AMENDMENT TO COMMITTEE PRINT

OFFERED BY M__. _____

(REMS__003, June 20, 2007)

Page 3, line 8, strike ''study'' and insert ''study or studies''.

Page 3, line 9, strike ''clinical trial'' and insert ''clinical trial or trials''.

Page 3, line 17, strike ''serious risks'' and insert ''serious risk''.

Page 3, line 24, strike ''postapproval study or postapproval trial'' and insert ''postapproval study or studies or postapproval trial or trials''.

Page 4, line 4, insert after ''information.'' the following: ''For each study required to be conducted under this subparagraph, the Secretary shall require that the applicant submit a timetable for completion of the study and shall require the applicant to periodically report to the Secretary on the status of the study. Unless the applicant demonstrates good cause for failure to comply with such timeline, the applicant shall be in violation of this subsection. The Secretary shall determine what constitutes good cause under the preceding sentence.''

Strike page 4, line 5, through page 5, line 8, and insert the following:

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

''(A) NEW SAFETY INFORMATION.—The Secretary shall promptly notify the responsible person if the Secretary becomes aware of new safety information that the Secretary believes should be included in the labeling of the drug.

''(B) RESPONSE TO NOTIFICATION.—Following notification pursuant to subparagraph (A), the responsible person shall within 30 days—

''(i) submit a supplement proposing changes to the approved labeling to reflect the new safety information, including changes to boxed warnings, contraindications, warnings, precautions, or adverse reactions; or

''(ii) notify the Secretary that the responsible person does not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.

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

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

''(E) ORDER.—Within 15 days of the conclusion of the discussions under subparagraph (D), the Secretary may issue an order directing the responsible person to make such a labeling change as the Secretary deems appropriate to address the new safety information. Within 15 days of such an order, the responsible person

shall submit a supplement containing the labeling change.

''(F) DISPUTE RESOLUTION.—Within 5 days of receiving an order under subparagraph (E), the responsible person may appeal using the Food and Drug Administration's normal dispute resolution procedures established by the Secretary in regulation and guidance.

''(G) VIOLATION.—If the change required by an order under subparagraph (E) is not made by the date so specified, the responsible person shall be considered to be in violation of this section.

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

Strike page 5, line 9, through page 5, line 13, and insert the following:

''(I) RULE OF CONSTRUCTION.—This paragraph shall not be construed to affect the responsibility of the responsible person to main-

tain its label in accordance with existing requirements, including subpart B and section 314.70 of title 21, Code of Federal Regulations (or any successor regulations).

Page 6, lines 21 and 22, strike ''an application referred to in paragraph (1)(A)'' and insert ''an application approved under subsection (b) or (j) for a new drug that is subject to section 503(b), or an application approved under section 351 of the Public Service Act,''.

Page 8, lines 22 and 23, strike ''with the application'' and insert ''as part of the application''.

Page 9, line 4, strike the period and insert the following:''and shall consider the following factors:

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

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

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

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

''(E) The seriousness of any known or potential adverse events that may be related to

the drug and the background incidence of such events in the population likely to use the drug.

''(F) The availability and safety of a drug or other treatment, if any, for such disease or condition to which the safety of the drug may be compared.

''(G) Whether the drug is a new molecular entity.''.

Page 9, lines 17 through 21, strike ''Not later than'' and all that follows through ''the holder shall submit'' and insert ''Not later than 120 days after the Secretary notifies the holder of an approved covered application that the Secretary has made a determination under subparagraph (A) with respect to the drug involved, or within such other time as the Secretary requires to protect the public health, the holder shall submit''.

Page 11, line 13, insert ''since the drug was approved, since the risk evaluation and mitigation strategy was required, or'' before ''since the last assessment''.

Page 13, after line 4, insert the following (and make such technical and conforming changes as may be necessary):

''(E) data derived from a postmarket risk identification and analysis system under section 505(k)(3).

Strike page 19, lines 15 through 17, and insert the following:

''(C) notify wholesalers of the drug of those health care providers—

Strike page 20, lines 1 through 13, and insert the following:

''(5) LIMITATION.—No holder of an approved application shall use any restriction on distribution required by the Secretary as necessary to assure safe use of the drug to block or delay approval of an application under section 505(b)(2) or (j) or to prevent application of such restriction under subsection (i)(1)(B) to a drug that is the subject of an abbreviated new drug application.

''(6) BIOEQUIVALENCE TESTING.—Notwithstanding any other provisions in this subsection, the holder of an approved application that is subject to distribution restrictions required under this subsection that limit the ability of a sponsor seeking approval of an application under subsection 505(b)(2) or (j) to purchase on the open market a sufficient

quantity of drug to conduct bioequivalence testing shall provide to such a sponsor a sufficient amount of drug to conduct bioequivalence testing if the sponsor seeking approval under section 505(b)(2) or (j)—

''(A) agrees to such restrictions on distribution as the Secretary finds necessary to assure safe use of the drug during bioequivalence testing; and

''(B) pays the holder of the approved application the fair market value of the drug purchased for bioequivalence testing.

''(7) LETTER BY SECRETARY.—Upon a showing by the sponsor seeking approval under section 505(b)(2) or (j) that the sponsor has agreed to such restrictions necessary to assure safe use of the drug during bioequivalence testing, the Secretary shall issue to the sponsor seeking to conduct bioequivalence testing a letter that describes the Secretary's finding which shall serve as proof that the sponsor has satisfied the requirements of subparagraph (6)(A).

''(8) EVALUATION OF ELEMENTS TO ASSURE SAFE USE.—The Secretary, acting through the Drug Safety and Risk Management Advisory Committee

(or any successor committee) of the Food and Drug Administration, shall—

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

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

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

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

''(i) assure safe use of the drug;

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

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

''(C) considering such input and evaluations—

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

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

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

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

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

Strike page 21, lines 13 through 24, and insert the following (and make such technical and conforming changes as may be necessary):

''(C) within a time period to be determined by the Secretary, if the Secretary determines that new safety or effectiveness information indicates that—

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

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

Page 24, after line 10, insert the following (and make such technical and conforming changes as may be necessary):

''(2) MARKETING PLAN.—As part of a review conducted under this subsection, the Secretary may require the applicant to submit information regarding its marketing plan and practices for the drug, so as to allow the Secretary to determine whether any of the proposed or ongoing marketing activities undermine any of the requirements of the risk evaluation and mitigation strategy.

Page 37, line 6, strike ''representatives'' and insert ''include such representatives as the Secretary shall designate''.

Page 48, lines 17 through 22, strike ''fails'' through ''to comply with'' and insert ''fails to comply with''.

Page 48, after line 24, insert the following:

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

Page 49, strike lines 12 through 22, and insert the following:

''(3) Any applicant (as such term is used in section 505A) who violates a requirement of section 505(o), section 505(p), or section 505A shall be subject to a civil monetary penalty of—

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

''(B) in the case of a violation that continues after the Secretary provides notice of such violation to the applicant, not more than $10,000,000 per violation, and not to exceed $50,000,000 for all such violations adjudicated in a single proceeding.

If a violation referred to in subparagraph (A) or (B) is continuing in nature and poses a substantial threat to the public health, the Secretary may impose a civil penalty not to exceed $1,000,000 per

day during such time period such person is in violation.''.

Page 50, line 25, insert after the period the following: ''As part of such study, the Commissioner shall consider the possibility of including in the labeling and any direct-to-consumer advertisements of a newly approved drug or indication a unique symbol indicating the newly approved status of the drug or indication for a period after approval.''.

At the appropriate place in the bill, insert the following:

SEC. ___. CLINICAL TRIAL GUIDANCE FOR ANTIBIOTIC DRUGS.

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

''SEC. 511. CLINICAL TRIAL GUIDANCE FOR ANTIBIOTIC DRUGS.

''(a) IN GENERAL.—Not later than 1 year after the date of enactment of this section, the Secretary, acting through the Commissioner of Food and Drugs, shall issue guidance for the conduct of clinical trials with respect to antibiotic drugs, including antimicrobials to treat acute bacterial sinusitis, acute bacterial otitis media, and acute

bacterial exacerbation of chronic bronchitis. Such guidelines shall indicate the appropriate animal models of infection, in vitro techniques, and valid microbiologic surrogate markers.

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

At the appropriate place in the bill, insert the following:

SEC. ___. PROHIBITION AGAINST FOOD TO WHICH DRUGS OR BIOLOGICAL PRODUCTS HAVE BEEN ADDED.

Section 301 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331) is amended by adding at the end the following:

''(____) The introduction or delivery for introduction into interstate commerce of any food to which has been added—

''(1) a drug approved under section 505,

''(2) a biological product licensed under section 351 of the Public Health Service Act, or

''(3) a drug or biological product for which substantial clinical investigations have been instituted and for which the existence of such investigations has been made public,

unless such drug or biological product was marketed in food before any approval of the drug under section 505 of this Act, before licensure of the biological product under section 351 of the Public Health Service Act, and before any substantial clinical investigations involving the drug or biological product have been instituted, or unless the Secretary, in the Secretary's discretion, has issued a regulation, after notice and comment, approving the addition of such drug or biological product to the food.''.

At the appropriate place in the bill, insert the following:

SEC. ___. ASSURING PHARMACEUTICAL SAFETY.

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

''SEC. 505C. PHARMACEUTICAL SECURITY.

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

''(b) STANDARDS DEVELOPMENT.—

''(1) IN GENERAL.—The Secretary shall, in consultation with the agencies specified in paragraph (3), prioritize and develop standards for the identification, validation, authentication, and tracking of prescription drugs.

''(2) PROMISING TECHNOLOGIES.—The standards developed under this subsection shall address promising technologies, including—

''(A) radio frequency identification technology;

''(B) nanotechnology;

''(C) encryption technologies; and

''(D) other track-and-trace technologies.

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

''(A) the Administrator of the Drug Enforcement Administration;

''(B) the Secretary of the Department of Homeland Security

''(C) the Secretary of Commerce; and

''(D) other appropriate Federal and State agencies.

''(c) INSPECTION AND ENFORCEMENT.—

''(1) IN GENERAL.—The Secretary shall expand and enhance the resources and facilities of the Office of Regulatory Affairs of the Food and Drug Administration to protect the prescription drug distribution system against counterfeit, diverted, subpotent, substandard, adulterated, misbranded, or expired drugs.

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

''(d) DEFINITION.—In this section, the term 'prescription drug' means a drug subject to section 503(b)(1).''.

At the appropriate place in the bill, insert the following new section (and make such technical and conforming changes as may be necessary):

SEC. _____. ORPHAN ANTIBIOTIC DRUGS.

(a) PUBLIC MEETING.—The Commissioner of Food and Drugs shall convene a public meeting regarding which serious and life threatening infectious diseases, such as diseases due to gram-negative bacteria and other diseases due to antibiotic-resistant bacteria, potentially qualify for

available grants and contracts under section 5(a) of the Orphan Drug Act (21 U.S.C. 360ee(a)) or other incentives for development.

(b) GRANTS AND CONTRACTS FOR THE DEVELOPMENT OF ORPHAN DRUGS.—Section 5(c) of the Orphan Drug Act (21 U.S.C. 360ee(c)) is amended to read as follows:

''(c) For grants and contracts under subsection (a), there is authorized to be appropriated $30,000,000 for each of fiscal years 2008 through 2012.''.