

COMMERCE COMMITTEE

NEWS RELEASE

Major Changes to H.R. 3201 in Staff Discussion Draft

- Provisions that permit an option to use an FDA Accredited third party reviewer are clarified to provide that they will be under strict FDA controls, FDA will select the panels of possible reviewers, and FDA will make all final decisions using current FDA standards.
 - The provision for good manufacturing inspections by FDA accredited persons is strengthened to meet agency concerns.
- Provisions that set time frames for FDA action have been expanded to meet agency concerns.
- Provisions that help patients by providing patients' treatment access to investigational devices or access to humanitarian devices have been strengthened to prevent misuse.
- Provisions that streamline procedures to permit companies to use performance standards have been tightened.
- Provisions that are used to determine device safety and effectiveness are clarified to make maintain current high standards.
- Provisions that exempt class I devices do not exempt devices that might present a risk to health.
- Provisions that permit FDA to reclassify new devices give FDA new flexibility to streamline the device approval process.
- Provisions relating to the dissemination of information have been substantially narrowed to make such dissemination meet exacting standards of scientific reliability. Specifically, only written products that come from the government's own health agencies, the recommendations of relevant medical professional societies, completed human clinical trial data or other high quality information (as judged by independent experts) can be given to health care professionals.
- Provisions to eliminate user reporting have been replaced by a new representative sampling system for user reporting.
- Provisions that were criticized as poorly drafted have been substantially modified.
- Deleted is the provision to eliminate certain malfunction reporting.

"THE MEDICAL DEVICE REFORM ACT OF 1996"

STAFF DISCUSSION DRAFT -- JULY 10, 1996

SUMMARY OF CHANGES MADE TO H.R. 3201

Sec. 1. Short title; reference; table of contents.

Sec. 2. FDA mission and annual report.

The discussion draft amends the FDA Mission to include specific responsibilities of the FDA to protect foods, human and veterinary drugs, medical devices, cosmetics, radiation from electronic products. The discussion draft shifts the responsibility assigned to FDA in H.R. 3201 to GAO for preparation of an annual report that compares the performance and resources of FDA and corresponding regulatory agencies in specified modern western countries.

Sec. 3. Dispute resolution.

The discussion draft revises the provision in H.R. 3201. Dispute resolution process is limited to a scientific controversy when no other specific provision of the Act or FDA regulations provides for a right for a review of the subject matter. This provision also adds a right, when a premarket submission is not completed within statutory time limits, to permit the sponsor to request a written explanation why the review is not completed, when to expect is completion, and to receive the answer in 14 days.

Sec. 4. Investigational device exemptions (IDE).

Of the new IDE regulation provisions required in H.R. 3201, the discussion draft narrows the use of investigational devices used outside of an ongoing clinical study. Such devices can be used in the treatment or diagnosis of diseases or conditions that are life-threatening or could be severely debilitating as determined by the treating physician when there is no legally marketed device alternative for the satisfactory treatment or diagnosis of the disease or condition.

The discussion draft also eliminates the right provided in H.R. 3201 to appear before a

classification panel in a dispute between FDA and an applicant over a clinical investigation plan and instead requires a meeting between FDA and the applicant.

The discussion draft adds to the provisions in H.R. 3201 a notice requirement to FDA prior to a implementation of a change to a investigational device or investigational device protocol, and adds that any dispute over such change shall be resolved under the dispute resolution provision established in Sec. 3.

Sec. 5. Special review for certain devices.

No change.

Sec. 6. Expanding humanitarian use of devices.

The discussion draft doubles the time permitted in H.R. 3201 for FDA to review an application of a humanitarian device from 30 to 60 days. Previous law had authorized special eased provisions for humanitarian devices that benefit patient populations of less than 4,000 people. The draft also adds a new provision permitting FDA to support or withdraw the exemption for a humanitarian device if any of the listed requirements for such exemption are no longer met. The draft also rescinds any regulations for humanitarian devices that the Secretary may have promulgated prior to the enactment of this Act.

Sec. 7. Performance standards.

H.R. 3201 authorized the use of FDA accepted performance standards by device manufacturers. The discussion draft makes clear that this provision applies only to FDA recognized performance standards to which a company may self-certify. Furthermore, the discussion draft requires that the data and information which support self-certification must be made available to FDA during an inspection. The discussion draft makes it a crime to falsify a certification or fail or refuse to provide this information during and FDA inspection.

Sec. 8. Effectiveness determination.

The discussion draft rewrites the provision in H.R. 3201 to make clear that the applicant and the FDA may agree on when a well-controlled clinical investigation may be appropriate. If they cannot agree, the dispute

is referred to a classification panel for resolution, and the final decision is made by FDA.

H.R. 3201 restricted when certain clinical outcome studies could be required. Because of concern that the provision might mean that clinical investigation might not be required to demonstrate device safety and effectiveness, the discussion revised the language when the evaluation of clinical outcomes is appropriate. Similarly, the discussion draft has revised language to make clear that the limitation on the use of relative effectiveness does not interfere with the necessary use of active clinical controls in clinical investigations.

The discussion draft specifies that various exclusions from effectiveness do not prohibit FDA from requiring warnings, precautions, contraindications or other similar label disclosures to provide a reasonable assurance of safety and effectiveness.

Sec. 9. Premarket notification.

While H.R. 3201 exempted all class I devices, the discussion draft does not exempt those class I devices which are intended to be life supporting or life sustaining, intended for a use which is of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury.

The discussion draft revises the initial classification provision contained in H.R. 3201 to permit the FDA to make a change from the initial class III classification without going to a classification panel. If the applicant disagrees with FDA's classification, or, if FDA fails to make a timely classification decision, the applicant's request for a risk-based study must be immediately referred to a classification panel for its recommendation and determination.

The discussion draft requires that all devices reviewed by an FDA accredited person for substantial equivalence must be submitted to FDA for a final classification. This is a major change to H.R. 3201 which permitted accredited persons to classify class II devices without FDA involvement.

The discussion draft narrows the device changes that H.R. 3201 would have allowed without FDA review. The

discussion draft no longer permits a significant change in operating principles even though the change would not adversely affect the safety or effectiveness of a device.

While H.R. 3201 permits the use of certain standards for determination of substantial equivalence, the discussion draft makes clear that compliance with standards that the Secretary might accept for the determination of substantial equivalence must be standards that have been accepted by the FDA. Furthermore, the discussion draft requires that the data and information which support self-certification must be made available to FDA during an inspection, and the discussion draft makes it a crime to falsify a certification or fail or refuse to provide this information during an FDA inspection.

Sec. 10. Classification panels.

The discussion draft reduces the specified number of annual panel meetings in H.R. 3201 from six to four and the number of meetings requiring the physical presence of members from three to two. Moreover, the provision states that such meetings will not be required unless persons request a panel review at least 30 days prior to a scheduled meeting. The discussion draft also narrows the rights found in H.R. 3201 regarding information about the panel review to persons whose devices are the subject of the review. Likewise, only such persons are guaranteed a response to any opposing views at a panel meeting.

Sec. 11. Premarket approval.

The discussion draft makes very clear that the FDA's decision to approve or disapprove a device based upon the recommendation of an FDA accredited person review shall be made upon the safety and effectiveness standard in the current law. The draft also clarifies that FDA must explain why it disagrees with a recommendation by the accredited person for the FDA to either approve or deny an application. The decision whether to have FDA or an accredited person conduct a review is up to the applicant. (Section 12 of the discussion draft establishes that FDA will provide an applicant a panel of three names of FDA accredited persons who would be qualified to conduct a review of its product.) If FDA determines that there is no FDA accredited person who is suitably qualified according to FDA's standards to conduct a review for a

particular type of product, then FDA alone would be the only entity that could conduct the review.

Sec. 12. Accreditation of third parties.

New language in the discussion draft makes clear that the Secretary will provide for accreditation through programs administered by the FDA, other government agencies, or other qualified non-government organizations. New language also establishes the process for withdrawal of accreditation, a requirement for performance auditing, and annual report listing the names of accredited persons and the particular activity for which such persons are accredited, and the names of all persons whose accreditation has been withdrawn during the year.

The discussion draft requires FDA to provide each person who wants to use an FDA accredited person to conduct a review the names of a panel of at least three accredited persons from which to select one that it would like to use. If FDA determines that there is not an FDA accredited person qualified to conduct the review of a particular type of device, then the use of an FDA accredited person for a review would not be possible, and FDA would conduct the review.

Sec. 13. Reclassification of preamendment devices.

No significant issue.

Sec. 14. Device tracking.

The discussion draft broadens the scope of H.R. 3201 for when device tracking can be required. The discussion draft authorizes device tracking for a device the failure of which would be reasonable likely to have serious adverse health consequences, and the device is intended to be permanently implantable or a life sustaining or life supporting device.

Sec. 15. Postmarket surveillance.

The discussion draft broadens the application of post-market surveillance by eliminating the restriction in H.R. 3201 on devices introduced prior to 1991 and includes such devices under post market surveillance. The draft adopts the broader language found in the device tracking provision (section 14. above). The period of a prospective postmarket surveillance shall

not be greater than 36 months, doubled from 18 in H.R. 3101.

Sec. 16. Harmonization.

The discussion draft removes the requirement that FDA participate "regularly and continuously" in meetings with other countries to discuss methods and approaches to reduce the burden of regulation, harmonize regulatory requirements, and seek reciprocal arrangements. Concern was raised that this provision as written could impose an unnecessary drain on FDA resources.

Sec. 17. Good manufacturing practice inspections.

The discussion draft permits 15 days, up from 10 in H.R. 3201, for a regulated person to respond to non-serious complaints about good manufacturers. However, in the discussion draft, the FDA is permitted to then take immediate regulatory action after such a response rather than after completing a review of the response.

When an accredited person conducts an inspection, the discussion draft tightens the obligation of the accredited person to report to FDA failures in compliance, and to provide to FDA all inspection observations and responses to observations. Also, the draft clarifies the FDA's right to conduct an inspection because of "good cause" doesn't limit the auditing of accredited persons.

Sec. 18. Use of scientific and medical information.

The provision limits the type of information that would qualify for dissemination to:

(i) recommendations of a Federal Government health agency,

(ii) recommendations of a medical speciality organization recognized by the Secretary,

(iii) reports on unapproved dosages or methods of administration for an approved drug or device,

(iv) reports of scientific research that would be sufficient for the submission of a supplemental application for a new use of an approved product under section 505 or section 515 or a notification under

section 510(k) whether or not such application or such notification has been filed,

(v) reports of a clinical investigation that would be considered to be scientifically sound by experts qualified by scientific training and experience to evaluate the effectiveness of a drug or device that is the subject of such clinical investigation, and

(vi) such other information that the Secretary may recognize.

The provision further permits FDA, through regulation and after an opportunity for public comment, to require that information representing inconsistent recommendations or inconsistent reports when disseminated be accompanied by conflicting information in order to achieve a balanced presentation of information to the recipient. The conflicting information would also have to be considered scientifically sound by experts qualified to make that determination.

The provision seeks to promote the availability of information about innovative medical research on new devices or drugs to private non-profit groups that could help provide patients access to this information. FDA would be authorized to provide technical assistance through the Food and Drug Administration, the National Institutes of Health, and the Centers for Disease Control to any not-for-profit entity recognized by the Secretary that seeks to make information widely available to the public on research and treatment conducted under the authority of section 505(I) and section 520(g). To be eligible for such technical assistance, such not-for-profit entity shall maintain registries of trials, protocols, eligibility, and experimental treatments, and the results of such research in the United States and other countries, with the consent of the sponsor, including information concerning potential toxicities or adverse effects associated with the use or administration of such experimental treatment.

Sec. 19. Reports.

The discussion draft eliminates the provision in H.R. 3201 that would have exempted certain malfunction device reporting when the failure resulted from improper servicing or maintenance.

The discussion draft deletes the provision in H.R. 3201 that would have eliminated the user reporting requirement. Instead, the discussion draft establishes a revised user reporting program that would limit user reports to a subset of hospitals and nursing homes to be identified by FDA that would create a representative profile of user reports for device deaths and serious illnesses or serious injuries.

Sec. 20. G.M.P. and device reports.

The discussion draft corrects a reference section of the Act from 301(g)(1)(B) in H.R. to 301(q)(1)(B)

Sec. 21. Civil penalties.

The discussion draft corrects a reference to a subsection (f)(2) to (g)(2)(a).

Sec. 22. Information system.

No change.

Sec. 23. Environmental impact review.

The language is revised to reflect the categorical exemption provision in the Council on Environmental Quality's regulations.

Sec. 24. Informal agency statements.

No change.

Sec. 25. Research and education; practice of medicine.

No change.

Sec. 26. Publication of notice of deviation.

H.R. 3201 prohibited FDA from releasing information to the public when investigating a concern about a product or its manufacture. The discussion draft changes this provision to permit FDA to disseminate information regarding a product that presents an imminent danger to health or gross deception to a consumer before FDA has completed an investigation on a concern regarding such product.

COMMERCE COMMITTEE

NEWS RELEASE

Major Changes to H.R. 3199 in Staff Discussion Draft

Provisions that specify the use of third party reviewers are clarified to provide that the FDA controls their use, accreditation and payment.

- Provisions that set time frames for FDA action have been expanded to meet agency concerns.
 - Provisions that detailed the exact nature of data that needed to be submitted for a new drug application have been deleted and replaced by a flexible regulatory process that encourages international harmonization.
 - Provisions that determine when a product has been proven to be safe and effective are clarified to make sure that the US high standard of safety and efficacy is maintained in a manner consistent with modern science.
 - Provisions relating to the dissemination of information have been substantially narrowed to make such dissemination meet exacting standards of scientific reliability. Specifically, only written products that come from the government's own health agencies, the recommendations of relevant medical professional societies, completed human clinical trial data or other high quality information (as judged by independent experts) can be given to health care professionals.
- New provisions have been added relating to:
 - A new data collection and dissemination program to help patients access information about pending clinical trials.
 - A new codification of the FDA's expanded access program to assure that patients have early access to promising new drugs.
 - New provisions for the regulation of human tissue.
- Provisions that were criticized as too costly, or poorly drafted have been either deleted or substantially modified.
- Deleted provisions include:
 - Substantial reform of blood products regulation.
 - The process of making manufacturing changes except to the extent that FDA and the regulated industry have agreed to changes.
 - Third party review of manufacturing practices.

"THE DRUG AND BIOLOGICAL PRODUCTS REFORM ACT OF 1996"

STAFF DISCUSSION DRAFT -- JULY 10, 1996

SUMMARY OF CHANGES MADE TO H.R. 3199

Sec. 1. Short title, reference, and table of contents.

Sec. 2. FDA mission and annual report.

The discussion draft amends the FDA Mission to include the specific responsibilities of the FDA to protect foods, human and veterinary drugs, medical devices, cosmetics, and radiation from electronic products. The discussion draft shifts the responsibility assigned to FDA in H.R. 3199 to GAO for preparation of an annual report that compares the performance and resources of FDA and corresponding regulatory agencies in specified modern western countries.

Sec. 3. Streamlining clinical research on drugs and biological products.

The discussion draft increases the time in H.R. 3199 for FDA's review of an investigational new drug (IND) from 21 days to 30 days in current practice. The submission requirements are broadened to include "information on design of the investigation." The discussion draft limits the reduced initial information requirements in H.R. 3199 for research applications to only phase I studies for drugs and well-characterized, therapeutic derived drugs. The discussion draft permits FDA to request additional information within 30 days increased from 21 days in H.R. 3199.

The discussion draft clarifies that the issuance of a clinical hold can be issued verbally but must be confirmed in writing, and its issuance may, in addition to other factors, take into account the qualifications of the clinical investigator and information about the drug. FDA is required to respond to a request to remove a clinical hold in 30 days, increased from 15 days in H.R. 3199.

The discussion draft also clarifies when FDA may accredit an institution, such as a medical college, to approve certain research. The authority is narrowed from H.R. 3199 to only permit such reviews for phase I and phase II non-commercial research for the specific

type of research that FDA accredits for a particular institution.

Sec. 4. The content and review of a new drug application.

The discussion draft eliminates the provision in H.R. 3199 that narrowed the amount of information FDA would routinely receive for a new drug application. Instead, in order to minimize the burden of unnecessary information submissions and to better harmonize international regulatory requirements, FDA is directed to complete within one year a determination of the type and amount of information that must be included in a new drug application after consultation with patient groups and the regulated industry. FDA is further directed to take into account the recommendations of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, an international group of which the US is a member. This provision is now similar to a provision in S.1477 reported by the Senate Labor and Human Resources Committee.

The discussion draft provides FDA with additional flexibility to respond to valid safety concerns in altering an agreement between FDA and a sponsor on the design of a study for proving the safety and effectiveness of a new drug.

The discussion draft clarifies that: (1) the written decisions of the office for the review of a new drug on all aspects of scientific and medical matters shall be binding upon field personnel unless in consultation with the reviewing office, such field personnel demonstrate why such decision should be modified; and, (2) that the action of the office responsible for review of new drug can not be delayed because of unavailability of information from or action by field personnel unless the delay is necessary to assure the marketing of a safe and effective drug.

The discussion draft adds a new section that provides provisions for generic drugs comparable to those for proprietary drugs that: requires FDA to establish review standards for applications, hold meetings between FDA and sponsors, restricts changes to the design of required studies, and proscribed actions of the field office regarding the medical and scientific matters, and the unavailability of field personnel to conduct inspections.

Sec. 5. Effectiveness determination.

The discussion draft makes substantial changes to assure that there is no diminution of the current effectiveness standard. The new language specifies when a single pivotal adequate and well-controlled investigation and other supporting information is sufficient: "Substantial evidence may, where there is a high level of confidence in the scientific validity of the results of an adequate and well-controlled investigation, consist of data from such adequate and well-controlled investigation and adequate supportive scientific evidence (obtained before or after such investigation)."

The provision in H.R. 3199 for expediting the approval of a new drug for serious or life threatening conditions is revised to adopt the language currently in FDA's "Subpart E" regulations that describes how to consider drugs for such conditions and further authorizes FDA to impose phase IV post-marketing testing requirements.

The provision in H.R. 3199 permitting a supplemental application for the new use of a previously approved drug has been revised to describe when the submission of retrospective information could support a supplement application for the new use of an approved drug. "For the purpose of making an evaluation of a new use of a previously approved new drug, the Secretary shall consider whether the new use is supported by adequate valid scientific information from clinical investigation reports in peer reviewed medical and scientific journals, patient registries or compendia, and other sources recognized by the Secretary. In carrying out the proceeding sentence, the Secretary may, when appropriate, consult with medical specialty societies."

The discussion draft modifies the restriction in H.R. 3199 on the FDA's ability to require consideration of relative effectiveness. The discussion draft permits its use when necessary for public health reasons.

Sec. 6. Scientific advisory panels.

The discussion draft removes a restriction in H.R. 3199 that would have prohibited federal employees from serving as a non-voting member of a scientific advisory panel. The discussion tightens conflict of interest

restriction by extending them to the immediate family of a member. The mandate in H.R. 3199 to hold a specified number of meetings per year is eliminated. While H.R. 3199 granted rights to all persons to receive all information regarding submissions to a panel, the provision is now limited to only the sponsor for written information submitted to a panel and certain other information is available to the public.

Sec. 7. Marketing approval.

The discussion draft narrows the use of FDA accredited persons to conduct reviews of new drug applications that was permitted in H.R. 3199. The discussion draft authorizes FDA accredited persons to review all or part of a new drug application when FDA requests the use of such accredited person, the sponsor concurs, and the cost is paid through funds collected under user fees. The accredited person is required to submit a report of its review including the basis for any recommendation to FDA. FDA makes the final approval decision on the same standards as it would to make a decision for a review conducted by FDA. A new comparable provision is added to permit the use of FDA accredited persons in the review of applications submitted for generic drugs. However, since generic drugs do not pay user fees, the cost of such review would be borne by the manufacturer.

Sec. 8. Accreditation of third parties.

The discussion draft makes clear that the Secretary will provide for accreditation of FDA accredited persons through programs administered by the FDA, other government agencies, or other qualified non-government organizations. New language also establishes a process for FDA to withdraw accreditation, a requirement for FDA to conduct performance auditing, and a requirement for FDA to prepare an annual report listing the names of FDA accredited persons and the particular activity for which accredited, and the names of all persons whose accreditation has been withdrawn during the year.

Sec. 9. Dispute resolution.

The discussion draft revises the provision in H.R. 3199. Dispute resolution process is limited to a scientific controversy when no other specific provision of the Act or FDA regulations provides for a right for a review of the subject matter. This provision also adds a right, when a premarket submission is not

completed within statutory time limits, to permit the sponsor to request a written explanation why the review is not completed, when to expect its completion, and to receive the answer in 14 days.

Sec. __. Good manufacturing practice inspections.

This provision is eliminated.

Sec. 10. Good manufacturing practices.

The discussion draft modifies H.R. 3199 to permit FDA to take action when there is a reasonable probability of harm, eliminating the requirement in H.R. 3199 for actual harm, and also eliminating the requirement for an informal hearing before FDA takes action.

Sec. 11. Pilot and small scale manufacture.

The discussion draft eliminates the opportunity for an informal hearing.

Sec. 12. Manufacturing changes.

The discussion draft revises this provision to conform to an agreement on this provision reached by FDA and the regulated industry. The new language requires the manufacturer of a new drug or animal drug to validate the effect of the change on the identity, strength, quality, purity, or potency as they may relate to the safety or effectiveness of the drug. Modifications are classified into: (1) minor manufacturing changes that can be made at any time and which must be annually reported to FDA, (2) major manufacturing changes that require prior FDA approval since these have a substantial potential to adversely affect the identify, strength, quality, purity, and potency as they may related to the safety or effectiveness of a drug, and (3) all other changes that require notice to FDA 30 in advance and which FDA will subsequently approve or disapprove. A transition period is established. It is expected that this provision will be added to the managers amendment to S.1477 in the Senate.

Sec. 13. Insulin and antibiotics.

No change.

Sec. 14. Nonprescription drugs.

No change.

Sec. 15. Information system.

No change.

Sec. 16. Environmental impact review.

The discussion draft modified this provision in order to reflect the categorical exemption provision in the Council on Environmental Quality's regulations.

Sec. 17. Application of State and Federal law to the practice of pharmacy compounding.

The discussion draft modifies this H.R. 3199 provision by including the compounding of devices, and by adding that compounding can be done by a licensed physician, that compounding must be conducted on the order of a licensed physician for an individual patient, that limited quantities can be premade under specified limited conditions to be determined by FDA in consultation with the National Association of State Boards of Pharmacy, and that advertising or promotion is prohibited except to extent that the pharmacist may advertise or otherwise promote the compounding service.

Sec. 18. Harmonization.

The discussion draft removes the requirement that FDA participate "regularly and continuously" in meetings with other countries to discuss methods and approaches to reduce the burden of regulation, harmonize regulatory requirements, and seek reciprocal arrangements. Concern had been raised that this provides would create an unnecessary drain on FDA resources.

Sec. 19. Use of scientific and medical information.

The provision defines when a manufacturer would be permitted to provide information regarding the unapproved uses of an approved drug. The type of information that would qualify for dissemination would be restricted to:

(I) recommendations of a Federal Government health agency,

(ii) recommendations of a medical speciality organization recognized by the Secretary,

(iii) reports on unapproved dosages or methods of administration for an approved drug or device,

(iv) reports of scientific research that would be sufficient for the submission of a supplemental application for a new use of an approved product under section 505 or section 515 or a notification under section 510(k) whether or not such application or such notification has been filed,

(v) reports of a clinical investigation that would be considered to be scientifically sound by experts qualified by scientific training and experience to evaluate the effectiveness of a drug or device that is the subject of such clinical investigation, and

(vi) such other information that the Secretary may recognize.

The provision further permits FDA, through regulation and after an opportunity for public comment, to require that information representing inconsistent recommendations or inconsistent reports when disseminated be accompanied by conflicting information in order to achieve a balanced presentation of information to the recipient. The conflicting information would also have to be considered scientifically sound by experts qualified to make that determination.

The provision seeks to promote the availability of information about innovative medical research on new drugs to private non-profit groups that could help provide patients access to this information. FDA would be authorized to provide technical assistance through the Food and Drug Administration, the National Institutes of Health, and the Centers for Disease Control to any not-for-profit entity recognized by the Secretary that seeks to make information widely available to the public on research and treatment conducted under the authority of section 505(I) and section 520(g). To be eligible for such technical assistance, such not-for-profit entity shall maintain registries of trials, protocols, eligibility, and experimental treatments, and the results of such research in the United States and other countries, with the consent of the sponsor, including information

concerning potential toxicities or adverse effects associated with the use or administration of such experimental treatment.

Sec. 20. Informal agency statements.

No change.

Sec. 21. Research and education; practice of medicine.

No change.

Sec. 22. Delegation of authority.

No change.

Sec. ____ Judicial review.

This provision is eliminated.

Sec. 23. Publication of notice of deviation.

H.R. 3199 prohibited FDA from releasing information to the public when investigating a concern about a product or its manufacture. The discussion draft changes this provision to permit FDA to disseminate information regarding a product that presents an imminent danger to health or gross deception to a consumer before FDA has completed an investigation on a concern regarding such product.

Sec. 24. Modern of Regulation of Biological Products.

This provision as drafted in H.R. 3199 is redrafted to modernize the regulation of biologics and add a new provision in Sec. 25 for the regulation of human tissue. The biologic provision are adapted from S.1477 that largely represent a codification of reforms in the regulation of biotechnology derived products currently underway at the FDA.

This provision, in order to strengthen and streamline the regulation of blood, requests the FDA to consult with patient advocacy groups and the regulated industry to develop the concept, as appropriate, of a single license for the regulation of blood and blood products that would cover multiple locations that fall under a single management.

Sec. 25. Requirements for Human Tissue.

This revised human tissue provision requires registration by persons that engage in human tissue recovery, processing, storage, and distribution. Initially, all human tissue is included that falls under FDA's current tissue regulation. FDA is authorized to add other human tissue for regulation when it finds that its voluntary regulation under generally accepted scientific standards is inadequate to protect the public health with respect to any particular type of human tissue or human tissue generally.

Registered persons are deemed to be authorized to conduct human tissue activities unless the FDA determines that the registered person fails to meet applicable operating standards, fails to comply with any patient registry or other retrospective patient data requirement, or presents an immediate danger of risk to public health. FDA is authorized to establish operating standards for human tissue. FDA may require a registered person to comply with the require for a patient registry or other retrospective patient data requirements if the human tissue has not been commercially available in the US for 5 years and such information is necessary to protect public health.

The provision permits the FDA to reclassify human tissue as a drug, biologic product, or device under specified conditions. Alternatively, it also permits a drug, biological product, or device to be reclassified as a human tissue. The provision grants recall authority, and other enforcement tools against prohibited acts. The provision regulates cord blood as human tissue.

Sec. 26. Access to unapproved therapies.

This section provides expanded access to unapproved therapies. For investigational products, any person may request, through a licensed health care practitioner, from the manufacturer or distributor, a product under an FDA approved investigation, for an immediately life-threatening or seriously debilitating disease or condition, and any other disease or condition designated by the FDA as appropriate for expanded access. This provision only applies if the person has no comparable or satisfactory alternative therapy, the risk to the person is not grater than the

risk from the disease or condition, and the sponsor and investigator complies with the requirements for an investigational drug or device. The manufacturer or distributor is to submit an expanded access protocol to FDA. The manufacturer or distributor may charge for an investigational product but the price may not be more than necessary to cover the cost of manufacturer and handling, and FDA must receive notice in advance of the assessment of such charge. FDA is required to inform national, State, and local medical associations and societies, voluntary health associations, and other appropriate persons about the availability of investigational drugs and devices under expanded access. This provision is identical to the provision in S.1477 as reported by the Senate Committee on Labor and Human Resources.

Sec. 27. Radiopharmaceuticals

This new provision establishes a streamlined process for regulating radiopharmaceuticals. The safety and effectiveness of radiopharmaceuticals shall be determined by weighing the probable benefit from the use of the radiopharmaceutical against any probable risk of injury or illness from such use and shall take into account the appropriate use of the radiopharmaceutical in the practice of medicine, the level of its pharmacological and toxicological activity, and the estimated absorbed radiation dose of such radiopharmaceutical. The provision permits a radiopharmaceutical used for diagnosis or monitoring, its indications may refer to manifestations of disease (such as biochemical, physiological, anatomical, or pathological processes) common to or present in one or more disease states or refer to a diagnostic procedure used in the diagnosis of one or more diseases or conditions. This provision is similar to a comparable provision in S.1477 as reported by the Senate Committee on Labor and Human Resources.

Sec. 28. Protection of Confidential Information.

H.R. 3199 restricted the release of confidential patient and donor information to when it use was needed for a public health reason. The discussion draft seeks to provide greater protection of this confidential information by making it a crime to release to the public confidential patient or donor information unless there is a critical public health reason.

Sec. 29. Funding for Medguide.

The discussion draft prohibits FDA from using appropriated funds to implement the proposed regulation "The Prescription Drug Product Medication Guide Requirements (60 Fed. Reg. 44182, August 24, 1995) or similar requirements. S. 1477 as reported by the Senate Labor and Human Resources committee has a provision that seeks to curtail Medguide with a different set of restrictions.

Sec. 30. State and Local Requirements for Drugs and Cosmetics.

This discussion draft provision prohibits a state from imposing certain regulation on drugs and cosmetics is inconsistent with FDA requirements. The provision is comparable to the provision contained in S.1477 as reported by the Senate Labor and Human Resources Committee for over-the-counter drugs. The discussion draft adds a provision to clarify that it does not preempt state tort law.

The discussion draft adds a provision to prohibit a state or local government from setting bioequivalence requirements for generic drugs different from those set by FDA.

Sec. 31. Demonstration Program Regarding Centers For Education And Research on Drugs, Devices, and Biological Products.

This provision establishes a demonstration grant program authorized to be funded at \$5 million over 2 years to encourage state-of-the-art clinical and laboratory research to evaluate effectiveness and safety of drugs, devices, or biological products.

OUTLINE OF A PROPOSAL

- **TO ASSURE THE QUALITY OF INFORMATION IS HIGH, THE NATURE OF THE INFORMATION DISSEMINATED SHOULD BE LIMITED TO RELEVANT PEER-REVIEWED DOCUMENTS, AS DEFINED BY THE SECRETARY, INCLUDING JOURNALS, TEXTBOOKS OR COMPENDIA. THE DATA DISCUSSED IN THE DOCUMENTS MUST BE SCIENTIFICALLY RELIABLE (E.G. NOT INCLUDING PRELIMINARY OR ANECDOTAL RESEARCH REPORTS).**
- **TO ASSURE BALANCE, COMPANIES SHOULD BE REQUIRED TO:**
 - ◊ Include prominent disclaimers with respect to such uses indicating that FDA has not approved these uses, along with a copy of the approved label for the product. Companies should also be required to certify that the material being disseminated is balanced.
 - ◊ Include a bibliography of alternative research (or an indication of such references accompanying the peer reviewed article).
 - ◊ Update the health care provider community with respect to any meaningful new information concerning such uses, including any FDA action that occurs with respect to such use after the dissemination occurs such as denial of a supplemental application. In the later situation dissemination would stop when the application is denied.

Balance Review

- ◊ Any such dissemination must be preceded by a notification of the proposed information dissemination to the FDA. In turn the FDA would have 30 days to consider that information, and may require that certain additional defined information be disseminated as well.

There is a presumption that such dissemination is appropriate:

- ◆ If the information relates only to the approved indication but such information discusses alternative dosage forms, routes of administration and frequency of use which are different from the approved labeling with certain exceptions.
- ◆ If the information relates to a new use for which a supplemental application has been filed, or data sufficient to lead to a supplemental approval has been collected and such application is "timely" filed.

- ◆ If the information relates to a use consistent with the recommendations of federal health agencies, including the National Institutes of Health (including the National Cancer Institute), Center for Disease Control, Agency for Health Care Policy and Research and other entities within the Public Health Service
- ◆ If the information is consistent with the practice guidelines issued by a medical specialty society, when such guidelines recommend the use of the product in a manner consistent with the proposed dissemination.

- ***To Improve Dissemination Of Information:***

- ◇ Authorize companies to provide free-of-charge access to text or electronic access to relevant third-party data bases maintained by independent third parties, including the United States Pharmacopeia/Drug Information, American Medical Association Drug Evaluation or other similar governmental or non-governmental data bases (as determined by the Secretary).
- ◇ Expansion of Sec. 2317 of PHS Act (data bank on clinical trials and treatment for AIDS) to include other diseases provided there is adequate trade secret and proprietary data protection.

- ***To Address Health Care Economic Claims:***

- ◇ FDA shall expend no funds to implement the "Draft Guidelines on Pharmacoeconomic Matters entitled ' Principles for the Review of Pharmacoeconomic Promotion (Draft)", or any other similar policy until the Agency fully complied with the rule making requirements of the Administrative Procedure Act (APA). In this instance, the FDA shall complete the above referenced rule making by the use of "negotiated rule making" actively involving the regulated industry in this process.

July 19, 1996

Elizabeth

DRY

Dissemination of Scientific Information

- ◆ Authorizes dissemination by a drug or biologics manufacturer to health care practitioners, managed care organizations and others of --
 1. written information on a treatment use of an investigational drug or biologic, and
 2. written information not included in the official labeling of an approved drug or biologic, including information on a new use, safety, effectiveness, cost or benefit.
- ◆ The information must be based on reports of clinical investigations in humans that are well designed and appropriately conducted. It must also be --
 1. a reprint of a peer-reviewed article from a scientific or medical journal, or a reference textbook;
 2. information the text of which has been approved by a CME accrediting agency as part of a scientific or medical program approved by the agency; or
 3. information recognized under Federal law for purposes of third party coverage or reimbursement, and part of a disease management program or treatment guideline.
- ◆ The information must be accompanied by a disclosure statement that includes (if applicable) a statement that the information is different from that in the approved labeling; that the information is being distributed at the

expense of the manufacturer; and the names of any authors who are employees of, or consultants to, the manufacturer. In addition, the information must be accompanied by a copy of the official labeling and an adequate bibliography of other articles about any new use covered by the disseminated information.

- ◆ If the information concerns an “off label” new use, then the manufacturer must submit it to the Secretary 30 days prior to dissemination. If FDA determines that the information “does not provide an appropriately balanced presentation” then the Secretary may require that additional information (and, where appropriate, a statement describing alternative published research findings) be included with the information being distributed. Information that describes a new use shall be presumed to be appropriately balanced if --

1. the new use is described in a recommendation of a Federal health agency, such as NIH, CDC or AHCPR;
2. the new use is consistent with medical practice guidelines of a generally recognized medical specialty society; or
3. the manufacturer has submitted a supplemental application for the new use and it has been accepted for filing.

- ◆ If concurrent or new information is published with respect to information disseminated under the new authority, the manufacturer is to notify the Secretary and if the Secretary determines that the new information

demonstrates that the drug or biologic presents a significant risk to public health, the Secretary shall require appropriate action by the manufacturer.

- ◆ HHS is required to enter into a negotiating rulemaking procedure with respect to the dissemination of pharmacoeconomic data. Until the proceedings are completed, FDA may not implement its current policy of restricting dissemination of economic data on pharmaceutical products.

Amendment to S. 1477

Insert the following after line 18, page 134:

SEC. 412. DISSEMINATION OF SCIENTIFIC INFORMATION.

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

**“SEC. 746. DISSEMINATION OF SCIENTIFIC INFORMATION ON
DRUGS AND BIOLOGICAL PRODUCTS.**

“(a) DISSEMINATION OF SCIENTIFIC INFORMATION.—

“(1) Notwithstanding sections 301(d), 502(f), and 505, and section 351 of the Public Health Service Act (42 U.S.C. 262), a manufacturer may disseminate to any person that is a health care practitioner or other provider of health care goods or services, a pharmacy benefit manager, a health maintenance organization or other managed health care organization, or a health care insurer or governmental agency, the following information:

“(A) written information concerning a treatment use for an investigational new drug or an investigational biological product; and

1 “(B) written information not included in the
2 official labeling of a drug or biological product for which
3 an approval of an application filed under section 505(b)
4 or 505(j), or a biologics license issued under section 351
5 of the Public Health Service Act, is in effect (including
6 information on a new use, safety, effectiveness, cost or
7 benefit of such product).

8 “(b) AUTHORIZED INFORMATION—A manufacturer
9 may disseminate information under paragraph (1)(B) only if --

10 “(1) the information is based on reports of one or more
11 clinical investigations in humans that are well designed and
12 appropriately conducted, and

13 “(2) the information meets at least one of the following
14 requirements:

15 “(A) the information is an unabridged —

16 “(i) reprint or copy of a peer-reviewed
17 article from a scientific or medical journal that is
18 published by an organization that is not controlled
19 by the pharmaceutical industry, or

20 “(ii) reference textbook that is published by
21 an organization that is not controlled by the
22 pharmaceutical industry;

1 “(B) the text of the information has been
2 approved by a continuing medical education accrediting
3 agency that is independent of the pharmaceutical
4 industry as part of a scientific or medical educational
5 program approved by the agency; or

6 “(C) the information is recognized under Federal
7 law for purposes of third-party coverage or reimbursement,
8 and the information is part of a disease management
9 program or treatment guideline.

10 “(c) DISCLOSURE STATEMENT ASSURING
11 BALANCE.—In order to afford a full and fair evaluation of the
12 information described in subsection (a), a manufacturer
13 disseminating the information shall include —

14 “(1) a prominently displayed statement that
15 discloses —

16 “(A) if applicable, that the new use or other
17 attribute of a drug or biological product described
18 in subparagraph (B) of subsection (i)(1) and the
19 information with respect to the new use or other
20 attribute is different from the information in the
21 official labeling;

1 “(B) if applicable, that the information is
2 being disseminated at the expense of the
3 manufacturer;

4 “(C) if applicable, the name of any authors of
5 the information being disseminated who are
6 employees of or consultants to the manufacturer;
7 and

8 “(D) the official labeling for the drug or
9 biological product, or in the case of a treatment use
10 of an investigational drug or biological product, the
11 investigator brochure and all updates thereof; and

12 “(2) an adequate bibliography of other articles from a
13 reference textbook or scientific or medical journal that have
14 been previously published about any new use covered by the
15 information disseminated (unless the information already
16 includes such bibliography).

17 “(d) INFORMATION ON NEW USES.—

18 “(1)(A) A manufacturer may disseminate
19 information under subsection (a)(1)(B) concerning the
20 new use of a drug or biological product only if the
21 manufacturer has submitted a copy of such information
22 to the Secretary 30 days prior to such dissemination.

1 “(B) If the Secretary determines that
2 information submitted under subparagraph (A) does not
3 provide an appropriately balanced presentation of
4 currently available published information of the type
5 described in subparagraphs (A), (B), or (C) of subsection
6 (b)(2), then the Secretary may, before the expiration of
7 the 30 day period described in subparagraph (A), require
8 that additional information described in such
9 subparagraphs (and, where appropriate, a statement
10 prescribed by the Secretary that describes alternative
11 published research findings based upon such additional
12 information) be included with the information being
13 disseminated. No other conditions may be imposed by
14 the Secretary.

15 “(C) The 30 day period described in clause (i) shall
16 begin on the first business day after mailing by first
17 class mail. Such period may not be extended.

18 “(2) Information that describes a new use shall be
19 presumed to be appropriately balanced for the purposes of
20 paragraph (3) if --

21 “(A) the new use is described in a recommendation of
22 a Federal health agency, including the National Institutes

1 of Health, the Agency for Health Care Policy and Research,
2 and the Centers for Disease Control of the Department of
3 Health and Human Services.

4 “(B) the new use is consistent with medical practice
5 guidelines adopted by a generally recognized, and
6 appropriate, medical specialty society; or

7 “(C) the person disseminating the information has
8 submitted to the Secretary an application for approval of
9 the new use under section 505(b), or section 351 of the
10 Public Health Service Act and such application has been
11 accepted for filing.

12 “(3) If a manufacturer has sponsored or
13 underwritten research that results in information described
14 in paragraph (1)(A), then only such manufacturer may
15 distribute the information under this section.

16 “(e) SPECIAL RULE.—If concurrent or new
17 information with respect to a use of a new drug or biological
18 product (including new information relating to safety or
19 efficacy of the new use of a drug or biological product) is
20 published with respect to any information disseminated
21 under this section, the manufacturer that disseminated the
22 information shall notify the Secretary with respect to the

1 new information. If the Secretary determines that the new
2 information demonstrates that a new drug or biological
3 product presents a significant risk to public health, the
4 Secretary shall, in consultation with the manufacturer, take
5 such appropriate action as the Secretary determines
6 necessary to ensure public health and safety.

7 “(f) DEFINITIONS. — As used in this section:

8 “(1) HEALTH CARE PRACTITIONER.—The term
9 ‘health care practitioner’ means a medical provider that is
10 licensed where applicable by state law to prescribe a drug
11 or biological product for the treatment of a disease or
12 other medical condition.

13 “(2) REFERENCE TEXTBOOK—The term ‘reference
14 textbook’ means a reference publication that the Secretary
15 determines --

16 “(A) has not been written, edited, excerpted,
17 or published specifically for, or at the request of, a
18 manufacturer of a drug or biological product;

19 “(B) has not been edited or significantly
20 influenced by a manufacturer of a drug or biological
21 product;

1 “(C) is not solely distributed through a
2 manufacturer of a drug or biological product, but is
3 generally available in bookstores or other
4 distribution channels where medical textbooks are
5 sold; and

6 “(D) does not focus on any particular drug or
7 biological product of a manufacturer that
8 disseminates information under subsection (a), and
9 does not have a primary focus on new uses of drugs
10 or biological products that are marketed or under
11 investigation by a manufacturer supporting the
12 dissemination of the information.

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

16 “(A) that is published by an organization
17 that—

18 “(i) has an editorial board and that
19 utilizes experts, who have demonstrated
20 expertise in the subject of the article under
21 review and who are not employees of the
22 organization, to review and objectively select,

1 reject, or provide comments about proposed
2 articles; and

3 “(ii) has publicly stated policy, to which
4 the organization adheres, of full disclosure of
5 any conflict of interest or biases for all
6 authors or contributors involved with the
7 journal or organization;

8 “(B) whose articles are peer-reviewed and
9 published in accordance with the regular peer-review
10 procedures of the organization;

11 “(C) that is generally recognized to be of
12 national or international scope and reputation;

13 “(D) that is indexed in the Index Medicus of
14 the National Library of Medicine of the National
15 Institutes of Health; and

16 “(E) that presents materials that are truthful
17 and not misleading.

18 “(4) NEW USE.—The term “new use” refers to the
19 conditions of use of a drug or biological product that are not
20 prescribed, recommended or suggested in the official
21 labeling of such product.

1 “(5) MANUFACTURER.—The term “manufacturer”
2 includes a person who manufactures, distributes or markets
3 a new drug or biological product.

4 “(e) This section does not prohibit a manufacturer from
5 disseminating information in response to an unsolicited request
6 from a health care practitioner.”

7 (2) (A) Until the negotiated rulemaking procedure required
8 under subparagraph (B) is completed, the Secretary of Health and
9 Human Services may not implement the Principles for the Review
10 of Pharmaceutical Economic Promotion, dated March 20, 1995 and
11 developed by the Food and Drug Administration or otherwise
12 restrict the dissemination by manufacturers of new drug and
13 biological products to physicians, managed care organizations or
14 other health providers of comparative economic information on
15 such products, including the results of cost studies about
16 prescription drug usage.

17 (B) Not later than 120 days following enactment of
18 the Food and Drug Administration Performance and
19 Accountability Act of 1996, the Secretary shall initiate negotiated
20 rulemaking proceedings under Subchapter III of Chapter 5 of the
21 Title V, United States Code, on the matters described in

- 1 subparagraph (A), whether or not such subchapter is in effect on
- 2 the date in which such proceedings are initiated.

CBO Estimate

EXECUTIVE OFFICE OF THE PRESIDENT

03-Jul-1996 08:38am

TO: John F. Morrall, III
TO: Daniel J. Chenok
TO: Sally Katzen
TO: Michael A. Fitzpatrick
TO: Lisa M. Jones

FROM: Paul Bugg
Office of Mgmt and Budget, OIRA

SUBJECT: CBO ESTIMATES BUDGETARY IMPACT OF REFORM BILL AT \$555 MILLION

CBO ESTIMATES BUDGETARY IMPACT OF REFORM BILL AT \$555 MILLION

Implementing the Food and Drug Administration reform measure reported out by the Senate Labor and Human Resources Committee (S 1477) would cost the federal government \$555 million over six years, according to Congressional Budget Office estimates.

The costs primarily would come as the result of ``the increased workload given to the FDA,`` CBO Director June E. O'Neill said in a July 1 letter to Sen. Nancy L. Kassebaum (R-Kan), Labor Committee chairwoman and chief sponsor of the bill.

The Labor Committee released its report on S 1477 June 20 without CBO estimates so the bill could be placed on the Senate calendar for debate. Senate Majority Leader Trent Lott (R-Miss) has indicated that the leadership is looking for a ``window`` of time to consider the bill, which could come after the week of July 15.

The bill is intended to streamline FDA's processes to expedite the availability of safe, effective new products while maintaining FDA's acknowledged role in protecting public health. A major complaint about agency performance has focused on FDA's failure to meet statutory deadlines for product review.

S 1477 responds to this concern with a provision triggering third-party review to help FDA meet statutory deadlines. Under the bill, if FDA failed to meet 95 percent of statutory deadlines within a product category in a given year, the secretary of health and human services would be required to contract with outside organizations to meet the deadlines. Moreover, FDA would have to act on recommendations by third-party reviewers within 60 days.

CBO noted that, with the exception of drugs approved under the Prescription Drug User Fee Act, FDA already has a backlog of products for review that are past their statutory deadlines. In addition, because of the enforced deadlines, the number of product applications may increase. According to CBO, ``the additional personnel and resources necessary to meet the proposed deadlines would exceed any savings realized through regulatory relief offered by S 1477. These provisions are estimated to cost the federal government \$430 million over six years.``

Furthermore, contracting with outside organizations would not save money, CBO said, because third-party reviewers would have to match FDA standards and quantity of work, which would require an equal level of resources.

Costs, Savings Estimated

Other provisions of S 1477 that CBO found had cost implications include:

- o A tracking system for product applications. Under the bill, FDA would set up a system to report on the progress of product applications, develop performance standards, and hold regular meetings with product sponsors. CBO estimated this provision would require additional staff at an increased cost of \$83 million over six years.
- o Radiopharmaceuticals. Beside setting up a new office for radiopharmaceuticals with the Center for Drug Evaluation and Research, and a separate scientific review group to handle product submissions, S 1477 sets deadlines for issuance of a final rule on regulation and approval of radiopharmaceuticals. The estimated cost would be \$7 million over six years.
- o Clinical pharmacology. S 1477 would reauthorize a pilot program in clinical pharmacology for fiscal 1997 through 1998 at the \$4 million level. In addition, the bill would provide \$51 million to establish a consortium for education and research on drug, device, and biologics, and a committee to oversee the consortium's activities, for fiscal years 1997 through 2000.

Some Cost Savings

According to the CBO estimates, several provisions in S 1477 would result in cost savings:

- o Waiving the premarket notification requirement for certain Class I and Class II medical devices (\$1 million in savings over six years);
- o Waiving a requirement that manufacturers must obtain an exemption from FDA to make minor changes to an investigational device file when the changes would not affect safety or efficacy (\$11 million in savings);
- o Allowing an advisory committee, at a sponsor's request, to recommend that FDA reconsider classifying a Class III device, the category of devices subject to the most rigorous level of review (\$7 million in savings); and
- o Repealing environmental impact reviews for products unless FDA determines that a particular product would have a ``sufficiently substantial'' impact to warrant such review (\$1 million in 1997).

Communications

EXECUTIVE OFFICE OF THE PRESIDENT

02-Jul-1996 06:51pm

TO: (See Below)

FROM: Daniel J. Chenok
Office of Mgmt and Budget, OIRA

SUBJECT: Consumer/Senior Citizen Coalition Hits Senate FDA Propos

GOVERNMENT OPERATIONS

Consumer/Senior Citizen Coalition Hits Senate FDA Proposal

A coalition of consumer, patient and senior citizen advocacy groups today joined former Sen. Howard Metzenbaum, D-Ohio, to denounce Senate FDA reform legislation. "The FDA has done and continues to do a very good job in protecting the efficacy of the system we have in place," Metzenbaum said, declaring the bill "would repeal the protections that are currently being provided." The Senate Labor and Human Resources Committee approved FDA reform legislation offered by Chairwoman Kassebaum, and it is expected to go to the floor at the end of July.

The groups -- calling themselves the Patients' Coalition -- argued the bill would limit the FDA's flexibility to prioritize certain drugs over others in the review process. The coalition also contended the legislation would encourage the United States to accept lower European standards for drug safety and effectiveness, thereby creating incentives for pharmaceutical companies to conduct research and testing overseas. Gary Rose, treatment and research representative at AIDS Action, said committee sources have told him Kassebaum is preparing to offer a "massive" manager's amendment -- but noted that if the changes meet the demands of his coalition, Kassebaum "is going to lose all support" from conservative Republicans.

Meanwhile, the House Commerce Committee is planning this month to take up the more extensive House version of FDA reform, sources said. The committee's FDA reform team probably will release revisions to the legislation prior to a markup, the sources added. Among the most controversial provisions in the legislation is a plan to privatize part of the approval process for new drugs and medical devices. Under the legislation, applicants for approval of new products could opt for testing of the products by private third-party organizations.

The Congress Daily --- Tuesday --- July 2, 1996

Distribution:

TO: Sally Katzen

hch 1800 Sky page
216-9191

Outline of Off-label amendment as of 7/22/96

1. A manufacturer may disseminate written information to health care practitioners or other providers of health care goods or services, pharmacy benefit managers, health maintenance organization or other managed care organizations or health care insurer or governmental agency. This information may concern the safety, effectiveness, cost, benefit, use, or comparison to other therapies of an already approved drug, biologic or device. The focus of this information may be about an unapproved use, dose, etc. of this approved drug, biologic or device.

2. The information disseminated must be of the following type:

a. peer-reviewed articles from scientific or medical journal reports of a clinical investigation that would be considered to be scientifically sound by experts qualified by scientific training or experience to evaluate the safety or effectiveness of a drug, biologic or device that is the subject of such clinical investigation.)

b. a reference text that is published independently of the manufacturer.
(Definition of referenced text defined later in the bill)

3. A manufacturer may disseminate this information only if the manufacturer has submitted a copy of the information to the Secretary 30 calander days prior to such dissemination. During this time,

a. if the Secretary determines that the information does not provide appropriate balance, then the Secretary, before the expiration of the 30 days, may require that additional information of the quality described under above 2 or, where appropriate, a statement that describes alternative research findings based upon such additional information be included with the disseminated information.

4. If concurrent or new information of the quality described in 2 with respect to the use addressed in the disseminated information is published, the manufacturer must notify the Secretary with respect to this new information. If the Secretary determines that the information demonstrates that the new use has a risk to public health or is not efficacious, the Secretary in consultation with the manufacturer will take appropriate action.

5. If the manufacturer sponsored the research contained in the disseminated information, then they would be the only ones allowed to disseminate this information.

6. Disclosure statement. The following must accompany the disseminated information and be prominently displayed:

- a. a statement that this article is about a use not approved by the FDA
- b. that the information is being disseminated at the expense of the manufacturer
- c. the names of any of the authors that are employees or consultants for the manufacturer
- d. a copy of the official label
- e. a bibliography of other articles from referenced texts or medical or scientific journals about the new use if appropriate bibliography is not contained in the article being disseminated
- [f. a statement concerning the sponsorship of the research- This is not in the version now in leg council but will be added]

7. Definitions:

- a. health care practitioner: medical provider licensed to prescribe
- b. referenced textbook: referenced publication that
 - 1. has not been written, edited, excerpted or published specifically for, or at the request of a manufacturer
 - 2. has not been edited or significantly influenced by a manufacturer
 - 3. is not solely distributed through a manufacturer but is available generally in a bookstore or other distribution channel where medical texts are generally sold
 - 4. does not focus on any particular drug, biologic or device or does not focus on the new use
- c. scientific or medical journal: one that is published by an organization that
 - 1. has an editorial board and utilizes experts, who have demonstrated expertise in the subject of the article. These experts must be independent of the journal.
 - 2. has a publicly stated policy, to which the organization adheres, of full disclosure of any conflict of interests or biases for all authors or contributors

07/23/96 TUE 09:50 FAX

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3. whose articles are peer-reviewed
4. that is generally recognized to be of national scope and reputation
5. that is indexed in the Index Medicus
6. that presents materials that are truthful and not misleading

d. new use: use not in the official label

e. manufacturer: person who manufactures, distributes or markets a new drug, biologic or device.

6. This amendment does not interfere with the current ability of the manufacturer to provide information in response to an unsolicited request from the health care practitioner.

7. The Secretary does not have authority in terms of cost and effects of drugs, biologics or devices in terms of price, cost effectiveness or quality of life.

E X E C U T I V E O F F I C E O F T H E P R E S I D E N T

22-May-1996 04:19pm

TO: Elizabeth E. Drye
TO: Michael A. Fitzpatrick

FROM: Robert J. Pellicci
 Office of Mgmt and Budget, LRD

CC: Jim R. Esquea
CC: Jonathan Winer
CC: Janet R. Forsgren

SUBJECT: Revised Justice Department language on dietary supplements

As I noted to you yesterday, Justice has crafted revised language for the Senate bill regarding treatment of certain dietary supplements. The following represents that new language (this would be a complete substitute for the Senate draft bill):

Section 201(g) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(g)(1)) is amended by adding at the end thereof the following new sentence:

"Notwithstanding the preceding sentence, a dietary supplement shall be considered a drug under clause (C) if the dietary supplement is intended to produce euphoria, heightened awareness, or similar mental, psychological, or stimulant, depressant, or hallucinogenic effects similar to those of a controlled substance (21 U.S.C. 802(6)), or if the dietary supplement poses a significant potential for harmful effect.".

I am also going to forward the above language to HHS/FDA for their review. Let me know how you want to proceed. Thanks.

E X E C U T I V E O F F I C E O F T H E P R E S I D E N T

23-May-1996 03:50pm

TO: Elizabeth E. Drye
TO: Michael A. Fitzpatrick

FROM: Robert J. Pellicci
 Office of Mgmt and Budget, LRD

SUBJECT: More on the dietary supplement language

Spoke to staff in HHS' office of the General Counsel who say that the D'Amato/Dodd language and Justice's revised language are basically identical except for one very critical difference. HHS strongly believes that the Justice language, by adding the phrase "or if the dietary supplement poses a significant potential for harmful effect" will cause a political "firestorm".

According to HHS, the D'Amato/Dodd bill is narrowly drafted to address the problems with certain herbal products that is making the news. On the other hand, Justice's language would undo the Dietary Supplement Health and Education Act of 1994 that the President signed on 10/25/94. That law prohibits FDA from regulating dietary supplements as food additives and limits the circumstances under which FDA could regulate these products as drugs. For example, under current law, dietary supplements can be marketed until FDA could affirmatively demonstrate that the product is unsafe. There is no requirement for safety data prior to marketing.

All this is to say that HHS prefers D'Amato/Dodd to the Justice language.



B A C K G R O U N D E R

U.S. FOOD & DRUG ADMINISTRATION

FDA: A Record Of Accomplishment

Faster Drug Approvals

- 82 new drugs approved in **16.5 months** (median) in Calendar Year (CY)1995, compared with 62 new drugs approved in **19 months** in 1994
- 28 of the 1995 approvals were new molecular entities (NMEs)—brand new drugs as opposed to new formulations—and were approved in **15.9 months** (median), compared with 22 NMEs approved in **17.5 months** in 1994
- 15 of the 1995 approvals were “priority” drugs—having important therapeutic value—and were approved in **6 months** (median), compared with 17 “priority” drugs approved in **15 months** in 1994
- 13 of the 1995 “priority” approvals were user fee drugs approved in **5.9 months** (median), compared with 12 “priority” user fee drugs approved in **10.4 months** in 1994

Improved Device Reviews

- 5,594 510(k)s (which account for about 98% of medical devices) reviewed by FDA in **138 days** (mean) in Fiscal Year (FY) 1995, compared with 5,498 in **182 days** in FY 1994
- 27 PMAs (premarket applications for certain Class III devices) reviewed by FDA in **20.2 months** (mean) in FY 1995, compared with 26 PMAs in **21.6 months** in FY 1994

The Record on Reinvention

As part of Vice President Gore’s National Performance Review, the FDA has announced more than 30 FDA regulatory reinvention initiatives since March 1995. These initiatives will reduce regulatory burdens and streamline the regulatory process, while maintaining vital public health safeguards and speeding the marketing of safe and effective new drugs and medical devices. Following is a partial listing of these initiatives:

- Speed up approval process for cancer drugs by using tumor shrinkage as surrogate marker for accelerated approval decisions
Impact: Cut years off development times and months off FDA review

- Expand patient access to experimental cancer drugs approved in other countries
Impact: Make it easier for patients to have access to promising but still experimental therapies
- Increase patient representation on cancer drug advisory committees
Impact: Give patients more of a voice in the drug review process
- Clarify requirements for doctors studying already approved cancer drugs
Impact: Reduce paperwork for doctors and free FDA staff for other priorities
- Eliminate Establishment License Application (ELA) for most biotech drugs
Impact: Reduce paperwork burden for industry and speed up marketing of biotech drugs
- Eliminate lot release requirement for biotech drugs
Impact: Save time and resources of industry and FDA
- Commit FDA to respond to clinical hold submissions on drugs, including biotech drugs, within 30 days
Impact: Speed up drug development
- Harmonize application forms for drugs and biologics
Impact: Improve quality of submissions and reduce paperwork for industry and FDA
- Eliminate preapproval requirement for promotional labeling for biotech drugs
Impact: Speed up marketing of products and free FDA staff for other priorities
- Allow companies to distribute certain textbooks and journal articles that discuss unapproved uses of drugs and devices
Impact: Increase access to important scientific information without threatening effectiveness standard
- Allow companies to submit toxicology findings based on first analysis of studies and reduce manufacturing data needed to begin drug tests in humans
Impact: Speed up drug development
- Develop pilot program for review of low- to moderate-risk medical devices by outside organizations
Impact: Determine if outside review speeds up process and if integrity of review process can be maintained while allowing FDA to focus resources on higher risk-devices
- Collect user fees for medical device reviews
Impact: Speed up device reviews using program similar to one already achieving success for drug reviews
- Expand opportunities for export of unapproved drugs and medical devices to industrialized countries
Impact: Widen industry markets for products and encourage American companies to keep operations in United States

- Exempt up to 125 categories of low-risk medical devices from premarket review, adding to 441 categories already exempted
Impact: Speed up marketing of medical devices and free FDA staff for other priorities
- Allow manufacturers of biological drugs to get licenses for pilot facilities instead of having to build full-scale manufacturing plants
Impact: Reduce manufacturers' start-up costs and speed up marketing of drugs
- Exclude drug and biologics manufacturers from requirements for most environmental assessments
Impact: Reduce industry costs in preparing assessments FDA has found unnecessary

The International Record

- The General Accounting Office reported in October 1995 that **approval times for NMEs were shorter in the United States than in the United Kingdom.**
 - in FY 1994, 32 NMEs were approved in the United Kingdom in a median time of 30 months
 - in CY 1994, 22 NMEs were approved in the United States in a median time of 18 months
- FDA's median approval time for new drugs approved in CY 1994 and 1995 was **as fast as** that in the United Kingdom and **faster than** those in France, Spain, Germany, Australia, Japan, Italy and Canada according to preliminary data from the Centre for Medicines Research (CMR), an industry-funded, not-for-profit research group in the United Kingdom. The median review time in the United States and the United Kingdom was approximately 1.3 years according to *CMR News*, Spring 1996.
- The United States has had **more first launches** of worldwide NMEs than any single European country since 1990. In fact, analysis of worldwide NMEs launched in the United States and Europe showed the United States has had a higher percentage of first launches than the top three European countries combined, according to *CMR News*, Spring 1996.
 - United States: 33%
 - United Kingdom: 14%
 - France: 9%
 - Germany: 7%

— Outline —

- Not trying to a supplemental —
- FDA Review for balance
- force attachments
- may be willing

Coats/others view deadlines as a commitment

- third party review — mkt. w/ Admin

Jane Wilkins said they are not on the schedule in the next 10 weeks —

E X E C U T I V E O F F I C E O F T H E P R E S I D E N T

19-Jul-1996 07:20pm

TO: Carol H. Rasco

FROM: Jeffrey Levi
AIDS Policy Council

CC: Patsy Fleming
CC: Jeremy D. Benami
CC: Elizabeth E. Drye

SUBJECT: Two things

(1) Jeremy mentioned your interest in activities around the quilt in October. There will be millions of things going on -- when it gets closer we will compile a list and make some recommendations.

If you would like to read names at the quilt display -- this can be arranged -- for you and other DPC staff (or other WH officials as well) -- let us know and we will speak to the Names Project people. If there are specific names you would like to read, I believe that can be arranged also.

(2) The Vice President is meeting on August 2nd with the Keystone Dialogue group working on AIDS clinical effectiveness research -- this is the public-private collaboration the VP asked for at the February meeting with the drug companies. The result is a recommendation for an on-going pilot project among government, researchers, industry, patients, and third party payors to become something of a "bully pulpit" for identifying key research questions that are not being answered. The federal government will be asked to kick in some money (about \$350,000) for the 18-month pilot project. It is actually a very positive outcome--it is the most positive interaction between industry and the rest of the AIDS community that I have seen in all my years in this business.

Is this something you want to attend or in some other way be involved with?

E X E C U T I V E O F F I C E O F T H E P R E S I D E N T

19-Jul-1996 09:12am

TO: Mark E. Miller

FROM: Farooq A. Khan
Office of Mgmt and Budget, HD

CC: Jim R. Esquea
CC: Richard J. Turman

SUBJECT: KENNEDY, PRYOR SAY PENDING REFORM BILLS COULD COMPROMISE PUB

KENNEDY, PRYOR SAY PENDING REFORM BILLS COULD COMPROMISE PUBLIC HEALTH, Sen. Edward Kennedy (D-Mass) and Sen. David Pryor (D-Ark) July 18 said Congress should kill pending Food and Drug Administration reform legislation because ultimately the measures would cripple the agency. Introduced by Senate Labor and Human Resources Committee Chairwoman Nancy Kassebaum (R-Kan), the FDA Performance and Accountability Act of 1996 (S 1477) drastically would reduce the ability of the FDA to ensure the safety and effectiveness of drugs and medical devices, said consumer advocacy organization Public Citizen. Kennedy's firm stance against S 1477 made him one of four Congressional members to vote against the rollback bill when it was approved by the Senate Labor and Human Resources Committee in March, noted a Public Citizen release. The House Commerce Committee is considering three separate reform bills--HR 3199, HR 3200, and HR 3201. Like S 1477, these pieces of pending legislation would weaken federal protection of drug, medical devices, and food supplies, Public Citizen charged. While acknowledging the pharmaceutical and medical device industries have made countless medical miracles from laboratory to bedside, Kennedy also noted these industries do make mistakes. During a panel discussion sponsored by Public Citizen, Kennedy, the ranking minority member of the Labor and Human Resources Committee, charged drug and device industries of sometimes placing private profit above public health. ``If product liability claims are pre-empted by the FDA rollback legislation, then an injured consumer could not receive any compensation for damages,'' said a Public Citizen statement echoing Kennedy's views. Campaign Contributions In a statement released by his office, Kennedy added that it is no accident that FDA-regulated companies have made almost \$900,000 in campaign contributions to sponsors of FDA reform bills and hundreds of thousands of more dollars in soft money have flowed from the industry to Republican Party committees. ``Public health is not negotiable. The FDA is not for sale to the highest bidder, and neither is Congress,'' said Kennedy before a six-member panel of women who survived medical device defects and unsafe drugs. ``No

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"SEC. 505A. PEDIATRIC STUDIES FOR NEW DRUG APPLICATIONS.

"(a) MARKET EXCLUSIVITY FOR APPROVED APPLICATIONS WITH PEDIATRIC STUDIES SUBMITTED BY AN APPLICANT.—If an application submitted under section 505(b)(1) is approved on or after the date of enactment of this section, and such application includes reports of pediatric studies described and requested in subsection (c), and such studies are completed and the reports thereof submitted in accordance with subsection (c)(2) or completed and the reports thereof accepted in accordance with subsection (c)(3), the Secretary may not make the approval of an application submitted under section 505(b)(2) or 505(j) that refers to the drug for which the section 505(b)(1) approval is granted effective prior to the expiration of ~~6 months~~ ^{the period of time determined to be appropriate pursuant to subsection (d)} from the earliest date in which the approval of such application for the drug under section 505(b)(2) or 505(j), respectively, could otherwise be made effective under the applicable provisions of this chapter.

"(b) MARKET EXCLUSIVITY FOR APPROVED APPLICATIONS WITH PEDIATRIC STUDIES REQUESTED BY THE SECRETARY.—If the Secretary makes a written request for pediatric studies described in subsection (c) to the holder of an approval under section 505(b)(1) for a drug, and such studies are completed and the reports thereof submitted in accordance with subsection (c)(2) or com-

505(j) designated application for a new drug.

based on a finding that such studies will significantly benefit children.

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1 pleted and the reports thereof accepted in accordance with
2 subsection (c)(3), the Secretary may not make the ap-
3 proval of an application submitted under section 505(b)(2)
4 or 505(j) that refers to the drug subject to the section
5 505(b)(1) approval effective prior to the expiration of ~~6-~~
6 ^{the period of time determined to be appropriate pursuant to subsection (d)}
7 ~~months~~ from the earliest date on which an approval of
8 such application under section 505(b)(2) or 505(j), respec-
9 tively, could otherwise be made effective under the applica-
10 ble provisions of this chapter. Nothing in this subsection
11 shall affect the ability of the Secretary to make effective
12 a section 505(b)(2) or 505(j) approval for a subject drug
13 if such approval is proper under such subsection and is
14 made effective prior to the submission of the reports of
15 pediatric studies described in subsection (c).

15 "(c) CONDUCT OF PEDIATRIC STUDIES.—

16 "(1) AGREEMENT FOR STUDIES.—The Sec-
17 retary may, pursuant to a written request for stud-
18 ies after consultation with the sponsor of an applica-
19 tion or holder of an approval for a drug under sec-
20 tion 505(b)(1), agree with the sponsor or holder for
21 the conduct of pediatric studies for such drug.

22 "(2) WRITTEN PROTOCOLS TO MEET THE
23 STUDIES REQUIREMENT.—If the sponsor or holder
24 and the Secretary agree upon written protocols for
25 such studies, the studies requirement of subsection

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1 (a) or (b) is satisfied upon the completion of the
2 studies in accordance with the protocols and the sub-
3 mission of the reports thereof to the Secretary. Not
4 later than 60 days after the submission of the report
5 of the studies, the Secretary shall determine if such
6 studies were or were not conducted in accordance
7 with the written protocols and reported in accord-
8 ance with the requirements of the Secretary for fil-
9 ing and so notify the sponsor or holder.

10 "(3) OTHER METHODS TO MEET THE STUDIES
11 REQUIREMENT.—If the sponsor or holder and the
12 Secretary have not agreed in writing on the proto-
13 cols for the studies, the studies requirement of sub-
14 section (a) or (b) is satisfied when such studies have
15 been completed and the reports accepted by the Sec-
16 retary. Not later than 90 days after the submission
17 of the reports of the studies, the Secretary shall ac-
18 cept or reject such reports and so notify the sponsor
19 or holder. The Secretary's only responsibility in ac-
20 cepting or rejecting the reports shall be to deter-
21 mine, within 90 days, that the studies fairly respond
22 to the written request, ^{under subsection (b)} that such studies have been
23 conducted in accordance with commonly accepted
24 scientific principles and protocols, and that such

1 studies have been reported in accordance with the
2 requirements of the Secretary for filing.

3 ^e
4 ~~“(d)~~ DELAY OF EFFECTIVE DATE FOR CERTAIN AP-
5 PPLICATIONS; PERIOD OF MARKET EXCLUSIVITY.—If the
6 Secretary determines that an approval of an application
7 under section 505(b)(2) or 505(j) for a drug may be made
8 effective after submission of reports of pediatric studies
9 under this section but before the Secretary has determined
10 whether the requirements of subsection (e) have been sat-
11 isfied, the Secretary may delay the effective date of any
12 approval under section 505(b)(2) or 505(j), respectively,
13 until the determination under subsection (e) is made, but
14 such delay shall not exceed 90 days. In the event that the
15 requirements of this section are satisfied, the ^{exclusivity} 6-month pe-
16 riod referred to in subsection (a) or (b) shall be deemed
17 to have begun on the date an approval of an application
18 under section 505(b)(2) or 505(j), respectively, would have
19 been permitted absent action under this subsection.

20 ^f
21 ~~“(f)~~ NOTICE OF DETERMINATIONS ON STUDIES RE-
22 QUIREMENT.—The Secretary shall publish notice of any
23 determination that the requirements of subsection (e) (2)
24 or (3) have been met and that approvals under section
25 (505)(b)(2) or (j) for a drug will be subject to deferred
26 effective dates under this section.

(d) Period of Market Exclusivity — When the sponsor or holder submits reports of pediatric studies in accordance with subsections (a) or (b), the sponsor or holder shall submit a request for a period of market exclusivity, not to exceed 6 months. The sponsor or holder must demonstrate that the value of such period is not disproportionate to the cost of conducting the pediatric studies. The secretary shall grant a period of marketing exclusivity that is proportionate to the cost of conducting such studies.

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1 ^g“(g) DEFINITIONS.—As used in this section, the term
2 ‘pediatric studies’ or ‘studies’ means at least 1 human
3 clinical investigation in a population of adolescent age or
4 younger. At the Secretary’s discretion, pharmacokinetic
5 studies may be considered as clinical investigations.”.

6 **SEC. 412. NOTIFICATIONS FOR DEVICE MARKET CLEAR-**
7 **ANCE.**

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

11 **TITLE V—FOOD AND DRUG**
12 **EXPORT REFORM**

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

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

16 **SEC. 502. EXPORT OF DRUGS AND DEVICES.**

17 (a) EXPORT AND IMPORTS.—Section 801 (21 U.S.C.
18 381) is amended—

19 (1) in subsection (d), by adding at the end
20 thereof the following new paragraphs:

21 “(3) No component, part, or accessory of a drug, bio-
22 logical product, or device, including a drug in bulk inform,
23 shall be excluded from importation into the United States
24 under subsection (a) if—

EXECUTIVE OFFICE OF THE PRESIDENT

07-Jun-1996 11:31am

TO: (See Below)

FROM: Jim R. Esquea
Office of Mgmt and Budget, HD

SUBJECT: REP. CONDIT SEEKS TO EXPEDITE DELANEY CLAUSE REPEAL IN HOUSE

REP. CONDIT SEEKS TO EXPEDITE DELANEY CLAUSE REPEAL IN HOUSE

Rep. Gary Condit (D-Calif) is attempting to have a food safety bill discharged from the House Commerce Committee so it can be considered on the House floor, an aide to the congressman told BNA June 6. The bill (HR 1627) is the proposed ``Food Quality Protection Act,'' which would make changes to two federal statutes governing use of and registration of pesticides. The portion of the bill currently in the Commerce Committee would revise the Federal Food, Drug, and Cosmetic Act by repealing the Delaney Clause, a 1958 provision found under Section 409 of the law. Provisions of the bill that would revise the Federal Insecticide, Fungicide, and Rodenticide Act -- the law governing the registration of pesticides -- are under the jurisdiction of the House Agriculture Committee. The Delaney Clause, a 1958 provision found under Section 409 of the Federal Food, Drug, and Cosmetic Act, prohibits the government from setting pesticide residue tolerances -- maximum residue limits -- for processed foods if the pesticides in question are linked to cancer, no matter how negligible the risk. There is no such zero risk provision governing raw food tolerances. HR 1627 would replace the zero-risk standard of Delaney with a negligible risk food safety standard for pesticide residues in processed and raw foods. Condit is one of the more than 240 co-sponsors of HR 1627. The bill is supported by industry groups including pesticide manufacturers, food processors, and growers. The Clinton administration and environmental groups have testified in opposition to the bill. On May 29, Condit and 20 other House members introduced a House Resolution, or rule, to provide for consideration on the floor of HR 1627. Under the proposed resolution (HRes 443), which is open, all amendments that are printed in the Congressional Record are made in order and general debate is set for two hours, according to a press release for Condit. To allow sufficient time for debate, the rule would allow a total of 10 hours for consideration of amendments. In addition, the rule would provide for one motion to recommit with or without instructions. Petition Possible June 10 Or 11 ``It is my sincere hope that the committees of jurisdiction will report out HR 1627, and the Rules Committee will vote out a rule that will allow for the House to consider this legislation,'' Condit said in the news release. ``Should these events not occur, we intend to file a discharge petition at the first possible date,'' Condit added. The aide to Condit told BNA June 6 that

the first possible date for filing a discharge petition is June 10 or 11, depending on the legislative calendar.

The FIFRA revisions of the bill would strengthen the Environmental Protection Agency's ability to remove dangerous pesticides from the market, according to Condit, who also said the bill would provide ``regulatory relief for minor use pesticides by streamlining the regulatory procedures for pesticides used in the production of smaller acreage crops, such as fruits and vegetables.''

Condit noted that the bill was introduced in May 1995, and that the FIFRA provisions of HR 1627 were ``essentially completed' by the House Agriculture Committee in June 1995. The agriculture panel may revisit the bill to consider new pesticide fee language, however.

While the Agriculture Committee moved forward quickly on HR 1627, Condit asserted that the Commerce panel ``has done little to move the legislation forward. HR 1627 is not new legislation, during the 103rd Congress this same bill had 225 co-sponsors yet it suffered the same fate this legislation may find.''

Rep. Thomas Bliley (R-Va), the chairman of the House Commerce Committee, is also a co-sponsor of the bill.

A spokesman for the Commerce Committee told BNA June 6 that Bliley is as eager as Condit to have food safety legislation passed. Bliley ``is second to none in wanting [the Delaney Clause] updated,' the spokesman said, noting that Bliley has co-sponsored HR 1627's predecessors in previous Congresses. The committee currently is working on bipartisan discussions on the bill, and a ``bipartisan package' is hoped for by the end of the month, the spokesman said.

Proposed Food Use Revocations

In February 1995, a federal judge approved a consent decree in a lawsuit that set out a schedule for EPA to consider whether dozens of processed food tolerances and raw food tolerances violate, or lead to violations of, the Delaney Clause (California v. EPA, DC ECalif, 89-0752, consent decree approved 2/7/95).

In March, EPA announced revocations for tolerances of five pesticides in 13 processed foods, but some of the revocations were stayed in May pending review of petitions to the agency. Revocations of nine raw food tolerances were proposed March 1 (61 FR 8173). Tolerances proposed for revocation include dicofol on apples, grapes, and plums; mancozeb on oats and wheat; propargite on apples and figs; simazine on sugarcane; and triadimefon on wheat.

At the time of the proposed raw food revocations, EPA said it was proposing revocations ``because it is otherwise impossible to guarantee that processed foods will be in compliance with the Delaney Clause.''

In his press release, Condit said, ``We cannot wait any longer for this legislation,' adding that the effects of the revocations under Delaney would be ``staggering' in California alone. The economic impact for apples, citrus, grapes, and plums would be over \$100 million annually, Condit asserted.

International Economics

Distribution:

TO: Nancy-Ann E. Min
TO: Barry T. Clendenin
TO: Richard J. Turman
TO: Gordon P. Agress
TO: Jonathan Winer

SERIOUS CONCERNS

1. Prompt and Efficient Review -- Shortened Review Times with Statutory Hammers

Bill Provision: Section 404 requires FDA to contract for outside review if FDA fails in any fiscal year to meet the statutory timeframe for 95 percent of the applications in a particular category. This provision applies to drug, biologic, device, and food additive reviews. Failure to meet the deadline for even one application could trigger the contracting out requirement. The provision also potentially eliminates FDA's ability to set priorities.

Also, the bill imposes many new requirements on FDA (e.g., the agency must meet with sponsors at defined periods and before such meetings provide the sponsor written information regarding application deficiencies and steps toward approval -- see sections 404 and 707). These requirements taken together would have the effect of further shortening the time frames by requiring FDA to complete its review of the application prior to the meetings.

FDA Concern: The bill sets shortened timeframes for the review of products without considering resources, apparently overlooking FDA's inability to meet currently-required timeframes. For example, it shortens the review times agreed to and funded under the Prescription Drug User Fee Act of 1992. Alternatively, if the agency rushes a decision to avoid the contracting out hammer, it may have to choose between having more disapprovals and compromising the safety and efficacy by approving products without a thorough review. If the contracting out is triggered, the agency will have to reduce its workforce to pay for it.

Prop. Position: Oppose the use of statutory hammers to force contracting-out of product review.

Oppose S.1477's shortened review times, and state support for an approach that would allow FDA to set priorities and would provide adequate resources (i.e. like PDUFA).

Oppose the bill's prescriptive requirement regarding FDA-applicant meetings. A possible compromise would be to require one pre-submission FDA-applicant meeting, one post-submission meeting, and consultation throughout the application's review.

2. Effective Medication Guides

Bill Provision: Section 607 (an amendment agreed to by the Committee) precludes FDA from implementing its proposed MedGuide program. The MedGuide program would ensure that patients receive useful written information when they get a new prescription (including information about how to take the drug, side-effects, and

dangerous interactions with foods or other drugs). The provision prohibits FDA from even providing guidance on the development of the voluntary program.

FDA Concern: The MedGuide proposal would defer a mandatory program until the year 2000 or 2006 to give the industry time to implement the voluntary program. It only requires that a small number of drugs which pose a serious and significant public health concern be immediately required to prepare FDA-approved prescription drug labeling. The proposal sets goals for distributing useful information for the rest, specifying that the hammer does not fall if these goals are met. The private sector is already approaching the fulfillment of the first of two performance standards.

Prop. Position: Oppose the bill provision.

3. Accredited Party Participation (Medical Device Review Pilot Program)

Bill Provision: Section 709 (an amendment adopted by the Committee) would require FDA, within one year, to certify third-party review of any device marketing application, at the request of the applicants. It would allow medical device companies to pay private companies to review applications to market devices.

FDA Concern: The provision leaves no discretion to the agency to retain review for class III devices, permitting third-party review of devices ranging from heart valves to products used to test the blood supply. It allows the party whose product FDA is reviewing to choose and directly compensate the third-party reviewer.

Prop. Position: To be discussed.

4. Health Claims of Food Products

Bill Provision: Section 903 (an amendment adopted by the Committee) would permit companies to include in the labeling of food products statements recommended by NIH, CDC, or the National Academy of Sciences (or any other Federal agency).

FDA Concern: Under the bill, there would be no single body to make decisions on health claims, resulting in potentially inconsistent decisions by different organizations using different standards.

Prop. Position: Oppose the bill provision, while supporting a streamlined FDA review process (e.g., make it a non-regulatory process) and maintaining current standard for food label claims.

5. Product Approval Standards

Bill Provision: Section 602, the **new drug approval standard**, states that substantial evidence may consist of data from one well-controlled clinical investigation and confirmatory evidence. This may lower the effectiveness requirement from two adequate and well-controlled studies to one.

FDA Concern: The provision may lower the effectiveness requirement

Prop. Position: To be discussed. However, FDA's proposed compromise position includes minor changes to the provision that would (1) add the phrase "adequate and" before the term "well-controlled" (to make the term consistent with its prior use in the statute) and (2) add the phrase "if appropriate" to ensure that while FDA may accept one trial, one trial is not the presumption.

exceptions - 1st big entry across centers - drug imp. get 2nd study later

Bill Provision: Section 703, the **medical device approval standard**, would require the agency to accept retrospective or historical clinical data as a control or for determining the effectiveness of a device if sufficient valid data are available and the effects of the device are clearly defined and well understood. The provision indicates a preference for a potentially lower quality of evidence.

FDA Concern: The provision may lower the effectiveness requirement

Prop. Position: To be discussed. However, FDA's compromise language would set forth the concept that retrospective or historical clinical data is acceptable if they are sufficient to demonstrate an assurance of effectiveness. Also, FDA could require concurrent clinical trials when the effects of the device are not clearly defined or well understood, when the retrospective or historical clinical data do not meet the statute's standards, or when there is a compelling health reason.

Bill Provision: Section 802(a), the **animal drug approval standard**, redefines the "substantial evidence" criteria that currently must be met to establish effectiveness. The requirement for adequate and well-controlled studies would be changed to "scientifically sound studies." Section 802 also replaces the requirement that the studies fairly and reasonably show effectiveness into a requirement that there is a reasonable assurance of effectiveness.

FDA Concern: The provision may lower the effectiveness requirement

Prop. Position: To be discussed. However, FDA's compromise position would be to revise the current standard to clarify that one study may be enough to establish effectiveness and the field investigations will only be required where appropriate.

OTHER CONCERNS

1. Off-Label Promotion

Bill Provision: Section 407 would have allowed companies to distribute journal articles and other types of information (such as textbooks, continuing medical education materials, etc.) to promote unapproved uses. However, it was removed from the bill. A substitute provision is likely to be considered when the bill goes to the floor.

FDA Concern: Any provision that would allow manufacturers to promote uses that have not been proven safe and effective by FDA is a concern. Moreover, although the stated purpose of the provision is the dissemination of information, its effect could be less information because it leaves little incentive for companies to do scientific research and have new uses reviewed by FDA.

Comments: Issue pending.

2. Manufacturing Changes

Bill Provision: Section 604 permits manufacturers of drugs and biologics to make changes in manufacturing without prior approval, as long as there is not a resulting change in formulation or release specifications and the changes are validated and records are made available during FDA inspections.

FDA Concern: Changes that do not affect formulations or release specifications can still change the safety and effectiveness of a product. For example, this provision would allow a company to change the strain of a virus for a vaccine or to change the detergent used to cleanse a blood derivative of HIV virus, both of which raise safety concerns.

Comments: The issue is being resolved.

As background, FDA recently published an NPRM, proposing to reduce the number of manufacturing changes that require pre-approval. If S.1477 adopts the approach of greater discretion for FDA, it is essentially codifying the agency's current regulatory initiative.

MEMORANDUM TO SALLY KATZEN AND NANCY-ANN MIN

From: Jonathan Winer
Jim Esquea

Date: April 4, 1996

Re: Draft Analysis of FDA's Most Serious Concerns Regarding S.1477

Attached is a draft OIRA and HD staff analysis of FDA's most serious concerns regarding Senator Kassebaum's FDA reform bill (S.1477). Each section contains three parts: a description of the *bill provisions* causing FDA the most concern, FDA's proposed *alternatives* to the provisions, and OMB *staff comments* on the merits along with possible Administration position.

Sec 202 - Access to unapproved therapies — it life threatening / seriously debilitating — no alternative + JOE or IND (involving animal dev. exempt; investigational need along).

Sec. 604 - Manufacturing Changes.
— drugs and biologics manufacturers can make changes in manufacturing w/out prior approval

Performance Standards (Sec. 103)

Policy statements — 7 opportunities for comment (Sec. 106)

Contracts for Expert review (expanded pilot?) Sec. 403

Env. Impact Review (REGO)

Pediatric studies marketing Exclusivity

Export
Animal Drugs

Pilot and small scale Manufacture. Sec 603 — Manufacture can obtain approval in sm. scale facilities

Device Performance Standards — FDA recognizing standards set by certain organizations (Sec. 708)

off-label use
deadlines
priorities
pharmaceuticals

unified view

Title IV -- Efficient, Accountable, and Fair Product Review

Contracts for Expert Review

Bill Provision: Section 403(a) permits FDA to contract for outside reviews to evaluate parts or all of applications or petitions. Section 403(b) appears to require FDA to contract out all applications, notifications, and conditions if certain conditions are met.

FDA Alternative: A proposed compromise would be to add language to ensure that the section 403(b) language is discretionary. Alternatively, the language could be revised to limit and tighten the conditions under which contracting out would be required.

Staff Comments: Support the bill provision as long as there is the assurance that the use of outside reviewers would be at the discretion of FDA.

Sound Medical Practice

Bill Provision: Section 407 would establish a procedure for approving new uses of previously approved drugs and devices based on sound medical practice (i.e., a use that has existed for five years, is "common" among experienced clinicians, and is reasonably based on experience and other confirmatory evidence). *What would you want in here*

FDA Alternative: This provision, which would create a standard for permitting new uses that completely bypasses the approval process and could result in marketing for unsafe or ineffective uses, is not acceptable to FDA.

Staff Comments: Committee removed language pertaining to dissemination of off-label use of information. Provision might be introduced again as an amendment to the bill on the Senate floor. *General*

Support the concept of the former bill provision which would establish a special process for approving drugs and devices based on professional experience and widespread application over a period of years. FDA considers the bill provision to be unacceptable.

Off-Label Promotion

Bill Provision: Section 407 would allow companies to distribute journal articles and other types of information (such as textbooks, continuing medical education materials, etc.) to promote unapproved devices. In other words, this provision allows manufacturers to promote uses that have not been proven safe and effective.

FDA Alternative: A proposed compromise would be to tie the distribution of articles to the submission of efficacy supplements. Under this approach, a manufacturer would be permitted to disseminate journal articles (as set forth in the section 407 of the bill) 90 days after an efficacy supplement has been submitted to FDA for review.

Staff Comments: Committee removed language pertaining to dissemination of off-label use of information. Provision might be introduced again as an amendment to the bill on the Senate floor.

Support the concept of the former bill provision if sufficient criteria is applied to the cited information to ensure that the off-label promotion of medical devices is based on clinically valid findings. FDA considers the bill provision to be unacceptable.

Struck and replaced w/ amended Amendment **Effectiveness, Outcome, and Cost-Effectiveness Standards** *

Bill Provision: Section 408 provides that the review of an application cannot include the evaluation of any potential use not included in the labeling. Section 408 also appears to prohibit FDA from including, in the labeling, warnings concerning indications for which a product is known not to be effective. *Review*

FDA Alternative: A proposed compromise would be to change section 408 so that it would not permit FDA to deny an application based on any potential use not included in the labeling. This change would permit FDA, where appropriate, to include in the labeling a warning that the product is not effective for a certain use.

Staff Comments: Support the alternative. The alternative allows FDA to maintain some oversight over the potential uses of products, while preventing the agency from denying an application over concerns with potential uses.

Alternative Approval of Supplemental New Drug Applications *CMT. Struck and replaced w/ acceptable Amendment*

Bill Provision: Section 410 provides that for efficacy supplements, the data may consist entirely of information published in medical literature if the proposed condition of use relates to treatment of a life-threatening disease. This suggests that information other than from adequate and well-controlled studies would be acceptable.

FDA Alternative: A proposed compromise would be to clarify that the information in the literature is about one or more adequate and well-controlled studies.

Staff Comments: Support the alternative which merely clarifies the term "information" to mean information from more than one adequate and well-controlled study.

Pediatric Studies Marketing Exclusivity

Bill Provision: Section 411 provides a six month marketing exclusivity for approved applications with pediatric studies submitted by an applicant.

FDA Alternative: It is important to provide incentives for conducting pediatric studies. However, there are concerns about whether the provision is sufficiently tailored so that it applies only to important new uses and whether the incentive is too generous in

light of the fact that these trials often are inexpensive. The compromise language should limit marketing exclusivity to life-saving drugs. The Secretary should have to find that the additional indication will advance public health.

Staff Comments: Concerns about both options due to the potential creation of an incentive to involve children in studies where there is no need to involve them. Of the two choices, the alternative is less restrictive than the bill provision, only focusing on potentially life-saving drugs.

Title VI -- Drug and Biological Products Regulatory Reform

New Drug Approval Standard

Bill Provision: Section 602 states that substantial evidence may consist of data from one well-controlled clinical investigation and confirmatory evidence. This may lower the effectiveness requirement from two adequate and well-controlled studies to one.

FDA Alternative: A compromise position could include minor changes to the provision that would (1) add the phrase "adequate and" before the term "well-controlled" (to make the term consistent with its prior use in the statute) and (2) add the phrase "if appropriate" to ensure that while FDA may accept one trial, one trial is not the presumption.

Staff Comments: Support the alternative due to its minor clarification of the bill provision.

Title VII -- Device Regulatory Reform

Automatic Exemption of All Class I Devices

Bill Provision: Section 702(a) exempts all class I devices from premarket notification (i.e., the submittance of the 510(k) application). FDA has already exempted 572 class I devices. Many of the 216 class I devices not exempted were due to public health reasons.

FDA Alternative: Compromise language could permit FDA to not exempt certain class I devices that have serious public health concerns. Alternatively, compromise language could simplify and expedite reclassification of the most problematic class I devices into class II.

Staff Comments: Support the bill provision which exempts all class I devices from premarket notification because FDA could reclassify those class I devices with serious public health concerns into class II. The second alternative -- the simplification of their reclassification process -- is also supportable given the impact of the bill provision.

Substantial Equivalence Determinations

Bill Provision: Section 702(c) would recognize any use "included with a general use for a predicate device" as an approved use for 510(k) devices. This would allow a device originally marketed for one clinical indication to later be marketed for other indications without documentation of the product's effectiveness for the new indication.

FDA Alternative: Compromise language could allow a new use of a device that is substantially similar to the use of the predicate device to be deemed a legally marketed use for the purposes of the section 510(k) premarket notifications.

Staff Comments: Support the alternative, considering the bill provision's potential effect to virtually eliminate approval of devices for specific uses and, thus, eliminate the requirement to show that these uses are safe and effective.

Medical Device Modifications

Bill Provision: Section 702(d) states that unless a manufacturer's own data shows the safety and effectiveness were to diminish, FDA could not require data on the modified product. It would eliminate FDA's role in assuring that changes made to a product do not adversely affect its safety and effectiveness.

FDA Alternative: Compromise language could ensure that FDA is not prevented from seeking a 510(k) when a change or modification could affect the safety or effectiveness of the device -- regardless of whether the effect is adverse.

Staff Comments: Support the alternative because it gives more discretion to FDA to use or not use the manufacturer's data. However, the compromise language could be improved to allow more medical devices to be eligible for exemption from 510(k) requirements.

Medical Device Approval Standards

Bill Provision: Section 703 would require the agency to accept retrospective or historical clinical data as a control or for determining the effectiveness of a device if sufficient valid data are available and the effects of the device are clearly defined and well understood. The provision indicates a preferences for a potentially lower quality of evidence.

FDA Alternative: Compromise language could set forth the concept that retrospective or historical clinical data are acceptable if they are sufficient to demonstrate an assurance of effectiveness. Also, FDA could require concurrent clinical trials when the effects of the device are not clearly defined or well understood, when the retrospective or historical clinical data do not meet the statute's standards, or when there is a compelling health reason.

CMT.
Accepted
Kennedy amendment
to let FDA
define "general
use!"

Staff Comments: Support the bill provision because it gives FDA the discretion to determine whether the retrospective or historical data is "sufficient(ly) valid" and whether the "effects of the device...are clearly defined and well understood."

Device Performance Standards

Bill Provision: Section 708 requires FDA to recognize performance standards of certain standard-setting organizations.

FDA Alternative: The concept of greater regulatory use of consensus standards is supportable. However, FDA should have the authority to decertify any standard-setting organization and to decide which standards it will recognize. FDA also should have authority to decide whether it is appropriate for companies to self-certify compliance with recognized standards.

Staff Comments: Support the alternative because FDA should be given the authority to decide which standards it will recognize. The bill is unclear how performance standards will be used.

Title VIII -- Animal Drug Regulatory Reform

Evidence of Effectiveness

Bill Provision: Section 802(a) redefines the "substantial evidence" criteria that currently must be met to establish effectiveness. The requirement for adequate and well-controlled studies would be changed to "scientifically sound studies." Section 802 also replaces the requirement that the studies fairly and reasonably show effectiveness into a requirement that there is a reasonable assurance of effectiveness.

FDA Alternative: A compromise position would be to revise the current standard to clarify that one study may be enough to establish effectiveness and the field investigations will only be required where appropriate.

Staff Comments: Support the alternative.

Miscellaneous Provisions

Shortened Review Times

Bill Provision: S. 1477 requires FDA to meet shorter product review deadlines (e.g., 4-6 months for drugs) than the agency is currently meeting. Also, it imposes a number of new requirements on FDA (e.g., the agency must meet with sponsors at defined time periods and prior to such meeting provide the sponsor written information regarding application deficiencies and steps toward approval -- see sections 404 and 707)). These requirements taken together would have the effect of further

shortening the time frames by requiring FDA to complete its review of the application prior to the meetings.

FDA Alternative: As to the time frames, a compromise should include the recognition of the Prescription Drug User Fee Act (PDUFA) times for drugs and biologics. A compromise to sections 404 and 707 could require one pre-submission meeting, one post-submission meeting (to be held at a time that is meaningful), and consultation throughout the application's review. The compromise language should also make the requirements for FDA's "deficiency" letters more reasonable (e.g., letters would include deficiencies known to date).

Staff Comments: Support the bill provision's concept of shortened review times and the alternative's compromise on FDA-applicant meetings. FDA needs to be consulted as to how and over what period any shortened review times are phased in. It should be recognized that PDUFA originated from negotiations between FDA, Congress, and industry on realistic product review time frames.

Amendments

Hammer - Sec. 404
(743 (d))

The following is a partial list of amendments approved during Committee debate. When the bill reaches the Senate floor, the addition of many more amendments is expected.

1. Initiate three-year pilot program under which sponsors could choose to use an outside review firm certified by FDA to approve all classes of medical devices. Approved 11-4. *JK*

Staff Comments: Support the amendment if additional discretion is given to FDA to select which devices are included in the pilot program and as long as the agency retains final authority over the device approval process. While FDA's announced pilot project for third-party review of Class I and II devices, is laudable, it excludes class III devices.

2. Halt FDA's rulemaking on the Medication Guide (MedGuide) proposed requirements. Approved 12-3.

Staff Comments: Oppose the amendment. The MedGuide proposal only requires that a small number of drugs which pose a serious and significant public health concern be immediately required to prepare FDA-approved prescription drug labeling. The proposal sets goals for distributing useful information for the rest, specifying that the hammer does not fall if these goals are met. The private sector is already approaching the fulfillment of the first of two performance standards.

3. Establish uniform labeling requirements for non-prescription drugs at the federal, state, and local levels. Approved 10-6.

Staff Comments: Support the amendment. FDA is preparing to formally submit to OMB a comparable NPRM.

4. Allow companies to make use of health claims information by other federal entities -- the National Cancer Institute and the National Institutes of Health, for example. Approved 10-6.

Staff Comments: Support the amendment.

5. Move ahead on mutual recognition agreements between the EU and the FDA on good manufacturing practice inspections after consultation by the Secretary of HHS with the Secretary of DOC. Approved by unanimous consent.

Staff Comments: Support the amendment.

6. At Kassebaum's request, remove the language pertaining to dissemination of off-label use of information, with the understanding that work would be done to reach consensus on these provisions before the bill reaches the Senate floor. Approved by voice vote.

OFF Label

CORR

KASSEBAUM BILL

A. Major Cross-Cutting Concerns

1. Timeframes/Hammers (Sections 103, 403, 404, 709, 806)
2. Third Party Reviews (Section 709)

B. Serious Concerns

1. Product Approval Standards (Sections 602, 703, 802(a))

drugs } agree to
devices } change
animal drug }

2. Manufacturing Changes/Modifications (Sections 604 & 702(d))

FDA getting back to them on bio

3. Health Claims (Section 903)

Ann Ford - working on it - procedural changes

4. Medication Guides (Section 607)

PHARMA in
diff place

FDA continues to set goals -
law prohibits FDA from doing it within certain time frame
Amr. report - says should be res, which FDA never
intended. - so disconnected.

C. Not Currently In The Bill

1. Off Label Use (Formerly Section 407)

- Can make it clear that this is a concern for ~~both~~
Democrats. -

D. Other Significant Concerns

- ① Mission Statement (Section 102) *potential pros*
 - ② Information ^{and optimistic} Systems/Policy ^{will c b} Statements (Sections 105 and 106)
 3. ^{web} Advisory Committees/Appeals (Sections 107 and 108)
 - Coats
Cares* ④ Access ^{will fix} to Unapproved Uses/HUD ^{open - but Coats} (Humanitarian Use Device) Exemptions (Section 202 and 203)
 5. Clinical Research of Drugs, Biologics, & Devices (Sections 302 and 303) *- no comment*
 6. Effectiveness Determination (Uses not on label) (Section 408) *maybe don't have part*
 7. Initial Classification of Devices (Section 702 (b)) *seem ok*
 8. Device Tracking (Section 704) *will fix*
 9. Combination Animal Drugs/Minor Species ^{- FDA in industry - we web} (Sections 802(b) and (d))
 10. Indirect Food Additives (Section 902) *- receptive*
 - ⑪ Pediatric Labeling (Section 411) *- NAM looking at - HOLD*
 - ⑫ State and Local Requirements Respecting OTC Drugs (Sections 608)
- * Section 406 - Environmental Assessment Provision
- CEO looking at* *- Rock at device law - HOLD*

FDA

~~Senate~~

Rich - met w/ Cassbaum -
recess activities

- reps of 3/4 Dems (not Hawkin) Bill, Bill, Rich

- Cassbaum wants to push Bill to floor in July
- has asked Jones to mount major effort to get issues resolved
- Sen. was somewhat frustrated ^{more not} ~~nothing~~ resolved at staff level.

- She's going to meet w/ R' labor and staff next week - clear out underbrush - may be followed by mtg. w/ Dems on big issues

- wants to set up Senators mtg w/ Phil Lee - Cassbaum, Daddo Mikulski, Phil;

HHS hasn't resolved internally (early the week of the 8th) -

(hold Donna back - let her be "solomenesque")
- Mikulski indicated to Donna that they want Phil as expert resource -

~~House~~

Drug bill looked more promising than Device or Food, following long mtg w/ Kessler

Series of mtgs on drugs only -

two issues

summary data
off label

off label — John Corsini — summarized/represented
in four pieces of paper.

- problem is in part FDA speed at reviewing efficacy Supplement —
 - is one companies don't think FDA takes this seriously
 - encouraged by RFGO Cancer

PDUFA deadline is 6/12 like for NDAs

In order to ~~submit~~ ^{distribute} outside you have to have finished studies for supplement. —

< talked about diff. b/w anecdotal NEM study and well controlled study >

Sally — VP letter to Shalala in March '95 →

- (data standards / consumer health info. / privacy, etc.)
- by discussion — Is it for DOCS? for the mother?
- Peter Edelman's shop —
 - ↳ what kind of info available and to whom
- AIDS database used by Dr.'s on Patients.

- #4 1984 Waxman Hatch — if you do research and file Supplement and get it approved for second use of drug — It has exclusive right to advertise for new use and put it on its label. —
- overrides state generic drug laws
 - industry is uninterested. —

Senate - we're under pressure to come up with resolution on off-label. -

— Mack, Frist, —

— Not saying that it has to be exactly like this —
basic concept that the work (research) has to be done. . .

— Paper exchange Tuesday — Conf. call —
following (7/8) week

— language — week after next (8)

— markup — week after that (15)

Sully here 2-3 hours now —

3rd Paragraph — 1st page

— Add States imposing mandates on localities

— Collapse first two ¶ on 2nd page.

The report captures . . . ; but as acknowledged
in the report it does not reflect. —

— Alleged costs — benefits to the public —
study which is fully appropriate

but the recommendation goes ^{on} to say

Availability of citizen suits has been
extraordinarily beneficial — to
the intent of the Congress —

IDEA

Winter

**Office of Policy
Food and Drug Administration
5600 Fishers Lane
Rm. 15-74, HF-23
Rockville, MD 20857**

PH: (301) 827-3380

FAX: (301) 443-6906

TO: Elizabeth Daye

FROM: Peggy Dotzel
Policy Research Staff

FAX: 202 456-7028

DATE: 6/10/96

TIME: _____
Number of pages including cover _____
Remarks: _____

FDA

*Per your voice mail (F&D)
Please call if you have any questions*

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12. STATE AND LOCAL REQUIREMENTS RESPECTING
OTC DRUGS (SECTION 608)

AMENDMENT NO. _____ Calendar No. _____

Purpose: To provide for the uniformity of Federal, State, and local requirements respecting nonprescription drugs intended for human use.

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 intended to be proposed by Mr. GREGG

Viz:

1 On page 64, between lines 7 and 8, insert the
2 following:

3 **SEC. 608. STATE AND LOCAL REQUIREMENTS RESPECTING**
4 **NONPRESCRIPTION DRUGS INTENDED FOR**
5 **HUMAN USE.**

6 Chapter V (21 U.S.C. 351 et seq.) is amended by
7 inserting after section 522 the following new section:

1 "SEC. 523. STATE AND LOCAL REQUIREMENTS RESPECTING
2 NONPRESCRIPTION DRUGS INTENDED FOR
3 HUMAN USE.

4 "(a) IN GENERAL.—Except as provided in subsection
5 (b), no State or political subdivision thereof may establish
6 or continue in effect any requirement relating to the regu-
7 lation of a drug intended for human use that is not subject
8 to the requirements of section 503(b)(1) which is different
9 from or in addition to, ~~or which is otherwise not identical~~
10 ~~with~~ a requirement of this Act or the Fair Packaging and
11 Labeling Act, ^{that is applicable to such drug} ~~and the administrative implementation~~
12 ~~thereunder~~. For purposes of this section, a requirement
13 relating to the regulation of such drug shall be deemed
14 to include any requirement relating to the subject matter
15 in any provision of this Act, the Fair Packaging and La-
16 beling Act, and any requirement relating to the dissemina-
17 tion of information in any manner about such drug, but
18 shall not include any requirement relating to the ~~dispens-~~ ^{approval or sanction}
19 ~~ing of~~ a drug only upon prescription of a practitioner li- ^{of any}
20 censed by law to administer such drug. ^{profession or}
^{occupation}
^{that}

21 "(b) EXEMPTION.—Upon application of a State, the ^{administers,}
22 Secretary may by regulation, after providing notice and ^{dispenses, or}
23 an opportunity for written and oral presentation of views, ^{sells}
24 exempt from the provisions of subsection (a), under such
25 conditions as the Secretary may impose, a proposed re-

1 quirement relating to the regulation of a drug intended
2 for human use—

3 “(1) that is justified by compelling local condi-
4 tions or protects an important public interest that
5 would otherwise be unprotected; and

6 “(2) that would not cause any drug intended
7 for human use that is not subject to the require-
8 ments of section 503(b)(1) to be in violation of any
9 applicable requirement or prohibition under Federal
10 law; and

11 “(3) that would not unduly burden interstate
12 commerce.”.

*ENVIRONMENTAL ASSESSMENT PROVISION (SECTION 406)

1 “(1) apply all relevant principles of good manu-
2 facturing practice established in this Act and in reg-
3 ulations promulgated by the Secretary;

4 “(2) provide to the Secretary and the manufac-
5 turer within 30 days after the completion of the in-
6 spection an adequate report of the findings of the in-
7 spection; and

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

11 **SEC. 406. ENVIRONMENTAL IMPACT REVIEW.**

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

15 **“SEC. 745. ENVIRONMENTAL IMPACT REVIEW.**

16 ~~“Notwithstanding any provision of other law, no ac-~~
17 ~~tion by the Secretary pursuant to this Act shall be subject~~
18 ~~to an environmental assessment, an environmental impact~~
19 ~~statement, or other environmental consideration unless the~~
20 ~~director of the office responsible for the action dem-~~
21 ~~onstrates, in writing and specifying the basis therefore—~~

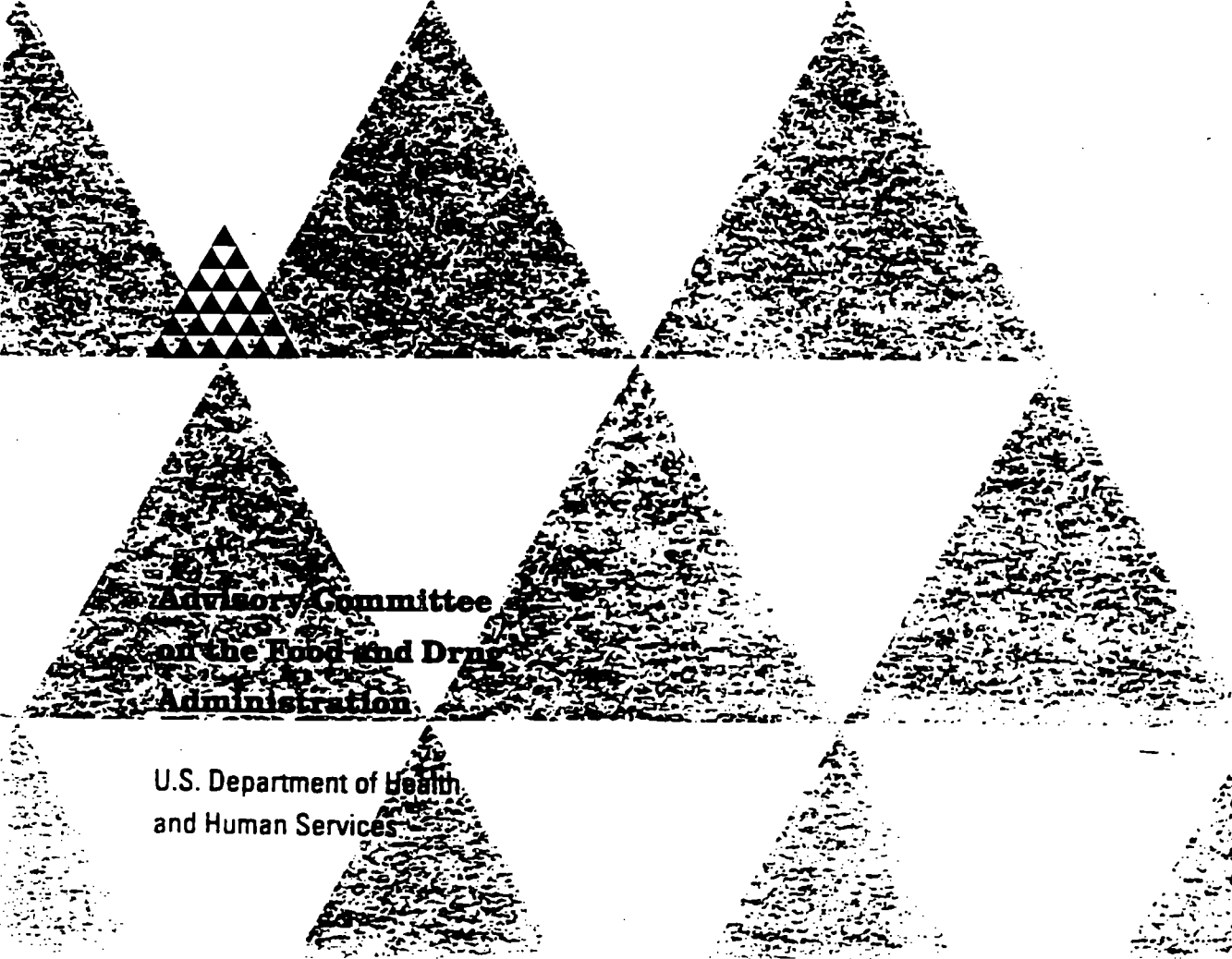
22 ~~“(1) that there is a reasonable probability that~~
23 ~~the environmental impact of the action is sufficiently~~
24 ~~substantial and within the factors that the Secretary~~
25 ~~is authorized to consider under this Act; and~~

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

1 “(2) that consideration of the environmental
2 impact will directly affect the decision on the ac-
3 tion.”.

**Final Report
of the Advisory Committee
on the Food and Drug
Administration**

May 1991



**Advisory Committee
on the Food and Drug
Administration**

**U.S. Department of Health
and Human Services**

CHAPTER 7

State and International Regulation

The FDA does not hold a monopoly on the regulation of foods, medicines and medical technology. There is growing interest in product regulation on both the state and international level.

In the domestic arena, the goal of national uniformity is widely accepted. There is not, however, agreement on how to achieve uniformity while preserving the rights of states to protect their residents.

In the international sphere, support for uniformity is comparatively recent. Although the FDA has worked for years on bilateral agreements to help foreign products conform to U.S. standards, two recent phenomena have helped bring international harmony into particular focus. First, the FDA has witnessed an increase in imported products that fall within the Agency's traditional jurisdiction. Second, the vigorous drive to create an internal market within the European Community (EC) has stimulated efforts to unify regulatory practices and requirements.

Federal Preemption and Domestic Uniformity

Uniform national regulatory standards, largely unobstructed by state regulations, have helped to create an efficient national market in the United States. But in the past decade, some states have moved into the FDA's traditional domain. In response, many companies that market FDA-regulated products have vigorously urged federal preemption. They argue that uniform national standards are essential ingredients of economic stability and public health and that additional state requirements are burdensome and disruptive. However, others disagree, including many consumer groups who emphasize the value of action and innovation at the state level.

After balancing the arguments, two subcommittees of the Committee endorsed national uniformity in the areas of food, veterinary drugs, cosmetics, over-the-counter drugs, and the blood supply. For the third subcommittee, such consideration was unnecessary since the medical device statutes already contain explicit preemption provisions.

In some areas, the Agency has already exercised preemption based on general administrative authority. (See the Appendix for a list of these instances.) In addition, the FDA administers seven laws that provide for preemption, the most recent being the labeling provisions of the 1990 Nutrition Labeling and Education Act.

Explicit preemption should play a greater role in FDA-state relations

After extensive discussion, the Committee has concluded that explicit preemption should play a greater role in FDA-state relations than it has in the recent past. Otherwise, the FDA's preeminence in consumer protection will be further eroded and unnecessary burdens will be imposed on the national economy. However, valid and growing state interests also must be recognized.

The Committee prefers that preemption be mandated through federal legislation that applies to all FDA regulated products. In areas where the FDA is active in regulation, the legislation should establish a procedure for states to petition the FDA for an exemption from preemption based on a convincing local need. Further, in those areas where the FDA has not acted, the legislation should provide for states to notify the FDA before regulating a product and allow the FDA 120 days to respond. The legislation should also include appropriate avenues for states to advance their interests by petitioning the Agency for the adoption or amendment of national standards.

We believe this legislation should be passed in the current Congress. If Congress has not enacted such legislation by the end of the 102nd Congress, the FDA should adopt a regulation of general applicability that would accomplish the same goals.

The Committee recognizes that there are additional ways to achieve uniformity. The Agency can further the goal of national uniformity by cooperating with state officials to develop model legislation, adopting state rules that explicitly utilize federal requirements, and participating in joint training. The Committee's subcommittee on foods, cosmetics, and veterinary medicine may have summed it up best:

...state requirements are often adopted because Congress or, more often, FDA is seen to be indifferent, inactive or incapable of addressing strongly felt concerns among consumers. A vigorous FDA is likely to be the most effective deterrent to the adoption of diverse and inconsistent state requirements.

A vigorous FDA is likely to be the most effective deterrent to diverse and inconsistent state requirements

Any approach to national uniformity, however, will be futile unless the FDA is substantially strengthened along the lines recommended in this report.

Approaches to Import Regulation

In testimony to the Committee, FDA enforcement officials described dramatic growth in imported foods, drugs, and devices subject to FDA regulation. The increase in food imports is particularly significant (see the Appendix), partly because of the sheer volume and also because food shipments come to the U.S. from thousands of foreign sources, many in countries where local regulatory standards are modest, mysterious, or nonexistent. It is particularly disturbing that foreign food inspections lag far behind import growth.

As in most nations, the keystone of import regulation in the United States is inspection at the point where foreign products enter the country. In cooperation with the U.S. Customs Service, FDA enforcement officers inspect thousands of shipments of regulated products every year. From 1985 through 1989, the number of FDA point-of-entry inspections doubled from 73,429 to 147,553.

Despite their wide use in the United States and most other nations, however, point-of-entry inspections are an anachronism. Inspecting a final product to determine if it conforms to standards, and rejecting products that do not—a concept called “inspecting-in quality”—has been totally discredited as a means of assuring manufacturing quality or regulatory compliance for domestic products. For that reason, the FDA has for many years specified and enforced good manufacturing practices within the U.S.

The FDA's dependence on point-of-entry inspections for imported products reflects both resource limits and political realities. It is very costly to send personnel to inspect production facilities abroad and many foreign countries do not welcome them. While arrangements are in place to inspect facilities where drugs and medical technologies are produced, further bilateral agreements

and other diplomatic initiatives are needed for foods. Despite the cost and complexity of developing on-site, and perhaps reciprocal, inspectional systems, however, the Committee is convinced this change must occur.

Harmony Within the European Community

Since 1985, the twelve-nation European Community has moved swiftly to develop new rules for regulating foods, drugs, and devices within member states. As of December 1990, there were 103 EC initiatives—about 19 percent of the total—that relate directly to FDA-regulated products, evidence that FDA-regulated products figure prominently in the development of the internal market of a unified Europe.

The number of EC directives dramatically illustrates the new challenges to the FDA. In the longer term, harmonization of European and U.S. regulatory standards may bring more efficient operations for all regulatory agencies. But to enjoy such benefits, much work needs to be done now. In particular, the broad impact of international harmonization on consumer protection and public health should be considered from a variety of perspectives, including health care costs, intellectual property rights, and world trade.

The FDA should be at the forefront of the movement toward international harmonization, but unfortunately it is not yet properly equipped to lead

The FDA should be at the forefront of the movement toward international harmonization, but unfortunately it is not yet properly equipped to lead. Although the Agency established an international affairs office in 1979, and individual Centers have taken some useful action, these steps are too small for the task ahead. Until very recently, international activities were not even formally recognized in food and drug legislation. The Safe Medical Devices Act of 1990 required the Secretary to establish an Office of International Relations that deals specifically with issues of international harmonization for devices. That model might serve for the food and drug areas as well.

Countless other developments in the global economy are likely to affect the FDA. An example is the ongoing diplomatic negotiations aimed at developing a North American Free Trade Agreement that includes Canada and Mexico. Such an agreement has many international health and safety implications and demands a more intensive and more sophisticated commitment than the FDA has shown in the past.

▲ Recommendations ▲

- ▲ 7-1. Congress should enact legislation that preempts additional and conflicting state requirements for all products subject to FDA jurisdiction. States should be permitted to seek an exemption from preemption in areas where the FDA has acted, based on a convincing local need. In areas where the FDA has not acted, a state would be required to notify the Agency that it intends to act and give the Agency 120 days to respond. States should, in addition, be allowed to petition for the adoption or amendment of national standards.**
- ▲ 7-2. If Congress has not enacted such legislation by the end of the 102nd Congress, the FDA should issue a preemption regulation that accomplishes the same goals.**
- ▲ 7-3. The FDA needs to be more aggressive in ensuring that the increased volume of imported foods, drugs, and devices meets health and safety standards prior to entering the country. FDA should work with other nations to encourage the implementation of uniform standards and systems here and abroad.**
- ▲ 7-4. The FDA must strengthen its efforts at harmonizing international regulatory standards, particularly with major trading partners.**

FDA BUDGET CONSIDERATIONS

I. TOTAL FDA BUDGET

- Total FDA budget is about \$870 million (FY 94)
- This is equivalent to less than \$3.00/person/year for all Americans

II. FDA BUDGET FOR FOODS

- FDA budget for foods responsibilities is about \$222 million
- This amounts to about 25% of the total FDA budget

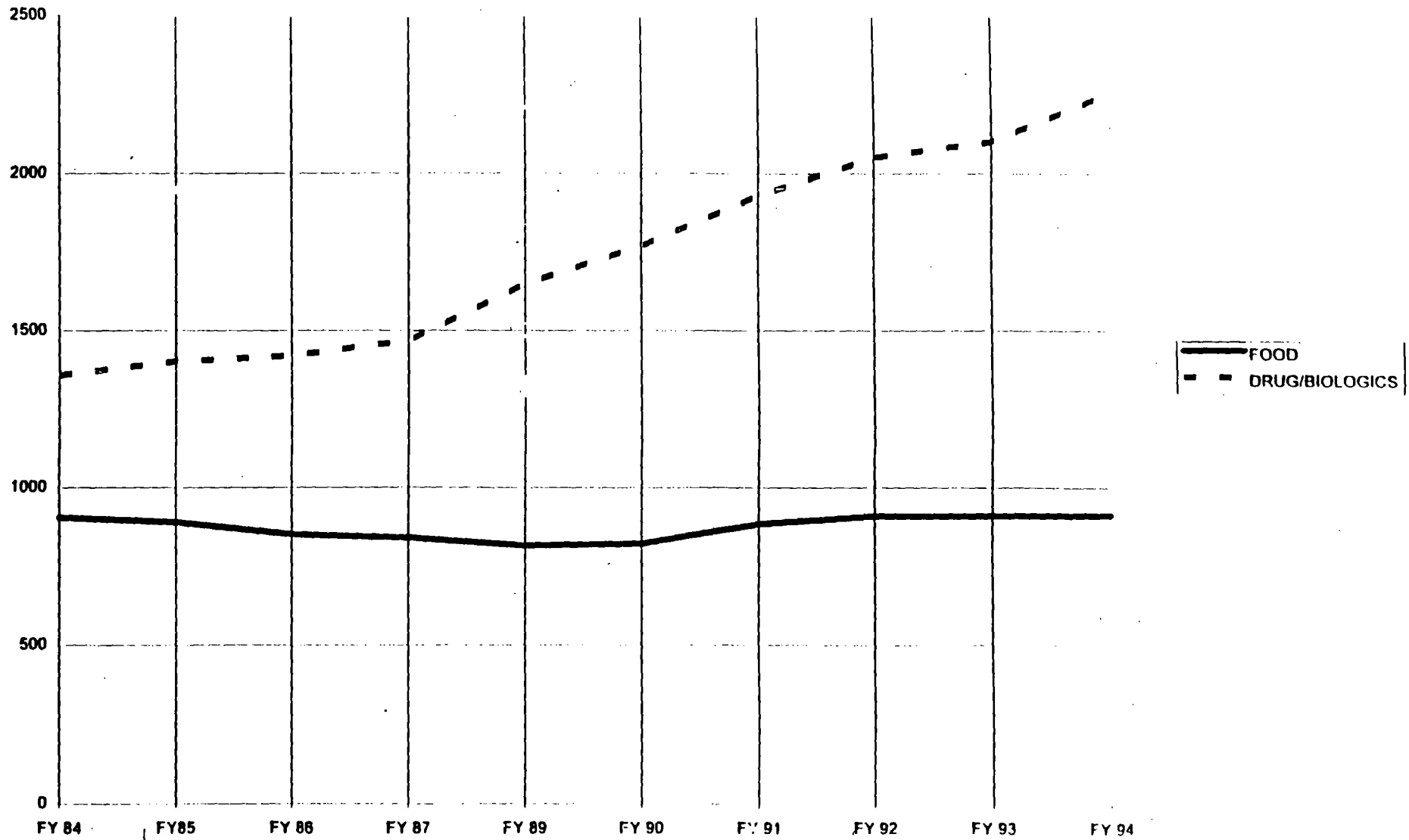
III. CFSAN OPERATING AND EXTRAMURAL BUDGET

- The Center for Food Safety and Nutrition (CFSAN) budget is about \$17 million
- The staffing levels are about the same as 10 years ago after dropping to their lowest levels in 1989
- This budget has remained about level for the last 4 years not adjusted for inflation
- Many added responsibilities have been added based on new legislation
- Comparison with budget changes for Centers for Drugs and Biologics shows a steady increase while CFSAN is not given sufficient budget priority

FDA RESOURCES
CENTER FOR FOOD SAFETY AND NUTRITION

- FDA resources for food in the Center for Food Safety and Nutrition (CFSAN) are the same as they were 10 years ago moving from 905 FTE's in 1984 to 912 FTE's in 1994. The actual staffing numbers went down to a low in FY 1989 and have remained basically flat for the last 3 years.
- On the other hand, for comparison, FDA resources for the Centers for Drugs and for Biologicals have consistently increased over the period from about 1357 FTE's in 1984 to 2253 FTE's in 1994, a 65 % increase.
- The very flat leveling of FDA resources for foods in recent years is in striked contrast with the increased responsibilities CFSAN has assumed due to new legislation such as in the areas of nutrition labeling, nutrition monitoring, pesticide monitoring, safe transport of food, etc.

FOOD AND DRUG ADMINISTRATION
CENTER PERSONNEL (FULL TIME EQUIVALENTS, FTE'S)



FOOD AND DRUG ADMINISTRATION
CENTER PERSONNEL (FULL TIME EQUIVALENTS, FTE'S)

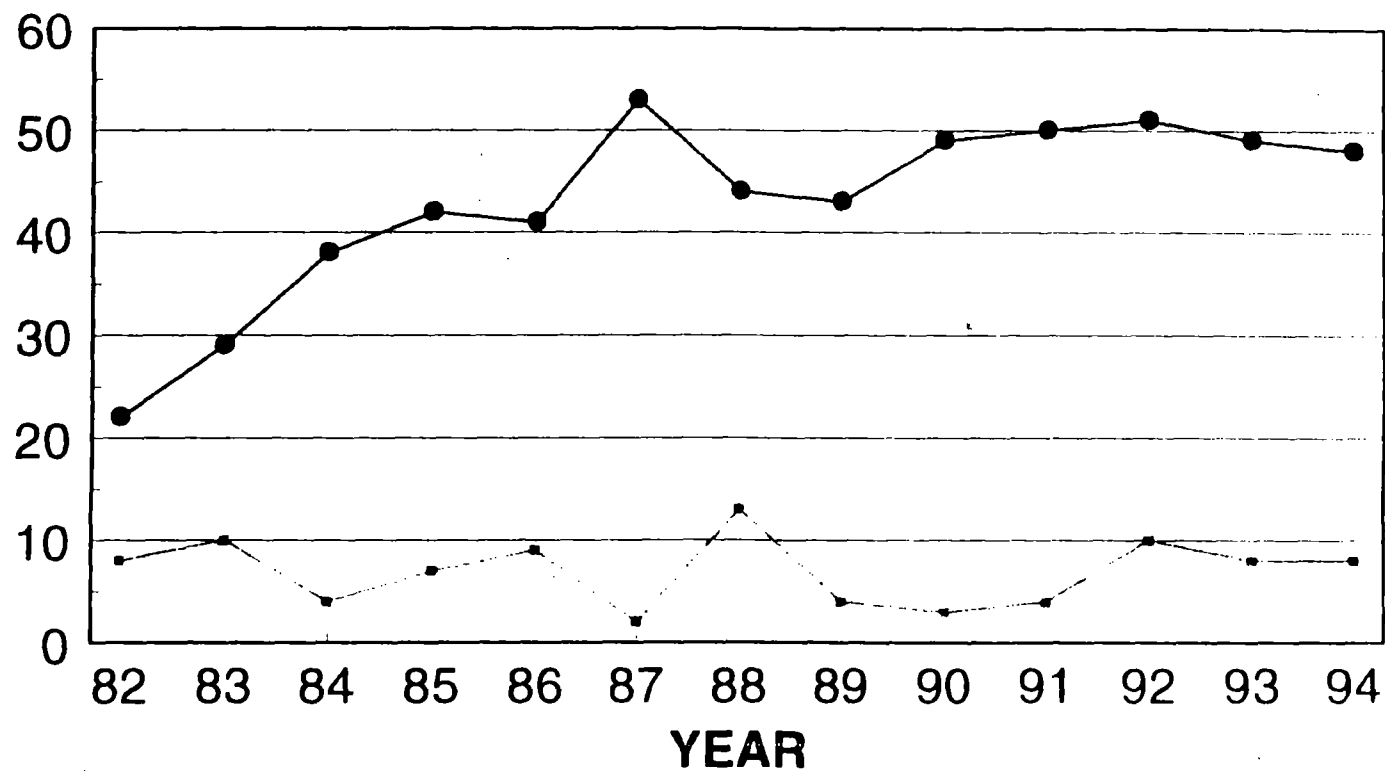
<u>Fiscal Year</u>	<u>Food</u>	<u>Drugs/Biologics</u>
FY 84	905	1357
FY 85	889	1401
FY 86	850	1419
FY 87	839	1467
FY 89	815	1648
FY 90	821	1768
FY 91	884	1929
FY 92	909	2051
FY 93	909	2101
FY 94	912	2253

FOOD AND DRUG ADMINISTRATION
CFSAN TOTAL OPERATING AND EXTRAMURAL BUDGET

<u>Fiscal Year</u>	<u>Total (in Thousands)</u>
FY 85	\$11,844
FY 86	11,844
FY 87	13,463
FY 88	13,463
FY 89	13,898
FY 90	14,590
FY 91	17,041
FY 92	18,553
FY 93	17,846
FY 94	16,748

FDA FOOD ADDITIVE APPROVAL TRENDS 1982-1994

Direct Additive and Irradiation Petitions Only



Petitions Pending Orders Issued



Testimony of

STEPHEN A. ZILLER, Ph.D.

VICE PRESIDENT, SCIENTIFIC AND TECHNICAL AFFAIRS

GROCERY MANUFACTURERS OF AMERICA, INC.

before the

HOUSE COMMITTEE ON GOVERNMENT REFORM AND OVERSIGHT
SUBCOMMITTEE ON
HUMAN RESOURCES AND INTERGOVERNMENTAL RELATIONS

on

THE EFFECTS OF REGULATORY DELAYS ON FOOD TECHNOLOGY RESEARCH
AND CONSUMER NUTRITION BENEFITS

JUNE 22, 1995

Mr. Chairman, I am Dr. Steve Ziller, Vice President, Scientific and Technical Affairs, for the Grocery Manufacturers of America, Inc. (GMA). GMA is the national trade association representing companies which manufacture and market branded grocery products that comprise 85% of the volume of food and grocery items sold in the United States. Member company annual sales exceed \$360 billion.

While virtually every GMA member company and their consumers have benefited from the increase in food quality, nutrition, safety, and availability made possible by food additives already approved or affirmed as safe by the Food and Drug Administration over the years, we strongly urge that substantial change be made in the food additive approval process to meet current and future consumer needs. GMA's members include a number of companies who have submitted some of the major direct food additive petitions, many of which are still pending before the Food and Drug Administration after too many years of review.

We strongly applaud this oversight subcommittee's action to take a close look at whether the way the food additive approval process is working today: 1) is still consistent with the Congressional intent when provisions were passed legislatively in 1958, 2) whether it is working as effectively as it can in the current environment, and 3) what changes would help make it most efficient for the future. Few processes that define such a very important interaction between government and industry can be expected to survive for over 35 years without a significant overhaul, both by regulatory and legislative means.

Mr. Chairman, I have had extensive experiences in working on important food ingredient approvals by FDA, both from the point of view of the petitioner, for example, in the case of Olestra (a complete fat substitute), and as part of a food processor wanting

to use a new food ingredient, for example in the case of an artificial sweetener. In my current position at GMA I have discussed the major problems with a number of companies with pending petitions for ingredients which have the capability of providing consumers a better and broader choice of foods to fit their individual nutrition and dietary needs. My comments are based on this background.

Before I begin specific comments, let me state a few general principles. First, both the food ingredient manufacturers and the food companies who use these in their most valued assets, i.e. their brands, demand that their products continue to be the safest in the world. These comments are made with that prerequisite. Secondly, the food industry believes that the FDA's participation in food additive approvals adds important credibility and assurance for consumers and we favor this. Third, the problems with the current food additive approval system are not due to a single reason but result from multiple causes. Fourth, the current global competitiveness and trade reality demands that all parts of industry and government continually improve their efficiency and effectiveness. For the food industry this includes expectation of a government that will support new technology and approval of new food ingredients.

While it is easy to say that the first and only cause of the breakdown of the FDA food additive approval process is reduced resources, I contend that this is more of a symptom and not a root cause. The fundamental causes are lack of a clear mission, a steadily decline in priority over the years, and the increasing lack of incentive and ability of the agency to make a final positive decision on a petition against the statutory criteria.

One of the recommendations of the Edwards Commission review of FDA and its operations was for FDA to develop a mission statement that included a strong statement

for new product approvals. There was some disappointment in the industry when this important role was relegated to a secondary and debatable status for food additives, "Be a positive force in making safe and effective products available to the consumer..." Of course, words on a piece of paper do not make things happen; however, they can give some clue as to the agency's lack of commitment to this area. Congress should give the agency more specific direction on this matter in the future as this relates to US competitiveness and leadership in nutrition, safety, and food technology worldwide.

A second cause for breakdown in the food additive approval process is a steadily decreasing priority. The general trend for food additive approvals over the last 12 years has been increased pending petitions and decreased approvals. For the direct food additives and irradiation petitions the numbers pending over the last 5 years has been about 50 and those approved each year have been less than 10. For the same group the pending petitions are averaging about 5 years to approval. Several of the major petitions still pending were submitted about 8 years ago.

We get a hint of the contributing factors by looking at the Center for Food Safety and Nutrition (CFSAN) staffing versus drugs and biologics. CFSAN staffing has remained essentially constant for the last 12 years (ranging from about 800 to 900) while that for drugs and biologics increased steadily from 1357 to 2253. Policy decisions were made on priorities which robbed the FDA CFSAN staff. Congress needs to provide direction to FDA on the need for higher priority for this effort within the resources they have. In the future, FDA will also have to leverage external resources more effectively as it will not be possible to maintain all needed expertise in-house.

A third major problem with the current food additive approval process is a growing inability to bring closure to the final decision and the replacement of sound scientific judgment with an infinite series of "what if" questions that delay the need for a decision. There seems to be a preoccupation by technical reviewers and the legal staff with fear of change and an obsession with an impossible standard of "zero risk" when the actual statutory standard is "reasonable certainty of no harm". This contributes to many associated problems such as no clear guidance on what the petitioner must do to satisfy the reviewers in advance of submission and further confusion after reviews are begun. This problem is very fundamental and must be addressed by bringing the best science and the best scientists together to determine decisive action steps to bring resolution. Importantly, the legal community must provide clearer guidance and support for final decisions. The inherent delays resulting from this inability to make final decisions is beginning to turn off major food companies from investing in new additives and technology. The system of approvals is now so unpredictable and uncertain that businesses cannot make even reasonable calculations about the costs of developing a new ingredient and the timing of related investments to commercialize it. Seven or eight years and a page full of new questions will kill all major new product development in the current world economy.

I will provide one example to illustrate that the long US timing delays are not necessary. Sucralose is still waiting for US approval since its submission February 9, 1987. Yet similar submissions in Canada and Australia have already been approved (9/91 and 10/93 respectively). These are well respected developed countries with food supplies as safe as the US. We should be able to do much better.

There should be much more commitment to approvals by FDA to be consistent with their other efforts to support a more nutritious and safe food supply. The same type of nutrition and public health yardstick should be used to justify increased FDA effort in promptly approving important new ingredients which can provide benefits such as lower calories, fat, and saturated fat. The secondary impact on expected reduction in risk of chronic disease is very important to consumers and society in general.

Based on an eight gram per day reduction in saturated fat, optimistic assumptions provide for a \$24 billion per year health care saving and two million fewer patients developing heart disease. One GMA member company has provided the following estimates of reduction in the incidence and costs of chronic disease associated with lower dietary saturated fat intake by use of a fat substitute only in the snacks and crackers food categories. Using a conservative "cost-of-illness" approach targeted at high risk groups for coronary heart disease produced estimated savings of \$2 billion over 10 years based on state of the art calculations. Extending the benefits to the entire population and including reduction in cancer risk would provide a \$4 billion saving over 20 years in direct medical costs and lost wages and 14,600 fewer deaths. Broader use of the fat substitute beyond snacks and crackers could provide savings of \$25 billion in health care costs and 112,400 fewer deaths over 20 years.

Mr. Chairman, I am not here to have a debate about the precise accuracy of these estimates. That can be done in another forum. However, I think the point is that important food additives with this magnitude of benefits should be encouraged with a speedy review and decision. The negative impact of their unavailability to consumers must be carefully considered in justifying continuing delay in approval.

Finally, the elements to the solution need to address all the critical elements of the underlying problems with the current system. Congress must make its position known to FDA about the importance of food additive approvals to the health and economy of Americans. There must be a positive and supportive attitude by FDA. While the details of the consensus industry legislative proposal will be provided later, let me summarize several key areas. FDA should be the "quarterback" for the review and approval process. FDA should approve and provide final regulations for direct food additives. Third parties listed by FDA as meeting agreed criteria may be selected by the petitioner to receive the petition from FDA in order to provide additional resources to FDA for review (including nationally renowned scientists in critical subject areas). The third party will have authority to make the primary safety judgment and to conduct a public hearing to receive input prior to completing the report to FDA. The petitioner will pay the third party for their effort. Appropriate time limits should be established for third party and FDA review and these should be strictly upheld.

Thank you for the opportunity to testify today. I would be happy to answer any questions you may have.

May 23, 1995



**Facilitating Innovation in the Food Industry--
Making the FDA Review Process for Food Ingredients Work**

- **The Problem**

Consumers in the United States enjoy the world's most varied, wholesome, and affordable food supply. Innovations in food processing and technology and in food packaging technology – the development of fat and sugar substitutes and new fiber sources, for example, as well as new types of packaging such as aseptic juice packages—enable food companies to develop and offer consumers increased food choices, including foods that have fewer calories, less fat, or more fiber, as well as enhanced convenience. Extraordinary delays in the FDA approval processes for new food ingredients impede much needed and desirable innovation in the food industry.

Since 1958, new food ingredients which qualify as "food additives" have been required to have FDA approval before marketing. Food additives include both those ingredients added directly to food to achieve a physical or technical function (sugar substitutes and antioxidants, for example—so-called "direct" food additives) and those substances that are used in food packaging or other food contact situations which may become part of the food through contact with it (so-called "indirect" food additives). Approximately seventy-five percent of the food additive petitions submitted to FDA are for indirect food additives.

Under the law, FDA has 180 days to review a food additive petition and to take action on it. Few, if any, food additive petitions are acted upon in the statutorily-prescribed time period. Rather, FDA action on a typical food additive petition, if it occurs at all, takes 4-6 years and, in some cases, twice as long as that. Increasingly, as the graphs attached to this paper show, food additive petitions remain in "pending" status in perpetuity. For example, in 1982, there were about twenty petitions pending for direct food additives; by 1994, the number had grown to nearly fifty. With the exception of 1988, FDA took action on fewer than ten petitions in each of the years in question. In five of the years in question, FDA acted on fewer than five petitions. If one looks at all pending petitions (direct and indirect), the numbers are equally distressing: there are nearly 200 petitions pending while only about half that number were pending in 1982. The trend on petitions acted on is decidedly downward with about twenty-five actions per year on average whereas fifty or more petitions were acted on in 1982 and 1983.

There are numerous reasons why the food ingredient review processes are not working. Most observers believe that FDA reviewers have become unduly cautious and conservative and thus unable to conclude that a particular substance under review is safe. This caution is frequently exhibited in requests that reviewers make for more

studies and data that have little, if any, relevance to the determination of safety for a food ingredient. A considerable part of the problem with the current system derives from the allocation of resources within the food ingredient review divisions of FDA—far too many resources are devoted to indirect additive review and far too few resources are devoted to the review of significant new ingredients. Of course, on occasion, petitioners also contribute to delays through submissions that are inadequate and because of the complexity of issues sometimes presented in petitions.

It is also apparent that FDA has perceived there to be no substantial harm to the public from its dysfunctional food ingredient processes and it therefore has invested no significant effort in repairing a broken process. FDA's perception is, of course, incorrect. By taking so long to act on petitions, if it acts at all, FDA depresses investment in new food ingredients and technologies which then deprives consumers of the benefits that these new ingredients and technologies can offer.

Reforming the FDA food ingredient review process does not mean eliminating FDA review or lowering the standards that help to provide consumers with a safe and wholesome food supply. Rather, reform means developing a system and processes that rely on sound science, helping to establish appropriate priorities, and requiring decisions in reasonable time periods. The proposals described below meet these criteria.

- Some Solutions

Solving the problems with the food ingredient review processes at FDA requires amendments to the food additive portions of the Federal Food, Drug, and Cosmetic Act to provide for a simplified procedure for indirects and to mandate the use of external scientific reviews for direct, when the petitioner requests that form of review and is willing to pay for the external review. These two relatively simple changes have the potential to improve dramatically the efficiency of the food additive review processes while maintaining the high level of consumer protection that the food industry and its consumers expect.

For direct human food and color additives (color additives are nothing more than food additives whose function in food is to impart color), a new system of "third party review" should be established. Under this system, FDA would enter into agreements with at least three independent organizations which are qualified to review the data contained in food additive petitions which demonstrate the safety and functionality of the additive. If the petitioner requests this form of review, it would designate which of the independent review organizations it wishes to conduct the review. FDA and the independent organization would review the data under appropriate but strict time periods. The FDA, the independent reviewing organization, and the petitioner would freely communicate with each other during the review. FDA would publish a notice of the filing of the petition within 30 days of receipt and thereafter the safety and functionality data in the petition would be available to the public (except for confidential

commercial information and trade secrets). The time periods for the review begin with the publication of the notice of filing.

After a suitable period of review (six months, perhaps) during which time FDA and the independent review organization would be required to raise all potential issues with the petitioner (so that the petitioner can respond and so that the review process is not simply an endless series of questions posed to the petitioner without closure ever being reached), the independent review organization would convene a public meeting to receive scientific testimony about the safety and functionality of the additive. FDA, the petitioner, and the public would participate in this meeting.

Within sixty days of the conclusion of the public meeting, the independent review organization would present to FDA a report and recommendation on the petition, concluding either that the additive had been shown to be safe (safety meaning a reasonable certainty of no harm from use of the additive under its intended conditions of use) or that safety has not been demonstrated. If the report concludes that safety has been demonstrated, a presumption of approvability will be created. The petitioner and the public will, of course, have access to the report. At the request of the petitioner, the time period for the report will be suspended (to allow, for example, analysis of existing data or the generation of additional data to respond to issues that have been raised during the review).

After receipt of the report, FDA will have ninety days to act on the recommendation by either accepting it and issuing a regulation to allow the use of the additive or by rejecting it and advising the petitioner in detail of the basis of the rejection. If FDA failed to take either action within the specified time period, it would be deemed to have accepted the report of the independent review organization and would have sixty days to issue a regulation to authorize the use of the additive.

The presumption of approvability arising from a favorable report of the independent review organization would be rebuttable by FDA only if it concluded that there existed substantial evidence to demonstrate that the additive had not been shown to be safe.

The costs of the review by the independent review organization would be borne entirely by petitioners who have requested this form of review. FDA would annually set forth the anticipated fees associated with the independent review (the actual fees incurred in a specific case would, of course, depend on the scope and complexity of the review required of a particular petition). Payment for the review would go directly from the petitioner to the independent review organization. FDA's contracts with the independent review organization would set forth the payment schedule for the petitioner (one-third initial payment, one-third at the conclusion of the public meeting, and one-third after delivery of the report and recommendations, for example). In addition, those contracts would provide for a refund of the petitioner's fee if the independent

review organization failed to perform its tasks under the contract or failed to meet the timeframes for completion of those tasks.

For petitions pending at the time that this new process is instituted, the petitioner would have the option of withdrawing the petition and resubmitting it under the new procedures or to have the petition continue to be reviewed under the existing procedures.

This process would enhance the efficiency of the process and bring some order and certainty to a process that is now anything but orderly and certain. Petitions would be reviewed in reasonable time periods because the independent review organizations would be contractually obligated to do so (and would respond as the private sector typically does—if more reviewers are needed to complete the reviews on time, more will be hired) and because real statutory time periods would be established under the law with teeth to enforce them. Consumer protection would be maintained because the standards for decisions on additives would remain rigorous.

The solution for indirects is simple. Indirect additives which are not, by definition, added directly to food and which rarely become a component of food in scientifically-meaningful quantities, do not require extensive food additive petitions nor elaborate FDA review. It simply makes no sense to burden the regulatory process with hundreds of petitions for indirects and for FDA to devote substantial resources to the review of this category of substances. Consumer protection can be maintained at equivalent levels by substituting a notification procedure for the current one.

Under the proposed process for indirects, a notification would be submitted to FDA at least ninety days before the "food contact substance" was intended to be used. The notification would contain the identity of the substance, its intended use, and data and information to show either that the substance was not reasonably expected to become a component of food or that the substance is safe (the identical safety standard for direct human food and color additives). The notification would take effect in ninety days and use of the substance therefore allowed, unless FDA concluded that there existed substantial evidence to show either: (1) that the substance is reasonably expected to become a component of food, if that contention was the basis for a notification; or, (2) that the substance was not safe (again, the same standard as would apply to the rejection of a favorable report from an independent review organization for a direct additive). The notification would be confidential during the ninety day period, but would, except for trade secrets and confidential commercial information, be made public after ninety days. FDA would maintain a list of food contact substances which are the subject of effective notifications.

The term "food contact substance" would be defined as a subset of "food additive." Existing food additive regulations would be unaffected; likewise, the categories of GRAS and prior sanction would continue to exist for food contact substances.

This simple notification system would facilitate the use of indirect additives and thus new or improved food packaging, while also ensuring that these substances are safe. FDA would continue to be made aware of new food contact substances and the basis for the manufacturer's conclusion that the substance is safe. Finally, FDA would have ample time and authority to prevent the use of a new food contact substance if it concluded that it was appropriate to do so.

Attachments

Direct Human Food and Color Additive Petition Review

- (a) Amend section 409(b)(2) by adding at the end thereof the following:

"(F) for a direct human food additive, a request for third party consideration under subsections (j) - (o) of this section and the identity of the independent review organization to review the petition."

- (b) Amend section 409(b)(5) to read as follows:

"(5) Notice of the regulation proposed by the petitioner, including the name and intended use of the additive, and a designation for third party consideration, if any, shall be published in general terms by the Secretary within thirty days after filing."

- (c) Amend section 409(b) by adding at the end thereof the following :

"(6) Upon request of the petitioner set forth in the petition for a direct human food additive, the Secretary shall designate a petition for third party consideration and such petition shall be subject to the procedures set forth in subsections (j) - (o) of this section."

- (d) Amend section 409 by adding at the end thereof the following new subsections:

Third Party Consideration

"(j)(1) Upon the publication of a notice of filing of a petition which contains a designation of third party consideration, the Secretary shall promptly place on public display in a location maintained for the examination of public documents a complete copy of the data and information contained in the petition which relate to the safety and functionality of the additive, except for data and information which are trade secrets or confidential commercial information.

"(2) Upon publication of a notice of filing of a petition which contains a designation of third party consideration, the Secretary shall promptly provide a complete copy of the data and information contained in the petition which relate to the safety and functionality of the additive to an independent review organization with which the Secretary has entered into an agreement under subsection (o). If the petitioner has designated a specific independent review organization to conduct the review, the Secretary shall refer the safety and functionality data and information to that organization. If the petitioner has not designated a specific organization to review the petition, the Secretary shall determine which organization shall conduct the review.

"(3) The Secretary and the independent review organization shall review the petition for a period not to exceed six months from the notice of filing. During the review period, the Secretary and the independent review organization may communicate with each other or with the petitioner in person or in writing; a complete record of all such communications and the petitioner's responses shall be maintained by the Secretary. Within the six month period provided for review of the petition, the Secretary and the independent review organization shall advise the petitioner in writing of all issues relevant to the evaluation of the petition. In evaluating a petition under this subsection, neither the Secretary nor the independent review organization may consider any data or information which is not filed with the Secretary within six months of the notice of filing or presented at the public meeting under subsection (k), unless such data and information were provided by the petitioner.

Public Meeting

"(k) Within sixty days of the completion of the review period under subsection (j)(3), the Secretary and the independent review organization shall convene a public meeting to consider the petition. The petitioner shall have the right to appear and to present testimony and to respond to questions. Members of the public shall also have the right to appear and present testimony concerning the safety and functionality of the additive. A verbatim record of the hearing shall be maintained. The meeting shall be chaired by a representative of the independent review organization.

Recommendation

"(l)(1) Within sixty days of the completion of the public meeting under subsection (k), the independent review organization shall provide to the Secretary a report and recommendations, together with a statement of the reasons or basis for the recommendations. The independent review organization shall recommend that the petition be approved if a fair evaluation of the data and information before it establishes that the proposed use of the additive under the conditions of use to be specified in the regulation will be safe within the meaning of section 201(u). The Secretary shall promptly provide a copy of the report and recommendations to the petitioner and shall promptly place a copy on public display in a location maintained by the Secretary for the examination of public documents, except that trade secret and confidential commercial data and information shall not be disclosed.

"(2) Upon request of the petitioner, the independent review organization shall defer submission of the report and recommendations provided for under subsection (1) for such period of time as the petitioner requests.

"(3) A report and recommendation from the independent review organization that concludes that an additive has been demonstrated to be safe shall create a presumption of approvability.

Action on the Recommendation

"(m)(1) Within ninety days of receipt of a report and recommendations under section (l), the Secretary shall either--

"(A) issue a regulation providing for the use of the additive under the conditions of use found by the independent review organization to be safe; or

"(B) reject the report and recommendations on the ground that there is substantial evidence to demonstrate that the additive has not been shown to be safe under the intended conditions of use. The decision of the Secretary to reject the report and recommendations of the independent review organization shall set forth the evidence on which the Secretary relies and the basis and rationale for the decision. A copy of the Secretary's decision under this subsection shall promptly be provided to the petitioner and independent review organization and placed on public display in a location maintained by the Secretary for the examination of public documents.

"(2) If the Secretary fails to take action under paragraph (1) within the required ninety days, the report and recommendations of the independent review organization shall be deemed to be the decision of the Secretary and the Secretary shall, within sixty days, issue a regulation providing for the use of the additive under the conditions of use found by the independent review organization to be safe.

Judicial Review

"(n) Upon issuance of a regulation under section (m)(1)(A), a rejection under section (m)(1)(B), or the failure of the Secretary to act within ninety days of receipt of a report and recommendation under section (l), any person who will be adversely affected by the decision of the Secretary, and without regard to the provisions of subsection (f) of this section, may obtain judicial review in accordance with subsection (g) of this section.

Independent Review Organization

"(o)(1) The Secretary shall enter into an agreement with at least three organizations qualified to evaluate petitions seeking approval for the use of food and color additives to review such petitions and to make reports and recommendations on them. In assessing the qualifications of any such organization, the Secretary shall consider, among other relevant factors--

"(A) the scientific and technical capabilities of the organization and the persons employed by it;

"(B) the experience of the organization in evaluating petitions or similar applications for approval, or data of the type typically contained in petitions;

"(C) the ability of the organization to protect the confidentiality of trade secret and confidential commercial information;

"(D) the ability of the organization to undertake balanced and objective reviews of petitions and to be free of bias; and,

"(E) the ability of the organization to undertake competent and timely reviews of petitions.

"(2) The agreement between the Secretary and an independent review organization shall require the organization to conduct its reviews in accordance with the provisions of section 409 and regulations issued by the Secretary to implement that section. In performing its responsibilities under an agreement with the Secretary, such organization shall not be subject to the provisions of the Federal Advisory Committee Act, 5 U.S.C. App. 2.

"(3)The Secretary shall publish annually the fee schedule in effect for each independent review organization for the review of petitions in the twelve-month period succeeding the notice. The Secretary shall also prescribe appropriate terms for payment by the petitioner to the independent review organization, including terms to ensure that the independent review organization completes the tasks required under this section within the time periods set forth and that payments by the petitioner are contingent on timely completion of those tasks."

(e) Amend section 721 by adding a new subsection (g) to read as follows:

"(g) Notwithstanding any provision to the contrary in this section or any other provision of this Act, any person may file with the Secretary a petition seeking the issuance of a regulation authorizing the use of a color in or on a food, drug, device or cosmetic which petition requests designation for third party consideration under section 409 (b)(2)(F). Upon the acceptance for filing of any such petition, the provisions for third party consideration in section 409 (j)- (o) shall apply."

Food Contact Substances

(a) Amend section 409(a) by deleting "or" at the end of paragraph (1) and the period at the end of paragraph (2); insert a semicolon at the end of paragraph (2), followed by "or," and insert the following new paragraph (3):

"(3) in the case of a food contact substance as defined in subsection (p)(4), there is in effect, and it and its use or intended use are in conformity with, a notification submitted under subsection (p) of this section."

(b) Amend the concluding paragraph of section 409(a) to read as follows:

"While such a regulation relating to a food additive, or, in the case of a food contact substance, a notification, is in effect, a food shall not, by reason of bearing or containing such an additive or food contact substance in accordance with the regulation or notification, be considered adulterated within the meaning of clause (1) of section 402(a)."

(c) Amend section 409 by adding at the end thereof the following new subsection (p):

"(p)(1) At least 90 days before being introduced or delivered for introduction into interstate commerce, the manufacturer of a food contact substance shall notify the Secretary of the identity and intended use of the substance and provide the Secretary with information to establish either that the substance is not reasonably expected to become a component of food, if the manufacturer has elected to file a notification in such circumstance, or that the risk of the use of the substance under the intended conditions of use is negligible or insignificant.

"(2) A notification submitted under this paragraph shall become effective after ninety days unless the Secretary concludes that there is substantial evidence to demonstrate either that the food contact substance is reasonably expected to become a component of food, if that was the basis of the notification, or that the risks of the food contact substance under the intended conditions of use are not negligible or insignificant, in which case the Secretary shall promptly notify in writing the person who submitted the notification of such conclusion and the basis for it. The decision of the Secretary to deny effectiveness to a notification shall constitute final agency action subject to judicial review.

"(3) The Secretary shall keep confidential any information provided in a notification under paragraph (1) for 90 days following receipt. After the expiration of 90 days, the Secretary shall place the information on public display, except for matters in the notification which are trade secrets or confidential commercial information.

"(4) For purposes of this section and section 402, the term "food contact substance" means any substance intended for use as a component of materials used in commercially manufacturing, packing, packaging, transporting or holding food or other substances used in commercial food contact surfaces if such substance may reasonably be expected to result, directly or indirectly, in its becoming a component of food, and is not intended to have any physical or other technical effect in such food."

Health Claims Regulations

Approved Claims

As mandated by the 1990 Nutrition Labeling and Education Act, FDA regulates health claims that are permitted in food labeling. Currently the Agency allows claims for seven different diet/disease relationships, including:

- Calcium and osteoporosis;
- Fat and cancer;
- Saturated fat and cholesterol and coronary heart disease (CHD);
- Fiber-containing grain products, fruits and vegetables and cancer;
- Fruits, vegetables and grain products that contain fiber and the risk of CHD;
- Sodium and hypertension; and
- Fruits and vegetables and cancer.

Additionally, FDA has approved the use of a health claim regarding folic acid and neural tube defects. However, use of this health claim on foods fortified with folic acid is prohibited until the Agency finalizes its regulation on folic acid fortification that was proposed in 1993.

FDA also has outlined a procedure for those interested in petitioning the Agency for use of additional health claims. In response to such a petition, FDA recently issued a proposed health claim regulation regarding the relationship between oat bran/oatmeal and CHD.

Eligibility Requirements

FDA has outlined a number of eligibility requirements for foods bearing health claims.

1. The food does not exceed disqualifying levels of: 13 grams of fat; 4 grams of saturated fat; 60 milligrams (mg.) of cholesterol or 480 mg. of sodium per serving.
2. If the health claim is based on consuming lower amounts of a nutrient, the levels have to meet the definition of "low" for that nutrient. For example, a food making a claim about fat and cancer should contain no more than 3 grams of fat per serving.
3. If the claim is about eating more of a nutrient, the levels have to meet the definition of "high" for that nutrient. For example, foods with health claims about calcium and osteoporosis must contain at least 200 mg. of calcium, 20 percent of the RDI.
4. Foods must contain 10 percent or more of the Daily Value or Recommended Daily Intake for vitamin A, vitamin C, iron, calcium, protein or fiber per serving, prior to fortification. (This requirement is commonly referred to as the jelly-bean rule).
5. The claim must be communicated in the context of the total diet.

Proposed Amendments

On December 21, 1995 FDA issued a proposed rule to add flexibility to the use of health claims. Specifically the Agency's proposal would:

1. Authorize use of an abbreviated calcium/osteoporosis health claim on the front panel, in conjunction with a referral statement to the full claim elsewhere on the label;
2. Simplify the required elements of information that must appear as part of currently approved health claims;

3. Exempt from the jelly bean rule products that are composed solely of fruits or vegetables and enriched grain and bread products that conform to a standard of identity; and
4. Authorize a health claim petition procedure by which manufacturers could gain exemptions from the disqualifying levels for foods on a case-by-case basis.

Problems that Remain

Despite FDA's proposed regulations to simplify health claims the following issues remain unresolved.

1. Health claims can be approved for use only by FDA. However, other federal agencies such as the National Cancer Institute, have expertise in this area. FDA should permit use of health claims about diet/disease relationships that have been authorized by authoritative federal agencies responsible for public health protection/nutrition research or by an objective panel of qualified experts. This would ensure more expedited approvals in a time of limited resources. FDA maintains that it lacks the statutory authority to defer approval authority to other agencies or expert panels.
2. FDA's proposal to exempt specific food categories from the jelly-bean rule is misguided. It continues to ignore the important contribution of food fortification and the value of essential nutrients beyond those FDA narrowly has determined to be of "public health significance." It also reinforces the focus on individual foods as opposed to a total diet approach to health promotion. The jelly-bean should include additional essential nutrients versus a select few.
3. FDA's proposal to simplify health claims is commendable; as a result health claims on fat and cancer, sodium and hypertension and saturated fat, cholesterol and heart disease are improved. However, the information required for a number of claims results in lengthy claims that are inappropriate for the limited space available on food labels. For example: Low fat diets rich in fruits and vegetables (foods that are low in fat and may contain dietary fiber, vitamin A and vitamin C), may reduce the risk of some types of cancer. This claim could be further simplified: Low fat diets rich in fruits and vegetables may reduce the risk of some types of cancer.
4. Additionally, FDA's proposal to abbreviate the calcium/osteoporosis health claim provides little relief, especially for manufacturers of dairy products that typically have small labels/packages (yogurt, cheese, single-serving milk cartons, etc.). The proposed abbreviated claim: "Adequate calcium in a healthful diet may reduce the risk of osteoporosis. See side panel for more information," would need to be accompanied by a complete health claim on the side panel, "Especially for teen and young adult women, adequate calcium in a healthful diet may reduce the risk of osteoporosis later in life."
5. FDA should amend the disqualifying nutrient levels to disclosure levels when the disqualifying nutrient is unrelated to the specific health claim. For example, foods that are high in calcium should be allowed to make calcium/osteoporosis claims, regardless of the levels of fat or sodium, as these nutrients have no impact on the development of osteoporosis.

OPTIONAL FORM 99 (7-90)

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GENERAL SERVICES ADMINISTRATION

22 *New York Times* Saturday, Apr. 16, 1996 Streamlining the F.D.A., Safely

The Clinton Administration is making it easier for cancer patients to get promising drugs that have not been fully tested. By loosening some of the Food and Drug Administration's rules to accelerate access to experimental drugs, the White House may defuse more sweeping and dangerous reforms under consideration by Congress.

The F.D.A.'s job is to insure that drugs and medical devices are safe and effective and that food additives are risk-free. The agency gives approval only after lengthy clinical trials by the manufacturer. But many companies complain that the F.D.A. is slow to respond, escalating costs. In addition, some groups representing AIDS and cancer patients say that its bureaucracy denies them faster access to promising remedies.

Congress, the companies and the agency are now struggling to get drugs and medical devices to needy patients as quickly as possible without jeopardizing public health or sacrificing the standards of safety and efficacy that give consumers confidence in F.D.A.-approved products.

The Clinton Administration proposes faster approval for cancer-fighting drugs. Previously, the F.D.A. asked for proof that an experimental drug would help a patient's chances for survival or improve that patient's quality of life. Under the new rules, a drug can be approved based on a "partial" positive response, like shrinkage of a tumor. In addition, companies making experimental drugs that have already been approved overseas can seek permission to distribute those drugs to American cancer patients even before the F.D.A. has given final approval. These measures, which need no further approval, will take effect immediately and could apply to about 100 drugs under study.

The new initiatives are welcome but unlikely to appease Congress, which is pressing for more sweeping F.D.A. reform. Last month the Senate Labor and Human Resources Committee approved a bill sponsored by Nancy Kassebaum, Republican of Kansas, that calls on the agency to expedite clinical investigations of new drugs, devices and biological products as well as breakthrough drugs for life-threatening diseases. If the agency fails to review most applications within six months, the product sponsors could force it to contract with outside experts to complete the process.

Similarly, a bill being pushed on behalf of the House G.O.P. by James Greenwood of Pennsylvania sets tight approval deadlines and would turn over some F.D.A. review authority to third parties.

The F.D.A. would retain a supervisory role. But the outside experts and "third parties" envisioned in both the Senate and House bills could, under the guise of regulatory reform, lead to the privatization of many of the F.D.A.'s functions and undermine its role as an independent government protector of public health.

The drive to reform the F.D.A. comes at a time when the agency has been improving its performance. In 1994, 96 percent of new drug applications were approved within the 12 months allotted under current law, and the agency has been streamlining many of its internal procedures. Important life-enhancing drugs and medical devices should obviously get to consumers as quickly as possible. That is what the Administration's new cancer drug initiative aims to do. But safety and effectiveness should not be sacrificed for efficiency. At the moment, the Administration seems more mindful of that than Congress.

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