

RISK MANAGEMENT

FDA Amendments Act of 2007

TITLE IX - ENHANCED AUTHORITIES REGARDING
POSTMARKET SAFETY OF DRUGS

SUBTITLE A- POSTMARKET STUDIES
AND SURVEILLANCE

SUBTITLE B- OTHER PROVISIONS TO
ENSURE DRUG SAFETY
AND SURVEILLANCE

Products Deemed to Have REMS
(as published in the Federal
Register, March 27, 2008)

IDENTIFICATION OF DRUG AND BIOLOGICAL
PRODUCTS DEEMED TO HAVE RISK EVALUATION
AND MITIGATION STRATEGIES (REMS) FOR
PURPOSES OF THE FOOD AND DRUG
ADMINISTRATION AMENDMENTS ACT OF 2007

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Preface

Congress and the Food and Drug Administration are increasingly focused on drug safety and risk management. With the passage of the Food and Drug Administration Amendments Act (FDAAA) in September 2007, the FDA is reauthorized with current and additional statutory authority for the next five years. An important new section of this public law (Title IX) deals specifically with risk management and serves to update and supplement the three Risk Management guidance documents issued in March 2005.

The new law also gives further authority to the FDA to enforce post-market safety and impose fines if the safety plans are not fully implemented. Importantly, FDAAA strengthens FDA's ability to request post-market safety studies for drugs that have already been approved.

In this volume you will find that FDA also has several new powers of enforcement for risk management, including civil monetary penalties. It introduces a new term to the risk management lexicon, "Risk Evaluation and Mitigation Strategies (REMS)." FDA is still developing guidances for this public law. These are much needed to explain the complexities of REMS in relation to the standard RiskMAPs (which were solidified with the above mentioned guidances in 2005). In the meantime, readers must draw upon precedents and experience, such as that accumulated by UBC, where we have worked on over 30 risk management programs.

In March 2008, the FDA released a list of 16 products which are deemed to have REMS because their RiskMAPs include elements to assure safe use. In releasing the list, the FDA gave the first indication

that REMS may be interpreted as being the most restrictive RiskMAPs, which link targeted outreach and training or specific tests with product distribution (e.g., performance linked access systems). We anticipate further direction from the FDA and guidance documents to be available in 2008 and 2009

We hope you find this copy of the public law helpful in understanding risk management and FDA regulatory requests in post-marketing risk management.



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FDA Amendments Act of 2007.

TITLE IX—ENHANCED AUTHORITIES REGARDING POSTMARKET SAFETY OF DRUGS

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Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for Purposes of the Food and Drug Administration Amendments Act of 2007

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TITLE IX—ENHANCED AUTHORITIES REGARDING POSTMARKET SAFETY OF DRUGS

Subtitle A—Postmarket Studies and Surveillance

Sec. 901. Postmarket Studies And Clinical Trials Re-
garding Human Drugs; Risk Evaluation And Mitigation
Strategies.

(a) IN GENERAL.—Section 505 of the Federal Food,
Drug, and Cosmetic Act (21 U.S.C. 355) is amended
by adding at the end the following subsections:

**“(o) POSTMARKET STUDIES AND CLINICAL
TRIALS; LABELING.**—

“(1) IN GENERAL.—A responsible person may not
introduce or deliver for introduction into interstate
commerce the new drug involved if the person is in
violation of a requirement established under para-
graph (3) or (4) with respect to the drug.

“(2) DEFINITIONS.—For purposes of this subsec-
tion:

“(A) RESPONSIBLE PERSON.—The term ‘respon-
sible person’ means a person who—

**“(i) has submitted to the Secretary a covered
application that is pending; or 42 USC 282 note.**

**“(ii) is the holder of an approved covered applica-
tion.**

“(B) COVERED APPLICATION.—The term ‘covered
application’ means—

**“(i) an application under subsection (b) for a drug
that is subject to section 503(b); and**

**“(ii) an application under section 351 of the Public
Health Service Act.**

“(C) NEW SAFETY INFORMATION; SERIOUS RISK.—The terms ‘new safety information’, ‘serious risk’, and ‘signal of a serious risk’ have the meanings given such terms in section 505–1(b).

“(3) STUDIES AND CLINICAL TRIALS.—

“(A) IN GENERAL.—For any or all of the purposes specified in subparagraph (B), the Secretary may, subject to subparagraph (D), require a responsible person for a drug to conduct a postapproval study or studies of the drug, or a postapproval clinical trial or trials of the drug, on the basis of scientific data deemed appropriate by the Secretary, including information regarding chemically-related or pharmacologically-related drugs.

“(B) PURPOSES OF STUDY OR CLINICAL TRIAL.—The purposes referred to in this subparagraph with respect to a postapproval study or postapproval clinical trial are the following:

“(i) To assess a known serious risk related to the use of the drug involved.

“(ii) To assess signals of serious risk related to the use of the drug.

“(iii) To identify an unexpected serious risk when available data indicates the potential for a serious risk.

“(C) ESTABLISHMENT OF REQUIREMENT AFTER APPROVAL OF COVERED APPLICATION.—The Secretary may require a postapproval study or studies or postapproval clinical trial or trials for a drug for which an approved covered application is in effect as of the date on which the Secretary seeks to establish such requirement only if the Secretary becomes aware of new safety information.

“(D) DETERMINATION BY SECRETARY.—

“(i) POSTAPPROVAL STUDIES.—The Secretary may not require the responsible person to conduct a study under this paragraph, unless the Secretary makes a determination that the reports under subsection (k)(1) and the active postmarket risk identification and analysis system as available under subsection (k)(3) will not be sufficient to meet the purposes set forth in subparagraph (B).

“(ii) POSTAPPROVAL CLINICAL TRIALS.—The Secretary may not require the responsible person to conduct a clinical trial under this paragraph, unless the Secretary makes a determination that a postapproval study or studies will not be sufficient to meet the purposes set forth in subparagraph (B).

“(E) NOTIFICATION; TIMETABLES; PERIODIC REPORTS.—

“(i) NOTIFICATION.—The Secretary shall notify the responsible person regarding a requirement under this paragraph to conduct a postapproval study or clinical trial by the target dates for communication of feedback from the review team to the responsible person regarding proposed labeling and postmarketing study commitments as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

“(ii) TIMETABLE; PERIODIC REPORTS.—For each study or clinical trial required to be conducted under this paragraph, the Secretary shall require that the responsible person submit a timetable for completion of the study or clinical trial. With respect to each study required to be conducted under this paragraph or otherwise undertaken by the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such study including whether any difficulties in completing the study have been encountered. With respect to each clinical trial required to be conducted under this paragraph or otherwise undertaken by

the responsible person to investigate a safety issue, the Secretary shall require the responsible person to periodically report to the Secretary on the status of such clinical trial including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to the requirements under section 402(j) of the Public Health Service Act. If the responsible person fails to comply with such timetable or violates any other requirement of this subparagraph, the responsible person shall be considered in violation of this subsection, unless the responsible person demonstrates good cause for such noncompliance or such other violation. The Secretary shall determine what constitutes good cause under the preceding sentence.

“(F) DISPUTE RESOLUTION.—The responsible person may appeal a requirement to conduct a study or clinical trial under this paragraph using dispute resolution procedures established by the Secretary in regulation and guidance.

“(4) SAFETY LABELING CHANGES REQUESTED BY SECRETARY.—

“(A) NEW SAFETY INFORMATION.—If the Secretary becomes aware of new safety information that the Secretary believes should be included in the labeling of the drug, the Secretary shall promptly notify the responsible person or, if the same drug approved under section 505(b) is not currently marketed, the holder of an approved application under 505(j).

“(B) RESPONSE TO NOTIFICATION.—Following notification pursuant to subparagraph (A), the responsible person or the holder of the approved application under section 505(j) shall within 30 days—

“(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, con-

traindications, warnings, precautions, or adverse reactions; or

“(ii) notify the Secretary that the responsible person or the holder of the approved application under section 505(j) does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

“(C) REVIEW.—Upon receipt of such supplement, the Secretary shall promptly review and act upon such supplement. If the Secretary disagrees with the proposed changes in the supplement or with the statement setting forth the reasons why no labeling change is necessary, the Secretary shall initiate discussions to reach agreement on whether the labeling for the drug should be modified to reflect the new safety information, and if so, the contents of such labeling changes.

“(D) DISCUSSIONS.—Such discussions shall not extend for more than 30 days after the response to the notification under subparagraph (B), unless the Secretary determines an extension of such discussion period is warranted.

“(E) ORDER.—Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person or the holder of the approved application under section 505(j) to make such a labeling change as the Secretary deems appropriate to address the new safety information. Within 15 days of such an order, the responsible person or the holder of the approved application under section 505(j) shall submit a supplement containing the labeling change.

“(F) DISPUTE RESOLUTION.—Within 5 days of receiving an order under subparagraph (E), the responsible person or the holder of the approved application under section 505(j) may appeal using dispute resolution procedures established by the Secretary in regulation and guidance.

“(G) VIOLATION.—If the responsible person or the holder of the approved application under section 505(j) has not submitted a supplement within 15 days of the date of such order under subparagraph (E), and there is no appeal or dispute resolution proceeding pending, the responsible person or holder shall be considered to be in violation of this subsection. If at the conclusion of any dispute resolution procedures the Secretary determines that a supplement must be submitted and such a supplement is not submitted within 15 days of the date of that determination, the responsible person or holder shall be in violation of this subsection.

“(H) PUBLIC HEALTH THREAT.—Notwithstanding subparagraphs (A) through (F), if the Secretary concludes that such a labeling change is necessary to protect the public health, the Secretary may accelerate the timelines in such subparagraphs.

“(I) RULE OF CONSTRUCTION.—This paragraph shall not be construed to affect the responsibility of the responsible person or the holder of the approved application under section 505(j) to maintain its label in accordance with existing requirements, including subpart B of part 201 and sections 314.70 and 601.12 of title 21, Code of Federal Regulations (or any successor regulations).

“(5) NON-DELEGATION.—Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

“(p) RISK EVALUATION AND MITIGATION STRATEGY.—

“(1) IN GENERAL.—A person may not introduce or deliver for introduction into interstate commerce a new drug if—

“(A)(i) the application for such drug is approved under subsection (b) or (j) and is subject to section 503(b); or

“(ii) the application for such drug is approved under section 351 of the Public Health Service Act; and

“(B) a risk evaluation and mitigation strategy is required under section 505–1 with respect to the drug and the person fails to maintain compliance with the requirements of the approved strategy or with other requirements under section 505–1, including requirements regarding assessments of approved strategies.

“(2) CERTAIN POSTMARKET STUDIES.—The failure to conduct a postmarket study under section 506, subpart H of part 314, or subpart E of part 601 of title 21, Code of Federal Regulations (or any successor regulations), is deemed to be a violation of paragraph (1).”.

(b) REQUIREMENTS REGARDING STRATEGIES.—Chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended by inserting after section 505 the following section:

“Sec. 505–1. Risk Evaluation And Mitigation Strategies.

“(a) SUBMISSION OF PROPOSED STRATEGY.—

“(1) INITIAL APPROVAL.—If the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, determines that a risk evaluation and mitigation strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug, and informs the person who submits such application of such determination, then such person shall submit to the Secretary as part of such application a proposed risk evaluation and mitigation strategy. In making such a determination, the Secretary shall consider the following factors:

“(A) The estimated size of the population likely to use the drug involved.

“(B) The seriousness of the disease or condition that is to be treated with the drug.

“(C) The expected benefit of the drug with respect to such disease or condition.

“(D) The expected or actual duration of treatment with the drug.

“(E) The seriousness of any known or potential adverse events that may be related to the drug and the background incidence of such events in the population likely to use the drug.

“(F) Whether the drug is a new molecular entity.

“(2) POSTAPPROVAL REQUIREMENT.—

“(A) IN GENERAL.—If the Secretary has approved a covered application (including an application approved before the effective date of this section) and did not when approving the application require a risk evaluation and mitigation strategy under paragraph (1), the Secretary, in consultation with the offices described in paragraph (1), may subsequently require such a strategy for the drug involved (including when acting on a supplemental application seeking approval of a new indication for use of the drug) if the Secretary becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks of the drug.

“(B) SUBMISSION OF PROPOSED STRATEGY.—Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other reasonable time as the Secretary requires to protect the public health, the holder shall

submit to the Secretary a proposed risk evaluation and mitigation strategy.

“(3) ABBREVIATED NEW DRUG APPLICATIONS.—The applicability of this section to an application under section 505(j) is subject to subsection (i).

“(4) NON-DELEGATION.—Determinations by the Secretary under this subsection for a drug shall be made by individuals at or above the level of individuals empowered to approve a drug (such as division directors within the Center for Drug Evaluation and Research).

“(b) DEFINITIONS.—For purposes of this section:

“(1) ADVERSE DRUG EXPERIENCE.—The term ‘adverse drug experience’ means any adverse event associated with the use of a drug in humans, whether or not considered drug related, including—

“(A) an adverse event occurring in the course of the use of the drug in professional practice;

“(B) an adverse event occurring from an overdose of the drug, whether accidental or intentional;

“(C) an adverse event occurring from abuse of the drug;

“(D) an adverse event occurring from withdrawal of the drug; and

“(E) any failure of expected pharmacological action of the drug.

“(2) COVERED APPLICATION.—The term ‘covered application’ means an application referred to in section 505(p)(1)(A).

“(3) NEW SAFETY INFORMATION.—The term ‘new safety information’, with respect to a drug, means

information derived from a clinical trial, an adverse event report, a postapproval study (including a study under section 505(o)(3)), or peerreviewed biomedical literature; data derived from the postmarket risk identification and analysis system under section 505(k); or other scientific data deemed appropriate by the Secretary about—

“(A) a serious risk or an unexpected serious risk associated with use of the drug that the Secretary has become aware of (that may be based on a new analysis of existing information) since the drug was approved, since the risk evaluation and mitigation strategy was required, or since the last assessment of the approved risk evaluation and mitigation strategy for the drug; or

“(B) the effectiveness of the approved risk evaluation and mitigation strategy for the drug obtained since the last assessment of such strategy.

“(4) SERIOUS ADVERSE DRUG EXPERIENCE.—The term ‘serious adverse drug experience’ is an adverse drug experience that—

“(A) results in—

“(i) death;

“(ii) an adverse drug experience that places the patient at immediate risk of death from the adverse drug experience as it occurred (not including an adverse drug experience that might have caused death had it occurred in a more severe form);

“(iii) inpatient hospitalization or prolongation of existing hospitalization;

“(iv) a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions; or

“(v) a congenital anomaly or birth defect; or

“(B) based on appropriate medical judgment, may jeopardize the patient and may require a medical or surgical intervention to prevent an outcome described under subparagraph (A).

“(5) SERIOUS RISK.—The term ‘serious risk’ means a risk of a serious adverse drug experience.

“(6) SIGNAL OF A SERIOUS RISK.—The term ‘signal of a serious risk’ means information related to a serious adverse drug experience associated with use of a drug and derived from—

“(A) a clinical trial;

“(B) adverse event reports;

“(C) a postapproval study, including a study under section 505(o)(3);

“(D) peer-reviewed biomedical literature;

“(E) data derived from the postmarket risk identification and analysis system under section 505(k)(4); or

“(F) other scientific data deemed appropriate by the Secretary.

“(7) RESPONSIBLE PERSON.—The term ‘responsible person’ means the person submitting a covered application or the holder of the approved such application.

“(8) UNEXPECTED SERIOUS RISK.—The term ‘unexpected serious risk’ means a serious adverse drug experience that is not listed in the labeling of a drug, or that may be symptomatically and pathophysiologically related to an adverse drug experience identified in the labeling, but differs from such adverse drug experience because of greater severity, specificity, or prevalence.

“(c) CONTENTS.—A proposed risk evaluation and mitigation strategy under subsection (a) shall—

“(1) include the timetable required under subsection (d); and

“(2) to the extent required by the Secretary, in consultation with the office responsible for reviewing the drug and the office responsible for postapproval safety with respect to the drug, include additional elements described in subsections (e) and (f).

“(d) MINIMAL STRATEGY.—For purposes of subsection (c)(1), the risk evaluation and mitigation strategy for a drug shall require a timetable for submission of assessments of the strategy that—

“(1) includes an assessment, by the date that is 18 months after the strategy is initially approved;

“(2) includes an assessment by the date that is 3 years after the strategy is initially approved;

“(3) includes an assessment in the seventh year after the strategy is so approved; and

“(4) subject to paragraphs (1), (2), and (3)—

“(A) is at a frequency specified in the strategy;

“(B) is increased or reduced in frequency as necessary as provided for in subsection (g)(4)(A); and

“(C) is eliminated after the 3-year period described in paragraph (1) if the Secretary determines that serious risks of the drug have been adequately identified and assessed and are being adequately managed.

“(e) ADDITIONAL POTENTIAL ELEMENTS OF STRATEGY.—

“(1) IN GENERAL.—The Secretary, in consultation with the offices described in subsection (c)(2), may under such subsection require that the risk evaluation and mitigation strategy for a drug include 1 or

more of the additional elements described in this subsection if the Secretary makes the determination required with respect to each element involved.

“(2) MEDICATION GUIDE; PATIENT PACKAGE INSERT.—The risk evaluation and mitigation strategy for a drug may require that, as applicable, the responsible person develop for distribution to each patient when the drug is dispensed—

“(A) a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations); and

“(B) a patient package insert, if the Secretary determines that such insert may help mitigate a serious risk of the drug.

“(3) COMMUNICATION PLAN.—The risk evaluation and mitigation strategy for a drug may require that the responsible person conduct a communication plan to health care providers, if, with respect to such drug, the Secretary determines that such plan may support implementation of an element of the strategy (including under this paragraph). Such plan may include—

“(A) sending letters to health care providers;

“(B) disseminating information about the elements of the risk evaluation and mitigation strategy to encourage implementation by health care providers of components that apply to such health care providers, or to explain certain safety protocols (such as medical monitoring by periodic laboratory tests); or

“(C) disseminating information to health care providers through professional societies about any serious risks of the drug and any protocol to assure safe use.

“(f) PROVIDING SAFE ACCESS FOR PATIENTS TO DRUGS WITH KNOWN SERIOUS RISKS THAT WOULD OTHERWISE BE UNAVAILABLE.—

“(1) ALLOWING SAFE ACCESS TO DRUGS WITH KNOWN SERIOUS RISKS.—The Secretary, in consultation with the offices described in subsection (c) (2), may require that the risk evaluation and mitigation strategy for a drug include such elements as are necessary to assure safe use of the drug, because of its inherent toxicity or potential harmfulness, if the Secretary determines that—

“(A) the drug, which has been shown to be effective, but is associated with a serious adverse drug experience, can be approved only if, or would be withdrawn unless, such elements are required as part of such strategy to mitigate a specific serious risk listed in the labeling of the drug; and

“(B) for a drug initially approved without elements to assure safe use, other elements under subsections (c), (d), and (e) are not sufficient to mitigate such serious risk.

“(2) ASSURING ACCESS AND MINIMIZING BURDEN.—Such elements to assure safe use under paragraph (1) shall—

“(A) be commensurate with the specific serious risk listed in the labeling of the drug;

“(B) within 30 days of the date on which any element under paragraph (1) is imposed, be posted publicly by the Secretary with an explanation of how such elements will mitigate the observed safety risk;

“(C) considering such risk, not be unduly burdensome on patient access to the drug, considering in particular—

“(i) patients with serious or life-threatening diseases or conditions; and

“(ii) patients who have difficulty accessing health care (such as patients in rural or medically underserved areas); and

“(D) to the extent practicable, so as to minimize the burden on the health care delivery system—

“(i) conform with elements to assure safe use for other drugs with similar, serious risks; and

“(ii) be designed to be compatible with established distribution, procurement, and dispensing systems for drugs.

“(3) ELEMENTS TO ASSURE SAFE USE.—The elements to assure safe use under paragraph (1) shall include 1 or more goals to mitigate a specific serious risk listed in the labeling of the drug and, to mitigate such risk, may require that—

“(A) health care providers who prescribe the drug have particular training or experience, or are specially certified (the opportunity to obtain such training or certification with respect to the drug shall be available to any willing provider from a frontier area in a widely available training or certification method (including an on-line course or via mail) as approved by the Secretary at reasonable cost to the provider);

“(B) pharmacies, practitioners, or health care settings that dispense the drug are specially certified (the opportunity to obtain such certification shall be available to any willing provider from a frontier area);

“(C) the drug be dispensed to patients only in certain health care settings, such as hospitals;

“(D) the drug be dispensed to patients with evidence or other documentation of safe-use conditions, such as laboratory test results;

“(E) each patient using the drug be subject to certain monitoring; or

“(F) each patient using the drug be enrolled in a registry.

“(4) IMPLEMENTATION SYSTEM.—The elements to assure safe use under paragraph (1) that are described in subparagraphs (B), (C), and (D) of paragraph (3) may include a system through which the applicant is able to take reasonable steps to—

“(A) monitor and evaluate implementation of such elements by health care providers, pharmacists, and other parties in the health care system who are responsible for implementing such elements; and

“(B) work to improve implementation of such elements by such persons.

“(5) EVALUATION OF ELEMENTS TO ASSURE SAFE USE.—The Secretary, through the Drug Safety and Risk Management Advisory Committee (or successor committee) of the Food and Drug Administration, shall—

“(A) seek input from patients, physicians, pharmacists, and other health care providers about how elements to assure safe use under this subsection for 1 or more drugs may be standardized so as not to be—

“(i) unduly burdensome on patient access to the drug; and

“(ii) to the extent practicable, minimize the burden on the health care delivery system;

“(B) at least annually, evaluate, for 1 or more drugs, the elements to assure safe use of such drug to assess whether the elements—

“(i) assure safe use of the drug;

“(ii) are not unduly burdensome on patient access to the drug; and

“(iii) to the extent practicable, minimize the burden on the health care delivery system; and

“(C) considering such input and evaluations—

“(i) issue or modify agency guidance about how to implement the requirements of this subsection; and

“(ii) modify elements under this subsection for 1 or more drugs as appropriate.

“(6) ADDITIONAL MECHANISMS TO ASSURE ACCESS.—The mechanisms under section 561 to provide for expanded access for patients with serious or life-threatening diseases or conditions may be used to provide access for patients with a serious or life-threatening disease or condition, the treatment of which is not an approved use for the drug, to a drug that is subject to elements to assure safe use under this subsection. The Secretary shall promulgate regulations for how a physician may provide the drug under the mechanisms of section 561.

“(7) WAIVER IN PUBLIC HEALTH EMERGENCIES.—The Secretary may waive any requirement of this subsection during the period described in section 319(a) of the Public Health Service Act with respect to a qualified countermeasure described under section 319F–1(a)(2) of such Act, to which a requirement under this subsection has been applied, if the Secretary has—

“(A) declared a public health emergency under such section 319; and

“(B) determined that such waiver is required to mitigate the effects of, or reduce the severity of, such public health emergency.

“(8) LIMITATION.—No holder of an approved covered application shall use any element to assure

safe use required by the Secretary under this subsection to block or delay approval of an application under section 505(b)(2) or (j) or to prevent application of such element under subsection (i)(1)(B) to a drug that is the subject of an abbreviated new drug application.

“(g) ASSESSMENT AND MODIFICATION OF APPROVED STRATEGY.—

“(1) VOLUNTARY ASSESSMENTS.—After the approval of a risk evaluation and mitigation strategy under subsection (a), the responsible person involved may, subject to paragraph (2), submit to the Secretary an assessment of, and propose a modification to, the approved strategy for the drug involved at any time.

“(2) REQUIRED ASSESSMENTS.—A responsible person shall, subject to paragraph (5), submit an assessment of, and may propose a modification to, the approved risk evaluation and mitigation strategy for a drug—

“(A) when submitting a supplemental application for a new indication for use under section 505(b) or under section 351 of the Public Health Service Act, unless the drug is not subject to section 503(b) and the risk evaluation and mitigation strategy for the drug includes only the timetable under subsection (d);

“(B) when required by the strategy, as provided for in such timetable under subsection (d);

“(C) within a time period to be determined by the Secretary, if the Secretary, in consultation with the offices described in subsection (c)(2), determines that new safety or effectiveness information indicates that—

“(i) an element under subsection (d) or (e) should be modified or included in the strategy; or

“(ii) an element under subsection (f) should be modified or included in the strategy; or

“(D) within 15 days when ordered by the Secretary, in consultation with the offices described in subsection (c)(2), if the Secretary determines that there may be a cause for action by the Secretary under section 505(e).

“(3) REQUIREMENTS FOR ASSESSMENTS.—An assessment under paragraph (1) or (2) of an approved risk evaluation and mitigation strategy for a drug shall include—

“(A) with respect to any goal under subsection (f), an assessment of the extent to which the elements to assure safe use are meeting the goal or whether the goal or such elements should be modified;

“(B) with respect to any postapproval study required under section 505(o) or otherwise undertaken by the responsible person to investigate a safety issue, the status of such study, including whether any difficulties completing the study have been encountered; and

“(C) with respect to any postapproval clinical trial required under section 505(o) or otherwise undertaken by the responsible party to investigate a safety issue, the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act.

“(4) MODIFICATION.—A modification (whether an enhancement or a reduction) to the approved risk evaluation and mitigation strategy for a drug may include the addition or modification of any element under subsection (d) or the addition, modification,

or removal of any element under subsection (e) or (f), such as—

“(A) modifying the timetable for assessments of the strategy as provided in subsection (d)(3), including to eliminate assessments; or

“(B) adding, modifying, or removing an element to assure safe use under subsection (f).

“(h) REVIEW OF PROPOSED STRATEGIES; REVIEW OF ASSESSMENTS OF APPROVED STRATEGIES.—

“(1) IN GENERAL.—The Secretary, in consultation with the offices described in subsection (c)(2), shall promptly review each proposed risk evaluation and mitigation strategy for a drug submitted under subsection (a) and each assessment of an approved risk evaluation and mitigation strategy for a drug submitted under subsection (g).

“(2) DISCUSSION.—The Secretary, in consultation with the offices described in subsection (c)(2), shall initiate discussions with the responsible person for purposes of this subsection to determine a strategy not later than 60 days after any such assessment is submitted or, in the case of an assessment submitted under subsection (g)(2)(D), not later than 30 days after such assessment is submitted.

“(3) ACTION.—

“(A) IN GENERAL.—Unless the dispute resolution process described under paragraph (4) or (5) applies, the Secretary, in consultation with the offices described in subsection (c)(2), shall describe any required risk evaluation and mitigation strategy for a drug, or any modification to any required strategy—

“(i) as part of the action letter on the application, when a proposed strategy is submitted under subsection (a) or a modification to the strategy is

proposed as part of an assessment of the strategy submitted under subsection (g)(1); or

“(ii) in an order issued not later than 90 days after the date discussions of such modification begin under paragraph (2), when a modification to the strategy is proposed as part of an assessment of the strategy submitted under subsection (g)(1) or under any of subparagraphs (B) through (D) of subsection (g)(2).

“(B) INACTION.—An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided under subparagraph (A).

“(C) PUBLIC AVAILABILITY.—Any action letter described in subparagraph (A)(i) or order described in subparagraph (A)(ii) shall be made publicly available.

“(4) DISPUTE RESOLUTION AT INITIAL APPROVAL.—If a proposed risk evaluation and mitigation strategy is submitted under subsection (a) (1) in an application for initial approval of a drug and there is a dispute about the strategy, the responsible person shall use the major dispute resolution procedures as set forth in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007.

“(5) DISPUTE RESOLUTION IN ALL OTHER CASES.—

“(A) REQUEST FOR REVIEW.—

“(i) IN GENERAL.—Not earlier than 15 days, and not later than 35 days, after discussions under paragraph (2) have begun, the responsible person may request in writing that a dispute about the strategy be reviewed by the Drug Safety Oversight Board under subsection (j), except that the determination of the Secretary to require a risk evaluation and mitigation strategy is not subject to review under

this paragraph. The preceding sentence does not prohibit review under this paragraph of the particular elements of such a strategy.

“(ii) SCHEDULING.—Upon receipt of a request under clause (i), the Secretary shall schedule the dispute involved for review under subparagraph (B) and, not later than 5 business days of scheduling the dispute for review, shall publish by posting on the Internet or otherwise a notice that the dispute will be reviewed by the Drug Safety Oversight Board.

“(B) SCHEDULING REVIEW.—If a responsible person requests review under subparagraph (A), the Secretary—

“(i) shall schedule the dispute for review at 1 of the next 2 regular meetings of the Drug Safety Oversight Board, whichever meeting date is more practicable; or

“(ii) may convene a special meeting of the Drug Safety Oversight Board to review the matter more promptly, including to meet an action deadline on an application (including a supplemental application).

“(C) AGREEMENT AFTER DISCUSSION OR ADMINISTRATIVE APPEALS.—

“(i) FURTHER DISCUSSION OR ADMINISTRATIVE APPEALS.—A request for review under subparagraph (A) shall not preclude further discussions to reach agreement on the risk evaluation and mitigation strategy, and such a request shall not preclude the use of administrative appeals within the Food and Drug Administration to reach agreement on the strategy, including appeals as described in the letters described in section 101(c) of the Food and Drug Administration Amendments Act of 2007 for procedural or scientific matters involving the review of human drug applications and supplemental ap-

plications that cannot be resolved at the divisional level. At the time a review has been scheduled under subparagraph (B) and notice of such review has been posted, the responsible person shall either withdraw the request under subparagraph (A) or terminate the use of such administrative appeals.

“(ii) AGREEMENT TERMINATES DISPUTE RESOLUTION.—At any time before a decision and order is issued under subparagraph (G), the Secretary (in consultation with the offices described in subsection (c)(2)) and the responsible person may reach an agreement on the risk evaluation and mitigation strategy through further discussion or administrative appeals, terminating the dispute resolution process, and the Secretary shall issue an action letter or order, as appropriate, that describes the strategy.

“(D) MEETING OF THE BOARD.—At a meeting of the Drug Safety Oversight Board described in subparagraph (B), the Board shall—

“(i) hear from both parties via written or oral presentation; and

“(ii) review the dispute.

“(E) RECORD OF PROCEEDINGS.—The Secretary shall ensure that the proceedings of any such meeting are recorded, transcribed, and made public within 90 days of the meeting. The Secretary shall redact the transcript to protect any trade secrets and other information that is exempted from disclosure under section 552 of title 5, United States Code, or section 552a of title 5, United States Code.

“(F) RECOMMENDATION OF THE BOARD.—Not later than 5 days after any such meeting, the Drug Safety Oversight Board shall provide a written recommendation on resolving the dispute to the Secretary. Not later than 5 days after the Board provides such written recommendation to the Secretary, the

Secretary shall make the recommendation available to the public.

“(G) ACTION BY THE SECRETARY.—

“(i) ACTION LETTER.—With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall issue an action letter that resolves the dispute not later than the later of—

“(l) the action deadline for the action letter on the application; or

“(ll) 7 days after receiving the recommendation of the Drug Safety Oversight Board.

“(ii) ORDER.—With respect to an assessment of an approved risk evaluation and mitigation strategy under subsection (g)(1) or under any of subparagraphs (B) through (D) of subsection (g)(2), the Secretary shall issue an order, which shall be made public, that resolves the dispute not later than 7 days after receiving the recommendation of the Drug Safety Oversight Board.

“(H) INACTION.—An approved risk evaluation and mitigation strategy shall remain in effect until the Secretary acts, if the Secretary fails to act as provided for under subparagraph (G).

“(I) EFFECT ON ACTION DEADLINE.—With respect to a proposal or assessment referred to in paragraph (1), the Secretary shall be considered to have met the action deadline for the action letter on the application if the responsible person requests the dispute resolution process described in this paragraph and if the Secretary—

“(i) has initiated the discussions described under paragraph (2) not less than 60 days before such action deadline; and

“(ii) has complied with the timing requirements of scheduling review by the Drug Safety Oversight

Board, providing a written recommendation, and issuing an action letter under subparagraphs (B), (F), and (G), respectively.

“(J) DISQUALIFICATION.—No individual who is an employee of the Food and Drug Administration and who reviews a drug or who participated in an administrative appeal under subparagraph (C)(i) with respect to such drug may serve on the Drug Safety Oversight Board at a meeting under subparagraph (D) to review a dispute about the risk evaluation and mitigation strategy for such drug.

“(K) ADDITIONAL EXPERTISE.—The Drug Safety Oversight Board may add members with relevant expertise from the Food and Drug Administration, including the Office of Pediatrics, the Office of Women’s Health, or the Office of Rare Diseases, or from other Federal public health or health care agencies, for a meeting under subparagraph (D) of the Drug Safety Oversight Board.

“(6) USE OF ADVISORY COMMITTEES.—The Secretary may convene a meeting of 1 or more advisory committees of the Food and Drug Administration to—

“(A) review a concern about the safety of a drug or class of drugs, including before an assessment of the risk evaluation and mitigation strategy or strategies of such drug or drugs is required to be submitted under any of subparagraphs (B) through (D) of subsection (g)(2);

“(B) review the risk evaluation and mitigation strategy or strategies of a drug or group of drugs; or

“(C) review a dispute under paragraph (4) or (5).

“(7) PROCESS FOR ADDRESSING DRUG CLASS EFFECTS.—

“(A) IN GENERAL.—When a concern about a serious risk of a drug may be related to the pharmaco-

logical class of the drug, the Secretary, in consultation with the offices described in subsection (c) (2), may defer assessments of the approved risk evaluation and mitigation strategies for such drugs until the Secretary has convened 1 or more public meetings to consider possible responses to such concern.

“(B) NOTICE.—If the Secretary defers an assessment under subparagraph (A), the Secretary shall—

“(i) give notice of the deferral to the holder of the approved covered application not later than 5 days after the deferral;

“(ii) publish the deferral in the Federal Register; and

“(iii) give notice to the public of any public meetings to be convened under subparagraph (A), including a description of the deferral.

“(C) PUBLIC MEETINGS.—Such public meetings may include—

“(i) 1 or more meetings of the responsible person for such drugs;

“(ii) 1 or more meetings of 1 or more advisory committees of the Food and Drug Administration, as provided for under paragraph (6); or

“(iii) 1 or more workshops of scientific experts and other stakeholders.

“(D) ACTION.—After considering the discussions from any meetings under subparagraph (A), the Secretary may—

“(i) announce in the Federal Register a planned regulatory action, including a modification to each risk evaluation and mitigation strategy, for drugs in the pharmacological class;

“(ii) seek public comment about such action; and

“(iii) after seeking such comment, issue an order addressing such regulatory action.

“(8) INTERNATIONAL COORDINATION.—The Secretary, in consultation with the offices described in subsection (c)(2), may coordinate the timetable for submission of assessments under subsection (d), or a study or clinical trial under section 505(o)(3), with efforts to identify and assess the serious risks of such drug by the marketing authorities of other countries whose drug approval and risk management processes the Secretary deems comparable to the drug approval and risk management processes of the United States. If the Secretary takes action to coordinate such timetable, the Secretary shall give notice to the responsible person.

“(9) EFFECT.—Use of the processes described in paragraphs (7) and (8) shall not be the sole source of delay of action on an application or a supplement to an application for a drug.

“(i) ABBREVIATED NEW DRUG APPLICATIONS.—

“(1) IN GENERAL.—A drug that is the subject of an abbreviated new drug application under section 505(j) is subject to only the following elements of the risk evaluation and mitigation strategy required under subsection (a) for the applicable listed drug:

“(A) A Medication Guide or patient package insert, if required under subsection (e) for the applicable listed drug.

“(B) Elements to assure safe use, if required under subsection (f) for the listed drug. A drug that is the subject of an abbreviated new drug application and the listed drug shall use a single, shared system under subsection (f). The Secretary may waive the requirement under the preceding sentence for a drug that is the subject of an abbreviated new drug

application, and permit the applicant to use a different, comparable aspect of the elements to assure safe use, if the Secretary determines that—

“(i) the burden of creating a single, shared system outweighs the benefit of a single, system, taking into consideration the impact on health care providers, patients, the applicant for the abbreviated new drug application, and the holder of the reference drug product; or

“(ii) an aspect of the elements to assure safe use for the applicable listed drug is claimed by a patent that has not expired or is a method or process that, as a trade secret, is entitled to protection, and the applicant for the abbreviated new drug application certifies that it has sought a license for use of an aspect of the elements to assure safe use for the applicable listed drug and that it was unable to obtain a license.

A certification under clause (ii) shall include a description of the efforts made by the applicant for the abbreviated new drug application to obtain a license. In a case described in clause (ii), the Secretary may seek to negotiate a voluntary agreement with the owner of the patent, method, or process for a license under which the applicant for such abbreviated new drug application may use an aspect of the elements to assure safe use, if required under subsection (f) for the applicable listed drug, that is claimed by a patent that has not expired or is a method or process that as a trade secret is entitled to protection.

“(2) ACTION BY SECRETARY.—For an applicable listed drug for which a drug is approved under section 505(j), the Secretary—

“(A) shall undertake any communication plan to health care providers required under subsection (e)(3) for the applicable listed drug; and

“(B) shall inform the responsible person for the drug that is so approved if the risk evaluation and mitigation strategy for the applicable listed drug is modified.

“(j) DRUG SAFETY OVERSIGHT BOARD.—

“(1) IN GENERAL.—There is established a Drug Safety Oversight Board.

“(2) COMPOSITION; MEETINGS.—The Drug Safety Oversight Board shall—

“(A) be composed of scientists and health care practitioners appointed by the Secretary, each of whom is an employee of the Federal Government;

“(B) include representatives from offices throughout the Food and Drug Administration, including the offices responsible for postapproval safety of drugs;

“(C) include at least 1 representative each from the National Institutes of Health and the Department of Health and Human Services (other than the Food and Drug Administration);

“(D) include such representatives as the Secretary shall designate from other appropriate agencies that wish to provide representatives; and

“(E) meet at least monthly to provide oversight and advice to the Secretary on the management of important drug safety issues.”.

(c) REGULATION OF BIOLOGICAL PRODUCTS.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended—

(1) in subsection (a)(2), by adding at the end the following:

“(D) POSTMARKET STUDIES AND CLINICAL TRIALS; LABELING; RISK EVALUATION AND MITIGATION STRATEGY.—A person that submits an application for a license under this paragraph is subject to sections 505(o), 505(p), and 505–1 of the Federal Food, Drug, and Cosmetic Act.”; and

(2) in subsection (j), by inserting “, including the requirements under sections 505(o), 505(p), and 505–1 of such Act,” after “, and Cosmetic Act”.

(d) ADVERTISEMENTS OF DRUGS.—The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.), as amended by section 801(b), is amended—

(1) in section 301 (21 U.S.C. 331), by adding at the end the following:

“(kk) The dissemination of a television advertisement without complying with section 503B.”; and

(2) by inserting after section 503A the following:

“Sec. 503b. Prereview Of Television Advertisements.

“(a) IN GENERAL.—The Secretary may require the submission of any television advertisement for a drug (including any script, story board, rough, or a completed video production of the television advertisement) to the Secretary for review under this section not later than 45 days before dissemination of the television advertisement.

“(b) REVIEW.—In conducting a review of a television advertisement under this section, the Secretary may make recommendations with respect to information included in the label of the drug—

“(1) on changes that are—

“(A) necessary to protect the consumer good and wellbeing; or

“(B) consistent with prescribing information for the product under review; and

“(2) if appropriate and if information exists, on statements for inclusion in the advertisement to address the specific efficacy of the drug as it relates to specific population groups, including elderly populations, children, and racial and ethnic minorities.

“(c) NO AUTHORITY TO REQUIRE CHANGES.—Except as provided by subsection (e), this section does not authorize the Secretary to make or direct changes in any material submitted pursuant to subsection (a).

“(d) ELDERLY POPULATIONS, CHILDREN, RACIALLY AND ETHNICALLY DIVERSE COMMUNITIES.—In formulating recommendations under subsection

(b), the Secretary shall take into consideration the impact of the advertised drug on elderly populations, children, and racially and ethnically diverse communities.

“(e) SPECIFIC DISCLOSURES.—

“(1) SERIOUS RISK; SAFETY PROTOCOL.—In conducting a review of a television advertisement under this section, if the Secretary determines that the advertisement would be false or misleading without a specific disclosure about a serious risk listed in the labeling of the drug involved, the Secretary may require inclusion of such disclosure in the advertisement.

“(2) DATE OF APPROVAL.—In conducting a review of a television advertisement under this section, the Secretary may require the advertisement to include, for a period not to exceed 2 years from the date of the approval of the drug under section 505 or section 351 of the Public Health Service Act, a specific disclosure of such date of approval if the Secretary determines that the advertisement would otherwise be false or misleading.

“(f) **RULE OF CONSTRUCTION.**—Nothing in this section may be construed as having any effect on requirements under section 502(n) or on the authority of the Secretary under section 314.550, 314.640, 601.45, or 601.94 of title 21, Code of Federal Regulations (or successor regulations).”.

(3) DIRECT-TO-CONSUMER ADVERTISEMENTS.—

(A) IN GENERAL.—Section 502(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(n)) is amended by adding at the end the following: “In the case of an advertisement for a drug subject to section 503(b)(1) presented directly to consumers in television or radio format and stating the name of the drug and its conditions of use, the major statement relating to side effects and contraindications shall be presented in a clear, conspicuous, and neutral manner.”.

(B) REGULATIONS TO DETERMINE CLEAR, CONSPICUOUS, AND NEUTRAL MANNER.—Not later than 30 months after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, the Secretary of Health and Human Services shall by regulation establish standards for determining whether a major statement relating to side effects and contraindications of a drug, described in section 502(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(n)) (as amended by subparagraph (A)) is presented in the manner required under such section.

(4) CIVIL PENALTIES.—Section 303 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 333), as amended by section 801(b), is amended by adding at the end the following:

“(g)(1) With respect to a person who is a holder of an approved application under section 505 for a drug subject to section 503(b) or under section 351 of the Public Health Service Act, any such person who disseminates or causes another party to disseminate a direct-to-consumer advertisement that

is false or misleading shall be liable to the United States for a civil penalty in an amount not to exceed \$250,000 for the first such violation in any 3-year period, and not to exceed \$500,000 for each subsequent violation in any 3-year period. No other civil monetary penalties in this Act (including the civil penalty in section 303(f)(4)) shall apply to a violation regarding direct-to-consumer advertising. For purposes of this paragraph: (A) Repeated dissemination of the same or similar advertisement prior to the receipt of the written notice referred to in paragraph (2) for such advertisements shall be considered one violation. (B) On and after the date of the receipt of such a notice, all violations under this paragraph occurring in a single day shall be considered one violation. With respect to advertisements that appear in magazines or other publications that are published less frequently than daily, each issue date (whether weekly or monthly) shall be treated as a single day for the purpose of calculating the number of violations under this paragraph.

“(2) A civil penalty under paragraph (1) shall be assessed by the Secretary by an order made on the record after providing written notice to the person to be assessed a civil penalty and an opportunity for a hearing in accordance with this paragraph and section 554 of title 5, United States Code. If upon receipt of the written notice, the person to be assessed a civil penalty objects and requests a hearing, then in the course of any investigation related to such hearing, the Secretary may issue subpoenas requiring the attendance and testimony of witnesses and the production of evidence that relates to the matter under investigation, including information pertaining to the factors described in paragraph (3).

“(3) The Secretary, in determining the amount of the civil penalty under paragraph (1), shall take into account the nature, circumstances, extent, and gravity of the violation or violations, including the following factors:

“(A) Whether the person submitted the advertisement or a similar advertisement for review under section 736A.

“(B) Whether the person submitted the advertisement for review if required under section 503B.

“(C) Whether, after submission of the advertisement as described in subparagraph (A) or (B), the person disseminated or caused another party to disseminate the advertisement before the end of the 45-day comment period.

“(D) Whether the person incorporated any comments made by the Secretary with regard to the advertisement into the advertisement prior to its dissemination.

“(E) Whether the person ceased distribution of the advertisement upon receipt of the written notice referred to in paragraph (2) for such advertisement.

“(F) Whether the person had the advertisement reviewed by qualified medical, regulatory, and legal reviewers prior to its dissemination.

“(G) Whether the violations were material.

“(H) Whether the person who created the advertisement or caused the advertisement to be created acted in good faith.

“(I) Whether the person who created the advertisement or caused the advertisement to be created has been assessed a civil penalty under this provision within the previous 1-year period.

“(J) The scope and extent of any voluntary, subsequent remedial action by the person.

“(K) Such other matters, as justice may require.

“(4)(A) Subject to subparagraph (B), no person shall

be required to pay a civil penalty under paragraph (1) if the person submitted the advertisement to the Secretary and disseminated or caused another party to disseminate such advertisement after incorporating each comment received from the Secretary.

“(B) The Secretary may retract or modify any prior comments the Secretary has provided to an advertisement submitted to the Secretary based on new information or changed circumstances, so long as the Secretary provides written notice to the person of the new views of the Secretary on the advertisement and provides a reasonable time for modification or correction of the advertisement prior to seeking any civil penalty under paragraph (1).

“(5) The Secretary may compromise, modify, or remit, with or without conditions, any civil penalty which may be assessed under paragraph (1). The amount of such penalty, when finally determined, or the amount charged upon in compromise, may be deducted from any sums owed by the United States to the person charged.

“(6) Any person who requested, in accordance with paragraph (2), a hearing with respect to the assessment of a civil penalty and who is aggrieved by an order assessing a civil penalty, may file a petition for de novo judicial review of such order with the United States Court of Appeals for the District of Columbia Circuit or for any other circuit in which such person resides or transacts business. Such a petition may only be filed within the 60-day period beginning on the date the order making such assessments was issued.

“(7) If any person fails to pay an assessment of a civil penalty under paragraph (1)—

“(A) after the order making the assessment becomes final, and if such person does not file a petition for judicial review of the order in accordance with paragraph (6), or

“(B) after a court in an action brought under paragraph (6) has entered a final judgment in favor of the Secretary, the Attorney General of the United States shall recover the amount assessed (plus interest at currently prevailing rates from the date of the expiration of the 60-day period referred to in paragraph (6) or the date of such final judgment, as the case may be) in an action brought in any appropriate district court of the United States. In such an action, the validity, amount, and appropriateness of such penalty shall not be subject to review.”

(5) **REPORT ON DIRECT-TO-CONSUMER ADVERTISING.**—Not later than 24 months after the date of the enactment of this Act, the Secretary of Health and Human Services shall report to the Congress on direct-to-consumer advertising and its ability to communicate to subsets of the general population, including elderly populations, children, and racial and ethnic minority communities. The Secretary shall utilize the Advisory Committee on Risk Communication established under this Act to advise the Secretary with respect to such report. The Advisory Committee shall study direct-to-consumer advertising as it relates to increased access to health information and decreased health disparities for these populations. The report required by this paragraph shall recommend effective ways to present and disseminate information to these populations. Such report shall also make recommendations regarding impediments to the participation of elderly populations, children, racially and ethnically diverse communities, and medically underserved populations in clinical drug trials and shall recommend best practice approaches for increasing the inclusion of such subsets of the general population. The Secretary of Health and Human Services shall submit the report under this paragraph to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives.

(6) **RULEMAKING.**—Section 502(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(n)) is amended by striking “the procedure specified in section 701(e) of this Act” and inserting “section 701(a)”.

(e) **RULE OF CONSTRUCTION REGARDING PEDIATRIC STUDIES.**— This title and the amendments made by this title may not be construed as affecting the authority of the Secretary of Health and Human Services to request pediatric studies under section 505A of the Federal Food, Drug, and Cosmetic Act or to require such studies under section 505B of such Act.

Sec. 902. Enforcement.

(a) **MISBRANDING.**—Section 502 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352) is amended by adding at the end the following:

“(y) If it is a drug subject to an approved risk evaluation and mitigation strategy pursuant to section 505(p) and the responsible person (as such term is used in section 505–1) fails to comply with a requirement of such strategy provided for under subsection (d), (e), or (f) of section 505–1.

“(z) If it is a drug, and the responsible person (as such term is used in section 505(o)) is in violation of a requirement established under paragraph (3) (relating to postmarket studies and clinical trials) or paragraph (4) (relating to labeling) of section 505(o) with respect to such drug.”

(b) **CIVIL PENALTIES.**—Section 303(f) of the Federal Food, Drug, and Cosmetic Act, as amended by section 801(b), is amended—(1) by inserting after paragraph (3), as added by section 801(b)(2), the following:

“(4)(A) Any responsible person (as such term is used in section 505–1) that violates a requirement of section 505(o), 505(p), or 505–1 shall be subject to a civil monetary penalty of—

“(i) not more than \$250,000 per violation, and not to exceed \$1,000,000 for all such violations adjudicated in a single proceeding; or

“(ii) in the case of a violation that continues after the Secretary provides written notice to the responsible person, the responsible person shall be subject to a civil monetary penalty of \$250,000 for the first 30-day period (or any portion thereof) that the responsible person continues to be in violation, and such amount shall double for every 30-day period thereafter that the violation continues, not to exceed \$1,000,000 for any 30-day period, and not to exceed \$10,000,000 for all such violations adjudicated in a single proceeding.

“(B) In determining the amount of a civil penalty under subparagraph (A)(ii), the Secretary shall take into consideration whether the responsible person is making efforts toward correcting the violation of the requirement of section 505(o), 505(p), or 505–1 for which the responsible person is subject to such civil penalty.”; and

(2) in paragraph (5), as redesignated by section 801(b)(2)(A), by striking “paragraph (1), (2), or (3)” each place it appears and inserting “paragraph (1), (2), (3), or (4)”.

Sec. 903. No Effect On Withdrawal Or Suspension Of Approval.

Section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)) is amended by adding at the end the following: “The Secretary may withdraw the approval of an application submitted under this section, or suspend the approval of such an application, as provided under this subsection, without first ordering the applicant to submit an

assessment of the approved risk evaluation and mitigation strategy for the drug under section 505–1(g)(2)(D).”.

Sec. 904. Benefit-Risk Assessments.

Not later than 1 year after the date of the enactment of this Act, the Commissioner of Food and Drugs shall submit to the Congress a report on how best to communicate to the public the risks and benefits of new drugs and the role of the risk evaluation and mitigation strategy in assessing such risks and benefits. As part of such study, the Commissioner may consider the possibility of including in the labeling and any direct-to-consumer advertisements of a newly approved drug or indication a unique symbol indicating the newly approved status of the drug or indication for a period after approval.

Sec. 905. Active Postmarket Risk Identification And Analysis.

(a) IN GENERAL.—Subsection (k) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) is amended by adding at the end the following:

“(3) ACTIVE POSTMARKET RISK IDENTIFICATION.—

“(A) DEFINITION.—In this paragraph, the term ‘data’ refers to information with respect to a drug approved under this section or under section 351 of the Public Health Service Act, including claims data, patient survey data, standardized analytic files that allow for the pooling and analysis of data from disparate data environments, and any other data deemed appropriate by the Secretary.

“(B) DEVELOPMENT OF POSTMARKET RISK IDENTIFICATION AND ANALYSIS METHODS.—The Secretary shall, not later than 2 years after the date of the enactment of the Food and Drug Administra-

tion Amendments Act of 2007, in collaboration with public, academic, and private entities—

“(i) develop methods to obtain access to disparate data sources including the data sources specified in subparagraph (C);

“(ii) develop validated methods for the establishment of a postmarket risk identification and analysis system to link and analyze safety data from multiple sources, with the goals of including, in aggregate—

“(I) at least 25,000,000 patients by July 1, 2010; and

“(II) at least 100,000,000 patients by July 1, 2012; and

“(iii) convene a committee of experts, including individuals who are recognized in the field of protecting data privacy and security, to make recommendations to the Secretary on the development of tools and methods for the ethical and scientific uses for, and communication of, postmarketing data specified under subparagraph (C), including recommendations on the development of effective research methods for the study of drug safety questions.

“(C) ESTABLISHMENT OF THE POSTMARKET RISK IDENTIFICATION AND ANALYSIS SYSTEM.—

“(i) IN GENERAL.—The Secretary shall, not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), establish and maintain procedures—

“(I) for risk identification and analysis based on electronic health data, in compliance with the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996, and in a manner that does not disclose individually identifiable health information in violation of paragraph (4)(B);

“(II) for the reporting (in a standardized form) of data on all serious adverse drug experiences (as defined in section 505–1(b)) submitted to the Secretary under paragraph (1), and those adverse events submitted by patients, providers, and drug sponsors, when appropriate;

“(III) to provide for active adverse event surveillance using the following data sources, as available:

“(aa) Federal health-related electronic data (such as data from the Medicare program and the health systems of the Department of Veterans Affairs);

“(bb) private sector health-related electronic data (such as pharmaceutical purchase data and health insurance claims data); and

“(cc) other data as the Secretary deems necessary to create a robust system to identify adverse events and potential drug safety signals;

“(IV) to identify certain trends and patterns with respect to data accessed by the system;

“(V) to provide regular reports to the Secretary concerning adverse event trends, adverse event patterns, incidence and prevalence of adverse events, and other information the Secretary determines appropriate, which may include data on comparative national adverse event trends; and

“(VI) to enable the program to export data in a form appropriate for further aggregation, statistical analysis, and reporting.

“(ii) TIMELINESS OF REPORTING.—The procedures established under clause (i) shall ensure that such data are accessed, analyzed, and reported in a timely, routine, and systematic manner, taking into consideration the need for data completeness, coding, cleansing, and standardized analysis and transmission.

“(iii) PRIVATE SECTOR RESOURCES.—To ensure the establishment of the active postmarket risk identification and analysis system under this subsection not later than 1 year after the development of the risk identification and analysis methods under subparagraph (B), as required under clause (i), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

“(iv) COMPLEMENTARY APPROACHES.—To the extent the active postmarket risk identification and analysis system under this subsection is not sufficient to gather data and information relevant to a priority drug safety question, the Secretary shall develop, support, and participate in complementary approaches to gather and analyze such data and information, including—

“(I) approaches that are complementary with respect to assessing the safety of use of a drug in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children); and

“(II) existing approaches such as the Vaccine Adverse Event Reporting System and the Vaccine Safety Datalink or successor databases.

“(v) AUTHORITY FOR CONTRACTS.—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subparagraph.

“(4) ADVANCED ANALYSIS OF DRUG SAFETY DATA.—

“(A) PURPOSE.—The Secretary shall establish collaborations with public, academic, and private entities, which may include the Centers for Education and Research on Therapeutics under section 912 of the Public Health Service Act, to provide for

advanced analysis of drug safety data described in paragraph (3)(C) and other information that is publicly available or is provided by the Secretary, in order to—

“(i) improve the quality and efficiency of postmarket drug safety risk-benefit analysis;

“(ii) provide the Secretary with routine access to outside expertise to study advanced drug safety questions; and

“(iii) enhance the ability of the Secretary to make timely assessments based on drug safety data.

“(B) PRIVACY.—Such analysis shall not disclose individually identifiable health information when presenting such drug safety signals and trends or when responding to inquiries regarding such drug safety signals and trends.

“(C) PUBLIC PROCESS FOR PRIORITY QUESTIONS.—At least biannually, the Secretary shall seek recommendations from the Drug Safety and Risk Management Advisory Committee (or any successor committee) and from other advisory committees, as appropriate, to the Food and Drug Administration on—

“(i) priority drug safety questions; and

“(ii) mechanisms for answering such questions, including through—

“(I) active risk identification under paragraph (3); and

“(II) when such risk identification is not sufficient, postapproval studies and clinical trials under subsection (o)(3).

“(D) PROCEDURES FOR THE DEVELOPMENT OF DRUG SAFETY COLLABORATIONS.—

“(i) IN GENERAL.—Not later than 180 days after the date of the establishment of the active post-market risk identification and analysis system under this subsection, the Secretary shall establish and implement procedures under which the Secretary may routinely contract with one or more qualified entities to—

“(l) classify, analyze, or aggregate data described in paragraph (3)(C) and information that is publicly available or is provided by the Secretary;

“(ll) allow for prompt investigation of priority drug safety questions, including—

“(aa) unresolved safety questions for drugs or classes of drugs; and

“(bb) for a newly-approved drugs, safety signals from clinical trials used to approve the drug and other preapproval trials; rare, serious drug side effects; and the safety of use in domestic populations not included, or underrepresented, in the trials used to approve the drug (such as older people, people with comorbidities, pregnant women, or children);

“(lll) perform advanced research and analysis on identified drug safety risks;

“(lV) focus postapproval studies and clinical trials under subsection (o)(3) more effectively on cases for which reports under paragraph (1) and other safety signal detection is not sufficient to resolve whether there is an elevated risk of a serious adverse event associated with the use of a drug; and

“(V) carry out other activities as the Secretary deems necessary to carry out the purposes of this paragraph.

“(ii) REQUEST FOR SPECIFIC METHODOLOGY.—The procedures described in clause (i) shall permit the Secretary to request that a specific methodol-

ogy be used by the qualified entity. The qualified entity shall work with the Secretary to finalize the methodology to be used.

“(E) USE OF ANALYSES.—The Secretary shall provide the analyses described in this paragraph, including the methods and results of such analyses, about a drug to the sponsor or sponsors of such drug.

“(F) QUALIFIED ENTITIES.—

“(i) IN GENERAL.—The Secretary shall enter into contracts with a sufficient number of qualified entities to develop and provide information to the Secretary in a timely manner.

“(ii) QUALIFICATION.—The Secretary shall enter into a contract with an entity under clause (i) only if the Secretary determines that the entity has a significant presence in the United States and has one or more of the following qualifications:

“(l) The research, statistical, epidemiologic, or clinical capability and expertise to conduct and complete the activities under this paragraph, including the capability and expertise to provide the Secretary de-identified data consistent with the requirements of this subsection.

“(ll) An information technology infrastructure in place to support electronic data and operational standards to provide security for such data.

“(lll) Experience with, and expertise on, the development of drug safety and effectiveness research using electronic population data.

“(lV) An understanding of drug development or risk/benefit balancing in a clinical setting.

“(V) Other expertise which the Secretary deems necessary to fulfill the activities under this paragraph.

“(G) CONTRACT REQUIREMENTS.—Each contract with a qualified entity under subparagraph (F)(i) shall contain the following requirements:

“(i) ENSURING PRIVACY.—The qualified entity shall ensure that the entity will not use data under this subsection in a manner that—

“(I) violates the regulations promulgated under section 264(c) of the Health Insurance Portability and Accountability Act of 1996;

“(II) violates sections 552 or 552a of title 5, United States Code, with regard to the privacy of individually-identifiable beneficiary health information; or

“(III) discloses individually identifiable health information when presenting drug safety signals and trends or when responding to inquiries regarding drug safety signals and trends. Nothing in this clause prohibits lawful disclosure for other purposes.

“(ii) COMPONENT OF ANOTHER ORGANIZATION.—If a qualified entity is a component of another organization—

“(I) the qualified entity shall establish appropriate security measures to maintain the confidentiality and privacy of such data; and

“(II) the entity shall not make an unauthorized disclosure of such data to the other components of the organization in breach of such confidentiality and privacy requirement.

“(iii) TERMINATION OR NONRENEWAL.—If a contract with a qualified entity under this subparagraph is terminated or not renewed, the following requirements shall apply:

“(I) CONFIDENTIALITY AND PRIVACY PROTECTIONS.—The entity shall continue to comply with the confidentiality and privacy requirements under this paragraph with respect to all data disclosed to the entity.

“(II) DISPOSITION OF DATA.—The entity shall return any data disclosed to such entity under this subsection to which it would not otherwise have access or, if returning the data is not practicable, destroy the data.

“(H) COMPETITIVE PROCEDURES.—The Secretary shall use competitive procedures (as defined in section 4(5) of the Federal Procurement Policy Act) to enter into contracts under subparagraph (G).

“(I) REVIEW OF CONTRACT IN THE EVENT OF A MERGER OR ACQUISITION.—The Secretary shall review the contract with a qualified entity under this paragraph in the event of a merger or acquisition of the entity in order to ensure that the requirements under this paragraph will continue to be met.

“(J) COORDINATION.—In carrying out this paragraph, the Secretary shall provide for appropriate communications to the public, scientific, public health, and medical communities, and other key stakeholders, and to the extent practicable shall coordinate with the activities of private entities, professional associations, or other entities that may have sources of drug safety data.”.

(b) RULE OF CONSTRUCTION.—Nothing in this section or the amendment made by this section shall be construed to prohibit the lawful disclosure or use of data or information by an entity other than as described in paragraph (4)(B) or (4)(G) of section 505(k) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a).

(c) REPORT TO CONGRESS.—Not later than 4 years after the date of the enactment of this Act, the

Secretary shall report to the Congress on the ways in which the Secretary has used the active postmarket risk identification and analysis system described in paragraphs (3) and (4) of section 505(k) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a), to identify specific drug safety signals and to better understand the outcomes associated with drugs marketed in the United States.

(d) **AUTHORIZATION OF APPROPRIATIONS.**—To carry out activities under the amendment made by this section for which funds are made available under section 736 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379h), there are authorized to be appropriated to carry out the amendment made by this section, in addition to such funds, \$25,000,000 for each of fiscal years 2008 through 2012.

(e) **GAO REPORT.**—Not later than 18 months after the date of the enactment of this Act, the Comptroller General of the United States shall evaluate data privacy, confidentiality, and security issues relating to accessing, transmitting, and maintaining data for the active postmarket risk identification and analysis system described in paragraphs (3) and (4) of section 505(k) of the Federal Food, Drug, and Cosmetic Act, as added by subsection (a), and make recommendations to the Committee on Energy and Commerce of the House of Representatives and the Committee on Health, Education, Labor and Pensions of the Senate, and any other congressional committees of relevant jurisdiction, regarding the need for any additional legislative or regulatory actions to ensure privacy, confidentiality, and security of this data or otherwise address privacy, confidentiality, and security issues to ensure the effective operation of such active postmarket identification and analysis system.

Sec. 906. Statement For Inclusion In Direct-To-Consumer Advertisements Of Drugs.

(a) **PUBLISHED DIRECT-TO-CONSUMER ADVERTISEMENTS.**—Section 502(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352), as amended by section 901(d)(6), is further amended by inserting “and in the case of published direct-to-consumer advertisements the following statement printed in conspicuous text: ‘You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.’” after “section 701(a).”

(b) **STUDY.**—

(1) **IN GENERAL.**—In the case of direct-to-consumer television advertisements, the Secretary of Health and Human Services, in consultation with the Advisory Committee on Risk Communication under section 567 of the Federal Food, Drug, and Cosmetic Act (as added by section 917), shall, not later than 6 months after the date of the enactment of this Act, conduct a study to determine if the statement in section 502(n) of such Act (as added by subsection (a)) required with respect to published direct-to-consumer advertisements is appropriate for inclusion in such television advertisements.

(2) **CONTENT.**—As part of the study under paragraph (1), such Secretary shall consider whether the information in the statement described in paragraph (1) would detract from the presentation of risk information in a direct-to-consumer television advertisement. If such Secretary determines the inclusion of such statement is appropriate in direct-to-consumer television advertisements, such Secretary shall issue regulations requiring the implementation of such statement in direct-to-consumer television advertisements, including determining a reasonable length of time for displaying the statement in such advertisements. The Secretary shall report to the appropriate committees of Congress

the findings of such study and any plans to issue regulations under this paragraph.

Sec. 907. No Effect On Veterinary Medicine.

This subtitle, and the amendments made by this subtitle, shall have no effect on the use of drugs approved under section 505 of the Federal Food, Drug, and Cosmetic Act by, or on the lawful written or oral order of, a licensed veterinarian within the context of a veterinarian-client-patient relationship, as provided for under section 512(a)(5) of such Act.

Sec. 908. Authorization Of Appropriations.

(a) **IN GENERAL.**—For carrying out this subtitle and the amendments made by this subtitle, there is authorized to be appropriated \$25,000,000 for each of fiscal years 2008 through 2012.

(b) **RELATION TO OTHER FUNDING.**—The authorization of appropriations under subsection (a) is in addition to any other funds available for carrying out this subtitle and the amendments made by this subtitle.

Sec. 909. Effective Date And Applicability.

(a) **EFFECTIVE DATE.**—This subtitle takes effect 180 days after the date of the enactment of this Act.

(b) **DRUGS DEEMED TO HAVE RISK EVALUATION AND MITIGATION STRATEGIES.**—

(1) **IN GENERAL.**—A drug that was approved before the effective date of this Act is, in accordance with paragraph (2), deemed to have in effect an approved risk evaluation and mitigation strategy under section 505–1 of the Federal Food, Drug, and Cosmetic Act (as added by section 901) (referred to in this section as the “Act”) if there are in effect on the effective date of this Act elements to assure safe use—

(A) required under section 314.520 or section 601.42 of title 21, Code of Federal Regulations; or

(B) otherwise agreed to by the applicant and the Secretary for such drug.

(2) **ELEMENTS OF STRATEGY; ENFORCEMENT.**—The approved risk evaluation and mitigation strategy in effect for a drug under paragraph (1)—

(A) is deemed to consist of the timetable required under section 505–1(d) and any additional elements under subsections (e) and (f) of such section in effect for such drug on the effective date of this Act; and

(B) is subject to enforcement by the Secretary to the same extent as any other risk evaluation and mitigation strategy under section 505–1 of the Act, except that sections 303(f)(4) and 502(y) and (z) of the Act (as added by section 902) shall not apply to such strategy before the Secretary has completed review of, and acted on, the first assessment of such strategy under such section 505–1.

(3) **SUBMISSION.**—Not later than 180 days after the effective date of this Act, the holder of an approved application for which a risk evaluation and mitigation strategy is deemed to be in effect under paragraph (1) shall submit to the Secretary a proposed risk evaluation and mitigation strategy. Such proposed strategy is subject to section 505–1 of the Act as if included in such application at the time of submission of the application to the Secretary.

Subtitle B—Other Provisions to Ensure Drug Safety and Surveillance

Sec. 911. Clinical Trial Guidance For Antibiotic Drugs.

Chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended by inserting after section 510 the following:

“Sec. 511. Clinical Trial Guidance For Antibiotic Drugs.

“(a) IN GENERAL.—Not later than 1 year after the date of the enactment of this section, the Secretary shall issue guidance for the conduct of clinical trials with respect to antibiotic drugs, including antimicrobials to treat acute bacterial sinusitis, acute bacterial otitis media, and acute bacterial exacerbation of chronic bronchitis. Such guidance shall indicate the appropriate models and valid surrogate markers.

“(b) REVIEW.—Not later than 5 years after the date of the enactment of this section, the Secretary shall review and update the guidance described under subsection (a) to reflect developments in scientific and medical information and technology.”.

Sec. 912. Prohibition Against Food To Which Drugs Or Biological Products Have Been Added.

(a) PROHIBITION.—Section 301 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331), as amended by section 901(d), is amended by adding at the end the following:

“(l) The introduction or delivery for introduction into interstate commerce of any food to which has been added a drug approved under section 505, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public, unless—

“(1) such drug or such biological product was marketed in food before any approval of the drug under section 505, before licensure of the biological product under such section 351, and before any substantial clinical investigations involving the drug or the biological product have been instituted;

“(2) the Secretary, in the Secretary’s discretion, has issued a regulation, after notice and comment,

approving the use of such drug or such biological product in the food;

“(3) the use of the drug or the biological product in the food is to enhance the safety of the food to which the drug or the biological product is added or applied and not to have independent biological or therapeutic effects on humans, and the use is in conformity with—

“(A) a regulation issued under section 409 prescribing conditions of safe use in food;

“(B) a regulation listing or affirming conditions under which the use of the drug or the biological product in food is generally recognized as safe;

“(C) the conditions of use identified in a notification to the Secretary of a claim of exemption from the premarket approval requirements for food additives based on the notifier’s determination that the use of the drug or the biological product in food is generally recognized as safe, provided that the Secretary has not questioned the general recognition of safety determination in a letter to the notifier;

“(D) a food contact substance notification that is effective under section 409(h); or

“(E) such drug or biological product had been marketed for smoking cessation prior to the date of the enactment of the Food and Drug Administration Amendments Act of 2007; or

“(4) the drug is a new animal drug whose use is not unsafe under section 512.”.

(b) CONFORMING CHANGES.—The Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) is amended—

(1) in section 304(a)(1), by striking “section 404 or 505” and inserting “section 301(l), 404, or 505”; and

(2) in section 801(a), by striking “is adulterated, misbranded, or in violation of section 505,” and inserting “is adulterated, misbranded, or in violation of section 505, or prohibited from introduction or delivery for introduction into interstate commerce under section 301(l),”.

Sec. 913. Assuring Pharmaceutical Safety.

Chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.), as amended in section 403, is amended by inserting after section 505C the following:

“Sec. 505d. Pharmaceutical Security.

“(a) IN GENERAL.—The Secretary shall develop standards and identify and validate effective technologies for the purpose of securing the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

“(b) STANDARDS DEVELOPMENT.—

“(1) IN GENERAL.—The Secretary shall, in consultation with the agencies specified in paragraph (4), manufacturers, distributors, pharmacies, and other supply chain stakeholders, prioritize and develop standards for the identification, validation, authentication, and tracking and tracing of prescription drugs.

“(2) STANDARDIZED NUMERAL IDENTIFIER.—Not later than 30 months after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, the Secretary shall develop a standardized numerical identifier (which, to the extent practicable, shall be harmonized with international consensus standards for such an identifier) to be applied to a prescription drug at the point of manufacturing and repackaging (in which case the numerical identifier shall be linked to the numerical

identifier applied at the point of manufacturing) at the package or pallet level, sufficient to facilitate the identification, validation, authentication, and tracking and tracing of the prescription drug.

“(3) PROMISING TECHNOLOGIES.—The standards developed under this subsection shall address promising technologies, which may include—

“(A) radio frequency identification technology;

“(B) nanotechnology;

“(C) encryption technologies; and

“(D) other track-and-trace or authentication technologies.

“(4) INTERAGENCY COLLABORATION.—In carrying out this subsection, the Secretary shall consult with Federal health and security agencies, including—

“(A) the Department of Justice;

“(B) the Department of Homeland Security;

“(C) the Department of Commerce; and

“(D) other appropriate Federal and State agencies.

“(c) INSPECTION AND ENFORCEMENT.—

“(1) IN GENERAL.—The Secretary shall expand and enhance the resources and facilities of agency components of the Food and Drug Administration involved with regulatory and criminal enforcement of this Act to secure the drug supply chain against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs including biological products and active pharmaceutical ingredients from domestic and foreign sources.

“(2) **ACTIVITIES.**—The Secretary shall undertake enhanced and joint enforcement activities with other Federal and State agencies, and establish regional capacities for the validation of prescription drugs and the inspection of the prescription drug supply chain.

“(d) **DEFINITION.**—In this section, the term ‘prescription drug’ means a drug subject to section 503(b)(1).”.

Sec. 914. Citizen Petitions And Petitions For Stay Of Agency Action.

(a) **IN GENERAL.**—Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), as amended by section 901(a), is amended by adding at the end the following:

“(q) **PETITIONS AND CIVIL ACTIONS REGARDING APPROVAL OF CERTAIN APPLICATIONS.**—

“(1) **IN GENERAL.**—

“(A) **DETERMINATION.**—The Secretary shall not delay approval of a pending application submitted under subsection (b)(2) or (j) because of any request to take any form of action relating to the application, either before or during consideration of the request, unless—

“(i) the request is in writing and is a petition submitted to the Secretary pursuant to section 10.30 or 10.35 of title 21, Code of Federal Regulations (or any successor regulations); and

“(ii) the Secretary determines, upon reviewing the petition, that a delay is necessary to protect the public health.

“(B) **NOTIFICATION.**—If the Secretary determines under subparagraph (A) that a delay is necessary with respect to an application, the Secretary shall

provide to the applicant, not later than 30 days after making such determination, the following information:

“(i) Notification of the fact that a determination under subparagraph (A) has been made.

“(ii) If applicable, any clarification or additional data that the applicant should submit to the docket on the petition to allow the Secretary to review the petition promptly.

“(iii) A brief summary of the specific substantive issues raised in the petition which form the basis of the determination.

“(C) **FORMAT.**—The information described in subparagraph (B) shall be conveyed via either, at the discretion of the Secretary—

“(i) a document; or

“(ii) a meeting with the applicant involved.

“(D) **PUBLIC DISCLOSURE.**—Any information conveyed by the Secretary under subparagraph (C) shall be considered part of the application and shall be subject to the disclosure requirements applicable to information in such application.

“(E) **DENIAL BASED ON INTENT TO DELAY.**—If the Secretary determines that a petition or a supplement to the petition was submitted with the primary purpose of delaying the approval of an application and the petition does not on its face raise valid scientific or regulatory issues, the Secretary may deny the petition at any point based on such determination. The Secretary may issue guidance to describe the factors that will be used to determine under this subparagraph whether a petition is submitted with the primary purpose of delaying the approval of an application.

“(F) FINAL AGENCY ACTION.—The Secretary shall take final agency action on a petition not later than 180 days after the date on which the petition is submitted. The Secretary shall not extend such period for any reason, including—

“(i) any determination made under subparagraph (A);

“(ii) the submission of comments relating to the petition or supplemental information supplied by the petitioner; or

“(iii) the consent of the petitioner.

“(G) EXTENSION OF 30-MONTH PERIOD.—If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

“(H) CERTIFICATION.—The Secretary shall not consider a petition for review unless the party submitting such petition does so in written form and the subject document is signed and contains the following certification: ‘I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/ or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the

party on whose behalf this petition is submitted on or about the following date: _____.

If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____.

I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.’, with the date on which such information first became known to such party and the names of such persons or organizations inserted in the first and second blank space, respectively.

“(I) VERIFICATION.—The Secretary shall not accept for review any supplemental information or comments on a petition unless the party submitting such information or comments does so in written form and the subject document is signed and contains the following verification: ‘I certify that, to my best knowledge and belief: (a) I have not intentionally delayed submission of this document or its contents; and (b) the information upon which I have based the action requested herein first became known to me on or about _____.

If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: _____. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.’, with the date on which such information first became known to the party and the names of such persons or organizations inserted in the first and second blank space, respectively.

“(2) EXHAUSTION OF ADMINISTRATIVE REMEDIES.—

“(A) FINAL AGENCY ACTION WITHIN 180 DAYS.—The Secretary shall be considered to have taken final agency action on a petition if—

“(i) during the 180-day period referred to in paragraph (1)(F), the Secretary makes a final decision within the meaning of section 10.45(d) of title 21, Code of Federal Regulations (or any successor regulation); or

“(ii) such period expires without the Secretary having made such a final decision.

“(B) DISMISSAL OF CERTAIN CIVIL ACTIONS.—If a civil action is filed against the Secretary with respect to any issue raised in the petition before the Secretary has taken final agency action on the petition within the meaning of subparagraph (A), the court shall dismiss without prejudice the action for failure to exhaust administrative remedies.

“(C) ADMINISTRATIVE RECORD.—For purposes of judicial review related to the approval of an application for which a petition under paragraph (1) was submitted, the administrative record regarding any issue raised by the petition shall include—

“(i) the petition filed under paragraph (1) and any supplements and comments thereto;

“(ii) the Secretary’s response to such petition, if issued; and

“(iii) other information, as designated by the Secretary, related to the Secretary’s determinations regarding the issues raised in such petition, as long as the information was considered by the agency no later than the date of final agency action as defined under subparagraph (2)(A), and regardless of whether the Secretary responded to the petition at or before the approval of the application at issue in the petition.

“(3) ANNUAL REPORT ON DELAYS IN APPROVALS PER PETITIONS.—The Secretary shall annually submit to the Congress a report that specifies—

“(A) the number of applications that were approved during the preceding 12-month period;

“(B) the number of such applications whose effective dates were delayed by petitions referred to in paragraph (1) during such period;

“(C) the number of days by which such applications were so delayed; and

“(D) the number of such petitions that were submitted during such period.

“(4) EXCEPTIONS.—This subsection does not apply to—

“(A) a petition that relates solely to the timing of the approval of an application pursuant to subsection (j)(5)(B)(iv); or

“(B) a petition that is made by the sponsor of an application and that seeks only to have the Secretary take or refrain from taking any form of action with respect to that application.

“(5) DEFINITIONS.—

“(A) APPLICATION.—For purposes of this subsection, the term ‘application’ means an application submitted under subsection (b)(2) or (j).

“(B) PETITION.—For purposes of this subsection, other than paragraph (1)(A)(i), the term ‘petition’ means a request described in paragraph (1)(A)(i).”.

(b) REPORT.—Not later than 1 year after the date of the enactment of this Act, the Secretary of Health and Human Services shall submit a report to the Congress on ways to encourage the early submission of petitions under section 505(q), as added by subsection (a).

Sec. 915. Postmarket Drug Safety Information For Patients And Providers.

Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), as amended by section 914(a), is amended by adding at the end the following:

“(r) POSTMARKET DRUG SAFETY INFORMATION FOR PATIENTS AND PROVIDERS.—

“(1) ESTABLISHMENT.—Not later than 1 year after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, the Secretary shall improve the transparency of information about drugs and allow patients and health care providers better access to information about drugs by developing and maintaining an Internet Web site that—

“(A) provides links to drug safety information listed in paragraph (2) for prescription drugs that are approved under this section or licensed under section 351 of the Public Health Service Act; and

“(B) improves communication of drug safety information to patients and providers.

“(2) INTERNET WEB SITE.—The Secretary shall carry out paragraph (1) by—

“(A) developing and maintaining an accessible, consolidated Internet Web site with easily searchable drug safety information, including the information found on United States Government Internet Web sites, such as the United States National Library of Medicine’s Daily Med and Medline Plus Web sites, in addition to other such Web sites maintained by the Secretary;

“(B) ensuring that the information provided on the Internet Web site is comprehensive and includes, when available and appropriate—

“(i) patient labeling and patient packaging inserts;

“(ii) a link to a list of each drug, whether approved under this section or licensed under such section 351, for which a Medication Guide, as provided for under part 208 of title 21, Code of Federal Regulations (or any successor regulations), is required;

“(iii) a link to the registry and results data bank provided for under subsections (i) and (j) of section 402 of the Public Health Service Act;

“(iv) the most recent safety information and alerts issued by the Food and Drug Administration for drugs approved by the Secretary under this section, such as product recalls, warning letters, and import alerts;

“(v) publicly available information about implemented RiskMAPs and risk evaluation and mitigation strategies under subsection (o);

“(vi) guidance documents and regulations related to drug safety; and

“(vii) other material determined appropriate by the Secretary;

“(C) providing access to summaries of the assessed and aggregated data collected from the active surveillance infrastructure under subsection (k)(3) to provide information of known and serious side-effects for drugs approved under this section or licensed under such section 351;

“(D) preparing, by 18 months after approval of a drug or after use of the drug by 10,000 individuals, whichever is later, a summary analysis of the adverse drug reaction reports received for the drug, including identification of any new risks not previously identified, potential new risks, or known risks reported in unusual number;

“(E) enabling patients, providers, and drug sponsors to submit adverse event reports through the Internet Web site;

“(F) providing educational materials for patients and providers about the appropriate means of disposing of expired, damaged, or unusable medications; and

“(G) supporting initiatives that the Secretary determines to be useful to fulfill the purposes of the Internet Web site.

“(3) POSTING OF DRUG LABELING.—The Secretary shall post on the Internet Web site established under paragraph (1) the approved professional labeling and any required patient labeling of a drug approved under this section or licensed under such section 351 not later than 21 days after the date the drug is approved or licensed, including in a supplemental application with respect to a labeling change.

“(4) PRIVATE SECTOR RESOURCES.—To ensure development of the Internet Web site by the date described in paragraph (1), the Secretary may, on a temporary or permanent basis, implement systems or products developed by private entities.

“(5) AUTHORITY FOR CONTRACTS.—The Secretary may enter into contracts with public and private entities to fulfill the requirements of this subsection.

“(6) REVIEW.—The Advisory Committee on Risk Communication under section 567 shall, on a regular basis, perform a comprehensive review and evaluation of the types of risk communication information provided on the Internet Web site established under paragraph (1) and, through other means, shall identify, clarify, and define the purposes and types of information available to facilitate the efficient flow of information to patients and providers, and shall recommend ways for the Food and Drug Administration to work with outside entities to help facilitate

the dispensing of risk communication information to patients and providers.”.

Sec. 916. Action Package For Approval.

Section 505(l) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(l)) is amended by—

(1) redesignating paragraphs (1), (2), (3), (4), and (5) as subparagraphs (A), (B), (C), (D), and (E), respectively;

(2) striking “(l) Safety and” and inserting “(l)(1) Safety and”; and

(3) adding at the end the following:

“(2) ACTION PACKAGE FOR APPROVAL.—

“(A) ACTION PACKAGE.—The Secretary shall publish the action package for approval of an application under subsection (b) or section 351 of the Public Health Service Act on the Internet Web site of the Food and Drug Administration—

“(i) not later than 30 days after the date of approval of such application for a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 351 of the Public Health Service Act; and

“(ii) not later than 30 days after the third request for such action package for approval received under section 552 of title 5, United States Code, for any other drug.

“(B) IMMEDIATE PUBLICATION OF SUMMARY REVIEW.—Notwithstanding subparagraph (A), the Secretary shall publish, on the Internet Web site of the Food and Drug Administration, the materials described in subparagraph (C)(iv) not later than 48 hours after the date of approval of the drug,

except where such materials require redaction by the Secretary.

“(C) CONTENTS.—An action package for approval of an application under subparagraph (A) shall be dated and shall include the following:

“(i) Documents generated by the Food and Drug Administration related to review of the application.

“(ii) Documents pertaining to the format and content of the application generated during drug development.

“(iii) Labeling submitted by the applicant.

“(iv) A summary review that documents conclusions from all reviewing disciplines about the drug, noting any critical issues and disagreements with the applicant and within the review team and how they were resolved, recommendations for action, and an explanation of any nonconcurrence with review conclusions.

“(v) The Division Director and Office Director’s decision document which includes—

“(I) a brief statement of concurrence with the summary review;

“(II) a separate review or addendum to the review if disagreeing with the summary review; and

“(III) a separate review or addendum to the review to add further analysis.

“(vi) Identification by name of each officer or employee of the Food and Drug Administration who—

“(I) participated in the decision to approve the application; and

“(II) consents to have his or her name included in the package.

“(D) REVIEW.—A scientific review of an application is considered the work of the reviewer and shall not be altered by management or the reviewer once final.

“(E) CONFIDENTIAL INFORMATION.—This paragraph does not authorize the disclosure of any trade secret, confidential commercial or financial information, or other matter listed in section 552(b) of title 5, United States Code.”.

Sec. 917. Risk Communication.

Subchapter E of chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360bbb et seq.), as amended by section 603, is amended by adding at the end the following:

“Sec. 567. Risk Communication.

“(a) ADVISORY COMMITTEE ON RISK COMMUNICATION.—

“(1) IN GENERAL.—The Secretary shall establish an advisory committee to be known as the ‘Advisory Committee on Risk Communication’ (referred to in this section as the ‘Committee’).

“(2) DUTIES OF COMMITTEE.—The Committee shall advise the Commissioner on methods to effectively communicate risks associated with the products regulated by the Food and Drug Administration.

“(3) MEMBERS.—The Secretary shall ensure that the Committee is composed of experts on risk communication, experts on the risks described in subsection (b), and representatives of patient, consumer, and health professional organizations.

“(4) PERMANENCE OF COMMITTEE.—Section 14 of the Federal Advisory Committee Act shall not apply to the Committee established under this subsection.

“(b) PARTNERSHIPS FOR RISK COMMUNICATION.—

“(1) IN GENERAL.—The Secretary shall partner with professional medical societies, medical schools, academic medical centers, and other stakeholders to develop robust and multi-faceted systems for communication to health care providers about emerging postmarket drug risks.

“(2) PARTNERSHIPS.—The systems developed under paragraph (1) shall—

“(A) account for the diversity among physicians in terms of practice, willingness to adopt technology, and medical specialty; and

“(B) include the use of existing communication channels, including electronic communications, in place at the Food and Drug Administration.”.

Sec. 918. Referral To Advisory Committee.

Section 505 of the Federal Food, Drug, and Cosmetic Act, as amended by section 915, is further amended by adding at the end the following:

“(s) REFERRAL TO ADVISORY COMMITTEE.—Prior to the approval of a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under this section or section 351 of the Public Health Service Act, the Secretary shall—

“(1) refer such drug to a Food and Drug Administration advisory committee for review at a meeting of such advisory committee; or

“(2) if the Secretary does not refer such a drug to a Food and Drug Administration advisory committee prior to the approval of the drug, provide in the action letter on the application for the drug a summary of the reasons why the Secretary did not refer the drug to an advisory committee prior to approval.”.

Sec. 919. Response To The Institute Of Medicine.

(a) IN GENERAL.—Not later than 1 year after the date of the enactment of this title, the Secretary shall issue a report responding to the 2006 report of the Institute of Medicine entitled “The Future of Drug Safety—Promoting and Protecting the Health of the Public”.

(b) CONTENT OF REPORT.—The report issued by the Secretary under subsection (a) shall include—

(1) an update on the implementation by the Food and Drug Administration of its plan to respond to the Institute of Medicine report described under such subsection; and

(2) an assessment of how the Food and Drug Administration has implemented—

(A) the recommendations described in such Institute of Medicine report; and

(B) the requirement under section 505–1(c)(2) of the Federal Food, Drug, and Cosmetic Act (as added by this title), that the appropriate office responsible for reviewing a drug and the office responsible for postapproval safety with respect to the drug work together to assess, implement, and ensure compliance with the requirements of such section 505–1.

Sec. 920. Database For Authorized Generic Drugs.

Section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), as amended by section 918, is further amended by adding at the end the following:

“(t) DATABASE FOR AUTHORIZED GENERIC DRUGS.—

“(1) IN GENERAL.—

“(A) PUBLICATION.—The Commissioner shall—
“(i) not later than 9 months after the date of the enactment of the Food and Drug Administration Amendments Act of 2007, publish a complete list on the Internet Web site of the Food and Drug Administration of all authorized generic drugs (including drug trade name, brand company manufacturer, and the date the authorized generic drug entered the market); and

“(ii) update the list quarterly to include each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug during the preceding 3-month period.

“(B) NOTIFICATION.—The Commissioner shall notify relevant Federal agencies, including the Centers for Medicare & Medicaid Services and the Federal Trade Commission, when the Commissioner first publishes the information described in subparagraph (A) that the information has been published and that the information will be updated quarterly.

“(2) INCLUSION.—The Commissioner shall include in the list described in paragraph (1) each authorized generic drug included in an annual report submitted to the Secretary by the sponsor of a listed drug after January 1, 1999.

“(3) AUTHORIZED GENERIC DRUG.—In this section, the term ‘authorized generic drug’ means a listed drug (as that term is used in subsection (j)) that—

“(A) has been approved under subsection (c); and

“(B) is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.”.

Sec. 921. Adverse Drug Reaction Reports And Post-market Safety.

Subsection (k) of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355), as amended by section 905, is amended by adding at the end the following:

“(5) The Secretary shall—

“(A) conduct regular, bi-weekly screening of the Adverse Event Reporting System database and post a quarterly report on the Adverse Event Reporting System Web site of any new safety information or potential signal of a serious risk identified by Adverse Event Reporting System within the last quarter;

“(B) report to Congress not later than 2 year after the date of the enactment of the Food and Drug Administration Amendments Act of 2007 on procedures and processes of the Food and Drug Administration for addressing ongoing post market safety issues identified by the Office of Surveillance and Epidemiology and how recommendations of the Office of Surveillance and Epidemiology are handled within the agency; and

“(C) on an annual basis, review the entire backlog of postmarket safety commitments to determine which commitments require revision or should be eliminated, report to the Congress on these determinations, and assign start dates and estimated completion dates for such commitments.”.

PRODUCTS DEEMED TO HAVE REMS AS OF
MARCH 27, 2008

Food and Drug Administration

[Docket No. FDA-2008-N-0174]

Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for Purposes of the Food and Drug Administration Amendments Act of 2007

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is issuing this notice to notify holders of certain prescription new drug and biological license applications that they will be deemed to have in effect an approved risk evaluation and mitigation strategy (REMS) under the Food and Drug Administration Amendments Act of 2007 (FDAAA). Holders of applications deemed to have in effect an approved REMS are required to submit a proposed REMS to FDA.

DATES: Submit proposed REMSs to FDA by September 21, 2008.

ADDRESSES: Written communications regarding the applicability of this notice to a specific product should be identified with Docket Number FDA-2008-N-0174 and submitted to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic communications to <http://www.regulations.gov>. Information about FDA implementation of FDAAA is available on the

Internet at <http://www.fda.gov/oc/initiatives/advance/fdaaa.html>.

FOR FURTHER INFORMATION CONTACT:

Mary Dempsey, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4326, Silver Spring, MD 20993-0002, 301-796-0147.

SUPPLEMENTARY INFORMATION:

I. Introduction

On September 27, 2007, the President signed into law FDAAA (Public Law 110-85). Title IX, subtitle A, section 901 of FDAAA created new section 505-1 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355-1). Section 505-1(a) of the act authorizes FDA to require persons submitting certain applications¹ to submit and implement a REMS if FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh the risks of the drug and informs the holder of the application for the drug of the determination. Section 909 of FDAAA provides that Title IX, subtitle A takes effect 180 days after its enactment, which is March 25, 2008.

FDAAA also contains REMS requirements for drug and biological products approved before the effective date of Title IX, subtitle A. Section 909(b)(1) of FDAAA specifies that a “drug that was approved before the effective date of this Act is * * * deemed to have in effect an approved risk evaluation and mitigation strategy under section 505-1 of the Federal Food, Drug, and Cosmetic Act * * * if there are in effect on the effective date of this Act elements to assure safe use— (A) required under section 314.520 or section 601.42 of title 21, Code

of Federal Regulations; or (B) otherwise agreed to by the applicant and the Secretary [of Health and Human Services] for such drug.”

Section 909(b)(3) of FDAAA states: “Not later than 180 days after the effective date of this Act, the holder of an approved application for which a risk evaluation and mitigation strategy is deemed to be in effect * * * shall submit to the Secretary a proposed risk evaluation and mitigation strategy. Such proposed strategy is subject to section 505–1 of the Act as if included in such application at the time of submission of the application to the Secretary.”²

Section 909(b)(2) of FDAAA states that a REMS for a drug deemed to have a REMS consists of the timetable required under section 505–1(d) of the act and any additional elements under section 505–1(e) and (f) of the act in effect for the drug on the effective date of FDAAA.

The purpose of this notice is to identify those drugs that FDA has determined will be deemed to have in effect an approved REMS and to notify holders of applications for such drugs that they are required to submit a proposed REMS by September 21, 2008. FDA is developing guidance on the preferred content and format of a proposed REMS required to be submitted under section 909(b) of FDAAA and will issue it as soon as possible.

II. List of Drug and Biological Products Deemed to Have a REMS

Drug and biological products deemed to have in effect an approved REMS are those that on March 25, 2008 (the effective date of Title IX, subtitle A of FDAAA), had in effect “elements to assure safe

use.” “Elements to assure safe use” include the following: (1) Health care providers who prescribe the drug have particular training or experience, or are specially certified; (2) pharmacies, practitioners, or health care settings that dispense the drug are specially certified; (3) the drug is dispensed to patients only in certain health care settings, such as hospitals; (4) the drug is dispensed to patients with evidence or other documentation of safe use conditions, such as laboratory test results; (5) each patient using the drug is subject to certain monitoring; or (6) each patient using the drug is enrolled in a registry (see section 505–1(f)(3) of the act).

Some applications approved before the effective date of FDAAA Title IX, subtitle A contain these elements to assure safe use.³ Some of these applications were approved under § 314.520 (21 CFR 314.520) or § 601.42 (21 CFR 601.42). Others were not approved under part 314, subpart H or part 601, subpart E, but still contain elements to assure safe use that were agreed to by the applicant and the Secretary for such drug. Since 2005, these elements typically appeared in approved risk minimization action plans (RiskMAPs) (see the guidance for industry entitled “Development and Use of Risk Minimization Action Plans” (70 FR 15866, March 29, 2005)). FDA has reviewed its records to identify applications that were approved before the effective date of Title IX of FDAAA with elements to assure safe use and has identified the drug and biological products listed in table 1 of this document as those that will be deemed to have in effect an approved REMS.

¹ Section 505(p)(1) of the act (21 U.S.C. 355(p)(1)) states that section 505–1 of the act applies to applications for prescription drugs approved under section 505(b) or (j) of the act and applications approved under section 351 of the Public Health Service Act (42 U.S.C. 262).

² Title IX, subtitle A of FDAAA, which includes section 909, takes effect March 25, 2008; 180 days after that date is September 21, 2008.

³ These plans sometimes contain other elements to minimize risk such as a Medication Guide (21 CFR part 208) or a communication/educational plan for health care providers or patients. A drug will not be deemed to have a REMS if it has only a Medication Guide, patient package insert, and/or communication plan (see section 505–1(e)(2) and (e)(3) of the act).

TABLE 1.—PRODUCTS DEEMED TO HAVE IN EFFECT AN APPROVED REMS

| Generic or Proper Name | Brand Name | Application Number ¹ | Date of Approval ² |
|------------------------|-----------------------|---|---|
| Abarelix | Plenaxis ³ | NDA 21-320 | 11/25/2003 |
| Alosetron | Lotronex | NDA 21-107 | 2/9/2000 |
| Ambrisentan | Letairis | NDA 22-081 | 6/15/2007 |
| Bosentan | Tracleer | NDA 21-290 | 11/20/2001 |
| Clozapine | Clozaril | NDA 19-758 ANDA 74-949 ANDA 75-417 ANDA 75-713 ANDA 75-162 ANDA 76-809 NDA 21-590 | 9/26/1989 11/26/1997 5/27/1999 11/15/2002 4/26/2005 12/16/2005 2/9/2004 |
| | Fazaclo ODT | | |
| Dofetilide | Tikosyn | NDA 20-391 | 10/1/1999 |
| Eculizumab | Soliris | BLA 125166 | 3/16/2007 |
| Fentanyl PCA | lonsys ³ | NDA 21-338 | 5//22/2006 |
| Fentanyl citrate | Actiq | NDA 20-747 | 11/14/1998 |
| Isotretinoin | Accutane Amnesteem | NDA 18-662 ANDA 75-945 ANDA 76-135 ANDA 76-356 ANDA 76-041 ANDA 76-503 | 5/7/1982 11/2002 4/2003 4/2003 12/2002 6/2003 |
| | Sotret | | |
| Lenalidomide | Revlimid | NDA 21-880 | 12/27/2005 |
| Mifepristone | Mifeprex | NDA 20-687 | 9/28/2000 |

| | | | |
|------------------------------------|----------|--------------------------|------------|
| Natalizumab | Tysabri | BLA 125104 | 11/23/2004 |
| Small pox (Vaccinia) Vaccine, Live | ACAM2000 | BLA 125158 | 8/31/2007 |
| Sodium oxybate | Xyrem | NDA 21-196 | 7/17/2002 |
| Thalidomide | Thalomid | NDA 20-785 NDA 21-430 | 7/16/1998 |

¹ New drug application (NDA), abbreviated new drug application (ANDA), biologics license application (BLA).

² The original date of approval of the drug. FDA may have required elements to assure safe use at a later date.

³ Product is not currently marketed in the United States.

FDA is further asking members of the public to please notify the agency if they are aware of applications that have not been identified in this document and that they believe should be deemed to have in effect an approved REMS. Please provide the information to Mary Dempsey, Risk Management Coordinator (see the FOR FURTHER INFORMATION CONTACT section of this document).

Any application holder that believes its product identified in this notice should not be on the list of drug or biological products that will be deemed to have in effect an approved REMS should submit a letter identified with Docket Number FDA–2008–N–0174 to the Division of Dockets Management (see ADDRESSES) stating why the application holder believes its product was improperly identified in this notice. FDA will notify the application holder within 30 days of receipt of the letter of its determination.

Dated: March 19, 2008.

Jeffrey Shuren, Associate Commissioner for Policy and Planning.

[FR Doc. E8-6201 Filed 3-26-08; 8:45 am]

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DEPARTMENT OF HEALTH AND
HUMAN SERVICES

Food and Drug Administration

Joint Meeting of the Anesthetic and Life Support
Drugs Advisory Committee and the Drug Safety and
Risk Management Advisory Committee; Notice
of Meeting

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

This notice announces a forthcoming of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public. Name of Committees: Anesthetic and Life Support Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee.