directed 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 under the FFDCA and biologics license applications under the PHSA. The guidance must describe the kinds of studies for which abbreviated reports are appropriate and the format of those reports.

Sec. 119. Content and Review of Applications

Previous Law or Policy. The FDA has promulgated several regulations encouraging manufacturers to meet with agency officials throughout the clinical investigation process.

FDAMA97. The Act codifies certain procedures about the review and content of applications. The FDA must issue guidance for employees who review applications. The Act also establishes that manufacturers can meet with officials to resolve controversial scientific issues and reach agreements on clinical trial protocols. The Secretary is directed to issue guidance to reviewers of applications about promptness in conducting the review, technical excellence, lack of bias and conflict of interest, and knowledge of regulatory and scientific standards. Such guidelines must apply equally to all who review applications.

The Secretary is required to meet with investigational drug sponsors or approval applicants, if they make a reasonable request for a meeting, to reach agreement on the design and size of clinical trials to establish effectiveness claims. Minutes of the meeting must be prepared. Any agreement between the Secretary and the sponsor about the parameters of the design and size of the clinical trial must be in writing and may not be changed after testing begins unless the sponsor agrees, or if the reviewing division director identifies a substantial scientific issue about safety and effectiveness. The Secretary must grant the sponsor an opportunity for a meeting at which the director will document that scientific issue. Written decisions by the reviewing division must be binding upon, and may not be changed by, the FDA field or compliance personnel unless the reviewing division demonstrates why the decision should be modified. Divisional review decisions may not be delayed due to unavailability of information from field personnel.

Those provisions must also apply when applicants submit abbreviated drug applications. The applicant or sponsor may also request a meeting with the Secretary to reach an agreement on the design and size of bioavailability and bioequivalence studies needed for approval of such applications.

Sec. 120. Scientific Advisory Panels

Previous Law or Policy. Current law (21 CFR 14.40) grants the FDA the regulatory authority to establish or renew advisory committees whenever appropriate.

FDAMA97. For purposes of providing expert scientific advice and recommendations about clinical investigation of a drug or approval for marketing of a drug under the FFDCAs or the PHSAs, the Secretary must establish panels of experts or use panels of experts previously established. Panels must have members who are qualified by training and experience to evaluate drugs; have diverse expertise in medicine and pharmacology; represent consumer interests; and are disease specialists (two or more diseases must be represented). Panel members must disclose all conflicts of interest. Conflict of interest waivers may be granted in special circumstances. As appropriate, panel members must be provided education and training. Within 90 days after an advisory panel makes a recommendation, the responsible FDA official must review the panel's conclusions and notify the affected persons of the agency's final decision. Final decisions must be documented and must include the rationale for the decision.

Sec. 121. Positron Emission Tomography

Previous Law or Policy. The FDA issued guidelines in 1995 to assist persons in determining whether certain manufacturing practices, procedures, and facilities used in the small-scale production of liquid injectable positron emission tomography (PET) radiopharmaceuticals are in compliance with the agency's current good manufacturing practice (GMP) regulations. In 1997, the FDA published a final rule to permit the agency to approve requests from manufacturers of PET drugs for exceptions or alternatives to its GMP regulations. The agency maintained that the action was necessary to relieve manufacturers from regulations that might result in unsafe handling of those products, that were inapplicable or inappropriate, and that did not enhance PET drug safety.

FDAMA97. The Act establishes a new statutory framework for the FDA to oversee the regulation of PET products, and nullifies the agency's earlier efforts to do so. The FFDCAs are amended to include the regulation of compounded positron emission tomography (PET) drugs. A compounded PET drug is defined as a drug that exhibits spontaneous disintegration of unstable nuclei by the emission of positrons and is used for providing dual photon emission tomographic diagnostic images. To be a PET drug, it must be compounded on the order of a practitioner who is licensed by a state to compound such a drug, and be compounded in accordance with State law, for a patient, research, teaching, or quality control. The definition also includes any non-radioactive reagent, reagent kit, ingredient, nuclide generator, accelerator, target material, electronic synthesizer, or associated software used to prepare any such drug.

To assure that PET drugs will meet the safety requirements of the FDCA, the drugs will be deemed by the FDA to be adulterated if procedures and facilities used for compounding do not conform to PET standards and the official monographs of the U. S. Pharmacopoeia. Additionally, PET drugs must have the identity and strength, and meet the quality and purity characteristics, that they are represented to possess. These criteria will no longer apply four years after the enactment date or two years after the Secretary establishes new procedures, whichever is later.

Two years after enactment, the Secretary must establish approval procedures and good manufacturing practices(GMPs) for PET drugs. In doing so, the Secretary must take due account of any relevant differences between commercial manufacturers of the drugs and not-for-profit institutions that compound the drugs for their patients. Before establishing these procedures the Secretary must consult with patient advocacy groups, professional associations, manufacturers, and physicians and scientists licensed to make or use PET drugs.

For a period of four years after enactment, or two years after establishing procedures, whichever is longer, the Secretary will no longer require the submission of new drug applications (NDAs) or abbreviated new drug applications (ANDAs) for PET drugs that are not considered adulterated under the criteria set forth in this Act. The Act does not prohibit voluntary submission of PET applications or their review by the agency. PET drugs are not to be exempted from the regulatory requirements for investigational drugs.

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.

Sec. 122. Requirements for Radiopharmaceuticals

Previous Law or Policy. Currently, radiopharmaceuticals are governed by the same safety and effectiveness requirement as other drugs.

FDAMA97. The Act establishes new criteria for regulations of radiopharmaceuticals. Within 180 days of enactment and after consultation with patient advocacy groups, associations, physicians licensed to use radiopharmaceuticals, and the regulated industry, the Secretary is required 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 the FDCA and the PHS Act, include (but not be limited to) consideration of the product's proposed medical use, its pharmacological and toxicological activity (including any carrier or ligand of the radiopharmaceutical), and its estimated absorbed radiation dose.

Within 18 months of enactment, the Secretary must issue final regulations governing the approval of radiopharmaceuticals. Further, a "special rule" is established stating that in the case of a radiopharmaceutical, its approved marketing indications may, in appropriate situations, refer to disease manifestations (such as biochemical, physiological, anatomic, or pathological processes) common to or present in one or more disease states. The term "radiopharmaceutical" is defined as

a drug to diagnosis or monitor a disease in humans, and which exhibits spontaneous disintegration of unstable nuclei emitting nuclear particles or photons. The definition also includes any nonradioactive reagent kit or nuclide generator that is intended to be used in its preparation.

Sec. 123. Modernization of Regulation

Previous Law or Policy. The FDA regulates biological drug products under the PHSa. Historically, both the biological product and its manufacturing establishment required licensing. The FDA recently announced that establishment license applications would be eliminated for well-characterized products.

FDAMA97. The Act codifies procedures, for the regulation of biological products, that are designed to streamline product review and approval. A biological product may not be introduced into interstate commerce unless it has a biologics license, and each 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. Approval of a license will be 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 is designed to assure those standards. 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.

Falsifying the labeling or marking of any package or container of a biological product is prohibited, and the requirement that biologics manufacturers obtain establishment licenses is eliminated. In addition, biological product are defined to mean a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, analogous product, or arsphenamine or its derivatives (or any other trivalent organic arsenic compound), applicable to the prevention, treatment, or cure of diseases or conditions of human beings.

A special rule directs 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 PHSa and a new drug application under section the FFDCa.

The FFDCa applies to biological products approved under this section, except that products with a license approved under the PHSa will not be required to have a new drug application approved as well.

Examinations and procedures that allow a laboratory to be granted a certificate of waiver under the PHSa if they are the only ones performed at that laboratory, are those that have been approved by the FDA for home use, or, as determined by the Secretary, are simple laboratory examinations and procedures that have an insignificant risk of erroneous result. These include methodologies that are so simple and accurate that there is little likelihood of error by the user, or the Secretary determines pose no unreasonable risk to the patient if performed incorrectly.

Sec. 124. Pilot and Small Scale Manufacture

Previous Law or Policy. In 1995, FDA issued a guidance document (60 FR 35750, July 11, 1995) that allowed manufacturers to use so-called "pilot" or small scale facilities for the development and manufacture of biological products. Previously, companies usually had to be manufacturing their products in scaled up commercial facilities before they would be granted establishment licenses.

FDAMA97. The Act codifies the use of pilot and small-scale manufacturing facilities in the production of drugs for approval. A 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. The same conditions hold for pilot or small scale animal drugs facilities.

Sec. 125. Insulin and Antibiotics

Previous Law or Policy. Under his Reinventing Government (ReGo) initiative, President Clinton proposed phasing out requirements for batch certification of insulin and antibiotic drugs. Also, drug marketing exclusivity, established under the 1983 Drug Price Competition and Patent Term Restoration Act, was not applicable to antibiotic products.

FDAMA97. The Act provides statutory authority for the phase out of batch certification, and establishes marketing exclusivity for new antibiotic drugs. Batch certification requirements for insulin and certain antibiotic products are eliminated, while current provisions for the export of insulin and antibiotics are preserved. A transition rule provides that an antibiotic drug that was approved under a regular or abbreviated application before the enactment of this Act will now be considered to be approved for safety and effectiveness under FDCA as amended by this Act.

For antibiotics, marketing applications for antibiotics received by the Secretary prior to enactment are not eligible for the marketing exclusivity provisions. If a marketing application for an antibiotic product whose active ingredient has never been approved is submitted to the Secretary after enactment, it is eligible for certain periods of market exclusivity. The Secretary is authorized to make publicly available a list of antibiotic drugs that were the subject of marketing applications received before the date of enactment.

Sec. 126. Elimination of Certain Labeling Requirements

Previous Law or Policy. Under the FDCA, a prescription drug could be deemed misbranded if its label did not carry the statement "Caution: Federal law prohibits dispensing without prescription." Under section 502 (d), drugs had to be deemed misbranded if they contained any quantity of certain habit forming substances (e.g., cocaine, heroin, marijuana) and did not carry the statement "Warning—May be habit-forming." In present-day prescription drug manufacturing

and dispensing, the need for those notices rarely occurs, and the warning requirements were believed to be anachronistic.

FDAMA97. The Act establishes labeling requirements for prescription drugs. A drug that can only be dispensed by a prescription is misbranded if at any time prior to dispensing, the drug's label does not bear, at a minimum, the symbol "Rx" only. A drug not so regulated is deemed to be misbranded if, at any time prior to dispensing, the label of the drug bears the symbol "Rx" only. Also, the Act eliminates the requirement that drugs containing portions of habit forming substances (e.g., cocaine, heroin, marijuana) be labeled with the statement "Warning—May be habit-forming."

Sec. 127. Application of Federal Law to Practice of Pharmacy Compounding

Previous Law or Policy. Pharmacy compounding became an issue when the FDA took regulatory action against several pharmacies and pharmacists who were, according to the agency, exceeding conventional compounding practices. The FDA felt that some of the examples it uncovered of nontraditional compounding were tantamount to the manufacture, promotion, and distribution of unapproved new drugs. In 1992, the agency issued policy guidelines for compounding, delineating which pharmacy practices were considered traditional and which were not.

FDAMA97. The Act clarifies the FDA's authority to regulate pharmacy compounding practices. Certain statutory restrictions on adulterated drugs, misbranded drugs, antibiotic drugs, and new drugs, will not apply to a drug product that is compounded for a specific patient based on an unsolicited prescription to meet a medical need. The compounding must be done by a licensed pharmacist in a state licensed pharmacy or federal facility, or a licensed physician on the prescription order of a physician or other licensed practitioner authorized by State law to prescribe drugs. Such compounding can be performed in limited quantities before receiving a valid prescription if there is a history of receiving valid orders solely within an established relationship between the pharmacist or licensed physician and the patient or other licensed practitioner who writes the prescription.

The restrictions do not apply to drug products if the pharmacist or physician compounds the drug product using bulk substances, as defined by the Secretary, that comply with applicable U.S. Pharmacopeia or National Formulary monographs, or are components of approved drugs. The restrictions also do not apply in situations where there is no monograph or where the drug is not a component of an approved drug, as long as the drug appears on a list developed by the Secretary. Further, the restrictions do not apply to drugs manufactured at registered establishments (including foreign establishments) and that are accompanied by valid certificates of analysis for each bulk drug.

Physicians and pharmacists may compound with ingredients that are not bulk substances and that comply with applicable standards from an applicable U.S. Pharmacopeia or National Formulary if the ingredients do not appear on a list of products that have been withdrawn or removed from the market due to a lack of

safety or efficacy, and if the physicians and pharmacists do not compound regularly or in inordinate amounts any drug that is a copy of a commercially available product.

Drugs may be compounded only if the compounding process does not adversely affect the product's safety and efficacy. They may be compounded in a state that has a memorandum of understanding (MOU) with the Secretary that addresses the interstate distribution of inordinate amounts of compounded products and provides for appropriate state investigations of complaints about distribution outside the state. Drugs can be compounded in a state that does not have an MOU only if the quantities of compounded products distributed out of state do not exceed 5% of the total prescription orders dispensed. The Secretary, in consultation with the National Association of Boards of Pharmacy, must develop a standard MOU that the states can use. A drug can be compounded only if the physician or pharmacist does not advertise or promote the compounding of any particular drug, class, or type of drug. Compounding services may be advertised or promoted.

The Secretary must issue regulations to implement this provision. Before issuing the regulations, the Secretary must convene and consult an advisory committee on compounding unless it is determined that new regulations are necessary, before such consultation, to protect the public health. Additionally, the Secretary is required, after consultation with the U.S. Pharmacopeia Convention, to develop regulations identifying drug substances that may be used in compounding for which a monograph does not exist or which are not components of approved drugs. This provision does not apply to compounded PET drugs or radiopharmaceuticals. The provisions on pharmacy compounding take effect one year after enactment.

Sec. 128. Reauthorization of Clinical Pharmacology Program

Previous Law or Policy. The Clinical Pharmacology Program established and authorized under the Health Education and Assistance Loans, P.L. 102-222, created an FDA-administered program for training in clinical pharmacology at medical schools without such a program. The legislation's sponsors maintain that the program can facilitate the agency's efforts in attracting the personnel needed to speed the drug approval process.

FDAMA97. The Act expands the definition of medical schools eligible for the FDA Clinical Pharmacology Program. The FDA is permitted to award grants for a pilot program for training in clinical pharmacology at appropriate medical schools, rather than medical schools without such a program. It reauthorizes the program for FY 1998 through FY 2002 at \$3 million annually.

Sec. 129. Regulations for Sunscreen Products

Previous Law or Policy. Sunscreens are currently regulated by the FDA as over-the-counter (OTC) drug products. In 1978, as part of its overall OTC review process, the agency published an advance notice of proposed rulemaking to establish a monograph for OTC sunscreen products. In 1993, the agency issued a tentative

final monograph that would establish conditions under which sunscreen products would be generally recognized as safe and effective and not misbranded.

FDAMA97. The Act sets a deadline of 18 months for the FDA for issuing regulations for over-the-counter sunscreen products.

Sec. 130. Reports of Postmarketing Approval Studies

Previous Law or Policy. Under section 505(k) of the FFDCA, the FDA has the authority to require drug manufacturers to maintain records and make reports of data relating to clinical experience and other information. The FFDCA specifies requirements for adverse drug reporting and other postmarketing reports. In addition, drugs approved under the FDA's accelerated approval process for treating serious or life-threatening illnesses, particularly where approval is based on a surrogate endpoint (i.e., not on actual clinical trials), are often required to undergo postmarket evaluation to further substantiate their clinical benefit.

FDAMA97. The Act codifies postmarketing evaluation report deadlines. Drug sponsors who enter into an agreement with the Secretary to conduct postmarketing studies must submit a report giving the study's progress within one year (and annually thereafter) of their product's approval. The Secretary must issue regulations delineating the form of the report. Agreements to conduct postmarketing studies that are entered into with the Secretary before the enactment of the Act are subject to the same requirements, and an initial report must be submitted within 6 months after the Secretary issues regulations governing this section.

To the extent necessary to identify the sponsor and to establish the status of postmarketing studies, any information about sponsors' annual reports must be considered public information. The Secretary must publish in the *Federal Register* a report that provides information on the status of the postmarketing studies. No later than Oct. 1, 2001, the Secretary must submit to Congress a report containing a summary of the annual reports, an evaluation of drug sponsors' performance in conducting postmarketing studies, the timeliness of the FDA's review, and any legislative recommendations.

Sec. 131. Notification of Discontinuance of a Life Saving Product

Previous Law or Policy. None.

FDAMA97. The Act establishes statutory procedures for notification of discontinued manufacturing of a life saving drug. When a manufacturer is the sole manufacturer of an approved drug that is life-supporting, life-sustaining, or intended for the prevention of debilitating disease or condition, and that is not a product originally derived from human tissue and replaced by a recombinant product, the manufacturer must notify the Secretary of intent to discontinue manufacturer of the drug at least six months before ceasing production.

The notification period may be reduced if the manufacturer certifies that there is good cause for the reduction. Good cause may be shown in situations where a public health problem may result, a liability problem exists, continued production

may cause economic hardship, bankruptcy has been sought, or where the drug's distribution can be maintained for six months. To the maximum extent practicable, the Secretary must distribute information on the drug's discontinuance to appropriate physicians and patient organizations.

Title II — Improving Regulation of Devices

Sec. 201. Investigational Device Exemption

Previous Law or Policy. Medical devices undergoing scientific investigation of their use, safety, and effectiveness may be exempted from certain requirements of the FDCA. The Secretary may grant investigational device exemptions (IDE) upon receipt of an application from the device manufacturer.

FDAMA97. The Act codifies procedures for granting exemptions to medical devices undergoing scientific investigation. For devices that have received an IDE, certain, specified developmental changes or modifications in the clinical protocols, are permitted without requiring additional approval of the original application or approval of a supplemental application. Regulations governing this provision are to be issued by the Secretary within one year of the date of enactment. The changes must not result in significant operational or design alterations. Protocol modifications must not affect the validity of data from the protocol invalid, or the safety and rights of human subjects in the investigation. The regulations must allow the changes if the investigation's sponsor determines that those conditions have been met on the basis of credible information.

Persons intending to submit an application for an IDE for a device in Class III or an implantable device may have their investigational plan reviewed by the Secretary before submitting the IDE application. The Secretary must meet with the applicant about this review within 30 days of receiving a request for such a meeting. Any agreements reached between the sponsor and the Secretary about the plan must be put in writing and made part of the administrative record. Changes are permitted if the Secretary and applicant agree to the change, or by the director of the device review office if it is decided that a substantial scientific issue has emerged that effects the safety and effectiveness of the device. The latter action can only be made after the sponsor has been given the opportunity to meet with the director.

The Act adds conditions under which the Secretary must accept data and information to determine whether a device that is subject to a pending IDE application is reasonably safe and effective. Such data and information can come from the investigation of an earlier version of the device provided any modifications made during or after that investigation do not result in significant operational or design changes, or the data and information come from an already approved and available device and is relevant to the device applying for the exemption.

Sec. 202. Special Review for Certain Devices

Previous Law or Policy. The FDA has a policy for the expedited review of premarket approval applications and notifications for devices that 1) offer a clinical advantage over the existing alternatives or 2) offer the promise of a technological breakthrough. The policy, however, has no statutory authority.

FDAMA97. The Act codifies procedures for expediting review of devices with significant potential. In consideration of applications submitted for premarket approval, the Secretary will give priority to review of devices that represent breakthrough technologies, have no approved alternative, offer significant advantages over existing alternatives, or would be in the best interest of patients.

Sec. 203. Expanding Humanitarian Use of Devices

Previous Law or Policy. Manufacturers may request exemptions from effectiveness requirements when a device is designated to treat conditions that affect fewer than 4,000 individuals in the United States. Upon receiving such an exemption, a so-called humanitarian exemption, a sponsor may use the device only in facilities that have an established local institutional review board (IRB).

FDAMA97. The Act clarifies procedures about the use of medical devices for humanitarian purposes. Requests for humanitarian use exemptions must be made by application to the Secretary and acted upon within 75 days. For a device granted an exemption, approval from a local IRB need not be obtained for emergency use, if such approval cannot be obtained in time to prevent serious harm or death to a patient. In such cases, the physician must notify the local IRB as soon as possible. The Secretary also may require that a holder of a humanitarian exemption demonstrate that the device continues to meet those requirements if it is found to be necessary to protect the public health or re-affirm eligibility for the exemption. The Secretary must provide an opportunity for informal hearing before suspending or withdrawing a humanitarian device exemption.

Sec. 204. Device Standards

Previous Law or Policy. If the Secretary determines that standards are needed to assure that a class II device is safe and effective, they may be established according to requirements set forth in the FFDCa.

FDAMA97. The Act gives statutory authority to a new procedure for setting and conforming with performance standards for medical devices. The Secretary must publish in the *Federal Register* all or part of a medical device standard that has been established by a nationally or internationally recognized organization for the development of standards and that would satisfy requirements for self-certification of a device. Manufacturers are given the option of submitting a declaration of conformity with such standards to meet any requirement of the Act to which the standard applies. However, a person has the option of submitting other types of data, in addition to recognized standards, to meet such requirements. The Secretary may withdraw recognition of a standard if it is found to be no longer appropriate. If conformity to a standard is declared, the Secretary must accept that declaration unless the submitted data do not demonstrate conformity with the standard or it is not applicable to the device. At any time, the Secretary may ask a person to submit data that substantiate a claim for conformity to a standard. Falsification of conformity to a recognized standard is prohibited, and a device is adulterated if it is falsely represented as in conformity with a recognized standard.

Sec. 205. Scope of Review; Collaborative Determinations of Device Data Requirements

Previous Law or Policy. In a decision by the Secretary about premarket notification for premarket approval applications (PMAs), the Secretary takes into consideration substantial equivalence or effectiveness. The former is defined in the FFDCAs as the technological and functional similarity that a candidate device has to one already approved and on the market. Meetings to discuss premarket notifications may be arranged between the applicant and the Secretary at the discretion of the Secretary.

The FFDCAs provide that the effectiveness of a device may be determined on the basis of multiple well-controlled investigations, including, where appropriate, clinical studies. Regulations are codified at CFR 814.39 for actions on a PMA supplement, and the FDA operates a pilot program for expedited approval of such supplements. General requirements under the FFDCAs for the labeling of a device apply to all submissions. Neither law nor policy suggest reliance on postmarket controls during premarket review to determine whether a device is substantially equivalent in its safety and effectiveness to one already on the market.

FDAMA97. The Act codifies procedures for enhancing collaboration between the FDA and device manufacturers during the approval process, and for expediting review. The Secretary must take into consideration the possibility that reliance on postmarket controls can expedite the review and classification of devices. Upon written request from a premarket approval applicant, the Secretary must meet with the applicant to determine the type of valid scientific evidence needed to establish safety and effectiveness for the proposed use of the device. Following the meeting, the Secretary has 30 days to specify in writing the type of evidence that will provide a reasonable assurance that the device is effective for its intended use.

Any clinical data, including those from one or more well-controlled investigations, that are determined by the Secretary as necessary to demonstrate the reasonable assurance of effectiveness of a device, must be requested from the applicant in writing. In such a case, the Secretary must consult with the applicant to determine the least burdensome means of evaluating effectiveness that would be reasonably likely to result in approval.

The Act adds new requirements for determining whether a device is substantially equivalent to one already on the market. The Secretary must take into consideration the extent to which reliance on postmarket controls may expedite classification of a device. Determinations for the intended use of a device must be based on the proposed labeling submitted with the premarket notification. In determining whether a device is substantially equivalent to one on the market, the device review director may require a statement on the device label that gives information about possible uses in ways that were not originally identified on the label, if those uses were likely and potentially harmful. The device review director may not delegate this responsibility. The requirement for unintended use identification is effective for five years from the date of enactment.

In deciding to approve or deny a premarket approval application, the Secretary must rely on conditions of use that have been included in the proposed labeling as the basis for determining whether there is reasonable assurance of safety and effectiveness. To determine whether the proposed label is false or misleading, the Secretary must evaluate all material facts pertinent to the proposed labeling.

A premarket approval supplement must be required for any changes to a device that affect its safety and effectiveness, unless the change is a modification in the manufacturing process. For the latter, the applicant must submit to the Secretary written details of the change, a summary of supporting data, and notice that the change conforms with the FDCA. The applicant may distribute the device 30 days after notification, unless the Secretary notifies the applicant within that period that additional information is needed. The Secretary must review that supplement within 135 days of receiving it. Incremental device changes that affect safety or effectiveness shall be approved if nonclinical data show that such changes enhance the device as intended, and if clinical data provide reasonable assurance of safety and effectiveness. When necessary, the Secretary may require additional clinical data.

Sec. 206. Premarket Notification

Previous Law or Policy. Each manufacturer must report to the Secretary intentions to market a device by way of the premarket notification process. The Secretary has the sole responsibility for the review and subsequent approval or denial of clearance for a premarket notification. The FDCA sets forth the process by which the devices may be exempted from premarket notification requirements.

FDAMA97. The Act establishes statutory authority for procedures exempting class II devices from premarket notification when the safety and effectiveness of such devices is clear. The Act clarifies an existing provision in the FDCA to exempt from premarket notification all class I devices except those that will be used to prevent illness or that have a high risk of injury or illness.

The Act requires the Secretary to publish, within 60 days of enactment, a list of each type of class II device that does not require premarket notification. Those exemptions are to become effective as of the date of publication in the *Federal Register*. After that date, the Secretary may exempt a class II device or may grant an exemption in response to a petition from an interested party. A notice of intent to exempt a device from premarket notification requirements must be published in the *Federal Register*, followed by a 30-day comment period. Within 120 days of issuing the notice in the *Federal Register*, the Secretary must publish final regulations for the device under consideration. If the Secretary fails to respond to a petition to reclassify a device within 180 days of receiving it, the petition shall be granted.

The Act prohibits the Secretary from withholding the classification of a device because of the applicant's failure to comply with provisions of the FDCA unrelated to a decision for substantial equivalence. Also, a decision to classify a device may not be withheld if the facility in which the device is manufactured is not in compliance with good manufacturing practices.

The Act clarifies that information to support claims of substantial equivalence may include “appropriate clinical or scientific data” that may be submitted to either the Secretary or an accredited person for consideration. The term “effectiveness” replaces the term “efficacy” of a device that is being compared to another for determination of substantial equivalence. Also, for determinations of substantial equivalence, the Secretary must issue guidance within 270 days of the Act’s enactment, listing the criteria to be used to determine if a specific intended use of a device is different from a general use.

Sec. 207. Evaluation of Automatic Class III Designation

Previous Law or Policy. The FFDCA requires that all new devices not substantially equivalent to a device already on the market must be automatically classified into class III.

FDAMA97. The Act expedites procedures for reclassifying medical devices that were initially given a class III designation. Applicants who submit a premarket notification for a device that has been automatically assigned to class III may now request the Secretary to reclassify the device without waiting for the Secretary to initiate actions for such requests. The Secretary must act upon the request within 60 days of its submission. Devices classified under this provision shall be considered predicate devices for the purpose of determining substantial equivalence.

Sec. 208. Classification Panels

Previous Law or Policy. The FFDCA requires the Secretary to establish panels of experts to make recommendations for device classification. Classification panels are exempt from those requirements of section 14 of the Federal Advisory Committee Act that relate to duration of the panel. Also, the FFDCA states requirements for composition of a classification panel, and its operation.

FDAMA97. The Act establishes schedule and procedural requirements for the classification panels. A classification panel must schedule its review of an application so that statutory deadlines for application review are met. Further, the Act clarifies the rights and privileges of the applicant to have equal access to data and information that have been submitted to the classification panel, the opportunity to submit certain information to the panel, and to participate in the meetings to the same degree as the Secretary. The panel meetings must provide adequate time for presentations and responses by those whose device is under review. If the decision by the Secretary for a premarket approval application differs from the classification panel’s decision, the Secretary must inform the applicant with a written explanation of the difference. Classification panels are not subject to annual chartering or annual reporting requirements of the Federal Advisory Committee Act.

Sec. 209. Certainty of Review Time Frames; Collaborative Review Process

Previous Law or Policy. The FFDCA requires manufacturers to submit premarket notifications to the Secretary within 90 days of distribution. In the

absence of a provision directing the Secretary to make decisions on such reviews within 90 days, final decisions frequently were determined after that period.

FDAMA97. The Act requires the Secretary to review premarket notifications and recommend device classification within 90 days of the notification's submission. If an applicant requests a meeting with the Secretary once a premarket approval application has been submitted for review, the Secretary must meet with the applicant within 100 days of receiving the request. Before the meeting, the Secretary must provide the applicant with a written description of any deficiencies that have been identified in the application. If the Secretary finds that there is a need for additional information to make a final decision on the application after the meeting has concluded, the Secretary must notify the applicant.

Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports

Previous Law or Policy. In August 1996, the FDA initiated a program for third-party review of medical devices. The ongoing program is a two-year pilot that allows third parties to review selected medical devices from class I and class II, and to make recommendations for the classification of those devices.

FDAMA97. The Act establishes authority to test third-party review of certain medical devices for the purposes of accelerating premarket review. The Secretary is to establish, within one year of enactment, a pilot program to permit third parties to review premarket notifications and make recommendations for regulatory classification. Persons accredited to perform such reviews must notify the Secretary of the reasons for the classification that they recommend. Once so notified, the Secretary must take action within 30 days. This procedure will not be used to review class III devices, devices that are implantable or life-sustaining or life-supporting, and devices that require the submission of clinical data.

Under the Act, accreditation programs for third-party review of medical devices will be provided through the FDA, other government agencies, or other qualified non governmental organizations. Within 180 days of enactment, the Secretary must publish, in the *Federal Register*, criteria for accrediting groups. Requests for accreditation must be acted upon within 60 days after being submitted. After providing notice and a hearing opportunity, the Secretary may withdraw or suspend accreditation if the accredited person is not in compliance with the Act.

The Secretary must complete performance audits of an accredited person by making onsite visits to examine performance. In the annual report submitted under section 903(g), the Secretary must list all accredited persons and all whose accreditation has been withdrawn during the year. An accredited person may not be employed by the federal government; can only be associated with an organization that is not owned or controlled by, and that does not have organizational, material, or financial affiliation, with a medical device manufacturer, supplier, or vendor; must be legally qualified to engage in accreditation activities; and must not be engaged in the design, manufacture, promotion or sale of devices.

The person must operate within generally accepted professional and ethical business practices. The person must also agree in writing to certify the accuracy of reported information, work only in areas of competency, treat all information and relevant materials received as proprietary, respond promptly to relevant complaints, and not use anyone for the review who has a financial interest in the device. Annual reports must be made about compliance with these requirements by the person and employees of the person.

At least two accredited persons must be made available to an applicant from which to choose. The applicant and the accredited person are responsible for making arrangements for compensation of the accredited party. The authority of the accreditation program ends five years after the Secretary notifies Congress that at least two accredited groups are available to review at least 60% of premarket notifications, or four years after the date Congress is notified that the Secretary has made decisions for at least 35% of devices subject to premarket notification, whichever occurs first.

Accredited persons are required to keep records about training, compensation, and procedures for maintaining confidentiality and avoidance of conflict of interest. Those records must be made available to the Secretary upon request. An accredited person is prohibited from submitting a false or misleading report in its recommendation. In addition, accredited persons are prohibited from disclosing confidential information or trade secrets without the written consent of the applicant, and from receiving bribes or engaging in corrupt activities.

Within five years of enactment, the General Accounting Office must submit to the House Committee on Commerce and the Senate Committee on Labor and Human Resources a report on the implementation of the accreditation program. Within six months of the end of the accreditation program, the General Accounting Office must submit to the House Committee on Commerce and the Senate Committee on Labor and Human Resources a report evaluating the program's assistance to the Secretary in carrying out premarket review and classification, and whether it resulted in actions contrary to the purposes of the Act.

Within three years of enactment, the Secretary must submit to the House Committee on Commerce and the Senate Committee on Labor and Human Resources a report stating whether Congress should rescind the limitation of certain class II devices from participation in the program.

Sec. 211. Device Tracking

Previous Law or Policy. Manufacturers must adopt a method of tracking (or tracing the path) of selected devices that are used outside of a user facility, as established under 21CFR Part 821.

FDAMA97. The Secretary can order manufacturers to track selected class II or class III devices that have potentially serious health consequences or functions. Patients do not have to release their name, address, Social Security number, or any other identifying information during such tracking.

Sec. 212. Postmarket Surveillance

Previous Law or Policy. The FDCA requires manufacturers to conduct postmarket surveillance, such as studies on safety and effectiveness, for certain devices in class I, II, or III devices that were marketed after January 1991. Manufacturers must obtain approval from the Secretary for a protocol for this surveillance.

FDAMA97 The Act makes procedures more flexible for ordering and planning for postmarket surveillance. Effective 90 days after enactment, manufacturers may be required to conduct postmarket surveillance for class II or class III devices whose failure would have serious adverse health consequences, devices intended to be implanted for more than 1 year, or life-supporting devices used outside of a user facility. Class II or III devices whose failure would be “reasonably likely” to have serious health consequences could be subject to this postmarket surveillance requirement. Manufacturers so required, must submit within 30 days after notification a surveillance plan. The Secretary must review the plan for adequacy within 60 days of receiving it. A trial surveillance period of up to 36 months may be required to determine if a longer period is necessary. If an agreement on duration of the postmarket surveillance cannot be reached, the manufacturer may seek redress through dispute resolution.

Sec. 213. Reports

Previous Law or Policy. Manufacturers, distributors and importers of medical devices must submit annual reports to the Secretary to acknowledge adverse events that were associated with medical devices.

FDAMA97 The Act establishes a new procedure to reduce the reporting burdens of medical device distributors and user facilities. Medical device distributors no longer need to establish and maintain a program for medical device reporting. However, manufacturers and importers are still subject to the FDCA reporting requirements. Regulations must be developed to require distributors to keep on file records of adverse events to be available to the Secretary upon request. Manufacturers, importers and distributors no longer need to certify whether they filed the reports required by the FDCA. Also, wholesale distributors of medical devices no longer need to register as device producers.

The Secretary must publish regulations that plan and implement a medical device reporting procedure that makes use of a representative sample of user facilities for reports about deaths and serious injuries or illnesses resulting from device use. User facilities that are not included in the sample group are not required to comply with user reporting requirements. Within two years of enactment, the Secretary must submit to the House Committee on Commerce and the Senate Committee on Labor and Human Resources a report on the plan that has been developed for medical device reporting at user facilities.

Sec. 214. Practice of Medicine

Previous Law or Policy. No previous law or policy.

FDAMA97. The Act clarifies the limitation of the Secretary’s authority about the practice of medicine. Health care practitioners are not limited by the FFDCA in prescribing or administering a device in the context of a legitimate patient-practitioner relationship.

Sec. 215. Noninvasive Blood Glucose Meter

Previous Law or Policy. No previous law or policy.

FDAMA97. The Act establishes a congressional declaration about noninvasive blood glucose meters. Congress finds that diabetes is a serious health problem in the United States, can be controlled by proper care, the absence of proper care results in serious adverse health consequences, blood testing is a critical tool for proper care but existing blood testing devices are painful creating a disincentive for their use, a safe and effective noninvasive blood glucose meter would probably improve diabetes care, and the FDA is responsible for medical device review in the United States. The Congress expresses its sense that accessibility to a non-invasive device for monitoring blood glucose would greatly enhance “the health and well-being of all people with diabetes across America and the world.”

Sec. 216. Use of Data Relating to Premarket Approval; Product Development Protocol

Previous Law or Policy. Certain data submitted as part of a premarket approval application are available for use by the Secretary in other device-related activities one year after the approval of the fourth device of the kind (known as the “four-of-a-kind” rule). Product development protocols (PDPs) must be referred to an advisory committee prior to approval.

FDAMA97. The Act repeals the four-of-a-kind rule for release of data. Data must be available for six years after the approval of the relevant application, and can be used to approve another device, determine whether a PDP has been completed, establish performance standards or special controls as covered by the Act, or classify or reclassify a device..

The Act repeals the requirement that PDPs be referred to an advisory committee before they are approved. At the request of the Secretary or the applicant, a PDP may be referred to an advisory committee for review unless the FDA finds that the PDP substantially duplicates one that was previously reviewed by the advisory committee.

Sec. 217. Clarification of the Number of Required Clinical Investigations for Approval

Previous Law or Policy. The FDCA requires one or more clinical investigations to establish a reasonable assurance of effectiveness.

FDAMA97. The Act directs that one or more well-controlled clinical investigations are appropriate for establishing the effectiveness of a device.

Title III — Improving Regulation of Food

Sec. 301. Flexibility for Regulations Regarding Claims

Previous Policy or Law. The previous policy required that any claim regulation had to become a final rule before it was allowed to be in effect. A regulation was not complete or final until it had undergone the full process of informal rulemaking (notice and comment on proposed regulatory language, and publication of the final rule), including provision of an effective implementation date.

FDAMA97. The Act allows the Secretary to make proposed regulations effective upon publication, pending consideration of public comment and publication of a final regulation. Such action would be warranted to allow prompt action on petitions that would provide consumer information that enables healthy dietary practices; results in prompt and effective communication of important nutrition and health benefits; or ensures that scientifically sound nutrition and health information is available as soon as possible. The Secretary also would be able to use this procedure to act promptly to ban or modify a claim. Such proposed regulations would be considered final agency action for purposes of judicial review.

Sec. 302. Petitions for Claims

Previous Policy or Law. Under the previous policy, when a claim was submitted, the Secretary had to issue a final decision either denying the claim or filing the petition within 100 days following its submission. If a petition was filed, the Secretary had an additional 90 days to deny or propose a regulation based on the action requested by the petitioner. Historically, until a regulation is proposed, information contained in the petition has not been made publically available.

FDAMA97. The Act requires that a petition not acted upon in 100 days will be considered denied, unless an extension is agreed upon by the Secretary and the petitioner. If the petition is denied, it would not be made publically available. If the petition is filed but not acted upon within 90 days, it will be considered to be denied, unless there is a mutually agreed upon extension. If the Secretary issues a proposed regulation, the rulemaking is to be completed within 540 days (18 months) of the date the petition is received. If a proposed regulation is not issued within that 540 days, the Secretary is required to provide the reason it was not completed to the House Committee on Commerce and the Senate Committee on Labor and Human Resources.

Sec. 303. Health Claims for Foods Products

Previous Policy or Law. Under the existing provisions for making health claims, a final regulation authorizing a claim is required to be in effect before it can be used on a food label or in labeling. The proponent of a claim can file a petition with the agency, providing the accumulated data on which the claim is based. The filing of a petition then triggers FDA review to determine whether, based on all of

the publically available scientific evidence, the diet-disease relationship meets the standard of significant scientific agreement, the food in question meets the minimum and maximum nutritional criteria required to bear the claim, and the food substance is safe and lawful. The message also must convey the relationship to the total diet, accurately convey the science, be truthful and nonmisleading, be generic and nonproprietary, and be understandable to consumers. If the standard was met along with all the other labeling requirements, then the agency would propose a regulation that, if finalized, would authorize the health claim.

FDAMA97. The Act creates an alternative mechanism for allowing health claims on food products. When a health claim is not authorized under an existing regulation, it can be authorized if it is based on a current authoritative statement about the relationship between a nutrient and a disease or health-related condition. A statement would be considered authoritative if published by a scientific body of the U.S. government that is responsible for public health protection or human nutrition research, such as NIH, or CDCP, or by the National Academy of Sciences (NAS).

At least 120 days prior its introduction into interstate commerce, the Secretary must be notified that the health claim will be used including the exact wording of the claim. A concise description of the basis on which the claim meets the requirements of the Act must be provided. A copy of the authoritative statement and a balanced representation of scientific literature about the relationship between the nutrient and a disease or health-related condition in the claim must also be included. During the 120 days, the Secretary may notify the individual wishing to make a claim if any of the required information needed for the notification has not been submitted.

The claim and the food on which the claim appears must comply with all other labeling requirements and accurately represent the authoritative statement. The claim must enable consumers to understand the relative significance of the information in the context of a total daily diet. The statement will be considered to be authoritative only if it is published by the scientific organization and not the statement of an individual employee.

A claim is allowed to be made under the requirements of this provision until the Secretary, by regulation, prohibits or modifies the claim, or a determination is made by either the Secretary or a U.S. district court (in an enforcement proceeding) that the requirements for making the claim have not been met.

Sec. 304. Nutrient Content Claims

Previous Policy or Law. Under the existing provisions, a specific nutrient content claim can be made only if it is allowed under an existing regulation. A nutrient content claim is a claim that either expressly or by implication characterizes the level of a nutrient contained in the food. It would appear on the principle display panel and is required to be listed on the nutrition label. The regulations identify the nutrient content claims that can be made and the circumstances under which they can be used. There are 11 core terms that can be used: free, low, lean, extra lean, high, good source, reduced, less, light, fewer, and more. Certain specific terms can be

used for calories, sugar, fat, cholesterol, sodium, and fiber. The level of a nutrient required to be present to make a given content claim is based in part on the existence of a daily value for the nutrient to which the amount of the nutrient present in the food can be compared.

FDAMA97. The Act creates an alternative mechanism for allowing nutrient content claims on food products. When a nutrient content claim is not authorized under an existing regulation, it can be authorized if the claim is based on a current authoritative statement that identifies the relevant nutrient level. A statement will be considered authoritative if it is published by a scientific body of the U.S. government that is responsible for public health protection or human nutrition research, such as NIH or CDCP, or by NAS.

At least 120 days prior to introduction into interstate commerce, the Secretary must be notified that a nutrient content claim will be used including the exact wording of the claim. A concise description of the basis on which the claim meets the requirements of the Act must be provided. A copy of the authoritative statement and a balanced representation of the scientific literature about the relationship between the nutrient and a disease or health-related condition in the claim must be included. During the 120 days, the Secretary may notify the individual wishing to make the claim if any of the required information has not been submitted.

The claim and the food on which the claim appears must comply with all other labeling requirements that include the accurate representation of the nutrient level and referral statements and must not contain either misleading labeling or advertising information. In addition, the claim must accurately represent the authoritative statement and enable consumers to understand the relative significance of the information in the context of a total daily diet. The statement will be considered to be authoritative only if it is published by the scientific organization and not the statement of an individual employee.

A claim is allowed to be made under the requirements of this provision until the Secretary, by regulation, prohibits or modifies the claim, or a determination is made by either the Secretary or a U.S. district court (in an enforcement proceeding) that the requirements for making the claim have not been met.

Sec. 305. Referral Statements

Previous Policy or Law. Under the previous policy, a food product that contained a nutrient at a level that increases the risk of a diet-related disease or other adverse health condition is not allowed to make a claim for that product. In most cases, however, a nutrient content claim could be made for a food containing a possible risk-increasing nutrient as long as the presence of a risk-increasing nutrient is disclosed on the label. Under the policy, a food was prohibited from making a nutrient content claim if it contains more than a certain level of fat, saturated fat, cholesterol, or sodium.

FDAMA97. The Act clarifies how information about possible health risks of a nutrient is conveyed on the label. When a nutrient claim is made about a food, and the Secretary determines that the food contains a nutrient at a level that increases a

diet-related health risk to the general population, the labeling must contain, prominently, and in immediate proximity to the claim, the following statement: “See nutrition information for _____ content” where the blank identifies the nutrient associated with the increased health risk. In determining that an increased risk may exist, the Secretary must take into account the significance of the food in the total daily diet.

Sec. 306. Disclosure of Irradiation

Previous Policy or Law. Under the existing regulations, there are several labeling requirements for irradiated foods. For packaged foods, the FDA’s rules require both a labeling statement and the internationally accepted logo. The label must state that the food has been “treated with irradiation” or “treated by radiation.” The labeling statement was originally included to inform consumers that the food had been treated with radiation, because they were not familiar with the logo if it appeared alone on the label. After an initial two-year period of using the statement, only the logo was to be required. The agency was to assess the labeling issue during that period. If the FDA determined that consumers still did not understand the meaning of the logo after the two-year period, then it was to propose extension of the wording requirement through regulation. Subsequently, the FDA amended the regulation on labeling of retail packages to extend for an additional two years the requirement that placed the wording with the irradiation logo, and continue to appear prominently on labels, labeling or at the point of purchase display for all foods that are irradiated. To date, few foods had been introduced into interstate commerce that are irradiated, so the use of the prominent wording along with the logo has been extended indefinitely until it is determined that consumers understand it.

FDAMA97. The Act prohibits any requirement of a separate radiation disclosure statement on labeling that is more prominent than the declaration of ingredients on the food package. The term “radiation disclosure statements” means a written statement that discloses that a food or a component of it has been intentionally exposed to radiation.

Sec. 307. Irradiation Petition

Previous Policy or Law. At the time of passage of FDAMA97, a petition for red meat irradiation had been pending before the FDA for three years. The agency published the final regulation approving the petition for the application of irradiation to red meat on December 3, 1997. Before the process can be used to treat red meat, however, USDA must also approve its use through regulation.

FDAMA97. The Act requires that, within 60 days of enactment, the Secretary is to make a final determination on any petition pending before the FDA that would permit irradiation for red meat. If such a determination is not made within that period, then the Secretary must provide the House Committee on Commerce and the Senate Committee on Labor and Human Resources with an explanation of the process followed by the FDA in reviewing the petition and the reasons action is delayed.

Sec. 308. Glass and Ceramic Ware

Previous Policy or Law. Under the existing regulation, if lead has been used in the glazes and decorative decals of ornamental and decorative ceramic ware, the containers must provide adequate information that they are not to be used for food-handling purposes. In 1979, the FDA and several other agencies entered into a voluntary agreement with the industry to end-test the lead content of glass containers in acetic acid solution. In 1997, newly identified problems related to lead paint led the agencies to decide that the old voluntary agreement was not stringent enough given advances in understanding the effects of lead in children. As a result, the agencies convened a meeting with industry and announced that the voluntary agreement was revoked.

FDAMA97. The Act prohibits the Secretary from implementing any requirement that would ban, as an unapproved food additive, lead and cadmium-based paints in the lip and rim area of glass and ceramic ware before one year after the regulation is published. Lead and cadmium-based paint may not be banned as an unapproved food additive, if the paint is on glass or ceramic ware that has less than 60 millimeters of decoration below the external rim, or is on an object that is not intended for use by children, unless the Secretary determines that it is unsafe. The Secretary may not take any action before January 1, 2003, to ban lead and cadmium-based enamel on glass and ceramic ware. Any action taken after that date to ban such enamel on those containers must be done by regulation and cannot be prohibited on those products before one year after the final regulation is published.

Sec. 309. Food Contact Substances

Previous Policy or Law. Since passage of the Food Additive Amendment of 1958, food contact substances (FCS) have been regulated in the same manner as food additives. The manufacturer wishing to use the FCS was required to submit a petition to the FDA for approval, if the FCS migration into the food was at a high level. Alternatively, the substance could be classified as “generally recognized as safe”, “prior sanctioned” or used under an existing regulation.

FDAMA97. The Act allows an FCS to be used in food products under either a regulation or a notification, and the substance cannot be considered to be adulterated while either is in effect. Under the notification process, at least 120 days prior to its introduction into interstate commerce, the manufacturer or supplier of an FCS may notify the Secretary of the name of the person, identity, and intended use of the FCS, and the determination that it is safe. The notification must contain the basis of the “safe” determination and all the information required to be submitted, as outlined in regulations promulgated by the Secretary.

The notification will become effective 120 days after it is submitted, and the substance may then be introduced into interstate commerce, unless within that period the Secretary has determined that, based on the information submitted, its use is unsafe. The manufacturer or supplier must be informed of an “unsafe” determination. A decision by the Secretary to object to a notification would constitute final agency action for purposes of judicial review. The term ‘food contact

substance' means the substance that is the subject of a notification, and does not include similar or identical substances manufactured or prepared by someone else.

The notification process can be used for marketing authorization for an FCS, except where the Secretary determines that submission and review of a petition is necessary for adequate assurance of safety, or the Secretary and any manufacturer or supplier agree that a petition should be submitted. The Secretary is authorized to promulgate regulations to identify the circumstances in which a petition is to be filed, including such criteria as the probable consumption and potential toxicity of the FCS.

For 120 days after receipt, the Secretary is to keep confidential any information provided in a notification. Except for any trade secrets or confidential commercial information, the material may then be made available to interested parties.

The notification program will not operate in any fiscal year, unless an appropriation of at least \$3 million is specifically made for that program that fiscal year. In addition, the Secretary is to certify that the amount appropriated for the FDA's Center for Food Safety and Applied Nutrition for each fiscal year is the same as or greater than the amount appropriated for the Center for FY1997. By April 1, 1999, the Secretary is to begin accepting and reviewing notifications, if a specific appropriation is made for the last six months of FY1999 and certified by the Secretary. The necessary sums are to be appropriated for each fiscal year from 1999 through 2003. Authorization of these appropriations, however, cannot be made for a fiscal year for any amount below that specified by the Act. Not later than April 1 of FY1998 and February 1 of each subsequent fiscal year, the Secretary must provide an estimate of the costs of operating the notification program for the next fiscal year to the House and Senate Committees on Appropriations, the House Committee on Commerce, and the Senate Committee on Labor and Human Resources.

The term "food contact substance" means any substance used in manufacturing, packing, packaging, transporting or holding food if such use is not intended to have any technical effect in the foods. The Secretary is to prescribe the procedure by which a notification is no longer to be in effect.

Title IV — General Provisions

Sec. 401. Dissemination of Information on New Uses

Previous Law or Policy. Prescription drugs and medical devices must be labeled to reflect properly the medical use or application for which they have been approved. By statute, drug and device manufacturers must provide evidence that their products are safe, and that they will have the effect prescribed, recommended, or suggested in their labeling. The FFDCA defines labeling to mean “all labels and other written, printed, or graphic matter, upon any article or any of its containers or wrappers, or accompanying such article.” Further, any drug or device whose labeling is “false or misleading in any particular,” is considered misbranded under that Act. Under its longstanding policy, the FDA considers virtually any material promoting a drug or device to be construed as part of its labeling. Manufacturers traditionally have been allowed to disseminate information or make promotional claims about a product as long as the information or claims are consistent with the product’s official labeling.

FDA modified its policy somewhat in 1996 when it published two guidance documents (61 FR 52800, Oct. 8, 1996) entitled “Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data,” and “Guidance for Industry Funded Dissemination of Reference Texts.” Those documents cover situations where drug and device sponsors may wish to distribute journal articles and reference texts containing information that may be inconsistent with the product’s approved labeling. In December 1997 (62 FR 64074, Dec. 3, 1997), the FDA issued another guidance document covering the dissemination of information about a drug or device’s unapproved (off-label) use at industry-supported scientific and educational activities. That document describes how industry may support those activities without being subjected to regulation under the FFDCA.

FDAMA97. The Act provides a means for health care practitioners to obtain scientific information about “off-label” uses of a drug or device when those uses are not included in the product’s approved labeling. The Act also creates a new regulatory mechanism for filing supplemental applications for such uses. If specific requirements are met, manufacturers may distribute written information about the safety, effectiveness, or benefit of a use not described in a product’s approved labeling.

Before off-label use information about a drug can be distributed, a new drug application filed under section 505(b) of the FFDCA or a biologics license issued under section 351 of the PHS Act must be in effect. Off-label use information about a device can only be disseminated if the product is in commercial distribution and complies with specified classification and premarket approval regulations. The off-label information must meet the requirements of section 552 (authorized information dissemination), and cannot be based on clinical research conducted by another manufacturer without their authorization to the results of such research. To disseminate the information, the manufacturer must, 60 days before distribution, submit to the Secretary a copy of the information, including clinical trials and

experience about the safety and effectiveness of the unapproved use, and must comply with the requirements for filing a supplemental application.

Manufacturers must include a prominent statement showing that the information, if applicable, concerns an unapproved use of a drug or device; that the disseminated information, if applicable, is being paid for by the manufacturer; the names of any authors who have financial ties with the manufacturer; the official labeling for the drug or device; a statement, if applicable, that there are other approved products or treatments for the use for which the information is being disseminated; the identification of all persons funding any study about the off-label new use; and a bibliography of published articles about the unapproved use from scientific or medical journals.

If the Secretary determines, after providing a notice and a meeting opportunity, that the off-label use information fails to provide data, analyses, or other objective material, dissemination of additional objective and scientifically sound information can be required, along with a statement of the Secretary, based on scientifically valid data, about the safety and effectiveness of the drug's unapproved use.

Manufacturers may disseminate information about an unapproved new use only if the information is in the form of an unabridged reprint or copy of an article peer reviewed by experts. The article must be from a medical journal and describe a scientifically sound clinical investigation, or else it must be from an unabridged reference publication that includes such information. A reference publication is one that has not been written, edited, or published specifically for, or significantly influenced by, a manufacturer; is generally available where medical texts are sold; does not focus on any particular manufacturer's drug or primarily on unapproved uses of drugs from a manufacturer supporting the dissemination; and does not present false or misleading material.

In addition, to disseminate off-label use information, manufacturers must prepare and submit biannually to the Secretary a list of articles and reference publications that are about their drug's unapproved uses and that were disseminated for the six-month period prior to the submission of the list. Additionally, manufacturers must submit lists that identify the categories of providers that received that material for the same period. Manufacturers that distribute off-label information must keep records that may be used in situations where the Secretary requires corrective action be taken. The records must be made available to the Secretary, upon request, for ensuring or taking corrective action. At the Secretary's discretion, the records may identify the recipient of the information.

To disseminate off-label use information manufacturers must also submit a supplemental application to the Secretary, be certified that they will file a supplemental application based on completed or planned studies, or be granted an exemption from submitting such an application.

In the case of completed studies, manufacturers can submit a certification that the necessary studies have been completed and the supplement will be submitted no later than six months after the initial information dissemination.

In the case of planned studies, manufacturers must submit an application with a proposed protocol and schedule for the studies needed for the supplemental application, and certify that it will be submitted no later than three years after the initial information dissemination (or, as applicable, not later than a date the Secretary may specify). The Secretary must determine whether the proposed protocol is adequate and whether the schedule is reasonable. Manufacturers must also submit periodic status reports. If the Secretary determines that the studies cannot be completed and submitted within three years, and that the manufacturer has diligently conducted the studies, an extension of up to two years may be provided.

To obtain an exemption from submitting a supplemental application, the manufacturer must submit an application for an exemption, it must be approved by the Secretary, and it must not be terminated due to corrective action. Exemptions may only be approved if the Secretary determines that the supplemental application would be economically prohibitive. In making that determination, the Secretary must consider the size of the patient population expected to benefit from the exemption approval, and whether the manufacturer would be entitled to any periods of exclusive marketing rights. In addition, an exemption may be granted if the Secretary determines that it would be unethical to conduct the necessary studies.

The Secretary must approve or deny an application for an exemption within 60 days, or the application is deemed approved. The Secretary, however, may at any time terminate such approval and order the manufacturer to cease distributing the information. The Secretary may prescribe the form and manner of applications submitted under this section.

If the Secretary determines that the unapproved use may not be effective or may present a significant risk to the public health, corrective action can be ordered. Manufacturers are responsible for reporting results of additional clinical research about the safety and effectiveness of the unapproved use involved. The extent of those responsibilities is to be set, by regulation, by the Secretary.

The Secretary, after notification, may order a manufacturer to stop dissemination of information if it is not in compliance. This order may be issued only after the Secretary provides a notice to the manufacturer and an opportunity for a meeting. If the compliance failure is minor, the Secretary must delay the order and provide to the manufacturer an opportunity to correct the violation.

Manufacturers can be ordered to stop dissemination when the supplemental application does not contain adequate information; the manufacturer, after certification, has not submitted the necessary supplemental application within six months; or the manufacturer, after certification, has not acted with due diligence to complete the required studies. In situations where the Secretary terminates an approved exemption, an order to stop dissemination will be made and complied with within 60 days. Manufacturers can be ordered to correct the information only if the unapproved use would pose a significant risk to human health.

Disseminating off-label use information to an unsolicited request from a health care practitioner is not prohibited by this Act. Information dissemination about off-label uses as defined in this provision is not to be considered evidence of

a new intended use of a drug or device that is different from the intended use described in its official labeling. The disseminated information may not be considered by the Secretary as labeling, adulteration, or misbranding under the FDCA. Nothing in this provision may affect patent rights or prohibit a publisher of a scientific journal from charging for reprints or requiring authorization to disseminate such article(s).

The Secretary must promulgate regulations to carry out this section no later than November 21, 1998. In addition, the amendments made in this section will cease September 30, 2006, or seven years after the Secretary's regulations to implement the section become effective, whichever is later. The General Accounting Office (GAO) is required to conduct a study to evaluate the impact of Section 401 on the resources of the Department of Health and Human Services. The report must be submitted to Congress no later than January 1, 2002. The Secretary must also request the Institute of Medicine (IOM) to conduct a study addressing scientific issues raised by this provision. If IOM is unwilling to do the study, then it must be conducted by GAO. The study must be submitted to Congress by September 30, 2005.

Sec. 402. Expanded Access to Investigational Therapies and Diagnostics

Previous Law or Policy. The FDA has implemented several regulatory policies to make it easier for patients to gain access to experimental therapies. In 1987, the agency promulgated its "Treatment Investigational New Drug" regulations which authorized the use of an experimental drug or biological product to treat a life-threatening or seriously debilitating disease if that use is under clinical investigation. In 1990, the U.S. Public Health Service, in response to the AIDS epidemic, initiated its "parallel track" policy allowing patients who could not participate directly in clinical trials to receive experimental drugs for treatment purposes while the drugs were being evaluated in clinical trials. In 1992, the FDA implemented its "accelerated approval" policy that speeds the review and approval process for drugs and biologics that may provide a significant benefit over existing therapy.

FDAMA97. The Act codifies and expands upon existing FDA policy to facilitate access to experimental drugs and devices. It gives the FDA the authority to broaden existing regulations to streamline drug accessibility so that they cover all life-threatening diseases and conditions. Patients are allowed expanded access to investigational therapies, and the Secretary has the authority in medical emergencies to allow the shipment of investigational drugs or devices for diagnosis, monitoring, or treatment.

Any person, acting through a physician, can request from and be provided by any manufacturer or distributor, an investigational drug or device for the diagnosis, monitoring, or treatment of a serious disease or condition. The physician must determine that the patient has no comparable or satisfactory alternative therapy, and that the risk from the investigational product is no greater than from the disease or condition. There must be sufficient evidence that the experimental drug or device is safe and effective, and that providing it will not interfere with clinical investigations for marketing approval. The sponsor or clinical investigator must

submit to the Secretary a clinical protocol for the use of the drug or device in a single patient or a small group of patients.

Upon submission of a protocol for expanded access, the Secretary must permit the drug or device to be made available under a treatment investigational new drug (IND) application or an investigational device exemption (IDE), if the drug or device is intended for a serious or immediately life-threatening disease, and no satisfactory alternative is available. The investigational drug or device must either be undergoing or have completed a controlled clinical trial under an investigational exemption; the sponsor must be diligently pursuing marketing approval; and use of the investigational drug or device for treatment purposes must not interfere with ongoing clinical investigations. In the case of a serious disease, there must be sufficient safety and effectiveness evidence to support the treatment exemption. For an immediately life-threatening disease, there must be enough scientific evidence to conclude that the product may be effective and would not expose patients to significant risk or injury.

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 or device under the expanded protocol. Expanded access may be terminated if this provision's requirements are no longer being met. The Secretary may determine, by regulation, the definition of "investigational drug," "investigational device," "treatment investigational new drug application," and "treatment investigational device exemption."

Sec. 403. Approval of Supplemental Applications for Approved Products

Previous Law or Policy. Current regulations permit the filing of supplemental applications for drug products already approved. Those applications usually modify a previously approved drug application to permit a change in the product or the addition of a new indication (new medical use). Regardless of the type of change involved, the manufacturer must notify the FDA about it in a supplemental application. A supplemental application for a new medical use for an already approved product usually requires the submission of safety and efficacy data from well-controlled clinical investigations.

FDAMA97. The Act expands the types of data that will qualify for support of a supplemental drug application to include, in certain circumstances, data from "published material". Within 180 days of enactment, the Secretary must publish standards for the prompt review of supplemental applications submitted for drugs and biologics previously approved under the FDCA and the PHS Act. Within this same period, the Secretary must also issue final guidance documents to clarify the requirements for and simplify the submission of supporting data. The documents must clarify when published material will qualify as the basis for approval, specify data requirements that will avoid duplication of data previously submitted, and define eligibility for priority review.

The Secretary must 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 help with the development and submission of data to support supplemental applications. In addition, the Secretary must take steps to foster collaboration between the FDA and the NIH, professional medical and scientific societies, and others to identify supporting studies. Moreover, the Secretary must implement policies that encourage sponsors to submit supplemental applications or conduct further research based on those studies.

Sec. 404. Dispute Resolution

Previous Law or Policy. FDA regulations provide administrative procedures for resolving differences between drug applicants and reviewing divisions (21 CFR 314.103). When disputes arise over technical requirements, the agency urges applicants to contact the consumer safety officer of the division responsible for handling the application. If resolution is not achieved, the issue can be taken up with an ombudsman. The regulations also note that at several stages of the review process, major scientific issues can be addressed at meetings of applicants, reviewing officials, and management representatives.

FDAMA97. The Act requires the establishment of a mechanism for resolving scientific disputes between the Secretary and sponsors, applicants, or manufacturers. The mechanism is to be used in situations where the FFDCIA contains no specific provision or regulation for a right to such review. The Secretary must establish, by regulation, a procedure by which sponsors, applicants, and manufacturers can request a review, including a review by an appropriate scientific advisory panel or committee. The regulations must be promulgated within one year of enactment.

Sec. 405. Informal Agency Statements

Previous Law or Policy. By FDA regulation (21 CFR 10.90), “guidelines relate to performance characteristics, preclinical and clinical test procedures, manufacturing practices, product standards, scientific protocols, compliance criteria, ingredient specifications, labeling, or other technical or policy criteria. Guidelines state procedures or standards of general applicability that are not legal requirements but are acceptable to the FDA for a subject matter which falls within the laws administered by the Commissioner.” Guidelines are filed with the agency’s Documents Management Branch and a notice of availability is published in the *Federal Register*. Public comments are accepted and given consideration when the agency decides that a guideline needs changing or amending.

FDAMA97. The Act clarifies procedures for and limitations of the FDA informal guidance statements. The Secretary must develop guidance documents with public participation. Also, the documents must be made available both in written, and if possible, electronic form. Those documents present the Secretary’s views on matter under FDA jurisdiction, but they do not create or confer any rights for any person.

The Secretary must ensure that FDA employees do not deviate from the guidance statements without justification. The Secretary must provide training in the

development and use of the documents and must monitor their issuance. For guidance documents that set initial interpretations of a statute or regulation, or changes in interpretation or policies that are significant or controversial, the Secretary must ensure public participation prior to implementation. For documents that establish existing practices or minor policy changes, the Secretary must receive public comment before implementation.

The Secretary must ensure uniform document nomenclature and uniform internal procedures for the approval of the document. In addition, the Secretary must indicate that the documents are nonbinding and ensure that they are properly dated. The secretary must periodically review all documents, and revise them as appropriate.

The Secretary must publish a list of the guidance documents in the *Federal Register*. Additionally, the Secretary must put in place an appeals mechanism for complaints about the development and use of these documents. No later than July 1, 2000, the Secretary, after evaluating the effectiveness of the Good Guidance Practices document published in the *Federal Register*, must promulgate regulations specifying FDA's policies and procedures for the development, issuance, and use of those documents.

Sec. 406. Food and Drug Administration Mission and Annual Report

Previous Law or Policy. Under current statutes, the FDA has neither a mission statement nor an obligation to submit an annual report.

FDAMA97. The Act establishes a mission statement for the FDA and requires it to prepare an annual report. The FDA must “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.” Public health must be protected by ensuring that “foods are safe, wholesome, sanitary, and properly labeled”; “human and veterinary drugs are safe and effective”; “there is reasonable assurance of the safety and effectiveness of devices intended for human use”; “cosmetics are safe and properly labeled”; and that “public health and safety are protected from electronic product radiation.” Furthermore, the FDA must participate with other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements. The Secretary should, as appropriate, meet these objectives in consultation with experts in science, medicine, and public health, and in cooperation with consumers, manufacturers, importers, packers, distributors, and retailers.

No later than one year after enactment, the Secretary must develop and publish in the *Federal Register* a plan to bring the agency into compliance with the Act. In formulating the plan, the Secretary must consult with appropriate scientific and academic experts, patient and consumer advocacy groups, and regulated industry. The Secretary must biannually review the plan and revise it as necessary. It must include objectives for maximizing availability and clarity of information about the review process, informing patients about new products, and for inspection and postmarket monitoring. Additionally, the plan must include goals to ensure access to needed scientific and technical expertise, to establish mechanisms by July

1, 1999, for meeting the required review periods, and to eliminate backlogs in the review of applications and submissions by January 1, 2000.

The Secretary must prepare and publish in the *Federal Register* an annual report with detailed statistical information on the Secretary's performance under the plan; a comparison of the Secretary's performance with the plan's objectives and the Secretary's statutory obligations; and identification of regulatory policies that have had a negative impact on compliance with the plan's objectives or statutory obligations. The plan must also include proposed revisions of any such policies.

Sec. 407. Information System

Previous Law or Policy. Currently, there is no information system, accessible by manufacturers, to monitor or track the review of marketing applications. The FDA does publish a cumulative compendium consisting of approved prescription drug products, over-the-counter drug products, orphan product designations, discontinued products, and abbreviated new drug suitability petitions. This compendium also provides drug patent and exclusivity information.

FDAMA97. The Act requires the Secretary to establish and maintain an information system to track the status of each application, petition, notification, or other request submitted to the agency for consideration. Also, no later than one year after enactment, the Secretary must submit a report to the Senate Committee on Labor and Human Resources and the House Committee on Commerce about the status of the system, its costs, and concerns about confidentiality.

Sec. 408. Education and Training

Previous Law or Policy. The FDA operates training programs for its personnel, as appropriate, but there is no general statutory guidance for those programs.

FDAMA97. The Act codifies certain education and training requirements for agency employees, and supports intramural training programs for scientists and physicians. The Secretary must conduct training and education programs, for FDA employees, about the regulatory responsibilities and policies of this Act. Those programs must include scientific training, training to improve the skills and develop product specialization of employees who conduct factory inspections, and training in administrative process and procedure, and in integrity issues. The Secretary may, through fellowships and other training programs, conduct and support intramural research training for predoctoral and postdoctoral scientists and physicians.

The Secretary, acting through the Director of the Centers for Disease Control and Prevention, is to establish fellowship and training programs for individuals in epidemiology, surveillance, laboratory analysis, and disease detection and prevention methods. The programs must be designed to enable health professionals to work on local, state, national, and international efforts in the prevention and control of diseases, injuries, and disabilities. The fellowships and training may be administered

by using either appointment or nonappointment procedures. This amendment is deemed to have taken effect on July 1, 1995.

Sec. 409. Centers for Education and Research on Therapeutics

Previous Law or Policy. This is a newly authorized program.

FDAMA97. The Act authorizes a demonstration program for research and education centers on therapeutics. The Secretary, through the Administrator of the Agency for Health Care Policy and Research, and in consultation with the FDA Commissioner, shall establish a demonstration program for the purposes of making grants to establish such centers. Activities to be carried out in those centers include clinical and laboratory research to increase awareness of new uses of drugs, biologics, and devices, ways to improve their effective use, and the risks associated with those uses and drugs and biologics in combination; to provide objective clinical information to various members of the health care industry and to consumers; and improve health care quality while reducing costs by appropriate use and prevention of adverse effects of drugs, biologics, or devices.

Research topics can also include the comparative effectiveness and safety of those products and other areas as considered appropriate by the Secretary. The grants may not, however, be used to help the Secretary review new drugs. Applications for grants must be complete and must undergo appropriate technical and scientific peer review. This program carries an authorization of \$2 million for FY1998, and \$3 million each year for FY1999 through 2002.

Sec. 410. Mutual Recognition Agreements and Global Harmonization

Previous Law or Policy. For several years, the FDA has been actively participating in meetings with representatives from other countries to explore developments in the international harmonization of regulatory standards. One example is FDA's participation in the International Conference on Harmonization (ICH), which was organized to develop harmonized technical requirements for the registration of pharmaceutical products between the United States, Japan, and the European Union. When the parties reach a consensus on a particular regulatory issue, a draft guideline is published for public comment. The draft undergoes further agency evaluation and eventually is published as an official agency guideline. According to the FDA, the guidelines represent the agency's current thinking, and do not necessarily create or confer any rights for or on any person and do not operate to bind the FDA or the private sector. However, the agency strongly recommends that its guidelines be followed.

FDAMA97. The Act provides statutory direction to the FDA for global harmonization of its regulatory responsibilities. Regulations about good manufacturing practices (GMP) for medical devices must conform with internationally recognized standards defining quality systems or parts of the standards. The Secretary is to support the Office of the U.S. Trade Representative, in consultation with the Secretary of Commerce, in meetings with representatives of other countries to discuss methods to reduce the burden of regulation and harmonize

regulatory requirements if the Secretary determines that such harmonization is consistent with the consumer protections supported by this Act.

The Secretary must support the Office of the U.S. Trade Representative and the Secretary of Commerce in moving toward acceptance of mutual recognition agreements (MRAs) between the United States and the European Union. Those MRAs cover the regulation of drugs, biological products, devices, foods, food additives, color additives, and GMPs. The Secretary must regularly participate in meetings with foreign governments over the harmonization of regulatory requirements. No later than 180 days after enactment, the Secretary is to make public a plan that establishes a framework for achieving mutual recognition of MRAs and GMPs. None of the Secretary's obligations under this section apply to dietary supplements.

Sec. 411. Environmental Impact Review

Previous Law or Policy. Under 21 CFR Part 25, the FDA recognizes the 1969 National Environmental Policy Act (NEPA) as the national charter for protection, restoration, and enhancement of the environment. The agency further states that all of its policies and programs will be planned, developed, and implemented to be consistent with NEPA policies and the Council on Environmental Quality regulations. However, on July 29, 1997, the FDA issued a final rule revising its environmental assessment policies and procedures. The agency said that the primary purpose of the revision was to increase the efficiency of NEPA implementation, and to reduce the number of NEPA evaluations, by developing categorical exclusions that individually or cumulatively have no significant effect on the human environment and for which, therefore, neither an environmental impact statement (EIS) nor an environmental assessment (EA) is required. The rule change was conceived as part of the President's reinventing government initiative (REGO) and became effective on August 28, 1997.

FDAMA97. The Act directs that an environmental impact statement, prepared in connection with an action carried out under this Act, will meet NEPA requirements.

Sec. 412. National Uniformity for Nonprescription Drugs and Cosmetics

Previous Law or Policy. The FFDCAs govern the sale or introduction of foods, drugs (both human and animal), cosmetics, and medical devices into interstate commerce. From time to time, a state legislature will impose a regulatory requirement (e.g., labeling or warning obligations) that exceeds that required at the federal level.

FDAMA97. With a few exceptions, the Act establishes federal regulatory preemption for products marketed in compliance with federal statutes. No state or political subdivision of a state may establish or continue to affect any requirement about a nonprescription drug that is not identical with requirements under this Act, the Poison Prevention Packaging Act (15 U.S.C. §§1471 et seq.), or the Fair Packaging and Labeling Act (15 U.S.C. §§1451 et seq.).

Upon application by a state, however, the Secretary may, by regulation, exempt a state requirement if it protects an important public interest that would otherwise not be done, would not cause any drug to be in violation of federal law, and would not unduly burden interstate commerce. The Secretary must make a decision on any exemption request within 120 days of receiving the application. The provisions of this section do not apply to any state or political subdivision requirement about the practice of pharmacy or to any state or political subdivision requirement that a drug be dispensed only by prescription. They do apply, however, to any requirement about providing warnings to the public about any kind of drug.

In the case of drugs not subject to an approved application, antibiotic certifications, and drugs subject to monographs, or action by the Secretary declaring the drug safe and effective, a national uniformity exception will apply only to a state or local requirement on the same subject as, but which does not duplicate, a regulation or other requirement in effect for the drug under the FFDCa, the Poison Prevention Packaging Act, or the Fair Packaging and Labeling Act. This section does not apply to a state requirement adopted by public referendum enacted before September 1, 1997 (e.g., California's Proposition 65), and it will not modify any action or liability under state product liability laws. Further, it cannot prevent a state from enforcing requirements identical to any of this Act's requirements.

This provision contains an amendment that extends the FDA's current factory inspection authority to nonprescription drug manufacturing facilities. Further, it amends the FFDCa's misbranding clause, making certain drug labeling requirements more specific than under existing law.

Except as described below, no state or political subdivision may have any labeling or packaging requirements for a cosmetic that are not the same as the requirements under the FFDCa, the Poison Prevention Packaging Act, or the Fair Packaging and Labeling Act. Only state requirements about aspects of the product's packaging and labeling, including public information or communication, that are covered by this Act are subject to this uniformity provision for cosmetics. The Secretary may, by regulation, prescribe an exemption if it protects an important public interest, does not make the cosmetic be in violation of federal law, and does not burden interstate commerce. Further, this section will not modify or affect any action or the liability under state product liability laws. Also, it does not apply to any state requirement adopted by public referendum enacted before September 1, 1997.

Sec. 413. Food and Drug Administration Study of Mercury Compounds in Drugs and Foods

Previous Law or Policy. Mercury compounds, in small amounts, have been used for years in prescription and over-the-counter drug products as either active (e.g., antibacterial) and inactive (e.g., preservative) ingredients. In recent decades, the use of mercury in pharmaceutical preparations has to a great extent been supplanted by safer and more effective compounds. The FDA has taken action, under its over-the-counter (OTC) review, to declare some mercury-containing products as "not generally recognized as safe and effective." Mercury-containing

products that remain on the market must be properly labeled to reflect this FDA conclusion.

FDAMA97. The Act codifies procedures for addressing concerns about the use of mercury in drugs and foods. By November 1999, the FDA must compile a list of drugs and foods to which mercury compounds have been added, and provide an analysis of those compounds. Further, within two years of enactment, the Secretary, acting through the FDA, must study the effects on humans of using mercury compounds in nasal sprays.

In addition, the Secretary, acting through the FDA, must conduct (or contract with the Institute of Medicine to conduct), a study of the effects on humans of elemental, organic, or inorganic mercury contained in drugs or dietary supplements. The study must evaluate the extent of mercury use as a drug or dietary supplement, and evaluate its adverse effects on children and other sensitive populations. In conducting the study, the FDA must 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.

If, in the opinion of the Secretary, such uses of elemental, organic, or inorganic mercury, pose a threat to public health, the Secretary must promulgate regulations restricting such use. The regulations must protect the health of children and other sensitive populations, but not necessarily interfere with mercury's availability for use in religious ceremonies.

Sec. 414. Interagency Collaboration

Previous Law or Policy. The FDA has an informal policy to collaborate with other science-based Federal agencies to coordinate programs and advance science-based issues.

FDAMA97. The Act codifies requirements for interagency collaboration by the FDA. The Secretary must implement programs and policies that will foster collaboration between the Administration, the National Institutes of Health, and other science-based federal agencies to enhance the scientific and technical expertise available to the Secretary. This requirement applies to the Secretary's duties relative to the development, clinical investigations, evaluation, and postmarket monitoring of emerging medical therapies.

Sec. 415. Contracts for Expert Review

Previous Law or Policy. With respect to scientific or technical assistance, under the FFDCA, the Secretary is authorized to establish technical and scientific review groups to help carry out the functions of the FDA.

FDAMA97. The Act establishes procedures to enhance FDA review of applications by obtaining advice from outside experts on technical and scientific matters. The FDA can enter into contracts with organizations or persons (not employees of the Department) with relevant expertise for review and evaluation, for

the purpose of making recommendations to the Secretary on part or all of any application or submission for the approval or classification of a product. This authority also includes the approval and classification processes or decisions made for a biological product under the Public Health Service Act. Contracts will be subject to the FFDCIA requirements concerning confidentiality of information.

The Secretary may use this authority to improve the timeliness and quality of review unless the authority would reduce the quality or unduly increase the costs of review. Improvements in timeliness or quality may include providing the Secretary increased scientific or technical expertise that is necessary to review or evaluate new therapies and technologies. The FDA official responsible for any matter for which the outside reviewer is used must review any recommendation made by the expert and make the final decision in a timely manner. A final decision by the Secretary must be made within the time period applicable to the matter under review.

Sec. 416. Product Classification

Previous Law or Policy. Under current policy, the FDA classifies a product—such as a drug, device, or combination product—sometimes using recommendations by classification panels—to denote the product’s regulatory classification and identify the FDA unit that would be assigned primary responsibility for its review. Current law does not provide for any default classification process.

FDAMA97. The Act clarifies the regulatory classification process. A person who submits an application or submission for a product can request a determination by the Secretary as to how the product will be classified—drug, device, biological product, device or combination product, and so forth—and which FDA unit will regulate the product. The person must recommend either a product classification or which component of the FDA should regulate its product, as appropriate. Within 60 days of receipt of the request, the Secretary must determine the product classification or the FDA regulatory component and provide that information and the reasons for the decision, in writing, to the requester. The Secretary cannot modify that statement except with the requester’s written consent, or for scientifically based public health reasons.

If the Secretary does not issue the written notice within the 60-day time period, the recommendation of the requester shall be considered final and may not be modified by the Secretary except with the requester’s written consent or for scientifically based public health reasons.

Sec. 417. Registration of Foreign Establishments

Previous Law or Policy. Under current law, producers of drugs and devices must register with the FDA. Among other things, foreign establishments, engaged in manufacturing, preparing, propagating, compounding, or processing a drug or device are permitted to register under this section and applicable regulations, and are required to provide certain additional information and filing statements.

FDAMA97. The Act clarifies requirements for registration of foreign establishments interested in importing its products. Any foreign establishment engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or device for importing into the United States must register its name and place of business and the agent's name with the Secretary. The establishment must also supply information required by the FFDCa. The Secretary has the authority to enter into cooperative agreements with foreign officials to ensure that means are available to determine, from time to time, whether such drugs and devices should be refused entry into the United States on grounds set forth in the FFDCa.

Sec. 418. Clarification of Seizure Authority

Previous Law or Policy. The FDA has the authority under the FFDCa to seize a product or article imported into the United States.

FDAMA97. The Act clarifies that a person seeking release for export of a seized imported article must establish that the product was intended for export.

Sec. 419. Interstate Commerce

Previous Law or Policy. Under the previous statutory provision, the FFDCa provided that the connection with interstate commerce required for jurisdiction was presumed for devices.

FDAMA97. The Act clarifies the connection with interstate commerce for products subject to regulation. In any action to enforce the requirements of the Act respecting a device, food, drug or cosmetic, the connection with interstate commerce is presumed to exist.

Sec. 420. Safety Report Disclaimers

Previous Law or Policy. The FFDCa requires that various reports and information be filed and/or kept by industry. For example, section 519 governs record keeping and reporting for devices, including the requirement that device manufacturers and others shall maintain records, make reports, and provide such information as required to ensure that the device is not adulterated or misbranded and to otherwise assure its safety and effectiveness. The reporting requirements include accounts of adverse experiences, injuries, and similar concerns.

FDAMA97. This Act establishes disclaimers for safety reports. Any report or other information about safety of a product—drug, food, device, dietary supplement, or cosmetic—and any release by the Secretary of this information shall not necessarily be interpreted that the product malfunctioned or caused or contributed to an adverse experience, death, serious injury, or serious illness. Those submitting such reports or information do not have to admit, and may deny, that the report or information that they are submitting constitutes an admission that the product malfunctioned or caused or contributed to an adverse experience, a death, serious injury or serious illness.

Sec. 421. Labeling and Advertising Regarding Compliance with Statutory Requirements

Previous Law or Policy. Section 301(l) of the FDCA prohibited the use, on the label of a drug or device or in any of their advertising, any representation or suggestion that an approved application for the product was in effect, or that it complied with applicable provisions for the drug or device.

FDAMA97. The Act repeals that prohibition.

Sec. 422. Rule of Construction

Previous Law or Policy. No provision.

FDAMA97. Nothing under the FDCA or amendments made by this Act shall be construed to affect the question of whether the Secretary has authority to regulate any tobacco product, tobacco ingredient, or tobacco additive. The Secretary's authority, if any, shall be exercised under the FDCA as in effect on the day before the date of the Act's enactment.

Title V — Effective Date

Sec. 501. Effective Date

Previous Law or Policy. Not applicable.

FDAMA97. Unless otherwise stated, these provisions take effect 90 days after the date of enactment.

Appendix — FDAMA97 Deadlines

The table below lists, with deadlines in chronological order, all the actions and activities that the Food and Drug Administration Modernization Act of 1997 (P.L. 105-115) requires FDA to take over the next 9 years and that involve congressional oversight. Included in the list are actions that are of general interest to Congress, to specific congressional committees, and to the public. I also included required activities that did not have specific deadlines but that are mandated by P.L. 105-115. The list does not include deadlines for actions between the agency and applicants for approval or sponsors of products.

Table 1. FDA Action Deadlines Established in P.L. 105-115, FDA Modernization Act of 1997

<i>Deadline</i>	<i>Statute Section and Title</i>	<i>Required Action</i>
11/21/97	P.L. 105-115. Enactment Date	Beginning date for some actions.
12/21/97 ¹	Sec. 121. Positron Emission Tomography	(d) Publication in the <i>Federal Register</i> revoking the inconsistent notice and final rules from 1995 and 1997.
2/19/98	Sec. 501. Effective date	Beginning date for some actions.
4/1/98	Sec. 309. Food Contact Substances	(b)(5)(C) Report to Congress estimating the costs of implementing the food contact substance notification program for the next fiscal year.
5/20/98	Sec. 111. Pediatric Studies of Drugs	(b) Secretary is to develop, prioritize, and publish a list of drugs for which additional pediatric information may be beneficial.

¹ The current criteria for approval of positron emission tomography drugs will no longer apply either 4 years after enactment or 2 years after the Secretary establishes new procedures.

5/20/98	Sec. 122. Requirements for Radiopharmaceuticals	(a)(1)(A) Develop proposed regulations on approvals of radiopharmaceuticals in consultation with patients, physicians, and the industry.
5/20/98	Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports. Sec. 523. Accredited Persons	(b)(2)(A) Establish and publish in the <i>Federal Register</i> criteria to accredit or deny accreditation to persons who request accreditation.
5/20/98	Sec. 403. Approval of Supplemental Applications for Approved Products	Publish performance standards for supplemental new drug applications.
5/20/98	Sec. 403. Approval of Supplemental Applications for Approved Products	Issue final guidelines to industry, clarifying and simplifying requirements for submission of supporting data.
5/20/98	Sec. 410. Mutual Recognition Agreements and Global Harmonization	Make public a plan that establishes a framework for achieving mutual recognition of inspections for good manufacturing practices.
8/18/98	Sec. 206. Premarket Notification	(c)(2)(F) Issue guidance on the principles that will be used when determining substantial equivalence for medical devices when the specific intended use of the device is different from the general use.
11/21/98	Sec. 112. Expediting Study and Approval of Fast Track Drugs	(b) Issue guidance to the industry on approval policies and procedures for fast track drugs.
11/21/98	Sec. 118. Data Requirements for Drugs and Biologics	Issue guidance to the industry regarding submissions of abbreviated study reports for new drug applications (NDAs) and biologic license applications.
11/21/98	Sec. 127. Application of Federal Law to Practice of Pharmacy Compounding	(d)(2) Promulgate regulations for drugs that must meet certain compounding requirements.

11/21/98	Sec. 201. Investigational Device Exemptions	(a)(6)(A) Establish procedures to permit developmental changes and modifications in the manufacturing of devices and in clinical protocols.
11/21/98	Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports. Sec. 523. Accredited Persons.	(a) Accredite persons for the reviewing reports submitted under 510(k) and for the classification of the device.
11/21/98	Sec. 401. Dissemination of Information on New Uses. Sec. 577. Rules of Construction	(c) Promulgate regulations on off-label information program.
11/21/98	Sec. 401. Dissemination of Information on New Uses. Sec. 577. Rules of Construction	(d) This section takes effect one year after date of enactment.
11/21/98	Sec. 404. Dispute Resolution. Sec. 562. Dispute Resolution.	The agency must develop regulations establishing procedures under which applicants, if a scientific controversy arises over a drug or device issue, may request a review of the scientific matter.
11/21/98	Sec. 406. Food and Drug Administration Mission and Annual Report	(f) Publish in the <i>Federal Register</i> a plan to bring FDA into compliance with all its statutory obligations.
11/21/98	Sec. 407. Information System. Sec. 741. Information System.	(b) Report to Congress on the status, costs, and confidentiality concerns of establishing an information system designed to track the progress of applications or submissions to the agency.
11/29/98	Sec. 104. Annual Reports	(a) Report on how well the agency met PDUFA goals for FY 1998.
1/28/99	Sec. 104. Annual Reports	(b) Report on use of PDUFA funds for FY 1999.

2/1/99	Sec. 309. Food Contact Substances	(b)(5)(C) Report to Congress estimating the costs of implementing the food contact substance notification program for the next fiscal year.
5/21/99	Sec. 122. Requirements for Radiopharmaceuticals	(a)(1)(B) Issue final regulations on approval procedures for radiopharmaceuticals.
5/21/99	Sec. 129. Regulations for Sunscreen Products	Issue regulations for over-the-counter sunscreen products for the prevention and treatment of sunburn.
7/1/99	Sec. 406. Food and Drug Administration Mission and Annual Report	(b) Establish mechanisms for meeting the review times specified in the act.
11/21/99	Sec. 113. Information Program on Clinical Trials for Serious or Life-threatening Diseases	(b)(2) Report to Congress of any public health need, or of any adverse impact on research/innovation of devices, if information on device investigations were included in the data bank on clinical trials for drugs for serious or life threatening diseases.
11/21/99 or when FDA implements regulations.	Sec. 116. Manufacturing Changes for Drugs	(b) Develop regulations implementing provisions on manufacturing changes.
11/21/99	Sec. 121. Positron Emission Tomography	(c)(1) Publish the requirements for approval procedures and current good manufacturing practices for compounded PET.
11/21/99	Sec. 213. Reports	(c) Submit a report to Congress describing the plan and progress of a program that would track device-caused deaths and serious illnesses or injuries in a representative number of device user facilities.

11/21/99	Sec. 413. Food and Drug Administration Study of Mercury Compounds in Drugs and Foods	Develop a list of drugs and foods that contain intentionally introduced mercury compounds and provide an analysis of those compounds.
11/29/99	Sec. 104. Annual Reports	(a) Report on how well the agency met PDUFA goals for FY 1999.
1/1/2000	Sec. 406. Food and Drug Administration Mission and Annual Report	The agency plan objectives should address eliminating backlogs in the review of applications and submissions.
1/28/00	Sec. 104. Annual Reports	(b) Report on use of PDUFA funds for FY 1999.
2/1/00	Sec. 309. Food Contact Substances	(b)(5)(C) Report to Congress estimating the costs of implementing the notification program for food contact substances for the next fiscal year.
7/1/00	Sec. 405. Informal Agency Statements	Publish in the <i>Federal Register</i> a list of guidance documents and update the list electronically, thereafter.
11/21/00	Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports. (d) Reports on Program Accreditation; (2) Inclusion of Certain Devices Within Program	Submit a report to Congress on whether the accreditation program should be eliminated.
11/29/00	Sec. 104. Annual Reports	(a) Report on how well the agency met PDUFA goals for FY 2000.

1/1/01	Sec. 111. Pediatric Studies of Drugs	(k) Report to Congress on the effectiveness and adequacy of the incentives for the pediatric drug program. The assessment should also include an assessment of the economic impact of the program on taxpayers and consumers, comparisons with costs of generic drugs, and suggestions for modifications of the program.
1/28/01	Sec. 104. Annual Reports	(b) Report on use of PDUFA funds for FY 2000.
2/1/01	Sec. 309. Food Contact Substances	(b)(5)(C) Report to Congress estimating the costs of implementing the notification program for food contact substances for the next fiscal year.
10/1/01	Sec. 130. Reports of Postmarketing Approval Studies	(b) Report to Congressional Committees, giving a summary and evaluation of industry performance in post marketing studies.
11/21/01 ²	Sec. 121. Positron Emission Tomography	The Secretary will no longer require (sunset) submission of applications for PET drugs.
11/29/01	Sec. 104. Annual Reports	(a) Report on how well the agency met PDUFA goals for FY 2001.
1/1/02	Sec. 401. Dissemination of Information on New Uses. Sec. 557. Rules of Construction.	(f)(1)(B) The General Accounting Office (GAO) must submit to Congress an evaluation of the impact of off-label information dissemination on the resources of DHHS.
1/28/02	Sec. 104. Annual Reports	(a) Report on use of PDUFA funds for FY 2001.

² Either 4 years after enactment or 2 years after establishing procedures for compounded PET drugs whichever is later.

2/1/02	Sec. 309. Food Contact Substances	(b)(5)(C) Report to Congress estimating the costs of implementing the notification program for food contact substances for the next fiscal year.
5/21/02	Sec. 114. Health Care Economic Information	(b) The General Accounting Office (GAO) shall study and report to Congress on the implementation of these provisions.
11/21/02	Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports. (d) Reports on Program Accreditation; (1) Comptroller General	(d)(1)(A) The General Accounting Office (GAO) must report to Congress on how well the agency implements the accreditation program for medical device reviewers (based on information to be provided by FDA).
11/29/02	Sec. 104. Annual Reports	(b) Report on how well the agency met PDUFA goals for FY 2002.
1/1/03	Sec. 308. Glass and Ceramic Ware	The Secretary may not take any action to ban lead- and cadmium-based enamel ceramic ware until this date. Regulations, if promulgated, cannot be implemented before one year after the final regulation is published.
1/28/03	Sec. 104. Annual Reports	(b) Report on use of PDUFA funds for the FY 2002.
2/1/03	Sec. 309. Food Contact Substances	(b)(5)(C) Report to Congress estimating the costs of implementing the notification program for the next fiscal year.
9/30/05	Sec. 401. Dissemination of Information on New Uses. Sec. 557. Rules of Construction	(f)(3)(A) Completion by the Institute of Medicine (IOM) of a study on the scientific issues raised by dissemination of off-label information program.

9/30/06 or 7 years after regulations are promulgated	Sec. 401. Dissemination of Information on New Uses. Sec. 557. Rules of Construction	(e) Cessation of the off-label information program (sunsets).
REQUIRED ACTIONS WITH CONDITIONAL OR NONSPECIFIED DEADLINES		
	Sec. 115. Clinical Investigations	(b) After consulting with the National Institutes of Health (NIH) and the drug industry, develop guidance to industry for inclusion of women and minorities in clinical trials.
	Sec. 119. Content and Review of Applications	(a) Issue guidance to FDA reviewers relating to standards used to review NDAs or biologic licenses.
	Sec. 123. Modernization of Regulation	(a) Establish, by regulation, requirements for the approval, suspension, and revocation of biologic licenses and eliminate existing license requirement.
	Sec. 125. Insulin and Antibiotics	(d)(3) Publish the established name of each antibiotic drug for which application was received by FDA under Section 507 before this Act repeals this provision.
	Sec. 127. Application of Federal Law to Practice of Pharmacy Compounding	(b)(3) Develop regulations in consultation with the National Association of Boards of Pharmacy to implement a standard memorandum of understanding for use by states.
	Sec. 130. Reports of Postmarketing Approval Studies	(a)(2)(c) Publish in the <i>Federal Register</i> an annual report that gives the status of postmarketing studies.
	Sec. 131. Notification of Discontinuance of a Life-Saving Product	Begin distributing, as much as possible, to appropriate physicians and patient organizations, information on the discontinuance of a drug.

	Sec. 204. Device Standards	(a) Publish in the <i>Federal Register</i> the acceptable international standards that, if met, could be used to meet a premarket submission requirement for devices.
Annually	Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports	(b)(2)(D) Include in the annual report to Congress, the names of all accredited persons who are certified to review medical device applications and the names of those whose accreditation has been withdrawn.
	Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports. (c) Duration	Authority for the accreditation program ends (sunsets) 5 years after Congress is notified that two or more accredited groups are available to review 60% or more of premarket notifications, or 4 years after FDA has made decisions for 35% of devices subject to premarket notification, whichever occurs first.
	Sec. 210. Accreditation of Persons for Review of Premarket Notification Reports. (d) Reports on Program Accreditation; (1) Comptroller General	(d)(1)(B) The General Accounting Office (GAO) must evaluate the use of accredited persons and present a report to Congress.
	Sec. 301. Flexibility for Regulations Regarding Claims	Propose regulations on nutrition information.
	Sec. 302. Petitions for Claims	If FDA formally proposes to regulate a health claim for a food product, rule making must be completed within 18 months, or, FDA must report to Congress the reason why it is not regulating a claim.

	Sec. 402. Expanded Access to Investigational Therapies and Diagnostics	Inform national, state, and local medical associations and voluntary health organizations of investigational drugs or devices in clinical trials. Expanded access may be terminated if FDA does not meet these requirements.
	Sec. 402. Expanded Access to Investigational Therapies and Diagnostics	By regulation, the Secretary will define “investigational drug and device” and “treatment investigational exemption.”
	Sec. 403. Approval of Supplemental Applications for Approved Products	Implement programs to foster collaboration between FDA, NIH, and other health organizations, to identify studies that may support supplemental applications.
	Sec. 405. Informal Agency Statements	Publish in the <i>Federal Register</i> a list of guidance documents and update that list electronically.
Annually	Sec. 406. Food and Drug Administration Mission and Annual Report	Publish in the <i>Federal Register</i> an annual report providing statistical information on FDA’s performance under the implementation plan.
	Sec. 413. Food and Drug Administration Study of Mercury Compounds in Drugs and Foods	Study the effect on humans of the use of mercury compounds in nasal sprays.
	Sec. 413. Food and Drug Administration Study of Mercury Compounds in Drugs and Foods	Study the effects on humans (include children and other sensitive populations) of elemental, organic, or inorganic mercury contained in drugs and dietary supplements, and evaluate its adverse effects. If adverse effects are found, restrict its use.

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