

110TH CONGRESS
1ST SESSION

S. 468

To amend the Federal Food, Drug, and Cosmetic Act with respect to drug safety, and for other purposes.

IN THE SENATE OF THE UNITED STATES

JANUARY 31, 2007

Mr. GRASSLEY (for himself, Mr. DODD, Ms. MIKULSKI, and Mr. BINGAMAN) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

A BILL

To amend the Federal Food, Drug, and Cosmetic Act with respect to drug safety, and for other purposes.

1 *Be it enacted by the Senate and House of Representa-*
2 *tives of the United States of America in Congress assembled,*

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the “Food and Drug Ad-
5 ministration Safety Act of 2007”.

6 **SEC. 2. CENTER FOR POSTMARKET EVALUATION AND RE-**
7 **SEARCH FOR DRUGS AND BIOLOGICS.**

8 (a) IN GENERAL.—Chapter V of the Federal Food,
9 Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amend-
10 ed by inserting after section 506C the following:

1 **“SEC. 507. DRUG SAFETY.**

2 “(a) ESTABLISHMENT OF THE CENTER FOR
3 POSTMARKET EVALUATION AND RESEARCH FOR DRUGS
4 AND BIOLOGICS.—There is established within the Food
5 and Drug Administration a Center for Postmarket Eval-
6 uation and Research for Drugs and Biologics (referred to
7 in the section as the ‘Center’). The Director of the Center
8 shall report directly to the Commissioner of Food and
9 Drugs.

10 “(b) DUTIES OF THE CENTER FOR POSTMARKET
11 EVALUATION AND RESEARCH FOR DRUGS AND BIO-
12 LOGICS.—

13 “(1) RESPONSIBILITIES OF DIRECTOR.—The
14 Director of the Center, in consultation with the Di-
15 rector of the Center for Drug Evaluation and Re-
16 search or the Director of the Center for Biologics
17 Evaluation and Research, as appropriate, shall—

18 “(A) conduct postmarket risk assessment
19 of drugs approved under section 505 of this Act
20 and of biological products licensed under section
21 351 of the Public Health Service Act;

22 “(B) conduct and improve postmarket sur-
23 veillance of approved drugs and licensed biologi-
24 cal products using postmarket surveillance pro-
25 grams and activities (including MedWatch),
26 risk-benefit analyses, adverse event reports, the

1 scientific literature, any clinical or observational
2 studies (including studies required under sub-
3 section (d) or (e)), and any other resources that
4 the Director of the Center determines appro-
5 priate;

6 “(C) determine whether a study is required
7 under subsection (d) or (e) and consult with the
8 sponsors of drugs and biological products to en-
9 sure that such studies are completed by the
10 date, and according to the terms, specified by
11 the Director of the Center;

12 “(D) contract, or require the sponsor of an
13 application or the holder of an approved appli-
14 cation or license to contract, with the holders of
15 domestic and international patient databases to
16 conduct epidemiologic and other observational
17 studies;

18 “(E) determine, based on postmarket sur-
19 veillance programs and activities (including
20 MedWatch), risk-benefit analyses, adverse event
21 reports, the scientific literature, and any clinical
22 or observational studies (including studies re-
23 quired under subsection (d) or (e)), and any
24 other resources that the Director of the Center
25 determines appropriate, whether a drug or bio-

logical product may present an unreasonable risk to the health of patients or the general public, and take corrective action if such an unreasonable risk may exist;

“(F) make information about the safety and effectiveness of approved drugs and licensed biological products available to the public and healthcare providers in a timely manner; and

“(G) conduct other activities as the Director of the Center determines appropriate to ensure the safety and effectiveness of all drugs approved under section 505 and all biological products licensed under section 351 of the Public Health Service Act.

“(2) DETERMINATION OF UNREASONABLE RISK.—In determining whether a drug or biological product may present an unreasonable risk to the health of patients or the general public, the Director of the Center, in consultation with the Director of the Center for Drug Evaluation and Research or the Director of the Center for Biologics Evaluation and Research, as appropriate, shall consider the risk in relation to the known benefits of such drug or biological product.

1 “(c) SECRETARIAL AUTHORITY.—

2 “(1) IN GENERAL.—Approval of a drug under
3 section 505 of this Act or issuance of a license for
4 a biological product under section 351 of the Public
5 Health Service Act may be subject to the require-
6 ment that the sponsor conduct 1 or more postmarket
7 studies as described in subsection (d) or (e) of this
8 section, or other postmarket studies as required by
9 the Secretary, to validate the safety and effective-
10 ness of the drug or biological product.

11 “(2) DEFINITION.—For purposes of this sec-
12 tion, the term ‘postmarket’ means—

13 “(A) with respect to a drug, after approval
14 of an application under section 505; and

15 “(B) with respect to a biological product,
16 after licensure under section 351 of the Public
17 Health Service Act.

18 “(d) PREAPPROVAL REVIEW.—

19 “(1) REVIEW OF APPLICATION.—

20 “(A) IN GENERAL.—

21 “(i) REVIEW.—At any time before a
22 drug is approved under section 505 of this
23 Act or a biological product is licensed
24 under section 351 of the Public Health
25 Service Act, the Director of the Center

1 shall review the application (or supplement
 2 to the application), and any analyses asso-
 3 ciated with the application, of such drug or
 4 biological product.

5 “(ii) EFFECT OF APPROVAL OR LI-
 6 CENSURE.—The approval of a drug under
 7 section 505 or the licensure of a biological
 8 product under such section 351 shall not
 9 affect the continuation and completion of a
 10 review under clause (i).

11 “(B) LIMITATION.—In no case shall the
 12 review under subparagraph (A) delay a decision
 13 with respect to an application for a drug under
 14 section 505 of this Act or for a biological prod-
 15 uct under section 351 of the Public Health
 16 Service Act.

17 “(2) RESULT OF REVIEW.—The Director of the
 18 Center may, based on the review under paragraph
 19 (1)—

20 “(A) require that the sponsor of the appli-
 21 cation agree to conduct 1 or more postmarket
 22 studies to determine the safety or effectiveness
 23 of a drug or biological product, including such
 24 safety or effectiveness as compared to other
 25 drugs or biological products, to be completed by

1 a date, and according to the terms, specified by
2 the Director of the Center; or

3 “(B) contract, or require the sponsor of
4 the application to contract, with a holder of a
5 domestic or an international patient database to
6 conduct 1 or more epidemiologic or other obser-
7 vational studies.

8 “(e) POSTMARKETING STUDIES OF DRUG SAFETY.—

9 “(1) IN GENERAL.—At any time after a drug is
10 approved under section 505 of this Act or a biologi-
11 cal product is licensed under section 351 of the Pub-
12 lic Health Service Act, the Director of the Center,
13 may—

14 “(A) require that the holder of an ap-
15 proved application or license conduct 1 or more
16 studies to determine the safety or effectiveness
17 of such drug or biological product, including
18 such safety and effectiveness as compared to
19 other drugs or biological products, to be com-
20 pleted by a date, and according to the terms,
21 specified by such Director; or

22 “(B) contract, or require the holder of the
23 approved application or license to contract, with
24 a holder of a domestic or an international pa-

1 tient database to conduct 1 or more epidemio-
2 logic or other observational studies.

3 “(2) REVIEW OF OUTSTANDING STUDIES.—Not
4 later than 90 days after the date of enactment of
5 the Food and Drug Administration Safety Act of
6 2007, the Director of the Center shall—

7 “(A) review and publish a list in the Fed-
8 eral Register of any postmarketing studies out-
9 standing on the date of enactment of the Food
10 and Drug Administration Safety Act of 2007;
11 and

12 “(B) as the Director determines appro-
13 priate, require the sponsor of a study described
14 in subparagraph (A) to conduct such study
15 under this subsection.

16 “(f) PUBLICATION OF PROGRESS REPORTS AND
17 COMPLETED STUDIES.—

18 “(1) IN GENERAL.—The Director of the Center
19 shall require that the sponsor of a study under sub-
20 section (d) or (e) submit to the Secretary—

21 “(A) not less frequently than every 90
22 days, an up-to-date report describing the
23 progress of such study; and

24 “(B) upon the completion date of such
25 study, the results of such study.

1 “(2) COMPLETION DATE.—For purposes of this
 2 section, the completion date of such study shall be
 3 determined by the Director of the Center.

4 “(g) DETERMINATIONS BY DIRECTOR.—

5 “(1) RESULTS OF STUDY.—The Director of the
 6 Center shall determine, upon receipt of the results of
 7 a study required under subsection (d) or (e)—

8 “(A) whether the drug or biological prod-
 9 uct studied may present an unreasonable risk to
 10 the health of patients or the general public; and

11 “(B) what, if any, corrective action under
 12 subsection (k) shall be taken to protect patients
 13 and the public health.

14 “(2) RESULTS OF EVIDENCE.—The Director of
 15 the Center may, at any time, based on the empirical
 16 evidence from postmarket surveillance programs and
 17 activities (including MedWatch), risk-benefit anal-
 18 yses, adverse event reports, the scientific literature,
 19 any clinical or observational studies (including stud-
 20 ies required under subsection (d) or (e)), or any
 21 other resources that the Director of the Center de-
 22 termines appropriate—

23 “(A) make a determination that a drug or
 24 biological product may present an unreasonable

1 risk to the health of patients or the general
2 public; and

3 “(B) order a corrective action under sub-
4 section (k) be taken to protect patients and the
5 public health.

6 “(3) REQUIRED CONSULTATION AND CONSIDER-
7 ATIONS.—Before making a determination under
8 paragraph (2), ordering a study under subsection
9 (d) or (e), or taking a corrective action under sub-
10 section (k), the Director of the Center shall—

11 “(A) consult with the Director of the Cen-
12 ter for Drug Evaluation and Research or the
13 Director of the Center for Biologics Evaluation
14 and Research, as appropriate; and

15 “(B) consider—

16 “(i) the benefit-to-risk profile of the
17 drug or biological product;

18 “(ii) the effect that a corrective ac-
19 tion, or failure to take corrective action,
20 will have on the patient population that re-
21 lies on the drug or biological product; and

22 “(iii) the extent to which the drug or
23 biological product presents a meaningful
24 therapeutic benefit as compared to other
25 available treatments.

1 “(h) PUBLIC INFORMATION.—Periodically, but not
2 less often than every 90 days, the Secretary shall make
3 available to the public, by publication in the Federal Reg-
4 ister and posting on an Internet website, the following in-
5 formation:

6 “(1) Studies required under subsection (d) or
7 (e) including—

8 “(A) the type of study;

9 “(B) the nature of the study;

10 “(C) the primary and secondary outcomes
11 of the study;

12 “(D) the date the study was required
13 under subsection (d) or (e) or was agreed to by
14 the sponsor;

15 “(E) the deadline for completion of the
16 study; and

17 “(F) if the study has not been completed
18 by the deadline under subparagraph (E), a
19 statement that explains why.

20 “(2) The periodic progress reports and results
21 of completed studies described under subsection (f).

22 “(3) Any determinations made by the Director
23 of the Center under subsection (g), including—

24 “(A) reasons for the determination, includ-
25 ing factual basis for such determination;

1 “(B) reference to supporting empirical
2 data; and

3 “(C) an explanation that describes why
4 contrary data is insufficient.

5 “(i) DRUG ADVISORY COMMITTEE.—The Drug Safe-
6 ty and Risk Management Advisory Committee within the
7 Center of the Food and Drug Administration shall—

8 “(1) meet not less frequently than every 180
9 days; and

10 “(2) make recommendations to the Director of
11 the Center with respect to—

12 “(A) which drugs and biological products
13 should be the subject of a study under sub-
14 section (d) or (e);

15 “(B) the design and duration for studies
16 under subsection (d) or (e);

17 “(C) which drugs and biological products
18 may present an unreasonable risk to the health
19 of patients or the general public; and

20 “(D) appropriate corrective actions under
21 subsection (k).

22 “(j) PENALTIES.—

23 “(1) IN GENERAL.—If the Secretary deter-
24 mines, after notice and opportunity for an informal
25 hearing, that a sponsor of a drug or biological prod-

1 uct or other entity has failed to complete a study re-
2 quired under subsection (d) or (e) by the date or to
3 the terms specified by the Secretary under such sub-
4 section, the Secretary may order such sponsor or
5 other entity to—

6 “(A) complete the study in a specified
7 time;

8 “(B) revise the study to comply with the
9 terms specified by the Secretary under sub-
10 section (d) or (e); or

11 “(C) pay a civil penalty.

12 “(2) AMOUNT OF PENALTIES.—

13 “(A) IN GENERAL.—The civil penalty or-
14 dered under paragraph (1) shall be \$250,000
15 for the first 30-day period after the date speci-
16 fied by the Secretary that the study is not com-
17 pleted, and shall double in amount for every 30-
18 day period thereafter that the study is not com-
19 pleted.

20 “(B) LIMITATION.—In no case shall a pen-
21 alty under subparagraph (A) exceed \$2,000,000
22 for any 30-day period.

23 “(3) NOTIFICATION OF PENALTY.—The Sec-
24 retary shall publish in the Federal Register any civil
25 penalty ordered under this subsection.

1 “(k) RESULT OF DETERMINATION.—

2 “(1) IN GENERAL.—If the Director of the Cen-
3 ter makes a determination that a drug or biological
4 product may present an unreasonable risk to the
5 health of patients or the general public under sub-
6 section (g), such Director shall order a corrective ac-
7 tion, as described under paragraph (2).

8 “(2) CORRECTIVE ACTIONS.—The corrective ac-
9 tion described under subsection (g)—

10 “(A) may include—

11 “(i) requiring a change to the drug or
12 biological product label by a date specified
13 by the Director of the Center;

14 “(ii) modifying the approved indica-
15 tion of the drug or biological product to re-
16 strict use to certain patients;

17 “(iii) placing restriction on the dis-
18 tribution of the drug or biological product
19 to ensure safe use;

20 “(iv) requiring the sponsor of the
21 drug or biological product or license to es-
22 tablish a patient registry;

23 “(v) requiring patients to sign a con-
24 sent form prior to receiving a prescription
25 of the drug or biological product;

1 “(vi) requiring the sponsor to monitor
2 sales and usage of the drug or biological
3 product to detect unsafe use;

4 “(vii) requiring patient or physician
5 education; and

6 “(viii) requiring the establishment of
7 a risk management plan by the sponsor;
8 and

9 “(B) shall include the requirements with
10 respect to promotional material under sub-
11 section (l)(1).

12 “(3) PENALTIES.—

13 “(A) IN GENERAL.—If the Secretary deter-
14 mines, after notice and opportunity for an in-
15 formal hearing, that a sponsor of a drug or bio-
16 logical product has failed to take the corrective
17 action ordered by the Director of the Center
18 under this subsection or has failed to comply
19 with subsection (l)(2), the Secretary may order
20 such sponsor to pay a civil penalty.

21 “(B) AMOUNT OF PENALTIES.—

22 “(i) IN GENERAL.—The civil penalty
23 ordered under subparagraph (A) shall be
24 \$250,000 for the first 30-day period that
25 the sponsor does not comply with the order

1 under paragraph (1), and shall double in
2 amount for every 30-day period thereafter
3 that the order is not complied with.

4 “(ii) LIMITATION.—In no case shall a
5 penalty under clause (i) exceed \$2,000,000
6 for any 30-day period.

7 “(C) NOTIFICATION OF PENALTY.—The
8 Secretary shall publish in the Federal Register
9 any civil penalty ordered under this paragraph.

10 “(l) PROMOTION MATERIAL.—

11 “(1) SAFETY ISSUE.—If the Director of the
12 Center makes a determination that a drug or bio-
13 logical product may present an unreasonable risk to
14 the health of patients or the general public under
15 subsection (g), such Director, in consultation with
16 the Division of Drug Marketing, Advertising, and
17 Communications of the Food and Drug Administra-
18 tion, shall—

19 “(A) notwithstanding section 502(n), re-
20 quire that the sponsor of such drug or biologi-
21 cal product submit to the Director of the Cen-
22 ter copies of all promotional material with re-
23 spect to the drug or biological product not less
24 than 30 days prior to the dissemination of such
25 material; and

1 “(B) require that all promotional material
2 with respect to the drug or biological product
3 include certain disclosures, which shall be dis-
4 played prominently and in a manner easily un-
5 derstood by the general public, including—

6 “(i) a statement that describes the
7 unreasonable risk to the health of patients
8 or the general public as determined by the
9 Director of the Center;

10 “(ii) a statement that encourages pa-
11 tients to discuss potential risks and bene-
12 fits with their healthcare provider;

13 “(iii) a description of the corrective
14 actions required under subsection (k);

15 “(iv) where appropriate, a statement
16 explaining that there may be products
17 available to treat the same disease or con-
18 dition that present a more favorable ben-
19 efit-to-risk profile, and that patients should
20 talk to their healthcare provider about the
21 risks and benefits of alternative treat-
22 ments;

23 “(v) a description of any requirements
24 of outstanding clinical and observational

1 studies, including the purpose of each
2 study; and

3 “(vi) contact information to report a
4 suspected adverse reaction.

5 “(2) NEW PRODUCTS; OUTSTANDING STUD-
6 IES.—For the first 2-year period after a drug is ap-
7 proved under section 505 of this Act or a biological
8 product is licensed under section 351 of the Public
9 Health Service Act, and with respect to drugs and
10 biological products for which there are outstanding
11 study requirements under subsection (d) or (e), the
12 Director of the Center, in consultation with the Divi-
13 sion of Drug Marketing, Advertising, and Commu-
14 nications of the Food and Drug Administration,
15 shall—

16 “(A) notwithstanding section 502(n), re-
17 quire that the sponsor of such drug or biologi-
18 cal product submit to the Director of the Cen-
19 ter copies of all promotional material with re-
20 spect to the drug or biological product not less
21 than 30 days prior to the dissemination of such
22 material; and

23 “(B) require that all promotional material
24 with respect to the drug or biological product
25 include certain disclosures, which shall be dis-

1 played prominently and in a manner easily un-
2 derstood by the general public, including—

3 “(i) a statement explaining that the
4 drug or biological product is newly ap-
5 proved or licensed or the subject of out-
6 standing clinical or observational studies,
7 as the case may be, and, as a result, not
8 all side effects or drug interactions may be
9 known;

10 “(ii) the number of people in which
11 the drug or biological product has been
12 studied and the duration of time during
13 which the drug or biological product has
14 been studied;

15 “(iii) a statement that encourages pa-
16 tients to discuss the potential risks and
17 benefits of treatment with their healthcare
18 provider;

19 “(iv) a description of any require-
20 ments of outstanding clinical and observa-
21 tional studies, including the purpose of
22 each study; and

23 “(v) contact information to report a
24 suspected adverse reaction.

1 “(3) EFFECT OF VOLUNTARY SUBMISSION.—
2 Paragraphs (1)(A) and (2)(A) shall not apply to the
3 sponsor of a drug or biological product if such spon-
4 sor has voluntarily submitted to the Division of
5 Drug Marketing, Advertising, and Communications
6 of the Food and Drug Administration all pro-
7 motional material with respect to the drug or bio-
8 logical product prior to the dissemination of such
9 material.

10 “(m) WITHDRAWAL OR SUSPENSION OF APPROVAL
11 OR LICENSURE.—

12 “(1) IN GENERAL.—The Director of the Center,
13 may withdraw or suspend approval of a drug or li-
14 censure of a biological product using expedited pro-
15 cedures (as prescribed by the Secretary in regula-
16 tions promulgated not later than 1 year after the
17 date of enactment of the Food and Drug Adminis-
18 tration Safety Act of 2007, which shall include an
19 opportunity for an informal hearing) after consulta-
20 tion with the Director of the Center for Drug Eval-
21 uation and Research or the Director of the Center
22 for Biologics Evaluation and Research, as appro-
23 priate, and any other person as determined appro-
24 priate by the Director of the Center, if—

1 “(A) the Director of the Center makes a
2 determination that the drug or biological prod-
3 uct may present an unreasonable risk to the
4 health of patients or the general public, and
5 that risk cannot be satisfactorily alleviated by a
6 corrective action under subsection (k); or

7 “(B) the sponsor fails to comply with an
8 order or requirement under this section.

9 “(2) PUBLIC INFORMATION.—The Secretary
10 shall make available to the public, by publication in
11 the Federal Register and posting on an Internet
12 website, the details of the consultation described in
13 paragraph (1), including—

14 “(A) the reason for the determination to
15 withdraw, suspend, or failure to withdraw or
16 suspend, approval for the drug or licensure for
17 the biological product;

18 “(B) the factual basis for such determina-
19 tion;

20 “(C) reference to supporting empirical
21 data;

22 “(D) an explanation that describes why
23 contrary data is insufficient; and

24 “(E) the position taken by each individual
25 consulted.

1 “(n) EFFECT OF SECTION.—The authorities con-
2 ferred by this section shall be separate from and in addi-
3 tion to the authorities conferred by section 505B.

4 “(o) ADMINISTRATION OF SECTION.—The provisions
5 of this section shall be carried out by the Secretary, acting
6 through the Director of the Center.”.

7 (b) MISBRANDING.—Section 502 of the Federal
8 Food, Drug, and Cosmetic Act (21 U.S.C. 352) is amend-
9 ed by inserting after subsection (j) the following:

10 “(k) If it is a drug or biological product for which
11 the sponsor of an application or holder of an approved ap-
12 plication or license has not complied with an order or re-
13 quirement under section 507.”.

14 (c) REPORT ON DEVICES.—Not later than 6 months
15 after the date of enactment of this Act, the Secretary of
16 Health and Human Services, in consultation with the
17 Commissioner of Food and Drugs, the Director of the
18 Center for Postmarket Evaluation and Research for Drugs
19 and Biologics, and the Director of the Center for Devices
20 and Radiological Health, shall submit to Congress a report
21 that—

22 (1) identifies gaps in the current process of
23 postmarket surveillance of devices approved under
24 the Federal Food, Drug, and Cosmetic Act (21
25 U.S.C. 321 et seq.);

1 (2) includes recommendations on ways to im-
2 prove gaps in postmarket surveillance of devices; and

3 (3) identifies the changes in authority needed to
4 make those improvements, recognizing the legitimate
5 differences between devices and other medical prod-
6 ucts regulated by the Food and Drug Administra-
7 tion.

8 (d) TRANSFER OF FUNCTIONS.—The functions and
9 duties of the Office of Surveillance and Epidemiology, in-
10 cluding the Drug Safety and Risk Management Advisory
11 Committee, of the Food and Drug Administration on the
12 day before the date of enactment of this Act shall be trans-
13 ferred to the Center for Postmarket Evaluation and Re-
14 search for Drugs and Biologics established under section
15 507 of the Federal Food, Drug, and Cosmetic Act (as
16 added by this section). The Center for Postmarket Evalua-
17 tion and Research for Drugs and Biologics shall be a sepa-
18 rate entity within the Food and Drug Administration and
19 shall not be an administrative office of the Center for
20 Drug Evaluation and Research or the Center for Biologics
21 Evaluation and Research.

22 (e) AUTHORIZATION OF APPROPRIATIONS.—There
23 are authorized to be appropriated to carry out this Act
24 (and the amendments made by this Act)—

25 (1) \$50,000,000 for fiscal year 2008;

- 1 (2) \$75,000,000 for fiscal year 2009;
- 2 (3) \$100,000,000 for fiscal year 2010;
- 3 (4) \$125,000,000 for fiscal year 2011; and
- 4 (5) \$150,000,000 for fiscal year 2012.

○