

REVISED
3/21/96
5:00 PM

AMENDMENT NO. _____

Calendar No. _____

Purpose: To provide for a substitute amendment.

IN THE SENATE OF THE UNITED STATES—104th Cong., 2d Sess.

S. 1477

To amend the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act to improve the regulation of food, drugs, devices, and biological products, and for other purposes.

Referred to the Committee on _____
and ordered to be printed

Ordered to lie on the table and to be printed

AMENDMENT IN THE NATURE OF A SUBSTITUTE intended
to be proposed by Mrs. KASSEBAUM

Viz:

1 Strike all after the enacting clause and insert the fol-

2 lowing:

3 **SECTION 1. SHORT TITLE.**

4 This Act may be cited as the "Food and Drug Ad-
5 ministration Performance and Accountability Act of
6 1996".

7 **SEC. 2. TABLE OF CONTENTS.**

8 The table of contents for this Act is as follows:

Sec. 1. Short title.

Sec. 2. Table of contents.

Sec. 3. References.

TITLE I—MISSION AND ACCOUNTABILITY

- Sec. 101. Short title.
- Sec. 102. The mission of the Food and Drug administration.
- * Sec. 103. Performance standards and review. ✓
- * Sec. 104. Interagency collaboration. ✓
- * Sec. 105. Information system. ✓
- * Sec. 106. Policy statements.
- Sec. 107. Scientific review groups. *new process*
- * Sec. 108. Appeals within the Food and Drug administration. *add'l appeals process*

TITLE II—EXPEDITED ACCESS TO PRODUCTS FOR SERIOUSLY ILL PATIENTS

- Sec. 201. Short title.
- * Sec. 202. Access to unapproved therapies.
- * Sec. 203. Expanding humanitarian use of devices.
- * Sec. 204. Expediting approval of new drugs, biologics, and medical devices for serious conditions.

*codifies FDA's
145 and PD
practice.*

TITLE III—REVITALIZING THE INVESTIGATION OF NEW PRODUCTS

- Sec. 301. Short title.
- * Sec. 302. Timely review and reasonable data requirements for clinical research on drugs and biological products.
- * Sec. 303. Timely review and reasonable data requirements for clinical research on devices.
- Sec. 304. Collaborative research design. (-)

*add more
products*

TITLE IV—EFFICIENT, ACCOUNTABLE, AND FAIR PRODUCT REVIEW

- Sec. 401. Short title.
- Sec. 402. The content and review of an application. (-)
- Sec. 403. Contracts for expert review. - depends
- * Sec. 404. Prompt and efficient review. (-)
- Sec. 405. Good manufacturing practice inspection. - contracting out for gmp
- Sec. 406. Environmental impact review. EIS
- * Sec. 407. Information exchange. (-) off label use - still big change
- * Sec. 408. Effectiveness, outcome, and cost-effectiveness standards. *codification of review*
- Sec. 409. Definition of a day for purposes of product review.
- * Sec. 410. Alternative approval of supplemental new drug applications. - process change/guidance on acceptable evidence
- * Sec. 411. Pediatric studies marketing exclusivity. *new*
- Sec. 412. Notifications for device market clearance.

TITLE V—FOOD AND DRUG EXPORT REFORM

- Sec. 501. Short title, reference.
- * Sec. 502. Export of drugs and devices.
- Sec. 503. Prohibited act.
- Sec. 504. Partially processed biological products.

TITLE VI—DRUG AND BIOLOGICAL PRODUCTS REGULATORY REFORM

- Sec. 601. Short title.
- * Sec. 602. New drug approval standard. (-) *where is a change - clarifications*

- Sec. 603. Pilot and small scale manufacture. + currently removed for most drugs (RIGG)
 XX Sec. 604. Manufacturing changes. (RIGG)
 Sec. 605. Insulin and antibiotics. ~~Depends on factor and how regular. FDA did under RIGG~~ (RIGG)
 Sec. 606. Modernization of regulation of biological products. ~~harmonizing~~ ^{reg} well characterized biologics as drugs. ~~up~~ ^{for} ~~forward~~ ^{for} ~~forward~~ ^{for} RIGG II + ~~up~~ ^{for} ~~forward~~ ^{for} ~~forward~~ ^{for}

TITLE VII—DEVICE REGULATORY REFORM

- Sec. 701. Short title. RIGG + not much
 Sec. 702. Premarket notification. ~~streamline process for exempting class II devices~~ 702(a)(-)
 XX Sec. 703. Medical device approval standards. (-) a 702(c)(-)
 X Sec. 704. Tracking. } significant change / places limits 702(d)(-)
 XX Sec. 705. Postmarket surveillance. }
 Sec. 706. Device distributor reporting. (eliminates)
 XX Sec. 707. Premarket approval. process - as for drugs
 X Sec. 708. Device performance standards. + FDA must require std's of certain self setting organizations. ~~New~~ but companies should not be able to self certify compliance w/ reciprocal std's.

TITLE VIII—ANIMAL DRUG REGULATORY REFORM

- Sec. 801. Short title.
 X Sec. 802. Evidence of effectiveness.
 Sec. 803. Limitation of residues. + change - positive - range of drugs
 X Sec. 804. Adulterated drugs.
 Sec. 805. Veterinary feed directives. + creates a new class of animal drugs (new)
 XX Sec. 806. Timeframes for approval.

TITLE IX—FOOD REGULATORY REFORM

- Sec. 901. Short title.
 XX Sec. 902. Indirect food additives. under FDA mark - big difference

1 SEC. 3. REFERENCES.

2 Except as otherwise expressly provided, whenever in
 3 this Act an amendment or repeal is expressed in terms
 4 of an amendment to, or repeal of, a section or other provi-
 5 sion, the reference shall be considered to be made to a
 6 section or other provision of the Federal Food, Drug, and
 7 Cosmetic Act (21 U.S.C. 321 et seq.).

8 TITLE I—MISSION AND 9 ACCOUNTABILITY

10 SEC. 101. SHORT TITLE.

11 This title may be cited as the "Food and Drug Ad-
 12 ministration Regulatory Reform Act of 1996".

1 **SEC. 102. THE MISSION OF THE FOOD AND DRUG ADMINIS-**
2 **TRATION.**

3 Section 903(a) (21 U.S.C. 393(a)) is amended by
4 adding at the end thereof the following: "The mission of
5 the Administration is to promote and protect the health
6 of the American public by—

7 ²
8 ~~(1)~~ facilitating the rapid and efficient develop-
9 ment and availability of ^{safe and effective} products subject to its regu-
10 lation: ^{and,}

11 ¹
12 ~~(2)~~ protecting the public from unsafe or inef-
13 fective products subject to its regulation; and

14 ~~(3)~~ enforcing the applicable statutes and regu-
15 lations in a timely, fair, consistent, and decisive
16 manner."

17 **SEC. 103. PERFORMANCE STANDARDS AND REVIEW.**

18 Section 903(b) (21 U.S.C. 393(b)) is amended by
19 adding at the end thereof the following new paragraph:

20 **"(3) PERFORMANCE STANDARDS AND RE-**
21 **VIEW.—**

22 **"(A) IN GENERAL.—**Within 180 days of
23 the date of enactment of this paragraph (3),
24 the Secretary, after consultation with experts in
25 the development, clinical investigation, and reg-
26 ulation of drugs, biological products, ^{new animal} drugs, de-
vices, and food additives, and representatives of
patient and consumer advocacy groups, health

1 and technology professionals, and the regulated
2 industries, shall publish in the Federal Register
3 quantifiable performance standards for action
4 by the Administration on—

5 “(i) applications or submissions (in-
6 cluding petitions, notifications, or any
7 other similar form of request) for review of
8 a protocol, a product investigation, a prod-
9 uct approval, a new use approval, a manu-
10 facturing change, a change in labeling, or
11 any other form of regulatory action relat-
12 ing to the review of a product that is a
13 new drug, biological product, new animal
14 drug, device, food additive, or color addi-
15 tive and that is subject to premarket re-
16 view or approval under this Act:

17 “(ii) letters, telephone calls, requests
18 for meetings, and the scheduling of re-
19 quested meetings relating to the applica-
20 tions and submissions described in clause
21 (i); and

*impossible
micromanagement*

22 “(iii) the scheduling of advisory com-
23 mittee meetings, and the action taken fol-
24 lowing an advisory committee recommenda-

1 tion, relating to the applications and sub-
2 missions described in clause (i).

“(B) REVIEW OF PERFORMANCE STANDARDS.—The performance standards required in subparagraph (A) shall be reviewed annually by the Secretary, and after consultation with experts in the development, clinical investigation, and regulation of drugs, devices, biological products, and food additives, and representatives of patient and consumer advocacy groups, health and technology professionals, and the regulated industries, may be revised, annually by the Secretary.

“(C) AGENCY OBJECTIVES.—The performance standards shall establish objectives for the Administration that—

“(i) expedite the clinical investigation of new drugs, devices, and biological products through closer collaboration between the Administration and new product sponsors;

21 sors,

22 “(ii) expedite ^{action on} applications for new

23 drugs, devices, and biological products—

“(I) for an immediately life-threatening disease or condition; or

1 “(II) for any other serious condi-
2 tion if a new drug, device, or biologi-
3 cal product provides therapy not avail-
4 able from other approved therapy or
5 offers significant improvement over
6 other approved therapy;

7 “(iii) reduce backlogs on all applica-
8 tions with the objective of eliminating all
9 backlogs by January 1, 1998;

10 “(iv) establish a schedule to bring the
11 Administration into full compliance by
12 July 1, 1998, with the time periods speci-
13 fied in this Act on all applications; and

14 “(v) improve the consistency and fair-
15 ness of the Administration's regulatory
16 process.

17 The Secretary shall also issue such other per-
18 formance standards that the Secretary deter-
19 mines will contribute to the efficient, fair, and
20 effective operation of the Administration.

21 “(D) ANNUAL REPORT.—The Secretary
22 shall prepare and publish in the Federal Reg-
23 ister for public comment an annual report—

24 “(i) providing detailed data on the ac-
25 tual performance of the Administration re-

*These dates
are a real
problem.*

*1st choice -
Reauthorizing
PDUFA and
conform food
additive and
PMA timelines
to those
required for
NDAs under
PDUFA.*

*2nd choice -
Change date
back to date
in draft -
2000, and
make review
times for
food additive
and devices
realistic.*

1 lating to each of the types of actions cov-
2 ered by this paragraph;

3 “(ii) comparing the performance of
4 the Administration with the applicable per-
5 formance standard for each of the types of
6 actions covered by this paragraph;

7 “(iii) describing any priorities estab-
8 lished with respect to the types of actions
9 covered by this paragraph, how such prior-
10 ities are implemented, and the data on
11 each priority category;

12 “(iv) analyzing any failure to achieve
13 any of the standards;

14 “(v) identifying regulatory policies
15 that have a significant impact on compli-
16 ance with the standards and analyzing how
17 such policies could be modified in order to
18 achieve compliance with the standards; and

19 “(vi) setting forth a plan to achieve
20 compliance with the standards that have
21 not been met.

22 “(E) STATISTICAL INFORMATION.—The re-
23 port described in subparagraph (D) shall in-
24 clude a full statistical presentation relating to
25 all applications and petitions for a new drug.

1 device, biological product, new animal drug,
2 food additive, or color additive approved by the
3 Administration during the year, taking into ac-
4 count the date of—

5 “(i) submission of any investigational
6 application;

7 “(ii) any clinical hold;

8 “(iii) submission of the application or
9 petition for approval;

10 “(iv) acceptance for filing of the appli-
11 cation or petition for approval;

12 “(v) any unapprovable action;

13 “(vi) any approvable action; and

14 “(vii) the approval.”

15 **SEC. 104. INTERAGENCY COLLABORATION.**

16 Section 903(b) (21 U.S.C. 393(b)), as amended by
17 section 103, is further amended by adding at the end
18 thereof the following new paragraph:

19 “(4) INTERAGENCY COLLABORATION.—The
20 Secretary shall implement programs and policies
21 that will foster collaboration between the Food and
22 Drug Administration, the National Institutes of
23 Health, and other science-based agencies, to enhance
24 the scientific expertise available to the Commissioner
25 for the evaluation of emerging medical therapies, in-

1 including complementary therapies, and advances in
2 nutrition and food science.”

3 **SEC. 105. INFORMATION SYSTEM.**

4 Chapter LX (21 U.S.C. 391 et seq.) is amended by
5 adding at the end thereof the following new section:

6 **“SEC. 906. INFORMATION SYSTEM.**

7 “The Secretary shall establish and maintain an infor-
8 mation system to track the status and progress of each
9 application or submission for the approval or clearance of
10 a drug, biological product, new animal drug, device, or
11 food additive (including a petition, notification, or other
12 similar form of request) submitted to the Food and Drug

13 Administration. The system shall permit access by the ap-
14 plicant or petitioner *to information regarding the status
and progress of specific applications.
Notwithstanding any other provision of*

15 **SEC. 106. POLICY STATEMENTS.** *the law and to the extent the
Secretary determines that*
16 Section 701(a) (21 U.S.C. 371(a)) is amended— *dissemination
of information*

17 (1) by striking “(a) The” and inserting “(a)(1) *Regarding*
18 The”; and *the safety and
efficacy of a
product would*

19 (2) by adding at the end thereof the following *enhance the
public health*
20 new paragraph: *such information*

21 “(2)(A) Within 180 days of the date of enactment *shall be
available to
the public.*
22 of Food and Drug Administration Performance and Ac-
23 countability Act of 1996, the Secretary shall establish a
24 procedure governing the development and use of all policy
25 statements of general applicability that provide guidance

1 relating to the conduct of preclinical or clinical investiga-
2 tions or other testing to support an application, petition,
3 or notification under section 409, 505, 510(k), 512, 515,
4 or 721 or that provide guidance on the submission of ap-
5 plications, petitions, or notifications under section 409,
6 505, 510(k), 512, 515, or 721 (including any guidance,
7 guideline, points-to-consider, protocol, recommendation, or
8 similar document regardless of the form or designation).

9 The procedure shall provide an opportunity for affected
10 persons ⁽ⁱ⁾ to participate in the development ^{or} ~~and~~ continued
11 use of a policy statement by sharing expertise, experience,

12 or providing comment before the policy statement is
13 ~~adopted and~~ ^{issued or (i) by providing an opportunity to comment} after the policy statement is ~~implemented, ex-~~ ^{issued}
14 ~~cept that if the Secretary determines that there is a public~~
15 ~~health need to issue the policy statement immediately, the~~
16 ~~Secretary shall provide an opportunity for affected persons~~
17 ~~to provide comment promptly after the policy statement~~
18 ~~is issued.~~

19 “(B) The Secretary shall establish a procedure for
20 the periodic compilation and publication of all policy state-
21 ments of general applicability (including any guideline,
22 points-to-consider, protocol, recommendation, or similar
23 document regardless of the form or designation).”

24 **SEC. 107. SCIENTIFIC REVIEW GROUPS.**

25 Section 904 (21 U.S.C. 394) is amended—

1 (1) by striking "Without" and inserting "(a) IN
2 GENERAL.—Without"; and

3 (2) by adding at the end thereof the following
4 new subsections:

5 "(b) DELEGATION OF APPOINTMENT AUTHORITY.—

6 The Commissioner may ^{not} delegate the appointment and
7 oversight authority granted under subsection (a).

8 "(c) MEMBERSHIP AND MEETING REQUIREMENTS.—

9 "(1) SCOPE.—The Commissioner shall consult
10 with a scientific review group in determining the
11 matters that the group will consider and in estab-
12 lishing an appropriate agenda with respect to the de-
13 termination of the matters.

14 "(2) NONVOTING MEMBERS.—A scientific re-
15 view group shall include a nonvoting industry rep-
16 resentative and a nonvoting public representative.

17 "(3) NOTIFICATION OF SCOPE OF DISCUS-
18 SION.—To the extent feasible, the specific matters
19 and questions to be discussed at a meeting of a sci-
20 entific review group shall be publicly announced and
21 published in the Federal Register at least 30 days
22 prior to the date of the meeting.

23 "(4) TERMS.—A member of a scientific review
24 group shall serve for a term of 3 years, which may
25 be renewed for a second term. An individual may

*Lab. Int
Adm*

1 serve on more than one scientific review group. The
2 chairperson of a scientific review group shall be a
3 member who has served at least 3 years. The term
4 of the chairperson may be renewed for not more
5 than 3 terms.

6 “(5) TRAINING.—Prior to service on a scientific
7 review group, a member of the group shall be given
8 adequate education and training relating to the re-
9 sponsibilities of the member.

10 “(6) FREQUENCY OF MEETINGS.—The Sec-
11 retary shall take whatever action is necessary to en-
12 sure that regular meetings are held by scientific re-
13 view groups, at appropriate intervals and for a suffi-
14 cient length of time. The meetings shall occur not
15 less than 3 times each year unless there are reasons
16 for fewer meetings.

17 “(d) ACCESS TO INFORMATION; PARTICIPATION BY
18 INTERESTED PERSONS IN MEETINGS.—

19 “(1) IN GENERAL.—When a scientific review
20 group reviews a product application, petition, or no-
21 tification for approval or clearance, or some part
22 thereof, submitted under section 409, 505, 510(k),
23 513(f), 512, 515, or 721, the Secretary shall provide
24 the product sponsor with copies of all documents
25 provided to the members of the scientific review

*except documents exempt from
public disclosure pursuant to
5 USC 552(b)(4)
and (b)(7).*

1 group in preparation for a meeting. The Secretary
2 shall provide such documents to the product sponsor
3 at the same time such documents are given to the
4 members of the scientific review group. Before the
5 meeting, the product sponsor shall have an oppor-
6 tunity to submit documents to the members of the
7 scientific review group in response to the Secretary's
8 documents. The product sponsor shall provide the
9 response to the Secretary, who shall immediately
10 provide copies to the members of the scientific re-
11 view group.

12 "(2) PARTICIPATION IN MEETINGS.—Any meet-
13 ings of a scientific review group shall provide ade-
14 quate time for initial presentations and for response
15 to any differing views and shall encourage free and
16 open participation by all interested persons.

17 "(c) FDA ACTIONS.—Within 60 days after the date
18 a scientific review group makes its conclusions and rec-
19 ommendations on any matter under review of the group,
20 the Food and Drug Administration official responsible for
21 the matter shall review the conclusions and recommenda-
22 tions of the group, ^{*and (c)*} shall make a final determination on
23 the matter, and shall notify the affected persons of the
24 determination in writing ~~and~~ if the determination differs *stet*

1 from the conclusions and recommendations of the group.
2 shall include the reasons for the difference, or (2) *notify the affected persons of the reasons why a decision has not been made and the time by which a decision will be made.*
3 ~~“(f) DEFINITION.—For purposes of this section, the~~
4 ~~term ‘center director’ means a director of a center within~~
5 ~~the Food and Drug Administration.”.~~

6 **SEC. 108. APPEALS WITHIN THE FOOD AND DRUG ADMINIS-**
7 **TRATION.**

8 Chapter LX (21 U.S.C. 391 et seq.), as amended by
9 section 105, is further amended by adding at the end
10 thereof the following new section:

11 **“SEC. 907. APPEALS WITHIN THE FOOD AND DRUG ADMIN-**
12 **ISTRATION.**

13 ~~“(a) EMPLOYEE DECISIONS.—The Secretary shall by~~
14 ~~regulation establish a system for the appeal within the~~
15 ~~Food and Drug Administration of any decision by an em-~~
16 ~~ployee of the Food and Drug Administration, except that~~
17 ~~this subsection shall not apply to decisions involving for-~~
18 ~~mal administrative or judicial proceedings. As the final~~
19 ~~stage in the internal appeal system, the Secretary shall~~
20 ~~provide for the right to request an evaluation by an appro-~~
21 ~~priate scientific review group~~ *under subsection (b)* ~~of a final decision of the Sec-~~
22 ~~retary on an appeal involving a significant scientific issue.~~
23 ~~Upon receipt of such a request, the Secretary shall refer~~
24 ~~the request to the chairperson of the appropriate scientific~~
25 ~~review group, or a member designated by the chairperson.~~

1 who shall review the request and determine whether the
2 scientific review group should conduct an evaluation. The
3 Secretary shall make publicly known the existence of the
4 internal appeal system and the procedures for an internal
5 appeal.

6 “(b) REVIEW BY SCIENTIFIC REVIEW GROUP.—

7 “(1) IN GENERAL.—The product sponsor or ap-
8 plicant shall have the right to request an evaluation
9 by an appropriate scientific review group established
10 under section 904 of any ~~significant scientific issue~~
11 ~~pending before, or~~ significant scientific decision
12 made by, the Secretary under this Act. An appro-
13 priate scientific review group ^{or representative thereof} shall review the request
14 and determine whether to conduct an evaluation
15 within 30 days after the date the request is received
16 by the Secretary.

17 “(2) SCOPE.—The significant scientific ^{decisions} ~~issues~~ a
18 scientific review group may evaluate ^{for a request under subsection (a)} ~~may~~ include,
19 but not be limited to, matters involving a decision by
20 the Secretary not to permit a clinical investigation to
21 begin or to continue, a refusal by the Secretary to
22 file an application, a protocol design, and decisions
23 relating to a pending application, petition, or notifi-
24 cation, where the same issue has not previously been
25 reviewed by a scientific review group.

1 “(3) TIME LIMITATION.—If a scientific review
2 group agrees to conduct an evaluation on an issue
3 under paragraph (1), the evaluation shall be sched-
4 uled for the next meeting of the group.

5 “(c) ADDITIONAL INFORMAL AND FORMAL PROCEDURE.—
6

7 “(1) IN GENERAL.—For purposes of obtaining
8 conclusions and recommendations regarding the res-
9 olution of any significant scientific dispute, the Sec-
10 retary is authorized to use such additional informal
11 and formal procedures as may be considered useful.
12 The procedures may include, but not be limited to,
13 the use of—

14 “(A) panels of qualified Food and Drug
15 Administration officials;

16 “(B) panels of qualified government em-
17 ployees who are not employees of the Food and
18 Drug Administration; and

19 “(C) outside mediators and arbitrators
20 who are not government employees.

21 “(2) APPLICATION OF FACCA.—The Federal Ad-
22 visory Committee Act (5 U.S.C. App) shall not apply
23 to a panel described in paragraph (1).

24 “(d) REVIEW OF RECOMMENDATIONS.—Within 60
25 days after any matter that is presented for resolution pur-

1 suant to this section has been the subject of conclusions
2 and recommendations, the Food and Drug Administration
3 official responsible for the matter shall personally review
4 the conclusions and recommendations, ^{and shall; (1)} make a final deter-
5 mination on the matter, and notify the parties of the de-
6 termination in writing, ^{or, (2) notify the parties of the} ~~and if the determination differs~~
7 ^{reasons why a decision has not been made and} ~~from the conclusions and recommendations, the reasons~~
8 ^{the time by which a decision will be made.} ~~for the difference."~~

9 **TITLE II—EXPEDITED ACCESS** 10 **TO PRODUCTS FOR SERI-** 11 **OUSLY ILL PATIENTS**

12 **SEC. 201. SHORT TITLE.**

13 This title may be cited as the "Patient Rights Regu-
14 latory Reform Act of 1996".

15 **SEC. 202. ACCESS TO UNAPPROVED THERAPIES.**

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

18 **"SEC. 543. EXPANDED ACCESS TO UNAPPROVED THERA-** 19 **PIES AND DIAGNOSTICS.**

20 "(a) IN GENERAL.—Any person, through a licensed
21 health care practitioner or licensed health care profes-
22 sional, ^{acting in accordance with state law,} may request from a manufacturer or distributor,
23 and any manufacturer or distributor may provide to a per-
24 son after compliance with the provisions of this section,
25 an investigational drug (including a biological product) or

1 device for the diagnosis, monitoring, or treatment of a se-
 2 rious disease or condition, an immediately life-threatening
 3 or seriously debilitating disease or condition, and any
 4 other disease or condition designated by the Secretary as
 5 appropriate for expanded access under this section by the
 6 person if *the Secretary determines--*

7
 8
 9
 10
 11
 12
 13
 14
 15

(3) Expanded access will not interfere with adequate enrollment in the ongoing clinical investigations authorized under section 505(i);

(4) The manufacturer or distributor is actively pursuing marketing approval with due diligence

“(1) the person has no comparable or satisfac-
 tory alternative therapy available to treat, diagnose,
 or monitor the disease or condition;

“(2) the risk to the person from the investiga-
 tional drug or device is not greater than the risk
 from the disease or condition; and

5
 6
 7
 8
 9
 10
 11
 12
 13
 14
 15
 16
 17
 18
 19
 20
 21
 22
 23
 24
 25

“(3) *for this use* an exemption for a drug or device is in ef-
 fect under a regulation promulgated pursuant to sec-
 tion 505(i) or 520(g) and the sponsor and investiga-
 tors comply with such regulation.

“(b) PROTOCOLS.—A manufacturer or distributor
 may submit to the Secretary one or more expanded access
 protocols covering expanded access use of a drug or device
 described in subsection (a). The protocols shall be subject
 to the provisions of section 505(i) for a drug and section
 520 (g) and (m) for a device and may include any form
 of use of the drug or device outside a clinical investigation,
 prior to approval of the drug or device for marketing, in-
 cluding but not limited to protocols for treatment, use,

1 parallel track, single patient protocols, emergency use, and
2 uncontrolled trials.

3 “(c) FEES.—A manufacturer or distributor may
4 charge for an investigational drug or device under an ex-
5 panded access protocol, but the price of the drug or device
6 may not be more than that necessary to recover the costs
7 of manufacture and handling for the drug or device, and
8 the Secretary shall be notified in advance of assessing any
9 such charges.

10 “(d) NOTIFICATION OF AVAILABILITY.—The Com-
11 missioner shall inform national, State, and local medical
12 associations and societies, voluntary health associations,
13 and other appropriate persons about the availability of in-
14 vestigational drugs and devices that are available under
15 expanded access protocols pursuant to this section. Such
16 notification shall identify—

17 “(1) the investigational product;

18 “(2) the expanded access use; and

19 “(3) the name and address of the manufacturer
20 or distributor that is providing the investigational
21 product for expanded access use.”.

22 **SEC. 203. EXPANDING HUMANITARIAN USE OF DEVICES.**

23 Section 520(m) (21 U.S.C. 360j(m)) is amended—

24 (1) in paragraph (2), by inserting at the end
25 thereof the following flush sentences:

(e) TERMINATION—
FDA may, at any
time, terminate
expanded access
under subsection
in (a) if the
requirements
under this
section are
no longer met.

{ I } within 120
days of enact-
ment final
regulations ha
not been issued
implementing Secti
522,

1 "The request shall be in the form of an application to the
2 Secretary. Within ¹⁸⁰~~90~~ days of the date of the receipt of
3 the application, the Secretary shall issue an order approv-
4 ing or denying the application.";

5 (2) by striking paragraph (5); and

6 (3) by striking paragraph (6).

This provision shall expire when final regulations are issued implementing section 522.

7 **SEC. 204. EXPEDITING APPROVAL OF NEW DRUGS, BIO-**
8 **LOGICS, AND MEDICAL DEVICES FOR SERI-**
9 **OUS CONDITIONS.**

time frame

10 (a) NEW DRUGS.—Section 505(c)(1) (21 U.S.C.
11 355(c)(1)) is amended by adding at the end thereof the
12 following flush sentence:

13 "In a case in which an application is submitted under sec-
14 tion 505(b)(1) for a new drug, or section 351(a) of the
15 Public Health Service Act for a biological product, that
16 is intended for use for an immediately life-threatening or
17 serious disease or condition and that provides therapy or
18 diagnosis not available from another approved drug or bio-
19 logical product or offers significant improvement over an-
20 other approved drug or biological product, the Secretary
21 shall approve or deny approval of the application within
22 ¹⁸⁰~~120~~ days after the receipt of the application."

23 (b) PREMARKET APPROVAL.—

1 (1) AMENDMENT.—Section 515(d)(1)(A) (21
2 U.S.C. 360e(d)(1)(A)) is amended by adding at the
3 end thereof the following flush sentence:

4 “For an application submitted under this subsection for
5 a device for a life-threatening disease or condition, a seri-
6 ously debilitating disease or condition, or for any other
7 serious disease or condition that provides therapy or diag-
8 nosis not available from another approved device or offers
9 a significant improvement over another approved device,
10 the Secretary shall take such action within ¹⁸⁰~~120~~ days.”.

11 (2) EFFECTIVE DATE.—The amendment made
12 by paragraph (1) shall take effect on ²⁰⁰⁰~~July 1, 1998~~.

13 **TITLE III—REVITALIZING THE**
14 **INVESTIGATION OF NEW**
15 **PRODUCTS**

16 **SEC. 301. SHORT TITLE.**

17 This title may be cited as the “Investigational Prod-
18 ucts Regulatory Reform Act of 1996”.

19 **SEC. 302. TIMELY REVIEW AND REASONABLE DATA RE-**
20 **QUIREMENTS FOR CLINICAL RESEARCH ON**
21 **DRUGS AND BIOLOGICAL PRODUCTS.**

22 Section 505(i) (21 U.S.C. 355(i)) is amended—

23 (1) by striking “(i) The” and inserting “(i)(1)
24 The”;

1 (2) by redesignating paragraphs (1), (2), and

2 (3) as subparagraphs (A), (B), and (C), respectively:

3 and

4 (3) by adding at the end thereof the following

5 new paragraphs:

6 “(2)(A) A clinical investigation of a new drug (includ-
7 ing a biological product) may begin 30 days after the date
8 the Secretary receives from the sponsor a notification con-
9 taining information about the drug and the clinical inves-
10 tigation unless, prior to the 30-day period, the Secretary

11 informs the sponsor ~~in writing~~ that the investigation may
12 not begin, and specifies the basis for the decision, ^{Within an additional 30 days,} and the
13 ~~the Secretary shall specify the deficiencies and the~~ information needed in order for the clinical investigation
14 to commence ^{in writing.}

15 “(B) Within 1 year after the date of enactment of
16 the Food and Drug Administration Performance and Ac-
17 countability Act of 1996, the Secretary, after consultation
18 with experts in the development, clinical investigation, and
19 regulation of drugs, physicians and other health care prac-
20 titioners and representatives of patient and consumer ad-
21 vocacy groups and the regulated industries, shall publish
22 in the Federal Register criteria for the type and amount
23 of information relating to the safety of an investigational
24 drug to be included in a notification described in subpara-
25 graph (A), taking into account the recommendations of

1 the International Conference on Harmonization of Tech-
2 nical Requirements for Registration of Pharmaceuticals
3 for Human Use. The Secretary shall periodically review,
4 and may revise, the criteria.

5 “(C) The Commissioner shall establish a mechanism
6 to ensure the fair and consistent application of safety
7 standards for clinical investigations.

8 “(3)(A) The Secretary may place a clinical hold on
9 any ongoing clinical investigation if the Secretary deter-
10 mines that such action is necessary for the protection of
11 human subjects *or for other reasons set forth*
by the Secretary in regulations.

12 “(B) If the Secretary places a clinical hold on a *ongoing* ~~clinical~~
13 cal investigation, the Secretary shall immediately advise
14 the applicant for such investigation in writing of such ac-
15 tion, and provide such applicant an opportunity to *confer* ~~meet~~
16 within 10 working days of the receipt of such a commu-
17 nication to discuss the clinical hold. Within 10 *working* ~~days~~ of
18 such *conference* ~~meeting~~, the Secretary shall provide to the sponsor
19 a written list of conditions for the withdrawal of the clini-
20 cal hold. Any written request from the sponsor requesting
21 that a clinical hold be removed shall receive a decision,
22 in writing and specifying the reasons therefor, within 20 *working*
23 days of the receipt of the request.”

*- currently place
hold on this*

1 **SEC. 303. TIMELY REVIEW AND REASONABLE DATA RE-**
2 **QUIREMENTS FOR CLINICAL RESEARCH ON**
3 **DEVICES.**

4 Section 520(g) (21 U.S.C. 360j(g)) is amended by
5 adding at the end thereof the following new paragraphs:

6 “(6) The procedures and conditions prescribed pursu-
7 ant to paragraph (2)(A) shall be subject to subparagraphs
8 (B) and (C) of section 505(i)(2), except that the provision
9 of subparagraph (B) of such section relating to the consid-
10 eration of the recommendations of the International Con-
11 ference on Harmonization of Technical Requirements for
12 Registration of Pharmaceuticals for Human Use shall not
13 apply to this paragraph.

14 “(7) The Secretary shall, within 120 days of the date
15 of enactment of this paragraph, by regulation amend the
16 content of parts 812 ~~and 813~~ of title 21 of the Code of
17 Federal Regulations to update the procedures and condi-
18 tions under which devices intended for human use may
19 upon application be granted an exemption from certain re-
20 quirements under this Act. The regulation shall—

21 “(A) permit developmental changes in devices,
22 including manufacturing changes, in response to in-
23 formation collected during an investigation without
24 requiring an additional approval of an application
25 for an investigational device exemption or the ap-
26 proval of a supplement to the application, if the

1 sponsor determines that, prior to making any
2 changes, the changes do not constitute a significant
3 change in design or a significant change in basic
4 principles of operation; and

5 “(B) permit, without approval of a supplement
6 to an application for an investigational device ex-
7 emption, changes or modifications to clinical proto-
8 cols that do not affect the validity of data or infor-
9 mation resulting from the completion of an approved
10 protocol so long as such changes do not affect any
11 patient protection provisions of the protocol.”.

12 **SEC. 304. COLLABORATIVE RESEARCH DESIGN.**

13 Chapter V (21 U.S.C. 351 et seq.), as amended by
14 section 202, is further amended by adding at the end
15 thereof the following new section:

16 **“SEC. 544. COLLABORATIVE RESEARCH DESIGN.**

17 **“(a) REVIEW OF DESIGN.—**

18 **“(1) REQUEST.—**Any person who intends to
19 sponsor a preclinical or clinical investigation of a
20 drug (including a biological product) or device may
21 request a meeting with the Secretary to review the
22 design of one or more protocols for the preclinical or
23 clinical testing of the drug or device.

24 **“(2) FORM.—**A request described in paragraph
25 (1) shall be in writing and shall include any protocol

1 for which the review is requested. A protocol shall be
 2 designed so that the fewest number of patients and
 3 procedures necessary to obtain data necessary for
 4 the approval of a new drug, biological product, or
 5 device are required, consistent with public health
 6 and safety.

*We don't know
 what this means.
 should be deleted
 a classified sec.
 not to limit
 evidence necessary
 to demonstration
 of safety and
 efficacy*

7 "(3) WRITTEN REVIEW.—The Secretary shall
 8 meet with the person within ⁶⁰~~30~~ days of the request
 9 and shall provide to the person a written review of
 10 the protocol, including any deficiencies in the proto-
 11 col. A written summary shall be made of the meet-
 12 ing. The summary shall include the written review of
 13 the protocol and, after agreement by the person and
 14 agency shall be made part of the product review file
 15 maintained by the Food and Drug Administration.

16 "(b) MODIFICATION OF AGREEMENTS.—Any agree-
 17 ments reached through meetings with respect to the design
 18 of any protocol under subsection (a) may be modified only
 19 in accordance with the following provisions:

20 "(1) At any time by mutual consent of the
 21 sponsor and the Secretary.

22 "(2) By the sponsor unilaterally, if the change
 23 is to a protocol and the change is one that would not
 24 require the approval of the Secretary under the ap-
 25 plicable regulations.

*This is not activity
 covered by PDUFA
 fees. Need longer
 timeline to allow
 management flexibility
 & meet PDUFA
 requirements.*

1 “(3) By the Secretary unilaterally, if the
2 change is made—

3 “(A) by the director of the office of the
4 Food and Drug Administration responsible for
5 regulating the drug or device that is the subject
6 of the agreement, who may not delegate such
7 responsibility; and

8 “(B) in writing and specifying the sci-
9 entific or clinical need therefor.

10 “(c) APPEALS.—Any person requesting a meeting
11 under subsection (a) may appeal the decision of the Sec-
12 retary to disapprove or modify an agreement or protocol
13 under section 907.

14 “(d) GUIDELINES AND LIMITATION.—The Secretary
15 shall issue guidelines to implement this section. Such
16 guidelines shall address the responsibilities of the person
17 requesting the meeting, as well as the Secretary’s respon-
18 sibilities. Repeated failure to follow the guidelines may be
19 grounds for a refusal by the Secretary to meet with a per-
20 son requesting a meeting under this section.”.

1 **TITLE IV—EFFICIENT, ACCOUNT-**
2 **ABLE, AND FAIR PRODUCT**
3 **REVIEW**

4 **SEC. 401. SHORT TITLE.**

5 This title may be cited as the “Product Review Regu-
6 latory Reform Act of 1996”.

7 **SEC. 402. THE CONTENT AND REVIEW OF AN APPLICATION.**

8 Chapter VII (21 U.S.C. 371 et seq.) is amended by
9 adding at the end thereof the following new subchapter:
10 “SUBCHAPTER D—REVIEW OF APPLICATIONS

11 **“SEC. 741. CONTENT AND REVIEW OF AN APPLICATION.**

12 “(a) **IN GENERAL.**—This section applies to any appli-
13 cation, petition, or notification submitted for approval or
14 clearance of a food additive, new drug, device, biological
15 product, new animal drug, animal feed bearing or contain-
16 ing a new animal drug, or color additive.

17 “(b) **FILING REQUIREMENTS.**—Within 60 days of the
18 date of enactment of this section, the Commissioner shall
19 establish and publish in the Federal Register a mechanism
20 to ensure the fair and consistent application of filing re-
21 quirements.

22 “(c) **CLASSIFICATION OF A PRODUCT.**—Within 60
23 days of the receipt of a written request of an applicant
24 for information respecting the classification of a product
25 as a drug, biological product, or device or the component

1 of the Food and Drug Administration that will regulate
2 the product (including a request respecting a combination
3 product subject to section 503(g)), the Secretary shall pro-
4 vide the person a written statement of the classification
5 of the product or the component of the Food and Drug
6 Administration that will regulate the product. The Sec-
7 retary's statement shall be binding and may not be
8 changed by the Secretary except with the written agree-
9 ment of the person who submitted the request. If the Sec-
10 retary does not provide the statement within the 60-day
11 period, the classification and component designated by the
12 person submitting the request shall be final and binding
13 and may not be changed by the Secretary except with the
14 written agreement of the person.

15 “(d) REASONABLE DATA REQUIREMENTS.—Within 1
16 year after the date of enactment of the Food and Drug
17 Administration Performance and Accountability Act of
18 1996, the Secretary, after consultation with experts in de-
19 velopment and testing of products that are drugs, biologi-
20 cal products, devices, and food additives, experts in the
21 regulation of such products, consumer and patient advoca-
22 cy groups, and the regulated industries, shall publish in
23 the Federal Register criteria for the type and amount of
24 information relating to safety and effectiveness to be in-
25 cluded in an application for the approval of a product, or

1 a new use of an approved product, described in subsection
2 (c). In developing the criteria for drugs, the Secretary
3 shall consider any recommendations of the International
4 Conference on Harmonization of Technical Requirements
5 for Registration of Pharmaceuticals for Human Use.”.

6 **SEC. 403. CONTRACTS FOR EXPERT REVIEW.**

7 Chapter VII (21 U.S.C. 371 et seq.), as amended by
8 section 402, is further amended by adding at the end
9 thereof the following new section:

10 **“SEC. 742. CONTRACTS FOR EXPERT REVIEW.**

11 **“(a) IN GENERAL.—**

12 **“(1) AUTHORITY.—**The Secretary may contract
13 with outside organizations and individuals, with ex-
14 pertise in relevant disciplines, to review, evaluate,
15 and make conclusions and recommendations to the
16 Secretary on parts or all of any application (includ-
17 ing a petition, notification, or other similar request
18 for Food and Drug Administration action). The Sec-
19 retary shall retain full authority to make determina-
20 tions with respect to the approval or disapproval of
21 any product. Any such contract shall be subject to
22 the requirements of section 708. Funds obtained
23 under part 2 of subchapter C may be used for exter-
24 nal review of any drug (including a biological prod-
25 uct) for which a user fee was paid.

1 “(2) INCREASED EFFICIENCY AND EXPERTISE
2 THROUGH CONTRACTS.—The Secretary, acting
3 through the Commissioner, shall ^{use the} ~~under the~~ authority
4 granted in paragraph (1) ^{to} ~~ensure~~

5 “(A) ^{improve} the efficiency, timeliness, and quality
6 of the review of applications, petitions, and no-
7 tifications for the approval or clearance of ~~new~~
8 ~~drugs, new animal drugs, biological products,~~
9 devices, and food additives; *or*

10 ~~“(C) the efficiency, timeliness, and quality~~
11 ~~of the review of applications and notifications~~
12 ~~for the approval of new uses for approved new-~~
13 ~~drugs, ^{devices} biological products;~~

14 “(D) ^{Be sure} that the agency has the scientific and
15 technical expertise ^{available to the agency} necessary to be keep in-
16 formed of emerging new therapies and tech-
17 nologies posing significant new scientific and
18 technical issues, and for the review of indirect
19 food additive petitions and submissions under
20 subsection ¹⁰¹(k).

21

22

23 The Secretary shall retain full authority to make de-
24 terminations with respect to the approval or dis-
25 approval a product.

*limit to
devices ~~to~~
and food
additives*

1 “(b) ELIGIBILITY REQUIREMENTS.—Within ^{one year}~~90 days~~
2 of the date of enactment of this section, the Secretary
3 shall by regulation establish the requirements that an or-
4 ganization shall meet to be eligible to conduct reviews
5 under subsection (a). Such regulations shall provide for
6 the protection of confidential or proprietary information
7 and shall provide for protection against conflicts of inter-
8 est.

9 “(c) REVIEW OF EXPERT’S EVALUATION.—

10 “(1) IN GENERAL.—Subject to paragraph (2),
11 the Food and Drug Administration official respon-
12 sible for any matter for which expert review is used
13 pursuant to this section shall personally review the
14 conclusions and recommendations of the expert re-
15 view organization or individual and shall make a
16 final decision regarding the matter ^{contracted out}~~under review~~
17 within 60 days after receiving the conclusions and
18 recommendation.

19 “(2) LIMITATION.—A final decision under para-
20 graph (1) shall be made within the applicable pre-
21 scribed time period for review of an application as
22 set forth in this Act.

23 “(d) REPORT TO CONGRESS.—Within 2 years of the
24 enactment of this section, the Secretary shall provide to
25 Congress a report on the use of the authority to contract

certification

1 with outside individuals and organizations for expert re-
2 views. Such report shall include an evaluation of the extent
3 to which such contracting improves the efficiency of review
4 and the expertise available to the agency.”.

5 **SEC. 404. PROMPT AND EFFICIENT REVIEW.**

6 Chapter VII (21 U.S.C. 371 et seq.), as amended by
7 section 403, is further amended by adding at the end
8 thereof the following new section:

9 **“SEC. 743. PROMPT AND EFFICIENT REVIEW.**

10 “(a) IN GENERAL.—The provisions of this section
11 shall apply to any of the following applications, petitions,
12 and notifications:

13 “(1) ~~An~~ petition for the issuance of a regulation
14 prescribing the safe use of a human food additive or
15 animal feed additive under section 409.

16 “(2) An application for approval of a new drug
17 under section 505.

18 “(3) An application for approval of a new ani-
19 mal drug or an animal feed bearing or containing a
20 new animal drug under subsection (b) or (m) of sec-
21 tion 512, respectively.

22 “(4) A notification submitted under section
23 510(k) for market clearance for a device.

24 “(5) An application for approval of a device
25 under section 515.

1 “(6) An petition for issuance of a regulation for
2 the listing of a color additive under section 721.

3 (b) REVIEW PROCEDURES AND POLICIES.—The
4 Secretary shall establish procedures and policies to facili-
5 tate a collaborative review process between the Food and
6 Drug Administration and the applicant with respect to an
7 application, petition, or notification described in sub-
8 section (a). As part of this collaborative process—

9 “(1) open, informal, and prompt communica-
10 tions shall be encouraged;

"(2) meetings (except meetings with respect to submissions to determine substantial equivalence of a device to a predicate device) shall be held ^{at the request} before ^{of the} applicant, ^{one pre-submission meeting}
~~the expiration of one half of the statutory time period for review of the application and before the expiration of three quarters of such period, or within 15 days after a scientific review group has convened and made recommendations on an application, unless the Food and Drug Administration and the applicant determine that a meeting is unnecessary; and~~ ^{one half-way through}
3) consultations throughout the process.

“(3) by mutual consent, the agency and the ap-
plicant or petitioner may establish a different sched-
ule for meetings required under paragraph (2);

24 “(4) the Secretary shall, prior to the meetings
25 described in paragraph (2), present to the applicant

1 in writing a description of any deficiencies of the ap-
2 identified to date with respect to those deficiencies,
3 what would
4 be necessary
5 to remedy
6 them.
7 plication) and ~~the information necessary to bring the~~
8 application into a form that would require approval.

4 The Secretary and the applicant may agree to supersede
5 any procedures and policies adopted under this section and
6 the requirements of paragraphs (2) and (3). Any such
7 agreement shall be in writing, and shall specify how any
8 such agreement shall be modified or set aside.

9 ~~“(c) APPROVAL, DISAPPROVAL, AND CLASSIFICA-~~
10 ~~TION—~~

11 ~~“(1) CONSIDERATION OF INTERNATIONAL AP-~~
12 ~~PROVALS.—Beginning July 1, 1998, if the Secretary~~
13 ~~fails to meet a time period for action on an applica-~~
14 ~~tion or notification for the approval or clearance of~~
15 ~~a new drug, device, biological product, or new animal~~
16 ~~drug that offers a significant improvement over ex-~~
17 ~~isting approved products or a petition for the ap-~~
18 ~~proval of a direct food additive that has the potential~~
19 ~~to make foods more wholesome and contribute to a~~
20 ~~healthier diet, and such a product has been approved~~
21 ~~for marketing in the European Union or the United~~
22 ~~Kingdom, at the request of the applicant or peti-~~
23 ~~tioner, the Secretary shall within 30 days either ap-~~
24 ~~prove or disapprove the application, notification, or~~
25 ~~petition and notify the person who submitted the ap-~~

*Agency
understands
it will
come out*

1 ~~plication, notification, or petitioner in writing of that~~
 2 ~~decision. In the case of a disapproval, such notifica-~~
 3 ~~tion shall set forth the reasons for disapproval.~~

4 ~~“(2) APPEAL.—A person whose application, no-~~
 5 ~~tification, or petition has been disapproved under~~
 6 ~~paragraph (1) may obtain judicial review under—~~

7 ~~“(A) section 505(h) for the disapproval of~~
 8 ~~a new drug under paragraph (1);~~

9 ~~“(B) section 517 for the disapproval of a~~
 10 ~~device or notification relating to a device under~~
 11 ~~paragraph (1);~~

12 ~~“(C) chapter VII of title 5, United States~~
 13 ~~Code, for the disapproval of a license for a bio-~~
 14 ~~logical product under paragraph (1);~~

15 ~~“(D) section 512(h) for the disapproval of~~
 16 ~~a new animal drug under paragraph (1); and~~

17 ~~“(E) section 109(g) for the disapproval of~~
 18 ~~a direct food additive under paragraph (1).~~

19 ^C“(1) CONTRACTS FOR EXPERT REVIEW.—

20 ~~“(1) IN GENERAL.—Beginning July 1, 1998, if~~
 21 ~~the Secretary in any fiscal year fails to meet the~~
 22 ~~statutory time period for action on an application,~~
 23 ~~notification, or petition for at least 95 percent of the~~
 24 ~~applications, notifications, and petitions in a particu-~~
 25 ~~lar product category, the Secretary shall in the fol-~~

Substitute with
 language that
 states:
 If the Secretary
 fails to meet
 the deadlines,
 the Secretary
 must report
 to Congress why
 the deadlines
 were not met
 and what actions
 are being taken to
 enable meeting the

at least
 broaden
 classification
 so not trigger
 by one
 missed
 application

1 ~~lowing fiscal year, with the consent of the persons~~
2 ~~who submit applications, notifications, or petitions,~~
3 ~~contract with expert individuals and organizations~~
4 ~~under section 742 to review new applications, notifi-~~
5 ~~cations, and petitions and review applications, notifi-~~
6 ~~cations, and petitions for which the Secretary has~~
7 ~~failed to meet the statutory time period for action~~
8 ~~for the particular product category.~~

9 “(2) APPROVAL.—If an individual or organiza-
10 tion selected to conduct a review under paragraph
11 (1) recommends the approval or clearance of an ap-
12 plication, notification, or petition described in para-
13 graph (1), the Secretary shall, within 60 days of re-
14 ceiving the determination of the individual or organi-
15 zation but not later than the time period for review
16 set forth in this Act, either approve or disapprove
17 the application or petition, and, in the case of a dis-
18 approval, notify the applicant or petitioner in writing
19 of the basis for the disapproval. An applicant or pe-
20 titioner may appeal the disapproval under subsection
21 (c)(2).”

*Conform language
w/ p. 14 &
allow for decis
on parts of
applications &
issue*

INSPECTIONS BY ACCREDITED ORGANIZATIONS

SEC. 405. ~~GOOD MANUFACTURING PRACTICE INSPECTION.~~

23 Chapter VII is (21 U.S.C. 371 et seq.), as amended
24 by section 404, is further amended by adding at the end
25 thereof the following new section:

INSPECTIONS BY ACCREDITED ORGANIZATIONS1 "SEC. 744. ~~GOOD MANUFACTURING PRACTICE INSPECTION.~~

2 "(a) IN GENERAL.—In order to comply with inspec-
3 tion requirements of this Act, the Secretary may accredit
4 organizations to conduct inspections under section 704 to
5 evaluate compliance of a manufacturer with applicable re-
6 quirements *including requirements for* for good manufacturing practice.

*eg.
Records
are approved*

7 "(b) ELIGIBILITY REQUIREMENTS.—If the Secretary
8 elects to accredit organizations to conduct inspections
9 under section 704, the Secretary shall by regulation, with-
10 in *one year* ~~90 days~~ of the date of enactment of this section, estab-
11 lish the requirements that an organization shall meet to
12 be eligible to be accredited to participate as a qualified
13 organization to conduct inspections under subsection (a).
14 Such regulation shall provide for the protection of con-
15 fidential or proprietary information and shall provide for
16 protection against conflicts of interest.

17 "(c) ACCREDITATION.—*If the Secretary elects to accredit organization* Within 90 days after the date *under*
subsection (b)
18 the Secretary receives an application for accreditation
19 under this section, the Secretary shall review the applica-
20 tion and determine whether an applicant is in compliance
21 with the requirements established under this section.
22 Within the 90-day period, the Secretary shall grant ac-
23 creditation or shall deny accreditation and specify in writ-
24 ing the reasons for the denial and the requirements that
25 shall be met to obtain accreditation.

1 “(d) REVOCATION OF ACCREDITATION.—The Sec-
2 retary may at any time revoke accreditation granted under
3 subsection (c) for failure to comply with the requirements
4 established under this section after specifying in writing
5 the reasons for the revocation and the requirements that
6 shall be met to retain accreditation and after an ~~informal~~ *opportunity to present*
7 *views* ~~hearing~~ on the revocation.

8 “(e) INSPECTIONS.—Any organization accredited
9 under this subsection that conducts an inspection under
10 this subsection at the request of the Secretary shall—

11 “(1) apply all relevant principles *including principles* of good manu-
12 facturing practice, established in this Act and in reg-
13 ulations promulgated by the Secretary;

14 “(2) provide to the Secretary and the manufac-
15 turer within 30 days after the completion of the in-
16 spection an adequate report of the findings of the in-
17 spection; and

18 “(3) immediately provide the Secretary with a
19 notice of any condition that could cause or contrib-
20 ute to a significant threat to the public health.”.

21 **SEC. 406. ENVIRONMENTAL IMPACT REVIEW.**

22 Chapter VII (21 U.S.C. 371 et seq.), as amended by
23 section 405, is further amended by adding at the end
24 thereof the following new section:

1 **"SEC. 745. ENVIRONMENTAL IMPACT REVIEW.**

2 ~~Notwithstanding any provision of other law, no ac-~~
3 ~~tion by the Secretary pursuant to this Act shall be subject~~
4 ~~to an environmental assessment, an environmental impact~~
5 ~~statement, or other environmental consideration unless the~~
6 ~~director of the office responsible for the action dem-~~
7 ~~onstrates, in writing and specifying the basis therefor—~~

8 ~~"(1) that there is a reasonable probability that~~
9 ~~the environmental impact of the action is sufficiently~~
10 ~~substantial and within the factors that the Secretary~~
11 ~~is authorized to consider under this Act; and~~

12 ~~"(2) that consideration of the environmental~~
13 ~~impact will directly affect the decision on the ac-~~
14 ~~tion."~~

15 **SEC. 407. INFORMATION EXCHANGE.**

16 Chapter VII (21 U.S.C. 371 et seq.), as amended by
17 section 406, is further amended by adding at the end
18 thereof the following new sections:

19 **"SEC. 746. DISSEMINATION OF TREATMENT INFORMATION**
20 **ON DRUGS AND BIOLOGICAL PRODUCTS.**

21 **"(a) DISSEMINATION OF TREATMENT INFORMA-**
22 **TION.—**

23 **"(1) IN GENERAL.—**Notwithstanding sections
24 301(d), 502(f), 505, and 507 and section 351 of the
25 Public Health Service Act (42 U.S.C. 262), and sub-
26 ject to the requirements of paragraph (2) and sub-

The Secretary shall,
by regulation, exclude
from the
requirement
to prepare
an
environmental
assessment
or an
environmental
impact
statement,
categories of
action which
the Secretary
finds are
not likely to
significantly
affect the
environment.

1 section (b), a manufacturer may disseminate to any
 2 person that is a health care practitioner or other
 3 provider of health care goods or services, a phar-
 4 macy benefit manager, a health maintenance organi-
 5 zation or other managed health care organization, or
 6 a health care insurer or governmental agency, writ-
 7 ten information, concerning—

8 “(A) a treatment use for an investigational
 9 new drug or an investigational biological prod-
 10 uct approved by the Secretary for such treat-
 ment use; or

“(B) a use (whether or not such use is
 contained in the official labeling) of a new drug
 (including any antibiotic drug) or a biological
 product for which an approval of an application
 filed under section 505(b), 505(j), or 507, or a
 product license issued under the Public Health
 Service Act, is in effect.

“(2) REQUIREMENTS.—A manufacturer may
 disseminate information under paragraph (1)(B)
 only if—

“(A) the information is an unabridged—

“(i) reprint or copy of a peer-reviewed
 article from a scientific or medical journal
 that is published by an organization that is

*Need language
 only if: a supplemental
 application
 has been filed
 with the Secretary
 and 90 days
 has passed
 with no decision.
 Once the Secretary
 renders a
 decision, if
 the decision
 is disapproval
 the manufacturer
 will be responsible
 for taking
 immediate
 corrective
 action on
 the denied
 use.*

1 independent of the pharmaceutical indus-
2 try; or

3 “(ii) reference textbook that is pub-
4 lished by an organization that is independ-
5 ent of the pharmaceutical industry; or

6 “(B) the information relates to a use that
7 is recognized under Federal law for purposes of
8 third-party coverage or reimbursement, and—

9 “(i) the text of the information has
10 been approved by an organization referred
11 to in such Federal law; and

12 “(ii) the information is part of a dis-
13 ease management program or treatment
14 guideline with respect to such use.

15 “(3) SPECIAL RULE.—If concurrent or new in-
16 formation (including new information relating to
17 safety or efficacy of the off-label use of a drug or
18 biological product) is published with respect to any
19 information disseminated under paragraph (1) and
20 (2), the manufacturer that disseminated the infor-
21 mation under paragraph (1) shall notify the Sec-
22 retary with respect to the new information. If the
23 Secretary determines that the new information dem-
24 onstrates that a new drug or biological product pre-
25 sents a significant risk to public health, the Sec-

1 retary shall, in consultation with the manufacturer,
2 take such appropriate action as the Secretary deter-
3 mines necessary to ensure public health and safety.

4 “(b) DISCLOSURE STATEMENT.—In order to afford
5 a full and fair evaluation of the information described in
6 subsection (a), a manufacturer disseminating the informa-
7 tion shall include—

8 “(1) a prominently displayed statement that
9 discloses—

10 “(A) if applicable, that the use of a new
11 drug or biological product described in subpara-
12 graph (B) of subsection (a)(1) and the informa-
13 tion with respect to the use have not been ap-
14 proved by the Food and Drug Administration:

15 “(B) if applicable, that the information is
16 being disseminated at the expense of the manu-
17 facturer;

18 “(C) if applicable, the name of any authors
19 of the information being disseminated who are
20 not employees of or consultants to the manufac-
21 turer; and

22 “(D) the official labeling for the drug and
23 biological product, or in the case of a treatment
24 use of an investigational drug or biological

1 product, the investigator brochure and all up-
2 dates thereof; and

3 "(2) a statement on whether there are other ar-
4 ticles that have been previously published about the
5 subject covered by the information disseminated.

6 "(c) DEFINITIONS.—As used in this section:

7 "(1) HEALTH CARE PRACTITIONER.—The term
8 'health care practitioner' means a medical provider
9 that is licensed to prescribe a drug or biological
10 product for the treatment of a disease or other medi-
11 cal condition.

12 "(2) REFERENCE TEXTBOOK.—The term 'ref-
13 erence textbook' means a reference publication
14 that—

15 "(A) has not been written, edited, ex-
16 cerpted, or published specifically for, or at the
17 request of, a manufacturer of a drug or biologi-
18 cal product;

19 "(B) has not been edited or significantly
20 influenced by a manufacturer of a drug or bio-
21 logical product;

22 "(C) is not solely distributed through a
23 manufacturer of a drug or biological product,
24 but is generally available in bookstores or other

1 distribution channels where medical textbooks
2 are sold; and

3 “(D) does not focus on any particular drug
4 or biological product of a manufacturer that
5 disseminates information under subsection (a).
6 and does not have a primary focus on off-label
7 uses of drugs or biological products that are
8 marketed or under investigation by a manufac-
9 turer supporting the dissemination of the infor-
10 mation.

11 “(3) SCIENTIFIC OR MEDICAL JOURNAL.—The
12 term ‘scientific or medical journal’ means a scientific
13 or medical publication—

14 “(A) that is published by an organization
15 that—

16 “(i) has an editorial board and that
17 utilizes experts, who have demonstrated ex-
18 pertise in the subject of the article under
19 review and who are not employees of the
20 organization, to review and objectively se-
21 lect, reject, or provide comments about
22 proposed articles; and

23 “(ii) has a publicly stated policy, to
24 which the organization adheres, of full dis-
25 closure of any conflict of interest or biases

1 for all authors or contributors involved
2 with the journal or organization;

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

6 "(C) that is generally recognized to be of
7 national scope and reputation;

8 "(D) that is indexed in the Index Medicus
9 of the National Library of Medicine of the Na-
10 tional Institutes of Health; and

11 "(E) that presents materials that are
12 truthful and not misleading.

13 "(d) SPECIAL RULE.—In the case of a professional
14 disagreement between the Secretary and other qualified
15 experts with respect to the application of section 502(a),
16 the Secretary may not use section 502 to prohibit the dis-
17 semination of information in the types of circumstances
18 and under the conditions set forth in subsections (a) and
19 (b).

20 **"SEC. 747. DISSEMINATION OF INFORMATION ON DEVICES.**

Same approach as drugs
21 "(a) DISSEMINATION OF INFORMATION.—Notwith-
22 standing sections 301, 501(f), 501(i), 502(a), 502(f), and
23 502(g), or any other provision of law, and subject to sub-
24 sections (b) and (c), a manufacturer may disseminate to
25 any person that is a health care practitioner or other pro-

1 vider of health care goods or services, a pharmacy benefit
2 manager, a health maintenance organization or other
3 managed health care organization, or a health care insurer
4 or governmental agency, written or oral information (in-
5 cluding information exchanged at scientific and edu-
6 cational meetings, workshops, or demonstrations) relating
7 to a use, whether or not the use is described in the official
8 labeling, of a device produced by a manufacturer reg-
9 istered pursuant to section 510.

10 “(b) DISCLOSURE STATEMENTS AND REQUIRE-
11 MENTS.—

12 “(1) DISCLOSURE STATEMENTS.—To the extent
13 practicable, the requirement with respect to a state-
14 ment of disclosure under subsection (b) of section
15 746 shall apply to the dissemination of written and
16 oral information under this section, except that this
17 paragraph shall not apply to the dissemination of
18 written or oral information with respect to the in-
19 tended use described in the labeling of a device.

20 “(2) ADDITIONAL REQUIREMENTS.—A person
21 may disseminate information under subsection (a)
22 only if—

23 “(A) the information is an unabridged—

24 “(i) reprint or copy of a peer-reviewed
25 article from a scientific or medical journal

1 that is published by an organization that is
2 independent of the medical device industry;
3 or

4 “(ii) recognized reference textbook
5 that is published by an organization that is
6 independent of the medical device industry;

7 “(B) the information has been approved by
8 a continuing medical education accrediting
9 agency that is independent of the medical de-
10 vice industry as part of a scientific or medical
11 educational program approved by such agency;

12 “(C) the information relates to a use that
13 is recognized under Federal law for purposes of
14 third-party reimbursement, and—

15 “(i) the text of the information has
16 been approved by an organization referred
17 to in such Federal law; or

18 “(ii) the information is part of a dis-
19 ease management program or treatment
20 guideline with respect to such use; or

21 “(D) the oral or written information is—

22 “(i) part of an exchange of informa-
23 tion solely among health care practitioners,
24 health care reimbursement officials, and
25 the industry;

1 “(ii) exchanged for educational or sci-
2 entific purposes; and

3 “(iii) presented at continuing medical
4 education programs, seminars, workshops,
5 or demonstrations.

6 “(3) SPECIAL RULE.—If concurrent or new in-
7 formation (including new information relating to
8 safety or efficacy of the off-label use of a device) is
9 published with respect to any information dissemi-
10 nated under paragraph (1), the manufacturer that
11 disseminated the information under paragraph (1)
12 shall notify the Secretary with respect to the new in-
13 formation. If the Secretary determines that the new
14 information demonstrates that a device presents a
15 significant risk to public health, the Secretary shall,
16 in consultation with the manufacturer, take such ap-
17 propriate action as the Secretary determines nec-
18 essary to ensure public health and safety.

19 “(4) APPLICABILITY.—The requirements under
20 subsection (a)(1)(A) and (B) of section 746 shall not
21 apply with respect to devices.

22 “(c) DEFINITIONS.—As used in this section:

23 “(1) HEALTH CARE PRACTITIONER.—The term
24 ‘health care practitioner’ means a medical provider

1 that is licensed to prescribe a device for the treat-
2 ment of a disease or other medical condition.

3 “(2) REFERENCE TEXTBOOK.—The term ‘ref-
4 erence textbook’ means a reference publication
5 that—

6 “(A) has not been written, edited, ex-
7 cerpted, or published specifically for, or at the
8 request of, a manufacturer of a device;

9 “(B) has not been edited or significantly
10 influenced by a manufacturer of a device;

11 “(C) is not solely distributed through a
12 manufacturer of a device, but is generally avail-
13 able in bookstores or other distribution channels
14 where medical textbooks are sold; and

15 “(D) does not focus on any particular de-
16 vice of a manufacturer that disseminates infor-
17 mation under subsection (a), and does not have
18 a primary focus on off-label uses of devices that
19 are marketed or under investigation by the
20 manufacturer supporting the dissemination of
21 the information.

22 “(3) SCIENTIFIC OR MEDICAL JOURNAL.—The
23 term ‘scientific or medical journal’ has the meaning
24 given to such term by section 746(c)(3).

1 **"SEC. 748. ESTABLISHMENT OF LIST OF ARTICLES AND**
2 **TEXTBOOKS DISSEMINATED AND LIST OF**
3 **PROVIDERS THAT RECEIVED ARTICLES AND**
4 **REFERENCE TEXTBOOKS.**

5 "A manufacturer that disseminates articles or ref-
6 erence textbooks as information under sections 746 and
7 747 shall prepare and submit to the Secretary bian-
8 nually—

9 "(1) a list containing the titles of the articles
10 and reference textbooks relating to off-label uses of
11 drugs, biological products, and devices that were dis-
12 seminated by the manufacturer to a person de-
13 scribed in sections 746(a)(1) and 747(a) for the 6-
14 month period preceding the date on which the manu-
15 facturer submits the list to the Secretary; and

16 "(2) a list that identifies the categories of pro-
17 viders (as described in sections 746(a)(1) and
18 747(a)) that received such articles and reference
19 textbooks for the 6-month period described in para-
20 graph (1).

21 **"SEC. 749. CONSTRUCTION.**

22 "(a) DISSEMINATION OF INFORMATION ON NEW
23 DRUGS OR DEVICES NOT EVIDENCE OF INTENDED
24 USE.—Notwithstanding section 502(a), 502(f), 502(o), or
25 any other provision of law, the written or oral dissemina-
26 tion of information relating to a new use of a new drug

1 or device, in accordance with section 746 or 747, shall not
2 be construed by the Secretary as evidence of a new in-
3 tended use of the new drug or device that is different from
4 the intended use of the new drug or device set forth on
5 the official labeling of the new drug or device. Such dis-
6 semination shall not be considered by the Secretary as la-
7 beling, adulteration, or misbranding of the new drug or
8 device.

9 “(b) DISSEMINATION POLICY OF MANUFACTUR-
10 ERS.—Nothing in sections 746 and 747 shall affect the
11 ability of manufacturers to respond fully to unsolicited
12 questions from health care practitioners and other persons
13 about drugs, biological products, or devices.

14 “(c) AUTHORIZATION FOR DISSEMINATION OF ARTI-
15 CLES AND FEES FOR REPRINTS OF ARTICLES.—Nothing
16 in sections 746 and 747 shall be construed as prohibiting
17 an entity that publishes a medical or scientific journal (as
18 defined in section 746(c)(3) of the Federal Food, Drug,
19 and Cosmetic Act) from requiring authorization from the
20 entity to disseminate an article published by such entity
21 and from charging fees for the purchase of reprints of
22 published articles from such entity.

23 “SEC. 750. APPROVAL OF ADDITIONAL USES.

24 ~~“(a) IN GENERAL.—As an alternative to the proce-~~
25 ~~dures established in section 505(c)(1) for a new drug (in-~~

Substitute
with language
that would require:
See attached

1 ~~including a biological product) and section 515(d)(1)(A) for~~
2 ~~a device, the Secretary may approve an application under~~
3 ~~this section for a new use of a previously approved new~~
4 ~~drug or device if experts qualified by scientific training~~
5 ~~and experience to evaluate the safety and effectiveness of~~
6 ~~drugs or devices conclude that a new use that has not been~~
7 ~~reviewed or approved by the Secretary represents sound~~
8 ~~medical practice based upon reliable clinical experience~~
9 ~~and other confirmatory information.~~

10 ~~“(b) PETITION: The holder of an approved applica-~~
11 ~~tion may submit a petition to the Secretary presenting in-~~
12 ~~formation that new use of a previously approved new drug~~
13 ~~or device meets the criteria for approval established in this~~
14 ~~subsection. The petition shall include data and informa-~~
15 ~~tion relating to the new use and shall demonstrate that~~
16 ~~the new use—~~

17 ~~“(1) has existed in clinical practice for at least~~
18 ~~five years;~~

19 ~~“(2) is common among clinicians experienced in~~
20 ~~the field; and~~

21 ~~“(3) represents reasonable medical practice~~
22 ~~based upon reliable clinical experience and other~~
23 ~~confirmatory information.~~

24 ~~“(c) ACTION ON PETITION: Upon receipt of the pe-~~
25 ~~tition, the Secretary shall obtain the conclusions and rec-~~

DRAFT

Supplement Legislation

Performance goals for supplements --

- o paper supplements
- o priority supplements
- o other supplements

Direct FDA to issue guidelines to simplify supplement submissions to reflect --

- o presumption that safety data often not required and typically not as extensive
- o if the indication is related, developing the protocol should be easier and it should be easy to give clear guidance as to what tests required

Require Center directors to establish small office whose job it would be to --

- o work with companies to explain requirements
- o work with centers to expedite and to make sure goals are met
- o work to identify journal articles, etc., that can be the basis for supplement; even have FDA consider whether to approve the new labeling without an application
- o work with NIH to identify new indications that should be studied

[probably could also be a single office that reports to the Commissioner]

Report back to Congress on the progress

IOM Study -

~~1 commendations of a scientific review group established~~
~~2 under section 904 and grant or deny the petition within~~
~~3 180 days of the receipt of the petition."~~

4 **SEC. 408. EFFECTIVENESS, OUTCOME, AND COST-EFFEC-**
5 **TIVENESS STANDARDS.**

6 Section 741, as added by section 402, is amended by
7 adding at the end thereof the following new subsection:

8 "(c) LIMITATION ON DETERMINATION OF EFEC-
9 TIVENESS.—In reviewing an application for a product that
10 is a new drug, biological product, new animal drug, animal
11 feed bearing or containing a new animal drug, or device
12 the determination of effectiveness shall not include the
13 evaluation of—

14 "(1) any potential use not included in the label-
15 ing;

16 "(2) the cost-effectiveness of the product de-
17 scribed in this subsection as compared to the cost-
18 effectiveness of a similar product, unless the pro-
19 posed labeling explicitly includes a representation
20 about cost-effectiveness; and

21 "(3) the clinical outcome resulting from the use
22 of a diagnostic device, unless the labeling explicitly
23 includes a representation regarding clinical out-
24 come."

*This section needs
to be revised to
permit agency to
evaluate all
relevant information
and to require in-
clusion on label
of warnings or
contraindications,
but not
to deny approval
because use not
in label.*

1 **SEC. 409. DEFINITION OF A DAY FOR PURPOSES OF PROD-**
 2 **UCT REVIEW.**

3 Section 201 (21 U.S.C. 321) is amended by adding
 4 at the end thereof the following:

5 “(gg) For purposes of reviewing any application, noti-
 6 fication or petition, or any document, with respect to a
 7 product that is a new drug, biological product, new animal
 8 drug, device, or food additive that is submitted to the Sec-
 9 retary to obtain approval of marketing, or to establish or
 10 clarify the regulatory status of the product, the term ‘day’
 11 means a calendar day (excluding any calendar day be-
 12 tween the date of receipt by the submitter of a written
 13 communication from the Secretary setting forth the action
 14 of the Secretary on a submission and the date of receipt
 15 by the Secretary of the written response of the submitter
 16 to the action) in which the Secretary has responsibility to
 17 review such a submission.”.

*Need clarification
of what this is
intended to do and
how it might
change current
procedures.*

18 **SEC. 410. ALTERNATIVE APPROVAL OF SUPPLEMENTAL**
 19 **NEW DRUG APPLICATIONS.**

20 Section 505(b) of the Federal Food, Drug, and Cos-
 21 metic Act is amended by adding the following new para-
 22 graph at the end:

23 “(4) The reports required by paragraph (1)(A) may
 24 consist entirely of ~~information~~ *one or more adequate and well-controlled* published in independent
 25 peer-reviewed scientific and medical literature, ~~in the case~~
 26 ~~of a supplement to a previously approved application that~~

*ambiguous
Doon's change
Std.*

1 ~~seeks approval for changes in the conditions of use pre-~~
2 ~~scribed, recommended, or suggested in the labeling of the~~
3 ~~drug subject to the application, if the proposed conditions~~
4 ~~of use relate to treatment of a life-threatening disease."~~

5 **SEC. 411. PEDIATRIC STUDIES MARKETING EXCLUSIVITY.**

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

9 **"SEC. 505A. PEDIATRIC STUDIES FOR NEW DRUG APPLICA-**
10 **TIONS.**

11 "(a) MARKET EXCLUSIVITY FOR APPROVED APPLI-
12 CATIONS WITH PEDIATRIC STUDIES SUBMITTED BY AN
13 APPLICANT.—If an application submitted under section
14 505(b)(1) is approved on or after the date of enactment
15 of this section, and such application includes reports of
16 pediatric studies described and requested in subsection (c),

17 and such studies are completed and the reports thereof
18 submitted in accordance with subsection (c)(2) or com-
19 pleted and the reports thereof accepted in accordance with
20 subsection (c)(3), the Secretary may not make the ap-
21 proval of an application submitted under section 505(b)(2)
22 or 505(j) that refers to the drug for which the section
23 505(b)(1) approval is granted effective prior to the expira-
24 tion of 6 months from the earliest date on which the ap-
25 proval of such application for the drug under section

*This should
be limited to
important.
life-saving
drugs.
The Secretary
should have
to find that
the additional
indication
will advance
public health.*

1 505(b)(2) or 505(j), respectively, could otherwise be made
2 effective under the applicable provisions of this chapter.

3 “(b) MARKET EXCLUSIVITY FOR APPROVED APPLI-
4 CATIONS WITH PEDIATRIC STUDIES REQUESTED BY THE
5 SECRETARY.—If the Secretary makes a written request
6 for pediatric studies described in subsection (c) to the
7 holder of an approval under section 505(b)(1) for a drug,
8 and such studies are completed and the reports thereof
9 submitted in accordance with subsection (c)(2) or com-
10 pleted and the reports thereof accepted in accordance with
11 subsection (c)(3), the Secretary may not make the ap-
12 proval of an application submitted under section 505(b)(2)
13 or 505(j) that refers to the drug subject to the section
14 505(b)(1) approval effective prior to the expiration of 6
15 months from the earliest date on which an approval of
16 such application under section 505(b)(2) or 505(j), respec-
17 tively, could otherwise be made effective under the applica-
18 ble provisions of this chapter. Nothing in this subsection
19 shall affect the ability of the Secretary to make effective
20 a section 505(b)(2) or 505(j) approval for a subject drug
21 if such approval is proper under such subsection and is
22 made effective prior to the submission of the reports of
23 pediatric studies described in subsection (c).

24 “(c) CONDUCT OF PEDIATRIC STUDIES.—

1 “(1) AGREEMENT FOR STUDIES.—The Sec-
2 retary may, pursuant to a written request for stud-
3 ies after consultation with the sponsor of an applica-
4 tion or holder of an approval for a drug under sec-
5 tion 505(b)(1), agree with the sponsor or holder for
6 the conduct of pediatric studies for such drug.

7 “(2) WRITTEN PROTOCOLS TO MEET THE
8 STUDIES REQUIREMENT.—If the sponsor or holder
9 and the Secretary agree upon written protocols for
10 such studies, the studies requirement of subsection
11 (a) or (b) is satisfied upon the completion of the
12 studies in accordance with the protocols and the sub-
13 mission of the reports thereof to the Secretary. Not
14 later than 60 days after the submission of the report
15 of the studies, the Secretary shall determine if such
16 studies were or were not conducted in accordance
17 with the written protocols and reported in accord-
18 ance with the requirements of the Secretary for fil-
19 ing and so notify the sponsor or holder.

20 “(3) OTHER METHODS TO MEET THE STUDIES
21 REQUIREMENT.—If the sponsor or holder and the
22 Secretary have not agreed in writing on the proto-
23 cols for the studies, the studies requirement of sub-
24 section (a) or (b) is satisfied when such studies have
25 been completed and the reports accepted by the Sec-

1 retary. Not later than 90 days after the submission
2 of the reports of the studies, the Secretary shall ac-
3 cept or reject such reports and so notify the sponsor
4 or holder. The Secretary's only responsibility in ac-
5 cepting or rejecting the reports shall be to deter-
6 mine, within 90 days, that the studies fairly respond
7 to the written request, that such studies have been
8 conducted in accordance with commonly accepted
9 scientific principles and protocols, and that such
10 studies have been reported in accordance with the
11 requirements of the Secretary for filing.

12 “(d) DELAY OF EFFECTIVE DATE FOR CERTAIN AP-
13 PLICATIONS; PERIOD OF MARKET EXCLUSIVITY.—If the
14 Secretary determines that an approval of an application
15 under section 505(b)(2) or 505(j) for a drug may be made
16 effective after submission of reports of pediatric studies
17 under this section but before the Secretary has determined
18 whether the requirements of subsection (c) have been sat-
19 isfied, the Secretary may delay the effective date of any
20 approval under section 505(b)(2) or 505(j), respectively,
21 until the determination under subsection (c) is made, but
22 such delay shall not exceed 90 days. In the event that the
23 requirements of this section are satisfied, the 6-month pe-
24 riod referred to in subsection (a) or (b) shall be deemed
25 to have begun on the date an approval of an application

*The value of
the extension
should be
limited,
suggestion 10
Times the
cost of the study.*

1 under section 505(b)(2) or 505(j), respectively, would have
2 been permitted absent action under this subsection.

3 “(c) NOTICE OF DETERMINATIONS ON STUDIES RE-
4 QUIREMENT.—The Secretary shall publish notice of any
5 determination that the requirements of subsection (c) (2)
6 or (3) have been met and that approvals under section
7 (505)(b)(2) or (j) for a drug will be subject to deferred
8 effective dates under this section.

9 “(f) DEFINITIONS.—As used in this section, the term
10 ‘pediatric studies’ or ‘studies’ means at least 1 human
11 clinical investigation in a population of adolescent age or
12 younger. At the Secretary’s discretion, pharmacokinetic
13 studies may be considered as clinical investigations.”.

14 **SEC. 412. NOTIFICATIONS FOR DEVICE MARKET CLEAR-**
15 **ANCE.**

16 Section 510(k) (21 U.S.C. 360(k) is amended by
17 striking “report to” and inserting “shall notify the Sec-
18 retary to report to”.

19 **TITLE V—FOOD AND DRUG**
20 **EXPORT REFORM**

21 **SEC. 501. SHORT TITLE, REFERENCE.**

22 This title may be cited as the “FDA Export Reform
23 and Enhancement Act of 1996”.

*Not commented on
because legislation
on this issue
being considered
separately.
No comments p-
through and
including page 76.*

NEXT PAGE AFTER 61.

717

1 **TITLE VI—DRUG AND BIOLOGI-**
2 **CAL PRODUCTS REGULATORY**
3 **REFORM**

4 **SEC. 601. SHORT TITLE.**

5 This title may be cited as the “Drug and Biological
6 Product Regulatory Reform Act of 1996”.

7 **SEC. 602. NEW DRUG APPROVAL STANDARD.**

8 Section 505(d) (21 U.S.C. 355(d)) is amended by
9 adding at the end thereof the following new sentence:
10 “Substantial evidence may ^{as appropriate} consist of data from one ^{adequate and} well-
11 controlled clinical investigation and confirmatory evidence
12 (obtained either before or after such investigation).”.

13 **SEC. 603. PILOT AND SMALL SCALE MANUFACTURE.**

14 Section 505(c) (21 U.S.C. 355(c)) is amended by
15 adding at the end thereof the following new paragraph:

16 “(4) A new drug or biological product manufactured
17 in a pilot or other small facility may be used to dem-
18 onstrate the safety and effectiveness of the drug or prod-
19 uct and to obtain approval prior to scaling up to a larger
20 facility, unless the Secretary demonstrates in writing and
21 specifying in detail the reasons, after an informal hearing,
22 that a full scale production facility is necessary to ensure
23 the safety or effectiveness of the drug or product.”.

Done by
Guidelines
and
regulations

1 SEC. 604. MANUFACTURING CHANGES.

2 Chapter VII (21 U.S.C. 371 et seq.), as amended by
 3 section 407, is further amended by adding at the end
 4 thereof the following new section:

5 "SEC. 751. MANUFACTURING CHANGES.

6 "(a) IN GENERAL.—A change in the manufacture of
 7 a new drug, biological product, or new animal drug, may
 8 be made in accordance with this section.

9 "(b) DRUG AND BIOLOGICAL PRODUCT.—~~A change~~
 10 ~~in the manufacture of a new drug, a biological product~~
 11 ~~that is the subject of a monograph in an official compen-~~
 12 ~~dium, a biological product that can be adequately charac-~~
 13 ~~terized by chemical, physical or biological means, or a new~~
 14 ~~animal drug shall require—~~

USP monographs

15 "(1) ~~validation, and~~

16 "(2)(A) ~~if there is no change in the approved~~
 17 ~~qualitative and quantitative formulation or in the~~
 18 ~~approved release specifications, or if there is a~~
 19 ~~change in the approved qualitative or quantitative~~
 20 ~~formula or in the approved release specifications of~~
 21 ~~a type permitted by the Secretary by regulation, may~~
 22 ~~be made at any time and shall be reported annually~~
 23 ~~to the Secretary, and—~~

24 "(B) ~~for any other change, shall require com-~~
 25 ~~pletion of an appropriate study demonstrating~~
 26 ~~equivalence according to criteria established by the~~

*Insert
attached
substitute*

[Substitute language for sec. 604 of S. 1477]

(b)(1) Before distributing a product made using a change in the manufacture of the product (including, if the Secretary determines it is appropriate, facilities and personnel) from that established in the approved new drug application, license application, or new animal drug application, the applicant must validate the effect on the safety, purity, potency, and effectiveness of the product.

(2) The applicant must report such changes to the Secretary and may distribute products as follows:

(i) If the change is of a type that the Secretary has determined has substantial potential to have an adverse effect on the safety, purity, potency, or effectiveness of the product, the applicant must submit a supplemental application to the Secretary and receive approval of the supplement before distribution of the product.

(ii) If the change is of a type that the Secretary has determined has moderate potential to have an adverse effect on the safety, purity, potency, or effectiveness of the product, the applicant must notify the Secretary at least 30 days before distribution of the product. Unless the Secretary notifies the applicant within 30 days not to distribute the product, the applicant may proceed with distribution.

(iii) If the change is of a type that the Secretary has determined has minimal potential to have an adverse effect on the safety, purity, potency, or effectiveness of the product, the applicant must report the change in a annual report. The applicant may distribute the product without prior notification to or approval by the Secretary.

1 ~~Secretary (unless such requirement is waived by the~~
2 ~~Secretary), may be made at any time, and shall be~~
3 ~~reported to the Secretary through a supplement or~~
4 ~~amendment submitted at the time the change is~~
5 ~~made.~~

6 ~~"(c) BIOLOGICAL PRODUCT NOT SUBJECT TO A~~
7 ~~MONOGRAPH. A change in the manufacture of a biologi-~~
8 ~~cal product that is not the subject of a monograph in an~~
9 ~~official compendium and cannot be adequately character-~~
10 ~~ized by chemical, physical, or biological means shall re-~~
11 ~~quire validation and--~~

12 ~~"(1) if the change relates solely to a modifica-~~
13 ~~tion of the manufacturing facility or change in per-~~
14 ~~sonnel, with no change in the approved manufactur-~~
15 ~~ing process or release specifications, may be made at~~
16 ~~any time and shall be reported annually to the Sec-~~
17 ~~retary, and~~

18 ~~"(2) for any other change, shall require comple-~~
19 ~~tion of a bioassay or other appropriate study dem-~~
20 ~~onstrating equivalence according to criteria estab-~~
21 ~~lished by the Secretary (unless such requirement is~~
22 ~~waived by the Secretary), may be made at any time,~~
23 ~~and shall be reported to the Secretary through an~~
24 ~~amendment submitted at the time the change is~~
25 ~~made.~~

1 ~~“(d) SPECIAL DETERMINATION FOR A BIOLOGICAL~~
 2 ~~PRODUCT.—A determination shall be made prior to ap-~~
 3 ~~proval of a biological product under section 351(a) of the~~
 4 ~~Public Health Service Act (42 U.S.C. 262(a)) whether the~~
 5 ~~product can be adequately characterized for purposes of~~
 6 ~~this subsection. With respect to biological products ap-~~
 7 ~~proved prior to the date of enactment of the Food and~~
 8 ~~Drug Administration Performance and Accountability Act~~
 9 ~~of 1996, the determination shall be made within 90 days~~
 10 ~~after the date of enactment of such Act. Any determina-~~
 11 ~~tion under this subsection is subject to change based upon~~
 12 ~~new scientific information.”.~~

13 SEC. 605. INSULIN AND ANTIBIOTICS.

14 (a) CERTIFICATION OF DRUGS CONTAINING INSU-
 15 LIN.—Section 506 (21 U.S.C. 356) is repealed.

16 (b) CERTIFICATION OF ANTIBIOTICS.—Section 507
 17 (21 U.S.C. 357) is repealed.

18 (c) EXPORTATION.—Section 802 (21 U.S.C. 382), as
 19 amended by section 502(b), is further amended by adding
 20 at the end thereof the following new subsection:

21 “(g) EXPORTATION OF UNAPPROVED PRODUCTS.—
 22 Insulin and antibiotics may be exported without regard to
 23 the requirements in this section if the insulin and anti-
 24 biotics meet the requirements in subsection (e)(1).”.

*See attached
language*

*Repealed Sec. 506, 507
under RIGG.
Also suggested
language deleted
w/ Sec. 505*

Recommended Statutory Language

"Section 506 of the Federal Food, Drug, and Cosmetic Act, Certification of Drugs Containing Insulin, is repealed. Section 507, of the Federal Food, Drug, and Cosmetic Act, Certification of Antibiotics, is repealed.

Section 505 is amended by adding at the end the following new subsection:

(n) Application to Antibiotic Drugs.--(1) In General.--On and after the effective date of this subsection, antibiotic drugs shall be considered new drugs subject to the provisions of this section, and an antibiotic drug certified pursuant to section 507 prior to such effective date shall be considered a new drug for which an application has been approved pursuant to subsection (b) (or, in the case of an abbreviated application under such section 507, pursuant to subsection (j)). (2) Exception.--The provisions of subsection (j) (4) (D) shall not apply in the case of an antibiotic drug certified prior to the effective date of this subsection."

*exempted
from
certification*

*, or exempted from certification
pursuant to section
507 prior to such
effective date,*

1 SEC. 606. MODERNIZATION OF REGULATION OF BIOLOGI-
2 CAL PRODUCTS.

3 (a) IN GENERAL.—Section 351 of the Public Health
4 Service Act (42 U.S.C. 262) is amended by striking “SEC.
5 351.(a)” and all that follows through “exchange the
6 same.” and inserting the following:

7 “SEC. 351. (a)(1) Except as provided in paragraph
8 (6), no person shall introduce or deliver for introduction
9 into interstate commerce any biological product unless—

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

12 “(B) each package of the biological product is
13 plainly marked with the proper name of the biologi-
14 cal product contained therein, the name, address,
15 and applicable license number of the manufacturer
16 of the biological product, and the expiration date of
17 the biological product.

18 “(2) The license required under paragraph (1)(A)
19 shall, as determined by the Secretary, cover the biological
20 product, any facility in which the biological product is
21 manufactured, processed, packed, or held, or both the
22 product and facility.

23 “(3)(A) The Secretary shall establish, by regulation,
24 requirements for license applications for biological prod-
25 ucts.

*Under
RJGO-abbreviated
establishment
licenses for
biologs...*

1 “(B) Except as provided in subparagraph (D), a li-
 2 cense application that covers a biological product shall be
 3 approved based upon a demonstration that the product
 4 that is the subject of the application—

5 ~~“(i) is safe and effective in accordance with sec-~~
 6 ~~tion 505(d) of the Federal Food, Drug, and Cos-~~
 7 ~~metic Act (21 U.S.C. 355(d)) for~~

8 “(ii) meets standards designed to ensure that
 9 such product is safe, pure, and where appropriate,

10 ~~and~~ *(iii) the methods used in, and facilities and*
 11 ~~“(C) A license application that covers a facility shall~~ *controls used for, the manufacture, processing,*
 12 ~~ensure that the product meets standards designed to en-~~ *such facility*
 13 ~~sure that the product meets applicable requirements of~~ *any therein manufactured, processed*
 14 ~~subparagraph (A).~~ *B*

15 “(D) A license application for blood or a blood com-
 16 ponent (including plasma) ~~shall~~ *but not blood derivatives* shall be approved based on a
 17 demonstration that the product is safe, pure, and where
 18 appropriate, potent, and that the facility in which the
 19 product is manufactured, processed, packed, or held meets
 20 standards designed to ensure that such product is safe,
 21 pure, and where appropriate, potent.

22 “(4) Requirements prescribed under paragraph (2)
 23 shall include a requirement for preapproval inspection
 24 under subsection (c).

(5) All licenses shall be approved upon condition that the licensee will permit inspection of their facilities in accordance with subsection (c).

1st Choice - delete

2nd - Substitute:

(i) meets the criteria in Section 505(c)(1)(A) of the FD+C Act (21 USC 355 (c)(1)(A))

standards designed to assure the continued safety, purity and where appropriate, potency of the product.

If reference to Section 505 of FD+C Act remains, need at a minimum report language making it clear that the bill does not intend to change FDA's longstanding interpretation of potency in Section 351 of the PHS Act.

1 ⁶~~(7)~~(A) Except as provided in subparagraph (C), an
2 approved license for a biological product may be revoked
3 if the Secretary determines, on the record after providing
4 opportunity for a hearing in accordance with section 554
5 of title 5, United States Code, that the requirements for
6 approval specified in paragraph (2) are no longer met with
7 respect to such product, or that other public health rea-
8 sons, prescribed by regulation, exist. No action to revoke
9 a license based on findings of an inspection shall be initi-
10 ated prior to submission and review by the Secretary of
11 a written response submitted by the licensee to a notice
12 of inspectional findings so long as such written response
13 is received within 30 days of the date of the receipt of
14 the findings. The revocation of any product license shall
15 not prevent the continued use of any licensed biological
16 product which has been sold and delivered by the licensee
17 unless the biological product is subject to recall under sub-
18 section (d).

19 “(B) If at any time before the Secretary has taken
20 final action to revoke a license, the licensee requests an
21 inspection by the Secretary to determine whether the li-
22 censee is in compliance with applicable standards, the Sec-
23 retary shall conduct an inspection within 30 days of the
24 date of the request. If the requested inspection confirms
25 that the licensee is not in compliance with applicable

1 standards, the 30-day requirement for inspection shall not
2 apply to any subsequent request by the licensee under this
3 subparagraph for inspection. If the inspection confirms
4 that the licensee is in compliance with all applicable re-
5 quirements, the Secretary shall withdraw any proposed ac-
6 tion within 30 days of the inspection.

7 “(C) If the Secretary determines that grounds for li-
8 cense revocation exist that constitute a danger to health,
9 the Secretary shall suspend the license, notify the licensee
10 that the licensee’s license is suspended, and require notifi-
11 cation of the suspension to any consignee. Within 30 days
12 thereafter, the Secretary shall initiate the hearing process
13 under subparagraph (A),

14 “(6) The requirements of paragraph (1) do not apply
15 to a biological product for which there is in effect an inves-
16 tigational new drug application under section 505(i) of the
17 Federal Food, Drug, and Cosmetic Act.”.

18 (b) DELETION OF ELA REQUIREMENT.—Section
19 351(d) of the Public Health Service Act (42 U.S.C.
20 262(d)) is amended—

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

23 (2) by redesignating paragraph (2)(A) as sub-
24 section (d)(1);

1 (3) by redesignating subparagraph (B) as para-
2 graph (2); and

3 (4) in paragraph (2) (as so redesignated) by
4 striking "subparagraph (A)" and inserting "para-
5 graph (1)".

6 (c) LABELING.—Section 351(b) of the Public Health
7 Service Act (42 U.S.C. 262(b)) is amended to read as fol-
8 lows:

9 "(b) No person shall falsely label or mark any pack-
10 age or container of any biological product or alter any
11 label or mark on the package, so as to falsify the label
12 or mark." *or container*

13 (d) INSPECTION.—Section 351(c) of the Public
14 Health Service Act (42 U.S.C. 262(c)) is amended by
15 striking "virus, serum," and all that follows through
16 "other product aforesaid" and inserting "biological prod-
17 uct".

18 (e) DEFINITION; APPLICATION.—Part F of title III
19 of the Public Health Service Act (42 U.S.C. 262 et seq.)
20 is amended by adding at the end thereof the following new
21 subsections:

22 "(i) For purposes of this section, the term 'biological
23 product' means a virus, therapeutic serum, toxin, anti-
24 toxin, vaccine, blood, blood component or derivative, aller-
25 genic ~~biologic~~ product, or arsphenamine or its derivative

(or any other analogous biological product) applicable to the prevention, treatment, or cure of diseases or conditions of human beings.

“(j)(1) Sections 505(i), 903, and 904 of the Federal Food, Drug, and Cosmetic Act shall apply to all biological products, and references in such sections to new drug applications shall be deemed to include product license applications.

“(2) Requirements involving labeling or advertising for biological products shall be established in accordance with sections 201(m) and 502(n) of the Federal Food, Drug, and Cosmetic Act.”.

TITLE VII —DEVICE REGULATORY REFORM

SEC. 701. SHORT TITLE.

This title may be cited as the “Medical Device Reform Act of 1996”.

SEC. 702. PREMARKET NOTIFICATION.

(a) EXEMPTION OF CERTAIN DEVICES.—Section 510 (21 U.S.C. 360) is amended—

(1) in subsection (k), by striking “intended for human use” and inserting “intended for human use (except a device that is classified into class I ~~under section 513 or 520 or a device that is classified into class II under section 513 or 520, and is exempt~~ *or class II and has been exempted by the Secretary*”

1 from the requirements of this subsection under sub-
 2 section (l))”;

3 (2) by adding at the end of subsection (k) (as
 4 amended by paragraph (1)) the following:

5 “The Secretary shall review the notification required by
 6 this subsection and make a determination under section
 7 513(f)(1)(A) within 90 days of receiving the notification.”;
 8 and

9 (3) by adding at the end thereof the following
 10 new subsections:

11 “(l) Within 30 days of the date of enactment of this
 12 subsection, the Secretary shall publish in the Federal Reg-
 13 ister a list of each type or class ^{or} II device that does not
 14 require a report under subsection (k) to provide reasonable
 15 assurance of safety and effectiveness. Each type of class ^{or} II
 16 II device so identified by the Secretary not to require the
 17 report shall be exempt from the requirement to file a re-
 18 port under subsection (k) as of the date of the publication
 19 of the list in the Federal Register. Beginning on the date
 20 that is 1 day after the date of the publication of a list
 21 under this subsection, any person may petition the Sec-
 22 retary to exempt a type of class ^{or} II device from subsection
 23 (k). The Secretary shall respond to the petition within 120
 24 days of the receipt of the petition and determine whether
 25 or not to grant the petition in whole or in part.

1 “(m) The Secretary may not withhold a determina-
 2 tion of the initial classification of a device under sub-
 3 section 513(f)(1) because of a failure to comply with any
 4 provision of this Act unrelated ^{to the device which is subject to} ~~to a substantial equivalent~~ ^{the initial}
 5 ~~decision.”.~~ ^{classification}

6 (b) INITIAL CLASSIFICATION.—~~Section 513(f)(1) (21~~ ^{See}
 7 ~~U.S.C. 360e(f)(1)) is amended in the second sentence, by~~ ^{attached}
 8 ~~striking the period at the end thereof and inserting the~~ ^{substitute}
 9 ~~following: “, unless within 30 days of receiving an order~~ ^{amendment}
 10 ~~classifying the device into class III, the individual who~~
 11 ~~submits a notification under section 510(k) requests an~~
 12 ~~advisory committee review and recommendation with re-~~
 13 ~~spect to the classification of the device and a final order~~
 14 ~~of classification from the Secretary. After the request, a~~
 15 ~~device classified into class III under this paragraph shall~~
 16 ~~not be deemed to be finally classified until an advisory~~
 17 ~~committee established under subsection (b) reviews the re-~~
 18 ~~quest with respect to the classification of the device and,~~
 19 ~~within 60 days of the date of receiving the request, rec-~~
 20 ~~ommends to the Secretary a classification for the device~~
 21 ~~based on the classification criteria set forth in subpara-~~
 22 ~~graphs (A) through (C) of subsection(a)(1). Thereafter,~~
 23 ~~the Secretary shall have 10 days to determine by order~~
 24 ~~the final classification of the device by applying the classi-~~

(b) INITIAL CLASSIFICATION -- Section 513(f)(1) (21 U.S.C. 360c(f)(1)) is amended by changing the last sentence to add "or (3)" following "paragraph (2)" and by adding a new paragraph (2) and redesignating "(2)" as "(3)" and "(3)" as "(4)." New paragraph (2) shall read as follows: "Within 30 days of receiving an order finding a device not substantially equivalent under section 513(i), the individual who submitted a notification under section 510(k) may request a de novo classification of the device and an order of classification from the Secretary if the device that has been determined to be not substantially equivalent under section 513(i) has risks that appear to be commensurate with other Class I and Class II devices and the submission has addressed new issues of safety and effectiveness, if any, in sufficient detail for the ^{Secretary}~~committee~~ to apply the classification criteria set forth in subparagraphs (A) through (C) of subsection (a)(1). If the Secretary concludes that the device should be classified into Class I or II, the Secretary shall issue an order of that classification. In lieu of issuing an order that classifies the device into Class I or II, the Secretary may, within 120 days, request an advisory committee review and recommendation with respect to the classification of the device. An advisory committee shall review the request with respect to the classification for the device based on the classification criteria set forth in subparagraphs (A) through (C) of subsection (a)(1). Following the committee's recommendation, the Secretary shall have 90 days to make a final

classification determination by applying the criteria set forth in subparagraphs (A) through (C) of subsection (a)(1).

1 ~~fication criteria set forth in subparagraphs (A) through~~
 2 ~~(C) of subsection (a)(1).~~

3 (c) SUBSTANTIAL EQUIVALENCE.—Section 513(i)(1)
 4 (21 U.S.C. 360c(i)(1)) is amended by adding at the end
 5 thereof the following new subparagraph:

6 “(C) For the purpose of determining the intended use
 7 of a predicate device under paragraph (A), each use ^{reasonably} in-
 8 cluded within a general use for the predicate device shall
 9 be deemed a legally marketed use of the predicate device
 10 for purposes of premarket notifications required under
 11 subsection 510(k).”

12 (d) DEVICE MODIFICATION.—Section 513(i) (21
 13 U.S.C. 360c(i)) is amended by adding at the end thereof
 14 the following new paragraph: *See attached.*

15 “(4) Any change or modification to a device initially
 16 classified under section 513(f), other than a major change
 17 (including any major modification) in the intended use,
 18 shall not require an additional submission under section
 19 510(k) if such change or modification is supported by ap-
 20 propriate data or information, and the change or modifica-
 21 tion ^{could not} ~~can be shown to not adversely~~ affect the safety or
 22 effectiveness of the device. All data or information relied
 23 upon to document that a change to (including any modi-
 24 fication of) the device does not require an additional notifi-
 25 cation under section 510(k) shall be made available to the

Provided such change or modification is made and validated in accordance with the requirements of the good manufacturing practice regulation promulgated under section 520(F).

Need language to ensure that Agency can require clinical data when necessary to establish safety and efficacy of new use.

Need language to clarify what changes will require approval and which will not.

"(4) Any change or modification to a LEGALLY MARKETED *device*

which is not intended to affect the device's safety or effectiveness and for which routine quality assurance testing establishes that the safety or effectiveness of the device has not been SIGNIFICANTLY affected, shall not require a notification under section 510(k) if the following requirements are met:

(A) such change or modification is made and validated in accordance with the requirements of the good manufacturing practice regulations promulgated under section 520(f) PRIOR TO ANY COMMERCIAL DISTRIBUTION; and

(B) all data and information relied upon to document that the requirements of subparagraph (A) have been met ARE made part of the device master records required under the good manufacturing practice regulations promulgated under section 520(f).

All data or other information relied upon to document that a change or modification does not require a notification under section 510(k) shall be made available to the Secretary upon request and shall be maintained FOR A PERIOD OF TIME EQUIVALENT TO THE DESIGN AND EXPECTED LIFE OF THE DEVICE, BUT IN NO CASE LESS THAN 2 YEARS FROM THE DATE OF RELEASE FOR COMMERCIAL DISTRIBUTION BY THE MANUFACTURER.

1 Secretary upon request and shall be maintained, at least
 2 for a period of time equal to the commercial life of the
 3 device.”.

4 (e) DEVICE CLASSES.—Section 513(a)(3) (21 U.S.C.
 5 360c(a)(3)) is amended—

6 (1) by striking “well-controlled” and inserting
 7 “one or more well-controlled”; and

8 (2) by striking “clinical investigations” and in-
 9 serting one or more clinical investigations”.

10 **SEC. 703. MEDICAL DEVICE APPROVAL STANDARDS.**

11 Section 513(a)(3) (21 U.S.C. 360c(a)(3)) is amended
 12 by adding at the end thereof the following new subpara-
 13 graphs:

14 “(C) The Secretary shall accept, for the purpose of
 15 facilitating a review of a premarket application, a supple-
 16 ment to a premarket application, or a premarket notifica-
 17 tion of a device, retrospective or historical clinical data as
 18 a control or for use in determining whether there is a rea-
 19 sonable assurance of effectiveness of a device if ^{*the data are sufficient*} ~~sufficient~~ ^{*to demonstrate*}
 20 ~~valid data are available~~ and the effects of the device on ^{*such*} ~~the~~ ^{*assurance*}
 21 the cure, mitigation, treatment, or prevention of a disease
 22 are clearly defined and well understood.

23 “(D) The Secretary may ~~not~~ require the sponsor of
 24 an application to conduct clinical trials for use in deter-
 25 mining whether there is a reasonable assurance of effec-

*burden
 issue*

1 tiveness for a device using prospective concurrent controls

2 ^{if} ~~unless~~—

3 “(i)(I) the effects of the device on the cure,
4 mitigation, treatment, or prevention of a disease or
5 condition are not clearly defined and well understood
6 as determined by the Secretary; or

7 “(II) retrospective or historical data are not
8 available that meet the standards of the Secretary
9 for quality and completeness; or

10 “(ii) there is a compelling public health reason
11 to not rely on retrospective or historical data as a
12 control.

13 SEC. 704. TRACKING.

14 Section 519(e) (21 U.S.C. 360i(e)) is amended to
15 read as follows:

16 “DEVICE TRACKING

17 “(e) The Secretary may by regulation require a man-
18 ufacturer to adopt a method of tracking a class II or class
19 III device—

20 “(1) the failure of which would be ^{reasonably likely to be} life-threaten-
21 ing or have permanently debilitating effects; ^{or} ~~and~~

22 “(2) which is—

23 “(A) ^{longer than 30 days} ~~permanently~~ implanted; or

24 “(B) life sustaining or life supporting and
25 used outside a device user facility.”

1 SEC. 705. POSTMARKET SURVEILLANCE.

2 Section 522 (21 U.S.C. 360l) is amended to read as
3 follows:

4 "SEC. 522. POSTMARKET SURVEILLANCE.

5 "(a) IN GENERAL.—The Secretary may require a
6 manufacturer to conduct postmarket surveillance for any
7 device ^{that} ~~of the manufacturer first introduced or delivered~~
8 ~~for introduction into interstate commerce after January~~
9 ~~1, 1991, that—~~

10 "(1) is a permanent implant the failure of
11 which may cause serious, adverse health con-
12 sequences or death;

13 "(2) is intended for a use in supporting or sus-
14 taining human life; or

15 "(3) potentially presents a serious risk to
16 human health.

17 "(b) SURVEILLANCE APPROVAL.—Each manufac-
18 turer required to conduct a surveillance of a device under
19 subsection (a) shall, within 30 days of receiving notice
20 from the Secretary that the manufacturer is required
21 under this section to conduct the surveillance, submit for
22 the approval of the Secretary, a protocol for the required
23 surveillance. The Secretary, within 60 days of the date of
24 the receipt of the protocol, shall determine if the principal
25 investigator proposed to be used in the surveillance has
26 sufficient qualifications and experience to conduct the sur-

*Current law,
this is mandatory*

1 veilance and if the protocol will result in collection of use-
 2 ful data or other information necessary to protect the pub-
 3 lic health and to provide safety and effectiveness informa-
 4 tion for the device. The Secretary may not approve the
 5 protocol until the protocol has been reviewed by a qualified
 6 scientific and technical review committee established by
 7 the Secretary.”.

8 **SEC. 706. DEVICE DISTRIBUTOR REPORTING.**

9 Section 519 (21 U.S.C. 360i) is amended—

10 (1) ~~by striking “, importer, or distributor” each~~
 11 ~~place it appears and inserting “or importer”;~~

12 ~~(2) in subsection (a)—~~

13 ~~(A) in paragraph (8), by striking “, and”~~
 14 ~~and inserting a period, and~~

15 ~~(B) by striking paragraph (9); and replacing it as~~
 16 ~~(3) by striking subsection (f).~~ *follows: (9) shall not*
 17 **SEC. 707. PREMARKET APPROVAL.** *impose adverse event*
reporting requirements
on distributors who are
not importers.

18 (a) ACTION ON APPLICATION.—Section 515(d) (21 ~~(2) in subsection~~
 19 U.S.C. 360e(d)) is amended— ~~(d) by striking~~
the words

20 (1) in paragraph (1)(A), by striking “paragraph *“importer,*
 21 (2) of this subsection” each place it appears and in- *and distributor*
 22 serting “paragraph (4)”; *and “importer*
or distributor

23 (2) in paragraph (1)(B), by adding at the end *each time they appear and inserting*
 24 thereof the following new clause: *“, or importer”*

1 “(iii) The Secretary shall accept and review data and
2 any other information from investigations conducted
3 under the authority of regulations required by section
4 520(g) to make a determination of whether there is a rea-
5 sonable assurance of safety and effectiveness of a device
6 subject to a pending application under this section if—

7 “(I) the data or information is derived from in-
8 vestigations of an earlier version of the device, the
9 device has been modified during or after the inves-
10 tigation, and the modification of the device does not
11 constitute a significant change in the design or in
12 the basic principles of operation of the device that
13 would invalidate the data or information; or

14 “(II) the data or information on a device ap-
15 proved under this section is available for use under
16 this Act and is relevant to the design and intended
17 use of the device subject to the pending applica-
18 tion.”;

19 (3) by redesignating paragraphs (2) and (3) as
20 paragraphs (4) and (5), respectively; and

21 (4) by inserting after paragraph (1) the follow-
22 ing new paragraphs:

23 “(2) Each application received under section 515(c)
24 shall be reviewed in the following manner to achieve final

1 action on the application within 180 days of the receipt
2 of the application:

3 “(A) The Secretary shall meet with an appli-
4 cant within 90 days of the receipt of the application
5 to discuss the review status of the application. If the
6 application does not appear in a form that would ~~re-~~
7 ~~quire an approval~~ ^{warrant review} under subsection (d), the Sec-
8 retary shall in writing, and prior to the meeting,
9 present to the applicant a description of any defi-
10 ciencies in the application ^{identified & date} and what information is
11 ~~required to bring the application into a form that~~ ^{would be necessary to remedy them.}
12 ~~would require an approval.~~

13 “(B) The Secretary shall refer an application to
14 a panel established under section 513 for review and
15 ~~an approval~~ recommendation, unless a panel is not
16 required under subsection (c)(2), within 30 days of
17 the date of the meeting referred to in subparagraph
18 (A) or at the next scheduled panel meeting following
19 the meeting referred to in subparagraph (A), which-
20 ever occurs later.

21 “(C) The Secretary shall meet with the appli-
22 cant within 15 days of the date of the panel review
23 to discuss the status of the application, including a
24 discussion on what action is necessary to bring the
25 application into a form that would ~~require approval~~ ^{warrant approval}

1 under this subsection. Prior to the meeting, the Sec-
2 retary shall in writing shall set forth an agenda for
3 the meeting (including a complete description of the
4 subject matter to be discussed at the meeting), and
5 a full description of the additional information nec-
6 essary to bring the application into a form that
7 would ~~require an approval~~ *warrant approval* under subsection (d). Par-
8 ticipation of the applicant at such a meeting shall be
9 at the discretion of the applicant.

10 “(D) The Secretary shall meet with the appli-
11 cant not later than 135 days after the receipt of an
12 application under subsection (c), if an advisory panel
13 is not required under subsection (c)(2), and inform
14 the applicant whether or not the application is in a
15 form that would ~~require approval~~ *warrant approval* under subsection
16 (d). If the application is in such form, the Secretary
17 shall, at or prior to the meeting, present in writing
18 to the applicant a description of all additional infor-
19 mation necessary to ~~require an approval~~ *warrant approval* of the appli-
20 cation under subsection (d). If the application is not
21 in such form, the Secretary shall deny approval of
22 the application and prior to the meeting, present in
23 writing to the applicant each basis for denying ap-
24 proval of the application and the additional informa-

1 tion required to bring the application into a form
 2 that would ~~require approval~~ *warrant approval*.

3 “(E) The Secretary shall issue an order approv-
 4 ing or denying an application within 180 days of the
 5 receipt of the application under subsection (c) or
 6 within 120 days for an application subject to an ex-
 7 pedited review under paragraph (1)(A).

8 “(3)(A) Except as provided in subparagraph (B), the
 9 time for the review of an application by the Secretary
 10 under this subsection shall not take more than 180 days.
 11 ~~and such time may not be extended if the application is~~ *This provision is*
 12 ~~amended.~~ *unreasonable.*

13 “(B) The Secretary shall not take more than 120
 14 days for the review of an application subject to an expe-
 15 dited review under paragraph (1)(A) and may not extend
 16 the 120-day period if the application is amended.”.

17 (b) REVISIONS OF REGULATIONS.—

18 (1) PREMARKET APPROVAL OF APPLICA-
 19 TIONS.—The Secretary of Health and Human Serv-
 20 ices shall revise through notice and comment proce-
 21 dures the regulations set forth in part 814 of title
 22 21 of the Code of Federal Regulations, to conform
 23 to the amendment made by subsection (a).

24 (2) PREMARKET APPROVAL OF SUPPLE-
 25 MENTS.—The Secretary of Health and Human Serv-

1 ices shall revise regulations relating to premarket
2 approval of a devices to eliminate premarket ap-
3 proval of supplements that relate to manufacturing
4 or product changes of a device that have been dem-
5 onstrated through appropriate protocols or other
6 methods as specified by the Secretary to validate the
7 safety or effectiveness of a device. The Secretary of
8 Health and Human Services shall require the manu-
9 facturer of a device to submit to the Secretary of
10 Health and Human Services any information relied
11 upon to support a device-related change that is not
12 subject to premarket approval of a supplement to an
13 application approved under section 515 of the Fed-
14 eral Food, Drug, and Cosmetic Act (21 U.S.C.
15 360e). The information shall be made a part of the
16 device master record. The information shall be main-
17 tained for a period of time equal to the period of
18 time for the design and expected life of the device,
19 but not less than 2 years after the date of release
20 of the device for commercial distribution by the
21 manufacturer.

22 **SEC. 708. DEVICE PERFORMANCE STANDARDS.**

23 (a) **ALTERNATIVE PROCEDURE.**—Section 514 (21
24 U.S.C. 360d) is amended by adding at the end thereof
25 the following new subsection:

"PRODUCT REVIEW"

1
2 “(c)(1) For the purpose of facilitating a review of a
3 device under sections 510(k), 515, or 520, the Secretary
4 ~~shall~~ ^{may} recognize appropriate medical device performance
5 standards developed by organizations accredited by the
6 American National Standards Institute (ANSI), the Inter-
7 national Standards Organization (ISO), the International
8 Electrotechnical Commission (IEC) and any other organi-
9 zation certified by the Secretary pursuant to paragraph
10 (2)(B).

11 “(2)(A) The Secretary shall establish a procedure
12 governing the certification by the Food and Drug Admin-
13 istration of the competence of any national or inter-
14 national standards-setting organization not identified in
15 paragraph (1) to develop standards for medical devices.

16 “(B) Certifications of standards-setting organizations
17 not identified in paragraph (1) shall be based on formal,
18 written criteria that include, but are not limited to, the
19 role of the organization in the scientific community, sci-
20 entific or medical expertise, standard writing experience,
21 conflict of interest considerations, and the openness of the
22 standard setting process of the organization.

23 “(C) The Secretary may impose a reasonable fee for
24 certifying standard-setting organizations pursuant to sub-
25 paragraph (B).

1 “(D) Upon being notified by a designated standard-
2 setting organization that a standard has been adopted, the
3 Secretary shall review and may recognize the standard by
4 publishing a notice in the Federal Register listing the
5 name of the standard, ~~and shall provide any person who~~
6 ~~so requests a copy of the standard.~~

7 “(E) The Secretary shall promulgate regulations
8 under which the Secretary may withdraw the certification
9 of a standard-setting organization, including an organiza-
10 tion described in paragraph (1), if the Secretary deter-
11 mines that the standard-setting organization does not
12 meet the requirements of subparagraph (B) or should oth-
13 erwise no longer be designated. Such regulation shall also
14 address the effect on standards of any withdrawal of a
15 designation.

16 “(3) As provided for in section 514, the Secretary
17 may promulgate performance standards for medical de-
18 vices that differ from or are not established by organiza-
19 tions recognized in paragraph (1) or (2).

20 “(4) The Secretary shall not require, as a condition
21 for approving an application under section 510(k), 515,
22 or 520, conformity with a medical device standard recog-
23 nized under this section if the sponsor of the application
24 submits evidence to demonstrate a reasonable assurance
25 that the device is substantially equivalent to a legally mar-

1 keted predicate device or provides reasonable assurance
2 that the device is safe and effective.

3 “(5) The Secretary may revoke ^{recognition of} the performance
4 standards recognized pursuant to paragraph (1) or (2) if,
5 in the discretion of the Secretary, the Secretary deter-
6 mines the standard is ^{no longer adequate} ~~insufficient to provide a reasonable~~
7 ~~assurance of safety and effectiveness~~. The Secretary shall
8 notify the standard-setting organization and specify the
9 basis for the revocation.

10 “(6) A performance standard recognized pursuant to
11 paragraph (1) or (2) for a medical device—

12 ~~“(A) shall include provisions to provide reason-~~
13 ~~able assurance of the safe and effective performance~~
14 ~~of the device;~~

15 ^A
16 “(B) shall, where necessary to provide reason-
17 able assurance of the safe and effective performance
18 of the device, include—

19 “(i) provisions with respect to the con-
20 struction, components, ingredients, and prop-
21 erties of the device and the compatibility of the
22 device with power systems and connections to
23 the systems;

24 “(ii) provisions for the testing (on a sam-
25 ple basis or, if necessary, on an individual
basis) of the device or, if it is determined that

no other more practicable means are available to the Secretary to assure the conformity of a device to the standard, provisions for the testing (on a sample basis or, if necessary, on an individual basis) of the device by the Secretary or by another person at the direction of the Secretary;

“(iii) provisions for the measurement of the performance characteristics of the device; and

“(iv) provisions requiring that the results of each or certain of the tests of the device required to be made under clause (ii) demonstrate that the device is in conformity with those portions of the standard for which the test or tests were required; and

^B
“(C) shall, where appropriate, require the use and prescribe the form and content of labeling for the proper installation, maintenance, operation, and use of the device.

“(7) The Secretary, in lieu of requiring data demonstrating conformity with a standard recognized under this section, ^{may} ~~shall~~ accept a certification, by an ^{(independent third} ~~applicant~~ ^{party} ~~who has made a submission pursuant to sections 510(k), 515, or 520~~ ^{competent to} ~~that the device conforms with each standard~~ ^{certify} ~~to standards~~

Submission pursuant to section 514(k), 515, or 520

1 identified in the ~~certification~~. Where appropriate, the Sec-
2 retary may require data demonstrating conformity with a
3 standard recognized under paragraph (1) or (2).

4 “(8) The Secretary shall require an applicant who
5 certifies that a device conforms to an applicable perform-
6 ance standard recognized under pursuant to paragraph
7 (1) or (2) or established under section 514 to maintain
8 data demonstrating conformance for a period of time
9 equal to the period of time for the design and expected
10 life of the device. Such data shall be made available to
11 the Secretary upon request.”.

12 (b) ADULTERATED DEVICE.—Section 501(c) (21
13 U.S.C. 351(c)) is amended—

14 (1) by striking “(e)” and inserting “(e)(1)”;

15 (2) by striking “section 514” and inserting
16 “section 514(b)”; and

17 (3) by inserting at the end thereof the follow-
18 ing:

19 “(2) If it is, or purports to be or is represented as,
20 a device which is certified to be in compliance with any
21 voluntary standard recognized under section 514(c), un-
22 less such a device is in all respects in conformity with such
23 a standard.”.

TITLE VIII—ANIMAL DRUG REGULATORY REFORM

SEC. 801. SHORT TITLE.

This title may be cited as the "Animal Drug Regulatory Reform Act of 1996".

SEC. 802. EVIDENCE OF EFFECTIVENESS.

(a) SUBSTANTIAL EVIDENCE.—Section 512(d) (21 U.S.C. 360b(d)) is amended by striking paragraph (3) and

by adding at the end the following: *replacing it with the following*

~~"(4)(A) As used in this subsection and subsections~~

~~(e)(2)(F)(iii) and (e)(1)(C), the term 'substantial evi-~~

~~dence' means evidence from 1 or more scientifically sound~~

~~studies, including as appropriate in vitro studies, studies~~

~~in laboratory animals (including a target species),~~

~~bioequivalence studies, and any studies voluntarily under-~~

~~taken by or for the applicant, that taken together provide~~

~~reasonable assurance that the drug will have the claimed~~

~~or intended effect of the drug.~~

~~"(B) For purposes of subparagraph (A), a study shall~~

~~be considered to be scientifically sound if the study is de-~~

~~signed and conducted in a manner that is consistent with~~

~~generally recognized scientific procedures and principles."~~

~~(b) COMBINATION OF DRUGS.—Section 512(d) (21~~

~~U.S.C. 360b(d)) is amended by inserting before paragraph~~

*new
paragraph:*

*(see
attached
language)*

*Replace (b)
COMBINATION
OF DRUGS
with
attached
language*

AMENDMENT 1

Section 802(a) - EVIDENCE OF EFFECTIVENESS

Page 104, strike line 7 through line 22 and replace it with the following language:

" Substantial Evidence - Section 512(d) (21 U.S.C. 360b(d)) is amended by striking paragraph (3) and replacing it with the following new paragraph:

'(3) As used in this section, the term 'substantial evidence' means evidence consisting of one or more adequate and well-controlled investigations, including field investigations where appropriate, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and reasonably be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.'"

AMENDMENT 2

Section 802 (b) COMBINATION OF DRUGS

Strike Page 104, line 23 through Page 105, line 20 and insert:

"(b) Concurrent Use of Animal Drugs in Animal Feed - Section 512(d)(1)(E) is amended by inserting after "thereof;", the following:

"but, if the drug contains multiple active ingredients and is intended for use in animal feed or the drug is intended for concurrent use with other drugs in animal feed, each of the active ingredients or drugs to be used concurrently have been previously approved individually for the particular indications and conditions of use for which they are intended to be used concurrently, and each of the active ingredients or drugs to be used concurrently is intended for at least one indication differing from any of the other active ingredients or drugs, the Secretary in determining the effectiveness of the drug shall consider only whether the drug when used in such manner represents appropriate concurrent therapy for the identified target population;"

1 ~~(1) (as added by subsection (a)) the following new para-~~
 2 ~~graph:~~

3 ~~“(3) In a case in which a new animal drug contains~~
 4 ~~more than 1 active ingredient, or the labeling of the drug~~
 5 ~~prescribes, recommends, or suggests use of the drug in~~
 6 ~~combination with another animal drug, and the active in-~~
 7 ~~gredients or drugs in the combination have been sepa-~~
 8 ~~rately approved for particular uses and species prior to~~
 9 ~~the approval of the application for the same uses and spe-~~
 10 ~~cies in combination (or, in the absence of such approvals,~~
 11 ~~after evaluating the safety and efficacy of the combination~~
 12 ~~itself), the Secretary may only consider with respect to the~~
 13 ~~combination whether any of the active ingredients or any~~
 14 ~~of the drugs in the combination, respectively, at the long-~~
 15 ~~est withdrawal time of any of the active ingredients or~~
 16 ~~drugs in the combination, respectively, is above its safe~~
 17 ~~concentration (such as exceeding its established tolerance,~~
 18 ~~as measured by its marker residue), or interferes with the~~
 19 ~~methods of analysis for another of the active ingredients~~
 20 ~~or drugs in the combination, respectively.”.~~

21 (c) SUPPLEMENTAL APPLICATIONS.—Section
 22 512(c)(2)(F)(iii) (21 U.S.C. 360b(c)(2)(F)(iii)) is amend-
 23 ed—

24 (1) by striking “reports of new clinical or field
 25 investigations (other than bioequivalence or residue

1 studies) and" and inserting "substantial evidence of
2 effectiveness as defined in subsection (d)(3), any
3 study of animal safety, or"; and

4 (2) by striking "essential to" and inserting "
5 required for".

6 ~~(d) MINOR SPECIES AND USES.—Section 512(d)(1)~~
7 ~~(21 U.S.C. 360b(d)(1)) is amended by adding at the end~~
8 ~~the following new sentence: "Subparagraph (E) shall not~~
9 ~~apply to a claim for use of the drug described in subpara-~~
10 ~~graph (E) in a minor species, or for a minor use of the~~
11 ~~drug, as the terms 'minor species' and 'minor use' are de-~~
12 ~~finied in regulations issued by the Secretary, if there is~~
13 ~~an application filed under subsection (b) for the drug, and~~
14 ~~the application is approved, prior to the submission of the~~
15 ~~claim."~~

16 ~~(e) WITHDRAWAL OF APPROVAL.—Section~~
17 ~~512(e)(1)(C) (21 U.S.C. 360b(e)(1)(C)) is amended by in-~~
18 ~~serting after "substantial evidence" the following: "(as de-~~
19 ~~finied in subsection (d)(4))"~~

20 (f) IMPLEMENTATION.—

21 (1) IN GENERAL.—Not later than ¹⁸~~6~~ months
22 after the date of enactment of this Act, the Sec-
23 retary shall issue proposed regulations implementing
24 the amendments made by this section. Not later
25 than ³⁰~~18~~ months after the date of enactment of this

1 Act, the Secretary shall issue final regulations imple-
2 menting the amendments.

3 (2) CONTENTS.—In issuing regulations imple-
4 menting the amendments made by this section, and
5 in taking an action to review an application for ap-
6 proval of a new animal drug under section 512 of
7 the Federal Food, Drug, and Cosmetic Act (21
8 U.S.C. 360b), or a request for an investigational ex-
9 emption for a new animal drug under subsection (j)
10 of such section, that is pending or has been submit-
11 ted prior to the effective date of the regulations, the
12 Secretary shall—

13 (A) further define the term “substantial
14 evidence”, as defined in subsection (d)(4) of
15 such section, in a manner that encourages the
16 submission of applications for production drugs
17 that conserve food resources, of applications for
18 veterinary prescription drugs whose use is de-
19 signed to rely on the experience and training of
20 practitioners in establishing effective doses for
21 such drugs, and of supplemental applications,
22 including applications seeking approval for uses
23 of animal drugs in minor species, for minor
24 uses of such drugs, and for permitted unlabeled
25 uses of such drugs;

1 (B) take into account the proposals con-
 2 tained in the citizen petition (FDA Docket No.
 3 91P-0434/CP) jointly submitted by the Amer-
 4 ican Veterinary Medical Association and the
 5 Animal Health Institute, dated October 21,
 6 1991;

7 (C)(i) provide for the opportunity for a
 8 conference prior to the submission of an appli-
 9 cation for approval of a new animal drug under
 10 such section, and prior to the submission of a
 11 request for an investigational exemption under
 12 subsection (j) of such section, to make a deci-
 13 sion establishing a submission or an investiga-
 14 tional requirement ~~(which decision shall bind~~
 15 ~~the Secretary and the applicant or requester~~
 16 ~~unless the Secretary by order determines that a~~
 17 ~~documented scientific requirement essential to~~
 18 ~~the determination of safety or effectiveness of~~
 19 ~~the animal drug involved has appeared after the~~
 20 ~~conference); and~~

21 (ii) not later than ³⁰~~10~~ days after each such
 22 conference, ~~by written order, provide a scientific~~
 23 ~~justification specific to the animal drug and in-~~
 24 ~~tended uses under consideration for requiring~~
 25 ~~studies of types other than the types of studies~~

FDA shall provide a written statement regarding what studies, including field investigations, are necessary to establish the safety and effectiveness of the new animal drug and how such studies are to be interpreted. Should more than one field investigation be necessary to establish substantial evidence for effectiveness for the intended uses of the drug, FDA will provide written scientific justification specific to the animal drug under consideration as to why more than one

1 ~~specified in subsection (d)(4) of such section, as~~
 2 ~~being essential to provide substantial evidence~~
 3 ~~of effectiveness for the intended uses of the~~
 4 ~~drug.~~

5 **SEC. 803. LIMITATION OF RESIDUES.**

6 Section 512(d)(1)(F) (21 U.S.C. 360b(d)(1)(F)) is
 7 amended to read as follows:

8 “(F) on the basis of information submitted to
 9 the Secretary as part of the application or any other
 10 information before the Secretary with respect to
 11 such drug, any use prescribed, recommended, or
 12 suggested in labeling proposed for such drug will re-
 13 sult in a residue of such drug in excess of a toler-
 14 ance found by the Secretary to be safe for such
 15 drug;”.

16 ~~SEC. 804. ADULTERATED DRUGS.~~

17 ~~Section 501(a)(2) (21 U.S.C. 351(a)(2)) is amend-~~
 18 ~~ed—~~

19 ~~(1) in subparagraph (A), by striking “health;~~
 20 ~~or” and inserting “health;”, and~~

21 ~~(2) in subparagraph (B), by striking “possess;”~~
 22 ~~and inserting the following: “possess; or (C) if it is~~

23 ~~a drug intended for use by animals other than man~~

24 ~~and the methods used in, or the facilities or controls~~

25 ~~used for, its manufacture, processing, packing, or~~

1st Choice -
 Strike the
 entire section
 2nd Choice -
 see substitute
 language
 attached

AMENDMENT 5

Section 804 - ADULTERATED DRUGS

Strike this section. (Page 109, line 16 - Page 110, line 9)
(See Talking Point)

Or, Alternatively, offer the following Amendment:

Strike Page 109, line 21 through Page 110, line 9, and insert the following:

“(2) in subparagraph (B), by striking ‘if it is a drug’ and inserting ‘if it is a drug intended for use in man’.

(3) in subparagraph (B) by striking ‘possess;’ and inserting the following: ‘possess; or (C) if it is a drug intended for use in animals other than man and the methods used in, or the facilities or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess;’”

Report language could also be drafted to make it clear (1) that FDA has regulations at 21 C.F.R. Parts 210 and 211 setting forth current good manufacturing practice requirements for human and animal drugs, (2) that those regulations continue to apply to both human and animal drugs, (3) that by letter dated February 16, 1996, FDA asked members of the animal industry and professional medical organizations to participate in a workshop to discuss whether current good manufacturing practice requirements are a significant obstacle to animal drug availability; (4) that through such workshops, FDA will determine whether the existing regulations need to be revised or clarified with respect to their application to animal drugs, and (5) that FDA will by notice and comment rulemaking propose any revisions or clarifying language to the existing regulations it finds appropriate to ensure animal drug availability and the manufacture of animal drug products that are safe and have the identity and strength, and meet the quality and purity characteristics, they are purported or represented to possess.

~~holding do not conform to or are not operated or administered in conformity with current good manufacturing practice requirements (appropriate for animal drugs) adopted pursuant to regulations issued by the Secretary to ensure that such drug meets the requirements of this Act as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess for use in animals other than man;".~~

10 SEC. 805. VETERINARY FEED DIRECTIVES.

11 (a) WRITTEN OR ORAL ORDERS.—Section
12 503(f)(1)(A) (21 U.S.C. 353(f)(1)(A)) is amended by
13 striking "other than man" and inserting the following:
14 "other than man, other than a veterinary feed directive
15 drug intended for use in animal feed or an animal feed
16 bearing or containing a veterinary feed directive drug,".

17 (b) GENERAL REQUIREMENTS.—Chapter V (21
18 U.S.C. 351 et seq.) is amended by inserting after section
19 503 the following new section:

20 "VETERINARY FEED DIRECTIVES DRUGS

21 "SEC. 504. (a)(1) A drug intended for use in or on
22 animal feed which is limited by an approved application
23 filed pursuant to section 512(b) to use under the profes-
24 sional supervision of a licensed veterinarian is a veterinary
25 feed directive drug. Any animal feed bearing or containing
26 a veterinary feed directive drug shall be fed to animals

1 only by or upon the lawful veterinary feed directive issued
2 by a licensed veterinarian in the course of the veterinar-
3 ian's professional practice. When labeled, distributed,
4 held, and used in accordance with this section, a veteri-
5 nary feed directive drug and any animal feed bearing or
6 containing a veterinary feed directive drug shall be exempt
7 from section 502(f).

8 “(2) A veterinary feed directive is lawful if it—

9 “(A) contains such information as the Secretary
10 may, by general regulation or by order, require; and

11 “(B) is in compliance with the conditions and
12 indications for use of the drug set forth in the notice
13 published pursuant to section 512(i).

14 “(3)(A) Any persons involved in the distribution or
15 use of animal feed bearing or containing a veterinary feed
16 directive drug and the licensed veterinarian issuing the
17 veterinary feed directive shall maintain a copy of the vet-
18 erinary feed directive applicable to each such feed, except
19 in the case of a person distributing such feed to another
20 person for further distribution, such person distributing
21 the feed shall maintain a written acknowledgment from
22 the person to whom the feed is shipped stating that that
23 person shall not ship or move such feed to an animal pro-
24 duction facility without a veterinary feed directive or ship
25 such feed to another person for further distribution unless

1 that person has provided the same written acknowledg-
2 ment to its immediate supplier.

3 “(B) Every person required under the subparagraph
4 (A) to maintain records, and every person in charge or
5 custody thereof, shall, upon request of an officer or em-
6 ployee designated by the Secretary, permit such officer or
7 employee at all reasonable times to have access to and
8 copy and verify such records.

9 “(C) Any person who distributes animal feed bearing
10 or containing a veterinary feed directive drug shall upon
11 first engaging in such distribution notify the Secretary of
12 that person's name and place of business. The failure to
13 provide such notification shall be deemed to be an act
14 which results in the drug being misbranded.

15 “(b) A veterinary feed directive drug and any feed
16 bearing or containing a veterinary feed directive drug shall
17 be deemed to be misbranded if the drug ^{or} ~~and~~ feed labeling
18 fails to bear such cautionary statement and such other in-
19 formation as the Secretary may, by general regulation or
20 by order, prescribe, or the drug ^{or} ~~and~~ feed advertising fails
21 to conform to the conditions and indications for use pub-
22 lished pursuant to section 512(i) or fails to contain the
23 general cautionary statement prescribed by the Secretary.

24 “(c) Neither a drug subject to this section, nor ani-
25 mal feed bearing or containing such a drug, shall be

1 deemed to be a prescription article under any Federal or
2 State law.”.

3 (c) CONFORMING AMENDMENTS.—Section 512 (21
4 U.S.C. 360b) is amended—

5 (1) in subsection (i), by striking “require-
6 ments)” and inserting “requirements and any re-
7 quirement that an animal feed bearing or containing
8 the new animal drug be limited to use under the
9 professional supervision of a licensed veterinarian”;

10 (2) in subsection (a)(2)(C) by striking “its la-
11 beling” and inserting “its labeling, its distribution,
12 its holding,”; and

13 (3) in subsection (m)(4)(B)(i)—

14 (A) by striking “paragraph (5)(A) of this
15 subsection” and inserting “paragraph (5)(A) or
16 under section 504(a)(3)(A)”;

17 (B) by striking “subparagraph (B) of such
18 paragraph” and inserting “subparagraph (B) of
19 such paragraph or section 504(a)(3)(B)”.

20 (d) PROHIBITED ACTS.—Section 301(e) (21 U.S.C.
21 331(e)) is amended—

22 (1) by striking “section 412” and inserting
23 “section 412, 504,”; and

24 (2) by striking “under section 412,” and insert-
25 ing “under section 412, 504,”.

Insert
substitute
amendment:
attached
language

114
FEED MILL LICENSING & IMPORT TOLERANCES

1 SEC. 806. ~~TIMEFRAMES FOR APPROVAL.~~

2 ~~The first sentence of section 512(c)(1) (21 U.S.C.~~
3 ~~360b(c)(1)) is amended by striking "one hundred and~~
4 ~~eighty" and inserting "90".~~

5 **TITLE IX—FOOD REGULATORY**
6 **REFORM**

7 SEC. 901. SHORT TITLE.

8 This title may be cited as the "Food Regulatory Re-
9 form Act of 1996".

FOOD CONTACT SUBSTANCES

10 SEC. 902. ~~INDIRECT FOOD ADDITIVES:~~

Insert
substitute
amendment.
attached
language

11 ~~.(a) APPROVAL. Section 409 (21 U.S.C. 348) is~~
12 ~~amended by adding at the end thereof the following new~~
13 ~~subsection:~~

14 ~~"ALTERNATIVE APPROVAL PROCEDURE-~~

15 ~~"(j)(1) As an alternative to the approval procedure~~
16 ~~established under subsection (b), any person may submit~~
17 ~~a notification for an indirect food additive under this sub-~~
18 ~~section.~~

19 ~~"(2) Any person who proposes to begin the introduc-~~
20 ~~tion or delivery for introduction into interstate commerce~~
21 ~~of a product intended for use as an indirect food additive~~
22 ~~may submit to the Secretary, at least 90 days prior to~~
23 ~~making such introduction or delivery, a notification con-~~
24 ~~taining information demonstrating that the labeled use of~~
25 ~~the product is safe.~~

AMENDMENT 8 - FEED MILL LICENSING

This is a new provision that is not currently found in S. 1477. It is one of the President's NPR Reinventing Government Initiatives.

FDA's Proposed Legislative Language to Implement the NPR on Feed Mill Licensing

1. Section 512(a) of the Federal Food, Drug, and Cosmetic Act (Act) is amended as follows:
 - (a) Section 512(a) is amended by striking section 512(a)(1)(i) and inserting "(i) holds a license issued under subsection (m) of this section and has in his possession current approved labeling for such drug in animal feed; or"
 - (b) Section 512(a)(1)(ii) is amended by striking "an approved application" and inserting "a license issued".
 - (c) Section 512(a)(2) is amended by striking 512(a)(2)(B) and inserting "(B) such animal feed is manufactured at a site for which there is in effect a license issued pursuant to subsection (m)(1) of this section to manufacture such animal feeds; and"
 - (d) Section 512(a)(2)(C) is amended by
 - (1) striking ", its labeling and such" and inserting ", bears approved labeling and its"; and
 - (2) striking " and to the application with respect thereto approved under subsection (m) of this section"
2. Section 512(m) of the Federal Food, Drug, and Cosmetic Act (Act) is amended as follows:
 - (a) Section 512(m) is amended by striking 512(m)(1) and inserting "(m)(1) Any person may file with the Secretary an application for a license to manufacture animal feeds bearing or containing new animal drugs. Such person shall submit to the Secretary as part of the application: (A) a full statement of the business name, location of the specific site at which the manufacturing is to take place, including the street, city, state, zip code, and FDA registration number; (B) the name and signature of the responsible persons at that facility; (C) certification that animal feed or feeds bearing or containing a new animal drug or drugs shall be manufactured and labeled in accordance with the regulation or regulations (relating to the new animal drug or drugs to be used in feed or feeds) published pursuant to subsection (i) of this section; and (D) certification that the methods used in, and the facilities and controls used for the manufacture, processing, packing, and holding of such animal feed or feeds are adequate to preserve the

identity, strength, quality, and purity of the new animal drug or drugs therein."

(b) Section 512(m)(2) is amended by striking "(c)" and inserting "(c)(1)".

(c) Section 512(m)(3) is amended as follows:

(1) by inserting after "part of the application" the following: ", on the basis of a preapproval inspection,";

(2) by striking 512(m)(3)(A), (B), and (D), moving 512(m)(3)(C) to 512(m)(3)(B), and inserting "(A) that the application is incomplete, false, or misleading in any particular;" and "(C) that the applicant manufactures animal feeds containing animal drugs in a manner that does not accord with the specifications for manufacture, or labels the animal feeds containing animal drugs in a manner that does not accord with the conditions or indications of use, that are published pursuant to subsection (i) of this section;"

(3) by striking in the paragraph following 512(m)(3)(C) "(A) through (D)" and inserting "(A) through (C)"; and

(4) by striking in the paragraph following 512(m)(3)(C) "with respect to an animal feed bearing or containing a new animal drug shall be effective only while there is in effect a regulation pursuant to subsection (i), on the basis of which such application (or a supplement thereto) was approved, relating to the use of such drug in or on such feed" and inserting "for a license to manufacture animal feeds bearing or containing a new animal drug or drugs shall permit a site to manufacture only those animal feeds containing new animal drugs for which there are in effect regulations pursuant to subsection (i) relating to the use of such drugs in or on such animal feed".

(d) Section 512(m)(4) is amended as follows:

(1) 512(m)(4)(A) is amended by striking "issue an order withdrawing approval of an application with respect to any animal feed" and inserting "revoke a license to manufacture animal feeds bearing or containing new animal drugs";

(2) 512(m)(4)(A)(ii) is amended by striking "any changes from the standpoint of safety or effectiveness beyond the variations provided for in the application" and inserting "changes that would cause the application to contain any untrue statements of material fact or that would affect the safety or effectiveness of the animal feeds manufactured at the site"; and

(3) 512(m)(4)(A)(ii) is amended by striking the last sentence;

(4) 512(m)(4)(A) is amended by striking "he may suspend the approval of such

application" and inserting "he may suspend the site's license" and replacing the word "applicant" with the word "licensee";

(5) 512(m)(4)(B) is amended by striking "issue an order withdrawing the approval of an application with respect to any animal feed" and inserting "revoke a license to manufacture animal feed";

(6) 512(m)(4)(B)(ii) is amended by striking "when such application was approved" and inserting "when such license was issued" and striking "processing, and packing" and inserting "processing, packing, and holding" and striking "or" at the end of (ii);

(7) 512(m)(4)(B)(iii) by striking "when the application was approved, the labeling of such animal feed" and inserting "when such license was issued, the labeling of any animal feeds" and striking the period at the end of the sentence and inserting "; or";

(8) inserting 512(m)(4)(B)(iv): "(iv) that on the basis of new information before him, evaluated together with the evidence before him when the license was issued, the firm has manufactured, processed, packed, or held animal feed bearing or containing a new animal drug adulterated under section 501(a)(6), and the licensee did not discontinue the manufacturing, processing, packing or holding of such animal feed within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of."; and,

(9) redesignating 512(m)(4)(C) as 512(m)(4)(D) and inserting "(C) The Secretary may also revoke a license to manufacture animal feeds under this subsection if a licensee gives notice to the Secretary of intention to discontinue the manufacture of all animal feed covered under this subsection, and waves an opportunity for a hearing on the matter."

(e) Section 512(m)(5) is amended by striking "of any animal feed for which an approval of an application filed pursuant to this subsection is in effect" and inserting "a license to manufacture animal feeds bearing or containing new animal drugs has issued" and by striking in 512(m)(5)(A) "applicant" and inserting "licensee".

(f) Section 512(m) is amended by inserting 512(m)(6) as follows: "(6) To the extent consistent with public health, the Secretary may promulgate regulations for exempting from the operation of this section sites that manufacture, process, pack, or hold animal feeds bearing or containing new animal drugs."

AMENDMENT 9 - IMPORT TOLERANCES

This is a new provision that is not currently found in S. 1477. It is one of the President's NPR Reinventing Government Initiatives.

FDA's Proposed Legislative Language to Implement the NPR on Import Tolerances

The statutory change would add a new section 512(a)(6) which provides as follows:

For purposes of section 402(a)(2)(D), a use or intended use of a new animal drug shall not be deemed unsafe under section 512 if the Secretary establishes a tolerance for such drug and any portion of any animal imported into the United States does not contain residues exceeding such tolerance.

In establishing such tolerance, the Secretary shall rely on data sufficient to demonstrate that a proposed tolerance is safe based on similar food safety criteria used by the Secretary to establish tolerances for applications for new animal drugs filed under subsection (b)(1). The Secretary may consider and rely on data submitted by the manufacturer, including data submitted to appropriate regulatory authorities in any country where the new animal drug is lawfully used, or data available from a relevant international organization, to the extent such data is not inconsistent with the criteria used by the Secretary to establish a tolerance for applications for new animal drugs filed under subsection (b)(1). For purposes of this paragraph, relevant international organization means the Codex Alimentarius Commission or other international organization deemed appropriate by the Secretary.

The Secretary may, under procedures specified by regulation, revoke such tolerances if information demonstrates that the use of the new animal drug under actual use conditions results in foods being imported into the United States with residues exceeding such tolerances.

This language was last updated on 3/21/96

TITLE IX -- FOOD REGULATORY REFORM

Sec. 901. Short Title.

This title may be cited as the "Food Regulatory Reform Act of 1996".

Sec. 902. Food Contact Substances

(a) Approval. -- Section 409 (21 U.S.C. 348) is amended by redesignating Subsection (h) as Subsection (j) and adding new Subsection (h) as follows:

"NOTIFICATION PROCEDURE FOR FOOD CONTACT SUBSTANCES".

"(h)(1) As an alternative to the procedure established under subsection (b), any person may submit a notification for a food contact substance under this subsection. For purposes of this subsection, the term 'food contact substance' means any substance intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use may reasonably be expected to result in such substance becoming a component of food, and is not intended to have any technical effect in such food."

(2) Any person who proposes to begin the introduction or delivery for introduction into interstate commerce of an article intended for use as a food contact substance may submit to the Secretary, at least 90 days prior to making such introduction or delivery, a notification that such person has determined that the labeled use of the article is safe. Such notification shall contain the data and information forming the basis for such determination.

(3) Within 90 days after the receipt of a notification by the Secretary, the Secretary may object to the notification if, on the basis of the data and information submitted, as well as other information available to the Secretary, the substance has not been shown to be safe for its labeled use under the standard of subsection (c)(3)(A), including the proviso thereof. In the absence of an objection, the article may be lawfully marketed for its labeled use on the 91st day after receipt of the notification, *unless the Secretary objects to the notification.*

(4) The Secretary shall publish on a quarterly basis a list of all food contact substances for which a notification has been received and to which the Secretary has not objected in the 90 day time period specified in Subsection (3). Such list shall include the identity of and specifications for use of each such substance."

(5) An objection by the Secretary under subsection (h)(3) shall be considered final agency action for the purposes of 5 U.S.C. § 706.

(b) Conformity With Adulteration Exemption. -- Section 409 (21 U.S.C. 348 (a)) is amended --

(1) in paragraph (1) by striking "or" at the end thereof;

(2) in paragraph (2) by striking the period at the end thereof and inserting "; or";

(3) by inserting after paragraph (2) the following new paragraph:

"(3) It is a food contact substance and more than 90 days have passed since the receipt of a notification under subsection (h) covering the use of such substance and the Secretary has not objected to such notification under subsection (h)(3)."

1 ~~“(3)(A) Within 90 days after the receipt of the notifi-~~
2 ~~cation by the Secretary, the Secretary shall either—~~
3 ~~“(i)(I) approve the notification if the article is~~
4 ~~safe for its intended use; or~~
5 ~~“(H) disapprove the notification if the article~~
6 ~~has not been shown to be safe for its intended use;~~
7 ~~and~~
8 ~~“(B) publish a notice of this determination in the~~
9 ~~Federal Register and, if the notification is approved, pro-~~
10 ~~mulgate an appropriate regulation pursuant to subsection~~
11 ~~(c).”.~~
12 ~~(b) DEFINITION. Section 201 (21 U.S.C. 321), as~~
13 ~~amended by section 409, is further amended by adding~~
14 ~~at the end thereof the following new subsection:~~
15 ~~“(ii) The term ‘indirect food additive’ means a food~~
16 ~~additive that is intended to contact food but that is not~~
17 ~~intended for consumption as a food ingredient.”.~~