

**AMENDMENT IN THE NATURE OF A SUBSTITUTE
TO THE COMMITTEE PRINT**

OFFERED BY _____

[Risk Evaluation and Mitigation Strategies]

Strike all after the enacting clause and insert the following:

**1 SECTION 1. POSTMARKET STUDIES AND CLINICAL TRIALS
2 REGARDING HUMAN DRUGS; RISK EVALUA-
3 TION AND MITIGATION STRATEGIES.**

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

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

9 “(1) IN GENERAL.—A responsible person may
10 not introduce or deliver for introduction into inter-
11 state commerce the new drug involved if the person
12 is in violation of a requirement established under
13 paragraph (3) or (4) with respect to the drug.

14 “(2) DEFINITIONS.—For purposes of this sub-
15 section:

16 “(A) RESPONSIBLE PERSON.—The term
17 ‘responsible person’ means a person who—

1 “(i) has submitted to the Secretary a
2 covered application that is pending; or

3 “(ii) is the holder of an approved cov-
4 ered application.

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

7 “(i) an application under subsection
8 (b) for a drug that is subject to section
9 503(b); and

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

12 “(C) NEW SAFETY INFORMATION; SERIOUS
13 RISK.—The terms ‘new safety information’, ‘se-
14 rious risk’, and ‘signal of a serious risk’ have
15 the meanings given such terms in section
16 505A(b).

17 “(3) STUDIES AND CLINICAL TRIALS.—

18 “(A) IN GENERAL.—For any or all of the
19 purposes specified in subparagraph (B), the
20 Secretary may, subject to subparagraph (C), re-
21 quire a responsible person for a drug to conduct
22 a postapproval study of the drug, or a post-
23 approval clinical trial of the drug, on the basis
24 of scientific information, including information

1 regarding chemically-related or pharmacologi-
2 cally-related drugs.

3 “(B) PURPOSES OF STUDY OR TRIAL.—
4 The purposes referred to in this subparagraph
5 with respect to a postapproval study or post-
6 approval clinical trial are the following:

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

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

11 “(iii) To identify a serious risk.

12 “(C) ESTABLISHMENT OF REQUIREMENT
13 AFTER APPROVAL OF COVERED APPLICATION.—
14 The Secretary may require a postapproval study
15 or postapproval trial for a drug for which an
16 approved covered application is in effect as of
17 the date on which the Secretary seeks to estab-
18 lish such requirement only if the Secretary be-
19 comes aware of new safety information.

20 “(4) LABELING.—

21 “(A) IN GENERAL.—The Secretary may re-
22 quire the responsible person for a drug to mod-
23 ify the labeling of the drug if the Secretary de-
24 termines that new safety information has be-
25 come available that is associated with the use of

1 the drug and should be communicated in the la-
2 beling of the drug.

3 “(B) DISCUSSIONS; ORDER TO MAKE
4 CHANGE; FAILURE TO COMPLY.—If the Sec-
5 retary determines that a change in labeling
6 should be required under subparagraph (A), the
7 following applies:

8 “(i) The Secretary shall provide the
9 responsible person a period of 45 days in
10 which to discuss the change with the Sec-
11 retary.

12 “(ii) Not later than 60 days after
13 making such determination, the Secretary
14 shall issue an order to make the change.

15 “(iii) The order shall specify the date
16 by which the responsible person is required
17 to complete implementation of the change,
18 not to 60 days.

19 “(iv) If the change is not made by the
20 date so specified, the responsible person
21 shall be considered to be in violation of
22 this section.

23 “(C) RULE OF CONSTRUCTION.—This sub-
24 section may not be construed as having any
25 legal effect on the provisions of section 314.70

1 of title 21, Code of Federal Regulations (or suc-
2 cessor regulations).

3 “(p) RISK EVALUATION AND MITIGATION STRAT-
4 EGY.—

5 “(1) IN GENERAL.—A person may not intro-
6 duce or deliver for introduction into interstate com-
7 merce a new drug if—

8 “(A)(i) the application for such drug is ap-
9 proved under subsection (b) or (j) and is sub-
10 ject to section 503(b); or

11 “(ii) the application for such drug is ap-
12 proved under section 351 of the Public Health
13 Service Act; and

14 “(B) a risk evaluation and mitigation
15 strategy is required under section 505A with re-
16 spect to the drug and—

17 “(i) the person fails to maintain com-
18 pliance with the requirements of the ap-
19 proved strategy or with other requirements
20 under section 505A, including require-
21 ments regarding assessments of approved
22 strategies; or

23 “(ii) in the case of a requirement for
24 such a strategy that is first established
25 after the applicable application referred to

1 in subparagraph (A) was approved with re-
2 spect to the drug, the Secretary, after no-
3 tice and opportunity for a hearing, pub-
4 lishes in the Federal Register a statement
5 the person is not cooperating with the Sec-
6 retary in developing such a strategy for the
7 drug.

8 “(2) REQUIRED STATEMENT DURING APPROVAL
9 PROCESS.—In the case of an application referred to
10 in paragraph (1)(A) or a supplement to such an ap-
11 plication that requires substantive data, the Sec-
12 retary may not approve the application or supple-
13 ment unless the person involved has complied with
14 the following:

15 “(A) The person has submitted to the Sec-
16 retary a statement that provides the following
17 information:

18 “(i) Whether the person believes that
19 a risk evaluation and mitigation strategy
20 should be required under section 505A.

21 “(ii) Whether a postmarket study or
22 clinical trial should be required under sub-
23 section (o)(3).

1 “(B) In making the statement under sub-
2 paragraph (A), the person took into account
3 each of the following factors:

4 “(i) The estimated size of the popu-
5 lation likely to use the drug involved.

6 “(ii) The seriousness of the disease or
7 condition that is to be treated with the
8 drug.

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

11 “(iv) The expected or actual duration
12 of treatment with the drug.

13 “(v) The seriousness of any known or
14 potential adverse events that may be re-
15 lated to the drug and the background inci-
16 dence of such events in the population like-
17 ly to use the drug.

18 “(3) CERTAIN POSTMARKET STUDIES.—The
19 failure to conduct a postmarket study under subpart
20 H of part 314 of title 21, Code of Federal Regula-
21 tions (or any successor regulation), is deemed to be
22 a violation of paragraph (1).”.

23 (b) REQUIREMENTS REGARDING STRATEGIES.—
24 Chapter V of the Federal Food, Drug, and Cosmetic Act
25 (21 U.S.C. 351 et seq.) is amended—

1 (1) by redesignating section 505A as 505A–1;

2 and

3 (2) by inserting after section 505 the following

4 section:

5 **“SEC. 505A. RISK EVALUATION AND MITIGATION STRATE-**
6 **GIES.**

7 “(a) SUBMISSION OF PROPOSED STRATEGY.—

8 “(1) INITIAL APPROVAL.—A person who sub-
9 mits an application referred to in section
10 505(p)(1)(A) (referred to in this section as a ‘cov-
11 ered application’) shall submit to the Secretary with
12 the application a proposed risk evaluation and miti-
13 gation strategy if the Secretary determines such a
14 strategy is necessary to ensure that the benefits of
15 the drug involved outweigh the risks of the drug. In
16 making such a determination, the Secretary shall
17 consider the statement submitted by the person
18 under section 505(p)(2) with respect to the drug.

19 “(2) POSTAPPROVAL REQUIREMENT.—

20 “(A) IN GENERAL.—If the Secretary ap-
21 proves a covered application and does not when
22 approving the application require a risk evalua-
23 tion and mitigation strategy under paragraph
24 (1), the Secretary may subsequently require
25 such a strategy for the drug involved if the Sec-

1 retary becomes aware of new safety information
2 and makes a determination that such a strategy
3 is necessary to ensure that the benefits of the
4 drug outweigh the risks of the drug.

5 “(B) SUBMISSION OF PROPOSED STRAT-
6 EGY.—Not later than 180 days after the Sec-
7 retary notifies the holder of an approved cov-
8 ered application that the Secretary has made a
9 determination under subparagraph (A) with re-
10 spect to the drug involved, the holder shall sub-
11 mit to the Secretary a proposed risk evaluation
12 and mitigation strategy.

13 “(3) APPROVAL OF NEW INDICATION FOR
14 USE.—The applicability of paragraph (2) includes
15 applicability to a drug for which an approved cov-
16 ered application was in effect on the day before the
17 effective date of this section and for which, on or
18 after such effective date, the holder of the approved
19 application submits to the Secretary a supplemental
20 application seeking approval of a new indication for
21 use of the drug.

22 “(4) ABBREVIATED NEW DRUG APPLICA-
23 TIONS.—The applicability of this section to an appli-
24 cation under section 505(j) is subject to subsection
25 (i).

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

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

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

9 “(B) an adverse event occurring from an
10 overdose of the drug, whether accidental or in-
11 tentional;

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

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

16 “(E) any failure of expected pharma-
17 cological action of the drug.

18 “(2) COVERED APPLICATION.—The term ‘cov-
19 ered application’ has the meaning indicated for such
20 term in subsection (a)(1).

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

24 “(A) a serious risk or an unexpected seri-
25 ous risk associated with use of the drug that

1 the Secretary has become aware of since the
2 last assessment of the approved risk evaluation
3 and mitigation strategy for the drug; or

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

8 “(4) SERIOUS ADVERSE DRUG EXPERIENCE.—

9 The term ‘serious adverse drug experience’ is an ad-
10 verse event that—

11 “(A) results in—

12 “(I) death;

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

19 “(iii) inpatient hospitalization or pro-
20 longation of existing hospitalization;

21 “(iv) a persistent or significant inca-
22 pacity or substantial disruption of the abil-
23 ity to conduct normal life functions; or

24 “(v) a congenital anomaly or birth de-
25 fect; or

1 “(B) based on appropriate medical judg-
2 ment, may jeopardize the patient and may re-
3 quire a medical or surgical intervention to pre-
4 vent an outcome described under subparagraph
5 (A).

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

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

12 “(A) a clinical trial;

13 “(B) adverse event reports;

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

16 “(D) peer-reviewed biomedical literature.

17 “(7) RESPONSIBLE PERSON.—The term ‘re-
18 sponsible person’ has the meaning indicated for such
19 term in subsection (e)(2).

20 “(8) UNEXPECTED SERIOUS RISK.—The term
21 ‘unexpected serious risk’ means a serious adverse
22 drug experience that is not listed in the labeling of
23 a drug, or that may be symptomatically and
24 pathophysiologically related to an adverse drug expe-
25 rience identified in the labeling, but differs from

1 such adverse drug experience because of greater se-
2 verity, specificity, or prevalence.

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

5 “(1) include the timetable required under sub-
6 section (d); and

7 “(2) to the extent required by the Secretary, in-
8 clude additional elements described in subsections
9 (e) and (f).

10 “(d) MINIMAL STRATEGY.—For purposes of sub-
11 section (c)(1), the risk evaluation and mitigation strategy
12 for a drug shall require a timetable for submission of as-
13 sessments of the strategy that—

14 “(1) is not less frequent than once annually for
15 the first 3 years after the strategy is initially ap-
16 proved;

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

19 “(3) subject to paragraph (2), for subsequent
20 years—

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

23 “(B) is increased or reduced in frequency
24 as necessary as provided for in subsection
25 (g)(4)(F); and

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

6 “(e) ADDITIONAL POTENTIAL ELEMENTS OF STRAT-
7 EGY.—

8 “(1) IN GENERAL.—The Secretary may under
9 subsection (c)(2) require that the risk evaluation
10 and mitigation strategy for a drug include 1 or more
11 of the additional elements described in this sub-
12 section if the Secretary makes the determination re-
13 quired with respect to the element involved.

14 “(2) MEDGUIDE; PATIENT PACKAGE INSERT.—
15 The risk evaluation and mitigation strategy for a
16 drug may require that, as applicable, the person sub-
17 mitting the covered application or the holder of the
18 approved such application (referred to in this section
19 as the ‘responsible person’) develop for distribution
20 to each patient when the drug is dispensed—

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

1 “(B) a patient package insert, if the Sec-
2 retary determines that such insert may help
3 mitigate a serious risk of the drug.

4 “(3) COMMUNICATION PLAN.—The risk evalua-
5 tion and mitigation strategy for a drug may require
6 that the responsible person conduct a communica-
7 tion plan to health care providers, if, with respect to
8 such drug, the Secretary determines that such plan
9 may support implementation of an element of the
10 strategy. Such plan may include—

11 “(A) sending letters to health care pro-
12 viders;

13 “(B) disseminating information about the
14 elements of the risk evaluation and mitigation
15 strategy to encourage implementation by health
16 care providers of components that apply to such
17 health care providers, or to explain certain safe-
18 ty protocols (such as medical monitoring by
19 periodic laboratory tests); or

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

24 “(4) PREREVIEW.—

1 “(A) IN GENERAL.—The risk evaluation
2 and mitigation strategy for a drug may require
3 that the responsible person submit to the Sec-
4 retary advertisements of the drug for prereview
5 not later than 45 days before dissemination of
6 the advertisement in any case in which the Sec-
7 retary determines that prereview of such adver-
8 tisements is necessary to ensure the inclusion of
9 a true statement in such advertisements of in-
10 formation in brief summary relating to—

11 “(i) a serious risk listed in the label-
12 ing of a drug; or

13 “(ii) a protocol to ensure the safe use
14 described in the labeling of the drug.

15 “(B) SPECIFICATION OF ADVERTISE-
16 MENTS.—The Secretary may specify the adver-
17 tisements required to be submitted under clause
18 (i).

19 “(5) SPECIFIC DISCLOSURES.—

20 “(A) IN GENERAL.—The risk evaluation
21 and mitigation strategy for a drug may require
22 that the responsible person include in advertise-
23 ments of the drug a specific disclosure—

24 “(I) of the date the drug was ap-
25 proved and that the existing information

1 may not have identified or allowed for full
2 assessment of all serious risks of using the
3 drug, if the Secretary determines that such
4 disclosure is necessary to protect public
5 health and safety; or

6 “(ii) about a serious adverse event
7 listed in the labeling of the drug or a pro-
8 tocol to ensure safe use described in the la-
9 beling of the drug, if the Secretary deter-
10 mines that such advertisements lacking
11 such disclosure would be false or mis-
12 leading.

13 “(B) SPECIFICATION OF ADVERTISE-
14 MENTS.—The Secretary may specify the adver-
15 tisements required to include a specific disclo-
16 sure under subparagraph (A).

17 “(6) TEMPORARY REVIEW PERIOD.—The risk
18 evaluation and mitigation strategy for a drug may
19 require that for a fixed period after initial approval,
20 not to exceed 3 years, the responsible person not
21 issue or cause to be issued direct-to-consumer adver-
22 tisements of the drug, if the Secretary determines
23 that disclosure under paragraph (7) is inadequate to
24 protect public health and safety, and that such pro-
25 hibition is necessary to protect public health and

1 safety while additional information about serious
2 risks of the drug is collected, considering—

3 “(A) the number of patients who may be
4 treated with the drug;

5 “(B) the seriousness of the condition for
6 which the drug will be used;

7 “(C) the serious adverse events listed in
8 the labeling of the drug;

9 “(D) the extent to which patients have ac-
10 cess to other approved drugs in the pharma-
11 cological class of the drug and with the same
12 intended use as the drug; and

13 “(E) the extent to which clinical trials
14 used to approve the drug may not have identi-
15 fied serious risks that might occur among pa-
16 tients expected to be treated with the drug.

17 “(f) RESTRICTIONS ON DISTRIBUTION OR USE.—

18 “(1) IN GENERAL.—If the Secretary determines
19 that a drug shown to be effective can be safely used
20 only if distribution or use of such drug is restricted,
21 the Secretary may under subsection (c)(2) require as
22 elements of the risk evaluation and mitigation strat-
23 egy such restrictions on distribution or use as are
24 needed to ensure safe use of the drug.

1 “(2) ASSURING ACCESS AND MINIMIZING BUR-
2 DEN.—Elements of a risk evaluation and mitigation
3 strategy included under paragraph (1) shall—

4 “(A) be commensurate with a specific seri-
5 ous risk listed in the labeling of the drug;

6 “(B) be posted publicly by the Secretary
7 with an explanation of how such elements will
8 mitigate the observed safety risk, which posting
9 shall be made within 30 days after the date on
10 which the Secretary requires the element in-
11 volved;

12 “(C) considering the risk referred to in
13 subparagraph (A) , not be unduly burdensome
14 on patient access to the drug, considering in
15 particular—

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

18 “(ii) patients who have difficulty ac-
19 cessing health care (such as patients in
20 rural or medically underserved areas); and

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

1 “(i) conform with elements to assure
2 safe use for other drugs with similar, seri-
3 ous risks; and

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

7 “(3) ELEMENTS.—The restrictions on distribu-
8 tion or use described in paragraph (1) shall include
9 1 or more goals to evaluate or mitigate a serious
10 risk listed in the labeling of the drug, and may re-
11 quire that—

12 “(A) health care providers that prescribe
13 the drug have special training or experience, or
14 are specially certified, which training or certifi-
15 cation with respect to the drug is available to
16 any willing provider from a frontier area;

17 “(B) pharmacies, practitioners, or health
18 care settings that dispense the drug are spe-
19 cially certified, which training or certification
20 with respect to the drug is available to any will-
21 ing provider from a frontier area;

22 “(C) the drug be dispensed to patients only
23 in certain health care settings, such as hos-
24 pitals;

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

4 “(E) each patient using the drug be sub-
5 ject to certain monitoring; or

6 “(F) each patient using the drug be en-
7 rolled in a registry.

8 “(4) IMPLEMENTATION SYSTEM.—The restric-
9 tions on distribution or use described in paragraph
10 (1) may require a system through which the respon-
11 sible person is able to—

12 “(A) monitor and evaluate implementation
13 of the restrictions by health care providers,
14 pharmacists, patients, and other parties in the
15 health care system who are responsible for im-
16 plementing the restrictions;

17 “(B) work to improve implementation of
18 the restrictions by health care providers, phar-
19 macists, patients, and other parties in the
20 health care system who are responsible for im-
21 plementing the restrictions; and

22 “(C) stop distribution of the drug to those
23 health care providers, pharmacists, and other
24 parties in the health care system—

1 “(I) who are responsible for imple-
2 menting the restrictions; and

3 “(ii) whom the responsible person
4 knows have failed to meet their responsibil-
5 ities for implementing the restrictions,
6 after the responsible person has informed
7 such party of such failure and such party
8 has not remedied such failure.

9 “(5) PATENTS.—The Secretary shall not ap-
10 prove a risk evaluation and mitigation strategy for
11 a drug, or any modification to the strategy, under
12 subsection (a) if—

13 “(A) the strategy includes a restriction on
14 distribution or use described in paragraph (1)
15 that is protected by a patent;

16 “(B) such patent was issued after the date
17 of the enactment of this section; and

18 “(C) such patent would prohibit or impair
19 the application of such restriction under sub-
20 section (j)(1)(G) to a drug that is the subject
21 of an abbreviated new drug application.

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

24 “(1) VOLUNTARY ASSESSMENTS.—After the ap-
25 proval of a risk evaluation and mitigation strategy

1 under subsection (a), the responsible person involved
2 may, subject to paragraph (2), submit to the Sec-
3 retary an assessment of, and propose a modification
4 to, the approved strategy for the drug involved at
5 any time.

6 “(2) REQUIRED ASSESSMENTS.—A responsible
7 person shall, subject to paragraph (5), submit an as-
8 sessment of, and may propose a modification to, the
9 approved risk evaluation and mitigation strategy for
10 a drug—

11 “(A) when submitting a supplemental ap-
12 plication for a new indication for use under sec-
13 tion 505(b) or under section 351 of the Public
14 Health Service Act, unless the drug is not sub-
15 ject to section 503(b) and the risk evaluation
16 and mitigation strategy for the drug includes
17 only the timetable under subsection (d);

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

21 “(C) within a time specified by the Sec-
22 retary, not to be less than 45 days, when or-
23 dered by the Secretary, if the Secretary deter-
24 mines that new safety or effectiveness informa-
25 tion indicates that an element under subsection

1 (d) or (e) should be modified or included in the
2 strategy;

3 “(D) within 90 days when ordered by the
4 Secretary, if the Secretary determines that new
5 safety or effectiveness information indicates
6 that an element under subsection (f) should be
7 modified or included in the strategy; or

8 “(E) within 15 days when ordered by the
9 Secretary, if the Secretary determines that
10 there may be a cause for action by the Sec-
11 retary under section 505(e).

12 “(3) REQUIREMENTS FOR ASSESSMENTS.—An
13 assessment under paragraph (1) or (2) of an ap-
14 proved risk evaluation and mitigation strategy for a
15 drug shall include—

16 “(A) with respect to any goal under sub-
17 section (f), an assessment of the extent to
18 which the restrictions on distribution or use are
19 meeting the goal or whether the goal or such
20 restrictions should be modified;

21 “(B) with respect to any postapproval
22 study required under section 505(o(3)), the sta-
23 tus of such study, including whether any dif-
24 ficulties completing the study have been en-
25 countered; and

1 “(C) with respect to any postapproval clin-
2 ical trial required under section 505(o), the sta-
3 tus of such clinical trial, including whether en-
4 rollment has begun, the number of participants
5 enrolled, the expected completion date, whether
6 any difficulties completing the clinical trial have
7 been encountered, and registration information
8 with respect to requirements under section
9 402(I) of the Public Health Service Act.

10 “(4) MODIFICATION.—A modification (whether
11 an enhancement or a reduction) to the approved risk
12 evaluation and mitigation strategy for a drug may
13 include the addition or modification of any element
14 under subsection (d) or the addition, modification,
15 or removal of any element under subsection (e) or
16 (f), such as—

17 “(A) modifying the timetable for assess-
18 ments of the strategy under subsection (d), in-
19 cluding to eliminate assessments;

20 “(B) adding, modifying, or removing a re-
21 striction on advertising under paragraph (4),
22 (5), or (6) of subsection (e); or

23 “(C) adding, modifying, or removing a re-
24 striction on distribution or use under subsection
25 (f);

1 “(5) NO EFFECT ON LABELING CHANGES THAT
2 DO NOT REQUIRE PREAPPROVAL.—In the case of a
3 labeling change to which section 314.70 of title 21,
4 Code of Federal Regulations (or any successor regu-
5 lation), applies for which the submission of a supple-
6 mental application is not required or for which dis-
7 tribution of the drug involved may commence upon
8 the receipt by the Secretary of a supplemental appli-
9 cation for the change, the submission of an assess-
10 ment of the approved risk evaluation and mitigation
11 strategy for the drug under paragraph (2) is not re-
12 quired.

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

15 “(1) IN GENERAL.—The Secretary shall
16 promptly review each proposed risk evaluation and
17 mitigation strategy for a drug submitted under sub-
18 section (a) and each assessment of an approved risk
19 evaluation and mitigation strategy for a drug sub-
20 mitted under subsection (g).

21 “(2) MARKETING PLAN.—**[*New text to be pro-***
22 ***vided.*]**

23 “(3) DISCUSSION.—The Secretary shall initiate
24 discussions with a responsible person for purposes of
25 this subsection to determine a strategy—

1 “(A) if the proposed strategy is submitted
2 as part of an application or supplemental appli-
3 cation under subsection (a) or subsection
4 (g)(2)(A), not less than 60 days before the ac-
5 tion deadline for the application that has been
6 agreed to by the Secretary and that has been
7 set forth in goals identified in letters of the
8 Secretary (relating to the use of fees collected
9 under section 736 to expedite the drug develop-
10 ment process and the process for the review of
11 human drug applications);

12 “(B) if the assessment is submitted under
13 subparagraph (B) or (C)) or subsection (g)(2),
14 not later than 20 days after such submission;

15 “(C) if the assessment is submitted under
16 subsection (g)(1) or subsection (g)(2)(D) , not
17 later than 30 days after such submission; or

18 “(D) if the assessment is submitted under
19 subsection (g)(2)(E), not later than 10 days
20 after such submission.

21 “(4) ACTION.—

22 “(A) IN GENERAL.—Unless the responsible
23 person requests the dispute resolution process
24 described under paragraph (5), the Secretary
25 shall approve and describe the risk evaluation

1 and mitigation strategy for a drug, or any
2 modification to the strategy—

3 “(i) as part of the action letter on the
4 application, when a proposed strategy is
5 submitted under subsection (a) or an as-
6 sessment of the strategy is submitted
7 under subsection (g)(1)(A); or

8 “(ii) in an order issued not later than
9 50 days after the date discussions of such
10 modification begin under paragraph (3),
11 when an assessment of the strategy is sub-
12 mitted under subsection (g)(1) or under
13 any of subparagraphs (B) through (E) of
14 subsection (g)(2).

15 “(B) INACTION.—An approved risk evalua-
16 tion and mitigation strategy shall remain in ef-
17 fect until the Secretary acts, if the Secretary
18 fails to act as provided under subparagraph
19 (A).

20 “(C) PUBLIC AVAILABILITY.—Any action
21 letter described in subparagraph (A)(I) or order
22 described in subparagraph (A)(ii) shall be made
23 publicly available.

24 “(5) DISPUTE RESOLUTION.—

25 “(A) REQUEST FOR REVIEW.—

1 “(i) IN GENERAL.—Not earlier than
2 15 days, and not later than 35 days, after
3 discussions under paragraph (3) have
4 begun, the responsible person may request
5 in writing that a dispute about the strat-
6 egy be reviewed by the Drug Safety Over-
7 sight Board under subsection (k), except
8 that the determination of the Secretary to
9 require a risk evaluation and mitigation
10 strategy is not subject to review under this
11 paragraph. The preceding sentence does
12 not prohibit review under this paragraph of
13 the particular elements of such a strategy.

14 “(ii) SCHEDULING.— Upon receipt of
15 a request under clause (i), the Secretary
16 shall schedule the dispute involved for re-
17 view under subparagraph (B) and, not
18 later than 5 business days of scheduling
19 the dispute for review, shall publish by
20 posting on the Internet or otherwise a no-
21 tice that the dispute will be reviewed by
22 the Drug Safety Oversight Board.

23 “(B) SCHEDULING REVIEW.—If a respon-
24 sible person requests review under subpara-
25 graph (A), the Secretary—

1 “(I) shall schedule the dispute for re-
2 view at 1 of the next 2 regular meetings of
3 the Drug Safety Oversight Board, which-
4 ever meeting date is more practicable; or

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

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

12 “(I) FURTHER DISCUSSION OR AD-
13 MINISTRATIVE APPEALS.—A request for
14 review under subparagraph (A) shall not
15 preclude further discussions to reach
16 agreement on the risk evaluation and miti-
17 gation strategy, and such a request shall
18 not preclude the use of administrative ap-
19 peals within the Food and Drug Adminis-
20 tration to reach agreement on the strategy,
21 including appeals as described in letters of
22 the Secretary (relating to the use of fees
23 collected under section 736 to expedite the
24 drug development process and the process
25 for the review of human drug applications)

1 for procedural or scientific matters involv-
2 ing the review of human drug applications
3 and supplemental applications that cannot
4 be resolved at the divisional level.

5 “(ii) AGREEMENT TERMINATES DIS-
6 PUTE RESOLUTION.—At any time before a
7 decision and order is issued under sub-
8 paragraph (G) , the Secretary and the re-
9 sponsible person may reach an agreement
10 on the risk evaluation and mitigation strat-
11 egy through further discussion or adminis-
12 trative appeals, terminating the dispute
13 resolution process, and the Secretary shall
14 issue an action letter or order, as appro-
15 priate, that describes the strategy.

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

20 “(I) hear from both parties; and

21 “(ii) review the dispute.

22 “(E) RECORD OF PROCEEDINGS.—The
23 Secretary shall ensure that the proceedings of
24 any such meeting are recorded, transcribed, and
25 made public within 30 days of the meeting. The

1 Secretary shall redact the transcript to protect
2 any trade secrets or other confidential informa-
3 tion described in section 552(b)(4) of title 5,
4 United States Code.

5 “(F) RECOMMENDATION OF THE
6 BOARD.—Not later than 5 days after any such
7 meeting, the Drug Safety Oversight Board shall
8 provide a written recommendation on resolving
9 the dispute to the Secretary. Not later than 5
10 days after the Board provides such written rec-
11 ommendation to the Secretary, the Secretary
12 shall make the recommendation available to the
13 public.

14 “(G) ACTION BY THE SECRETARY.—

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

20 “(I) the action deadline referred
21 to in paragraph (3)(A); or

22 “(II) 7 days after receiving the
23 recommendation of the Drug Safety
24 Oversight Board.

1 “(ii) ORDER.—With respect to an as-
2 sessment of an approved risk evaluation
3 and mitigation strategy under subsection
4 (g)(1) or under any of subparagraphs (B)
5 through (E) of subsection (g)(2), the Sec-
6 retary shall issue an order, which shall be
7 made public, that resolves the dispute not
8 later than 7 days after receiving the rec-
9 ommendation of the Drug Safety Oversight
10 Board.

11 “(H) INACTION.—An approved risk evalua-
12 tion and mitigation strategy shall remain in ef-
13 fect until the Secretary acts, if the Secretary
14 fails to act as provided for under subparagraph
15 (G).

16 “(I) EFFECT ON ACTION DEADLINE.—
17 With respect to a proposal or assessment re-
18 ferred to in paragraph (1), the Secretary shall
19 be considered to have met the action deadline
20 referred to in paragraph (3)(A) with respect to
21 the application involved if the responsible per-
22 son requests the dispute resolution process de-
23 scribed in this paragraph and if the Secretary—

1 “(I) has initiated the discussions de-
2 scribed under paragraph (3) not less than
3 60 days before such action deadline; and

4 “(ii) has complied with the timing re-
5 quirements of scheduling review by the
6 Drug Safety Oversight Board, providing a
7 written recommendation, and issuing an
8 action letter under subparagraphs (B),
9 (F), and (G), respectively.

10 “(J) DISQUALIFICATION.—No individual
11 who is an employee of the Food and Drug Ad-
12 ministration and who reviews a drug or who
13 participated in an administrative appeal under
14 subparagraph (C)(I) with respect to such drug
15 may serve on the Drug Safety Oversight Board
16 at a meeting under subparagraph (D) to review
17 a dispute about the risk evaluation and mitiga-
18 tion strategy for such drug.

19 “(K) ADDITIONAL EXPERTISE.—The Drug
20 Safety Oversight Board may add members with
21 relevant expertise from the Food and Drug Ad-
22 ministration, including the Office of Pediatrics,
23 the Office of Women’s Health, or the Office of
24 Rare Diseases, or from other Federal public
25 health or health care agencies, for a meeting

1 under subparagraph (D) of the Drug Safety
2 Oversight Board.

3 “(6) USE OF ADVISORY COMMITTEES.—The
4 Secretary may convene a meeting of 1 or more advi-
5 sory committees of the Food and Drug Administra-
6 tion to—

7 “(A) review a concern about the safety of
8 a drug or class of drugs, including before an as-
9 sessment of the risk evaluation and mitigation
10 strategy or strategies of such drug or drugs is
11 required to be submitted under any of subpara-
12 graphs (B) through (E) of subsection (g)(2);

13 “(B) review the risk evaluation and mitiga-
14 tion strategy or strategies of a drug or group
15 of drugs; or

16 “(C) review a dispute under paragraph (5).

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

19 “(A) IN GENERAL.—When a concern about
20 a serious risk of a drug may be related to the
21 pharmacological class of the drug, the Secretary
22 may defer assessments of the approved risk
23 evaluation and mitigation strategies for such
24 drugs until the Secretary has convened 1 or
25 more public meetings to consider possible re-

1 sponses to such concern. If the Secretary defers
2 an assessment under this subparagraph, the
3 Secretary shall give notice to the public of the
4 deferral not later than 5 days of the deferral.

5 “(B) PUBLIC MEETINGS.—Such public
6 meetings may include—

7 “(I) 1 or more meetings of the re-
8 viewed entities for such drugs;

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

13 “(iii) 1 or more workshops of sci-
14 entific experts and other stakeholders.

15 “(C) ACTION.—After considering the dis-
16 cussions from any meetings under subpara-
17 graph (B), the Secretary may—

18 “(I) announce in the Federal Register
19 a planned regulatory action, including a
20 modification to each risk evaluation and
21 mitigation strategy, for drugs in the phar-
22 macological class;

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

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

4 “(8) INTERNATIONAL COORDINATION.—The
5 Secretary may coordinate the timetable for submis-
6 sion of assessments under subsection (d), or a study
7 or clinical trial under section 505(o)(3), with efforts
8 to identify and assess the serious risks of such drug
9 by the marketing authorities of other countries
10 whose drug approval and risk management processes
11 the Secretary deems comparable to the drug ap-
12 proval and risk management processes of the United
13 States. If the Secretary takes action to coordinate
14 such timetable, the Secretary shall give notice to the
15 public of the action not later than 5 days after the
16 action.

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

21 “(i) ABBREVIATED NEW DRUG APPLICATIONS.—

22 “(1) IN GENERAL.—A drug that is the subject of an
23 abbreviated new drug application under section 505(j) is
24 subject to only the following elements of the risk evalua-

1 tion and mitigation strategy required under subsection (a)
2 for the applicable listed drug:

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

6 “(B) Prereview of advertising, if required under sub-
7 section (e)(4) for the applicable listed drug.

8 “(C) Specific disclosures in advertising, if required
9 under subsection (e)(5) for the applicable listed drug.

10 “(D) A temporary review period during which direct-
11 to-consumer advertising will not occur, if required under
12 subsection (e)(6) for the applicable listed drug.

13 “(E) Restrictions on distribution or use, if required
14 under subsection (f) for the listed drug. A drug that is
15 the subject of an abbreviated new drug application and
16 the listed drug shall use a single, shared system under
17 subsection (f)(4). The Secretary may waive the require-
18 ment under the preceding sentence for a drug that is the
19 subject of an abbreviated new drug application if the Sec-
20 retary determines that—

21 “(I) it is not practical for the drug to use such
22 single, shared system; or

23 “(ii) the burden of using the single, shared sys-
24 tem outweighs the benefit of using the single system.

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

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

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

10 “(j) DRUG SAFETY OVERSIGHT BOARD.—

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

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

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

19 “(B) include representatives from offices
20 throughout the Food and Drug Administration;

21 “(C) include at least 1 representative from
22 each of the National Institutes of Health and
23 the Department of Health and Human Services
24 (other than the Food and Drug Administra-
25 tion);

1 “(D) representatives from other appro-
2 priate agencies that wish to provide representa-
3 tives; and

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

7 (c) REGULATION OF BIOLOGICAL PRODUCTS.—Sec-
8 tion 351 of the Public Health Service Act (42 U.S.C. 262)
9 is amended—

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

12 “(D) RISK EVALUATION AND MITIGATION STRAT-
13 EGY.—A person that submits an application for a license
14 under this paragraph is subject to section 505(p) of the
15 Federal Food, Drug, and Cosmetic Act.”; and

16 (2) in subsection (j), by inserting “, including
17 the requirements under section 505(p) of such Act,”
18 after “, and Cosmetic Act”.

19 (d) CONFORMING AMENDMENT; PREREVIEW OF AD-
20 VERTISEMENTS.—Section 502(n)(3)(A) of the Federal
21 Food, Drug, and Cosmetic Act (21 U.S.C. 352(n)(3)(A))
22 is amended by inserting “(or when required under section
23 505A(e)(4))” after “except in extraordinary cir-
24 cumstances”.

1 (e) RULE OF CONSTRUCTION REGARDING PEDIATRIC
2 STUDIES.—This Act and the amendments made by this
3 Act may not be construed as affecting the authority of
4 the Secretary of Health and Human Services to request
5 pediatric studies under section 505A–1 of the Federal
6 Food, Drug, and Cosmetic Act or to require such studies
7 under section 505B of such Act.

8 **SEC. 2. ENFORCEMENT.**

9 (a) MISBRANDING.—Section 502 of the Federal
10 Food, Drug, and Cosmetic Act (21 U.S.C. 352) is amend-
11 ed by adding at the end the following:

12 “(y) If it is a drug subject to an approved risk evalua-
13 tion and mitigation strategy pursuant to section 505(p)
14 and the person responsible for complying with the strategy
15 fails—

16 “(1) to make a labeling change required by
17 such strategy after the Secretary has completed re-
18 view of, and acted on, an assessment of such strat-
19 egy under section 505A(g); or

20 “(2) to comply with a requirement of such
21 strategy provided for under subsection (d), (e), or (f)
22 of section 505A.”.

23 (b) CIVIL PENALTIES.—Section 303 of the Federal
24 Food, Drug, and Cosmetic Act (21 U.S.C. 333(f)) is
25 amended—

1 (1) by redesignating subsection (g) (relating to
2 civil penalties) as subsection (f); and

3 (2) in subsection (f) (as so redesignated)—

4 (A) by redesignating paragraphs (3), (4),
5 and (5) as paragraphs (4), (5), and (6), respec-
6 tively;

7 (B) by inserting after paragraph (2) the
8 following:”.

9 “(3)(A) Any person who violates a requirement of
10 this Act which relates to drugs shall be liable to the United
11 States for a civil penalty in an amount not to exceed
12 \$20,000,000 for each such violation and, for all such viola-
13 tions adjudicated in a single proceeding, in an amount not
14 to exceed \$100,000,000.

15 “(B) If a violation referred to in subparagraph (A)
16 is continuing in nature and poses a substantial threat to
17 the public health, the Secretary may impose a civil penalty
18 not to exceed \$1,000,000 per day during such time period
19 such person is in violation.”.

20 (C) in paragraph (2)(C)), by striking
21 “paragraph (3)(A)” and inserting “paragraph
22 (4)(A)”;

23 (D) in paragraph (4), as so redesignated,
24 by striking “paragraph (1) or (2)” each place

1 it appears and inserting “paragraph (1), (2), or
2 (3)”; and

3 (E) in paragraph (6), as so redesignated,
4 by striking “paragraph (4)” each place it ap-
5 pears and inserting “paragraph (5)”.

6 **SEC. 3. NO EFFECT ON WITHDRAWAL OR SUSPENSION OF**
7 **APPROVAL.**

8 Section 505(e) of the Federal Food, Drug, and Cos-
9 metic Act (21 U.S.C. 355(e)) is amended by adding at
10 the end the following: “The Secretary may withdraw the
11 approval of an application submitted under this section,
12 or suspend the approval of such an application, as pro-
13 vided under this subsection, without first ordering the ap-
14 plicant to submit an assessment of the approved risk eval-
15 uation and mitigation strategy for the drug under section
16 505A(g)(2)(E).”.

17 **SEC. 4. BENEFIT-RISK ASSESSMENTS.**

18 Not later than 1 year after the date of the enactment
19 of this Act, the Commissioner of Food and Drugs shall
20 submit to the Congress a report on how best to commu-
21 nicate to the public the risks and benefits of new drugs
22 and the role of the risk evaluation and mitigation strategy
23 in assessing such risks and benefits.

1 **SEC. 5. ROUTINE ACTIVE SURVEILLANCE AND ASSESS-**
2 **MENT.**

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

6 “(3) ROUTINE ACTIVE SURVEILLANCE AND AS-
7 SESSMENT.—

8 “(A) DEVELOPMENT OF THE POSTMARKET
9 RISK IDENTIFICATION AND ANALYSIS SYS-
10 TEM.—The Secretary shall, not later than 2
11 years after the date of enactment of the En-
12 hancing Drug Safety and Innovation Act of
13 2007, act in collaboration with academic insti-
14 tutions and private entities to—

15 “(I) establish minimum standards for
16 collection and transmission of post-
17 marketing data elements from electronic
18 health data systems; and

19 “(ii) establish, through partnerships,
20 a validated and integrated postmarket risk
21 identification and analysis system to inte-
22 grate and analyze safety data from mul-
23 tiple sources, with the goals of including,
24 in aggregate—

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

1 “(II) at least 100,000,000 pa-
2 tients by July 1, 2012.

3 “(B) DATA COLLECTION ACTIVITIES.—

4 “(I) IN GENERAL.—The Secretary
5 shall, not later than 1 year after the estab-
6 lishment of the minimum standards and
7 the identification and analysis system
8 under subparagraph (A), establish and
9 maintain an active surveillance infrastruc-
10 ture—

11 “(I) to collect and report data for
12 pharmaceutical postmarket risk iden-
13 tification and analysis, in compliance
14 with the regulations promulgated
15 under section 264(c) of the Health
16 Insurance Portability and Account-
17 ability Act of 1996; and

18 “(II) that includes, in addition to
19 the collection and monitoring (in a
20 standardized form) of data on all seri-
21 ous adverse drug experiences (as de-
22 fined in section 505A(b)) required to
23 be submitted to the Secretary under
24 paragraph (1), and those events vol-
25 untarily submitted from patients, pro-

1 viders, and drug, when appropriate,
2 procedures to—

3 “(aa) provide for adverse
4 event surveillance by collecting
5 and monitoring Federal health-
6 related electronic data (such as
7 data from the Medicare program
8 and the health systems of the
9 Department of Veterans Affairs);

10 “(bb) provide for adverse
11 event surveillance by collecting
12 and monitoring private sector
13 health-related electronic data
14 (such as pharmaceutical purchase
15 data and health insurance claims
16 data);

17 “(cc) provide for adverse
18 event surveillance by monitoring
19 standardized electronic health
20 records, as available;

21 “(dd) provide for adverse
22 event surveillance by collecting
23 and monitoring other information
24 as the Secretary deems necessary
25 to create a robust system to iden-

1 tify adverse events and potential
2 drug safety signals;

3 “(ee) enable the program to
4 identify certain trends and pat-
5 terns with respect to data re-
6 ported to the program;

7 “(ff) enable the program to
8 provide regular reports to the
9 Secretary concerning adverse
10 event trends, adverse event pat-
11 terns, incidence and prevalence of
12 adverse events, laboratory data,
13 and other information determined
14 appropriate, which may include
15 data on comparative national ad-
16 verse event trends; and

17 “(gg) enable the program to
18 export data in a form appropriate
19 for further aggregation, statis-
20 tical analysis, and reporting.

21 “(ii) TIMELINESS OF REPORTING.—
22 The procedures developed under clause (I)
23 shall ensure that such data are collected,
24 monitored, and reported in a timely, rou-
25 tine, and automatic manner, taking into

1 consideration the need for data complete-
2 ness, coding, cleansing, and transmission.

3 “(iii) PRIVATE SECTOR RESOURCES.—
4 To ensure the establishment of the active
5 surveillance infrastructure by the date de-
6 scribed under clause (I), the Secretary
7 may, on a temporary or permanent basis,
8 implement systems or products developed
9 by private entities.

10 “(iv) COMPLEMENTARY AP-
11 PROACHES.—To the extent the active sur-
12 veillance infrastructure established under
13 clause (I) is not sufficient to gather data
14 and information relevant to priority drug
15 safety questions, the Secretary shall de-
16 velop, support, and participate in com-
17 plementary approaches to gather and ana-
18 lyze such data and information, includ-
19 ing—

20 “(I) approaches that are com-
21 plementary with respect to assessing
22 the safety of use of a drug in domestic
23 populations not included in the trials
24 used to approve the drug (such as
25 older people, people with

1 comorbidities, pregnant women, or
2 children); and

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

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

11 “(C) RISK IDENTIFICATION AND ANAL-
12 YSIS.—

13 “(I) PURPOSE.—To carry out this
14 paragraph, the Secretary shall establish
15 collaborations with other Government, aca-
16 demic, and private entities, including the
17 Centers for Education and Research on
18 Therapeutics under section 912 of the
19 Public Health Service Act, to provide for
20 the risk identification and analysis of the
21 data collected under subparagraph (B) and
22 data that is publicly available or is pro-
23 vided by the Secretary, in order to—

1 “(I) improve the quality and effi-
2 ciency of postmarket drug safety risk-
3 benefit analysis;

4 “(II) provide the Secretary with
5 routine access to expertise to study
6 advanced drug safety data; and

7 “(III) enhance the ability of the
8 Secretary to make timely assessments
9 based on drug safety data.

10 “(ii) PUBLIC PROCESS FOR PRIORITY
11 QUESTIONS.—At least biannually, the Sec-
12 retary shall seek recommendations from
13 the Drug Safety and Risk Management
14 Advisory Committee (or successor com-
15 mittee) and from other advisory commit-
16 tees, as appropriate, to the Food and Drug
17 Administration on—

18 “(I) priority drug safety ques-
19 tions; and

20 “(II) mechanisms for answering
21 such questions, including through—

22 “(aa) routine active surveil-
23 lance under subparagraph (B);
24 and

1 “(bb) when such surveillance
2 is not sufficient, postmarket
3 studies under paragraph (4) of
4 section 505A(e) and postapproval
5 clinical trials under paragraph
6 (5) of such section.

7 “(iii) PROCEDURES FOR THE DEVEL-
8 OPMENT OF DRUG SAFETY COLLABORA-
9 TIONS.—

10 “(I) IN GENERAL.—Not later
11 than 180 days after the date of the
12 establishment of the active surveil-
13 lance infrastructure under subpara-
14 graph (B), the Secretary shall estab-
15 lish and implement procedures under
16 which the Secretary may routinely col-
17 laborate with a qualified entity to—

18 “(aa) clean, classify, or ag-
19 gregate data collected under sub-
20 paragraph (B) and data that is
21 publicly available or is provided
22 by the Secretary;

23 “(bb) allow for prompt in-
24 vestigation of priority drug safety
25 questions, including—

1 “(AA) unresolved safety
2 questions for drugs or class-
3 es of drugs; and

4 “(BB) for a newly-ap-
5 proved drug: safety signals
6 from clinical trials used to
7 approve the drug and other
8 preapproval trials; rare, seri-
9 ous drug side effects; and
10 the safety of use in domestic
11 populations not included in
12 the trials used to approve
13 the drug (such as older peo-
14 ple, people with
15 comorbidities, pregnant
16 women, or children);

17 “(cc) perform advanced re-
18 search and analysis on identified
19 drug safety risks;

20 “(dd) convene an expert ad-
21 visory committee to oversee the
22 establishment of standards for
23 the ethical and scientific uses for,
24 and communication of, post-
25 marketing data collected under

1 subparagraph (B), including ad-
2 vising on the development of ef-
3 fective research methods for the
4 study of drug safety questions;

5 “(ee) focus postmarket stud-
6 ies under paragraph (4) of sec-
7 tion 505A(e) and postapproval
8 clinical trials under paragraph
9 (5) of such section more effec-
10 tively on cases for which reports
11 under paragraph (1) and other
12 safety signal detection is not suf-
13 ficient to resolve whether there is
14 an elevated risk of a serious ad-
15 verse event associated with the
16 use of a drug; and

17 “(ff) carry out other activi-
18 ties as the Secretary deems nec-
19 essary to carry out the purposes
20 of this paragraph.

21 “(II) REQUEST FOR SPECIFIC
22 METHODOLOGY.—The procedures de-
23 scribed in subclause (I) shall permit
24 the Secretary to request that a spe-
25 cific methodology be used by the

1 qualified entity. The qualified entity
2 shall work with the Secretary to final-
3 ize the methodology to be used.

4 “(iv) USE OF ANALYSES.—The Sec-
5 retary shall provide the analyses described
6 under this subparagraph, including the
7 methods and results of such analyses,
8 about a drug to the sponsor or sponsors of
9 such drug.

10 “(v) QUALIFIED ENTITIES.—

11 “(I) IN GENERAL.—The Sec-
12 retary shall enter into contracts with
13 a sufficient number of qualified enti-
14 ties to develop and provide informa-
15 tion to the Secretary in a timely man-
16 ner.

17 “(II) QUALIFICATION.—The Sec-
18 retary shall enter into a contract with
19 an entity under subclause (I) only if
20 the Secretary determines that the en-
21 tity—

22 “(aa) has the research capa-
23 bility and expertise to conduct
24 and complete the activities under
25 this paragraph;

1 “(bb) has in place an infor-
2 mation technology infrastructure
3 to support adverse event surveil-
4 lance data and operational stand-
5 ards to provide security for such
6 data;

7 “(cc) has experience with,
8 and expertise on, the develop-
9 ment of drug safety and effec-
10 tiveness research using electronic
11 population data;

12 “(dd) has an understanding
13 of drug development and risk/
14 benefit balancing in a clinical set-
15 ting; and

16 “(ee) has a significant busi-
17 ness presence in the United
18 States.

19 “(vi) CONTRACT REQUIREMENTS.—
20 Each contract with a qualified entity shall
21 contain the following requirements:

22 “(I) ENSURING PRIVACY.—The
23 qualified entity shall provide assur-
24 ances that the entity will not use the

1 data provided by the Secretary in a
2 manner that violates—

3 “(aa) the regulations pro-
4 mulgated under section 264(e)
5 of the Health Insurance Port-
6 ability and Accountability Act of
7 1996; or

8 “(bb) sections 552 or 552a
9 of title 5, United States Code,
10 with regard to the privacy of in-
11 dividually-identifiable beneficiary
12 health information.

13 “(II) COMPONENT OF ANOTHER
14 ORGANIZATION.—If a qualified entity
15 is a component of another organiza-
16 tion—

17 “(aa) the qualified entity
18 shall maintain the data related to
19 the activities carried out under
20 this paragraph separate from the
21 other components of the organi-
22 zation and establish appropriate
23 security measures to maintain
24 the confidentiality and privacy of
25 such data; and

1 “(bb) the entity shall not
2 make an unauthorized disclosure
3 of such data to the other compo-
4 nents of the organization in
5 breach of such confidentiality and
6 privacy requirement.

7 “(III) TERMINATION OR NON-
8 RENEWAL.—If a contract with a
9 qualified entity under this subpara-
10 graph is terminated or not renewed,
11 the following requirements shall apply:

12 “(aa) CONFIDENTIALITY
13 AND PRIVACY PROTECTIONS.—
14 The entity shall continue to com-
15 ply with the confidentiality and
16 privacy requirements under this
17 paragraph with respect to all
18 data disclosed to the entity.

19 “(bb) DISPOSITION OF
20 DATA.—The entity shall return
21 to the Secretary all data dis-
22 closed to the entity or, if return-
23 ing the data is not practicable,
24 destroy the data.

1 “(vii) COMPETITIVE PROCEDURES.—

2 The Secretary shall use competitive proce-
3 dures (as defined in section 4(5) of the
4 Federal Procurement Policy Act) to enter
5 into contracts under clause (v).

6 “(viii) REVIEW OF CONTRACT IN THE

7 EVEN OF A MERGER OR ACQUISITION.—

8 The Secretary shall review the contract
9 with a qualified entity under this para-
10 graph in the event of a merger or acquisi-
11 tion of the entity in order to ensure that
12 the requirements under this subparagraph
13 will continue to be met.

14 “(D) COORDINATION.—In carrying out

15 this paragraph, the Secretary shall provide for
16 appropriate communications to the public, sci-
17 entific, public health, and medical communities,
18 and other key stakeholders, and provide for the
19 coordination of the activities of private entities,
20 professional associations, or other entities that
21 may have sources of surveillance data.”.

22 (b) AUTHORIZATION OF APPROPRIATIONS.—To carry

23 out activities under the amendment made by subsection

24 (a) for which funds are made available under section 736

25 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C.

1 379h), there are authorized to be appropriated to carry
2 out the amendment made by this section, in addition to
3 such funds, \$25,000,000 for each of fiscal years 2008
4 through 2012.

5 **SEC. 6. AUTHORIZATION OF APPROPRIATIONS.**

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

10 (b) RELATION TO OTHER FUNDING.—The authoriza-
11 tion of appropriations under subsection (a) is in addition
12 to any other funds available for carrying out this Act and
13 the amendments made by this Act.

14 **SEC. 7. EFFECTIVE DATE AND APPLICABILITY.**

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

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

19 (1) IN GENERAL.—A drug that was approved
20 before the effective date of this Act is, in accordance
21 with paragraph (2), deemed to have in effect an ap-
22 proved risk evaluation and mitigation strategy under
23 section 505A of the Federal Food, Drug, and Cos-
24 metic Act (as added by section 1 of this Act) (re-
25 ferred to in this section as the “Act”) if there are

1 in effect on the effective date of this Act restrictions
2 on distribution or use—

3 (A) required under section 314.520 or sec-
4 tion 601.42 of title 21, Code of Federal Regula-
5 tions; or

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

8 (2) ELEMENTS OF STRATEGY; ENFORCE-
9 MENT.—The approved risk evaluation and mitigation
10 strategy in effect for a drug under paragraph (1)—

11 (A) is deemed to consist of the elements
12 described in paragraphs (1) and (2) of section
13 505A(d) of the Act and any additional elements
14 under subsections (d) and (e) of such section in
15 effect for such drug on the effective date of this
16 Act; and

17 (B) is subject to enforcement by the Sec-
18 retary to the same extent as any other risk
19 evaluation and mitigation strategy under sec-
20 tion 505A of the Act.

21 (3) SUBMISSION.—Not later than 180 days
22 after the effective date of this Act, the holder of an
23 approved application for which a risk evaluation and
24 mitigation strategy is deemed to be in effect under
25 paragraph (1) shall submit to the Secretary a pro-

1 posed risk evaluation and mitigation strategy. Such
2 proposed strategy is subject to section 505A of the
3 Act as if included in such application at the time of
4 submission of the application to the Secretary.

5 (c) OTHER DRUGS APPROVED BEFORE THE EFFEC-
6 TIVE DATE.—The Secretary, on a case-by-case basis, may
7 require the holder of an application approved before the
8 effective date of this Act to which subsection (b) does not
9 apply to submit a proposed risk evaluation and mitigation
10 strategy in accordance with the timeframes provided for
11 in subparagraphs (C) through (E) of section 505A(g)(2)
12 of the Act if the Secretary determines (with respect to
13 such drug or with respect to the group of drugs to which
14 such drug belongs) that—

15 (1) an element described under 505A(d)(1) of
16 the Act may require modification; or

17 (2) a standard for adding an element described
18 in subsection (e) or (d) of the Act that is not in ef-
19 fect with respect to such drug or class of drugs may
20 apply.

21 (d) USE OF ADVISORY COMMITTEES; PROCESS FOR
22 ADDRESSING DRUG CLASS EFFECTS.—In imposing a re-
23 quirement under subsection (c), the Secretary—

24 (1) may convene a meeting of 1 or more advi-
25 sory committees of the Food and Drug Administra-

1 tion in accordance with paragraph (6) of section
2 505A(h) of the Act; and

3 (2) may use the process described in paragraph
4 (7) of such section 505A(h) (relating to addressing
5 drug class effects).