

Calendar No. 105

105TH CONGRESS }
1st Session }

SENATE

{ REPORT
{ 105-43

FOOD AND DRUG ADMINISTRATION MODERNIZATION AND
ACCOUNTABILITY ACT OF 1997

JULY 1, 1997.—Ordered to be printed

Filed, under authority of the order of the Senate of June 27, 1997

Mr. JEFFORDS, from the Committee on Labor and Human
Resources, submitted the following

REPORT

together with

ADDITIONAL AND MINORITY VIEWS

[To accompany S. 830]

The Committee on Labor and Human Resources, to which was referred the bill (S. 830) to amend the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act to improve the regulation of food, drugs, and biological products, and for other purposes, having considered the same, reports favorably thereon with an amendment in the nature of a substitute and recommends that the bill (as amended) do pass.

CONTENTS

	Page
I. Purpose and summary	2
II. Background and need for the legislation	6
III. Legislative history and votes in committee	11
IV. Explanation of the legislation and committee views	15
V. Cost estimate	69
VI. Regulatory impact statement	74
VII. Section-by-section analysis	75
VIII. Additional views	101
IX. Minority views	107
X. Changes in existing law	113

to it to contract for outside expert review when such contracts would achieve more timely and efficient reviews.”

Information program on clinical trials for serious or life-threatening diseases

Sec. 808 amends section 402 of the Public Health Services Act to establish a registry of clinical trials, both publicly or privately funded, of experimental drugs and biologicals for serious or life-threatening medical conditions. Registry information must be understandable to the general public and include the purpose of the experimental protocol, trial eligibility criteria, and sites and contact points for people wishing to enroll in a trial. Patients, health care providers, researchers and the public would access the registry through toll-free telephone communications and other information systems. Sec. 808 also requires the Secretary of HHS, within 2 years after enactment, to investigate and report on whether it is necessary or feasible to include medical device trials in the registry. The purpose of the registry is to simplify the process through which individuals with serious or life-threatening medical conditions obtain information about opportunities to participate in clinical trials of experimental therapies.

Pharmacy compounding

Section 809 of S. 830 is intended to clarify the application of the Federal Food, Drug and Cosmetic Act to the professional practice of pharmacist compounding of drug products. States currently have the authority to license pharmacists and regulate pharmacies, including the scope of pharmacy practice. All States include compounding as a core component of the profession of pharmacy. While the Food, Drug and Cosmetic Act specifically exempts pharmacies from inspection and registration provisions of the Act, it has been the contention of the Food and Drug Administration that compounded products are not exempt from the Act's new drug provisions. The committee has found that clarification is necessary to address current concerns and uncertainty about the Food and Drug Administration's regulatory authority over pharmacy compounding.

The committee has worked extensively with the Food and Drug Administration and other interested parties to reach consensus on how to ensure continued availability of compounded drug products as a component of individualized therapy, while limiting the scope of compounding so as to prevent small-scale manufacturing under the guise of compounding. Section 809 establishes parameters under which compounding is appropriate and lawful. This section is not intended to subvert the requirements that apply to investigational new drugs or to result in experimentation without appropriate human subject protections, including proper informed consent.

The views of the Committee with respect to certain subsections of Section 809 are outlined below:

The exemptions in section (h)(1) are limited to compounding for an individual patient based on the medical need of such patient for the particular drug compounded. To qualify for the exemptions, the pharmacist or physician must be able to cite a legitimate medical need for the compounded product that

would explain why a commercially available drug product would not be appropriate. Although recording the medical need directly on each prescription order would not be required, this technique would be one of many acceptable ways of documenting the medical need for each compounded drug product. This medical need would not include compounding drugs that are essentially copies of commercially available drug products for largely economic reasons. The pharmacist may rely on appropriately documented input from the physician as to whether a commercially available drug product is not appropriate for the identified individual patient.

Implementation of subsection (h)(1)(B)(I)(I)(bb), regarding bulk drug substances, is expected to coincide with the implementation of subsection (h)(3), except that compliance with the standards of an applicable United States Pharmacopeia monograph is not dependent on any further implementation under subsection (h)(3).

Among other requirements, a bulk drug substance used for compounding must have been manufactured in an establishment that has registered under section 510 of the Act. In addition to applying to domestic manufacturing establishments, this requirement shall also apply to foreign establishments, once the requirement in section 801 of this Act, which requires foreign establishments to register and list under section 510 of the Act, becomes effective.

In compliance with subsection (h)(1)(B)(I)(III), pharmacists may retain each certificate of analysis until the supply of such bulk drug substance has been exhausted, and must record in the compounding record the manufacturer, repackager (if any), and the lot number of the bulk drug substance.

The list published pursuant to subsection (h)(1)(B)(iv) includes drug products that have been withdrawn or removed from the market because the finished drug product and/or a component thereof has been found to be unsafe or not effective. The Federal Register document that includes the list should briefly describe the basis for the withdrawal or removal and provide interested parties with an opportunity to comment. The list should not include products that have been withdrawn or removed solely because of manufacturing issues.

Interested parties should be allowed to petition, under 21 CFR § 10.30, to change the listing of a particular drug product under subsection (h)(1)(B)(v) should research and technology yield advances which correct the compounding difficulties.

Regarding subsection (h)(2)(B), until the State agency of jurisdiction in which the pharmacy is located enters into a memorandum of understanding (MOU) with the Secretary or 180 days after the development of the standard MOU, whichever comes first, the exemption shall not apply if inordinate quantities of compounded products are distributed outside of the State in which the compounding pharmacy or physician is located. "Inordinate" quantities means amounts typically associated with ordinary commercial drug manufacturing.

As required under subsection (h)(3), the Secretary will be required to promulgate regulations limiting compounding to drug

substances that are components of drug products approved by the Secretary and to other drug substances as the Secretary may identify. It is expected that the Secretary's regulations would allow compounding with drug products, or the components of drug products, that are lawfully distributed, including drug products that are not new drugs under 21 U.S.C. § 321(p) and drug substances that authorized for use under an effective Investigational New Drug application (IND) protocol under 21 U.S.C. § 355(I) and 21 CFR Part 312. The FDA may, in development of the list for other substances approved for compounding, consult with pharmacy organizations and other interested parties, beyond the United States Pharmacopeia.

V. COST ESTIMATE

U.S. CONGRESS,
CONGRESSIONAL BUDGET OFFICE,
Washington, DC, June 27, 1997.

Hon. JAMES M. JEFFORDS,
Chairman, Committee on Labor and Human Resources, United States Senate, Washington, DC.

DEAR MR. CHAIRMAN: The Congressional Budget Office has prepared the enclosed cost estimate for S. 830, the Food and Drug Administration Modernization and Accountability Act of 1997.

If you wish further details on this estimate, we will be pleased to provide them. The CBO staff contact is Anne Hunt.

Sincerely,

JUNE E. O'NEILL, *Director.*

S. 830—Food and Drug Administration Modernization and Accountability Act of 1997

Summary: S. 830 would reauthorize the Prescription Drug User Fee Act (PDUFA) of 1992, which empowers the Food and Drug Administration (FDA) to collect user fees from the pharmaceutical industry. The user fee program would be reauthorized, with some modifications, for an additional five years. The bill would also amend the Food, Drug and Cosmetic Act (FD&CA) and the Public Health Service Act to reform the FDA's regulatory and approval processes for drugs, biological products, devices, foods and animal drugs. One provision would grant a six-month extension of market exclusivity for pharmaceutical manufacturers who conduct pediatric studies on select prescription drugs.

CBO estimates that enacting S. 830 would result in net additional discretionary spending of \$63 million in 1998 and \$445 million over the 1998–2002 period, assuming appropriation of the authorized amounts. Reauthorizing the user fee program would yield \$601 million in offsetting collections over five years; these amounts would also be authorized to be spent, subject to appropriation. Extending market exclusivity for certain drugs would increase direct spending by \$65 million over the 1998–2002 period.

By preempting state and local laws that regulate nonprescription drugs differently than federal law, S. 830 would impose an intergovernmental mandate as defined in the Unfunded Mandates Reform Act (UMRA). CBO estimates that compliance with this man-

the Director of the CDC, the Secretary shall establish a data bank of information on clinical trials for drugs, and biologicals, for serious or life-threatening diseases and conditions. The Secretary shall collect, catalog, store and disseminate this information through information systems, which must include toll-free telephone communications and be available to persons with serious or life-threatening diseases and conditions, the public, health care providers and researchers.

The Data Bank must include: (A) a registry of clinical trials of experimental treatments for serious or life-threatening diseases or condition that describes the purpose of each experimental drug or biological protocol, either with the consent of the sponsor or when a trial to test efficacy begins. The information shall consist of eligibility criteria, location of trial sites, point of contact, in a form readily understood by the public, and must be forwarded to the data bank by the sponsor of the trial not later than 21 days after the approval by the FDA; (B) information pertaining to treatments that may be available under a treatment investigational new drug application that has been submitted to the FDA under pertinent regulations or as a Group C cancer drug. The Bank may include information relating to the results of clinical trials, with the consent of the sponsor, including potential toxicities or adverse effects. It shall not include information relating to an investigation if the sponsor has certified to the Secretary that disclosure will substantially interfere with the timely enrollment of subjects in the investigation. To carry out the program, the bill authorizes to be appropriated such sums as may be necessary, and fees collected under section 736 of the Act shall not be used or appropriated for this.

Section 808(b) provides that the Secretary, the Director of NIH, and the Commissioner shall collaborate to determine the feasibility of including device investigations within the registry. Within two years of enactment, the Secretary must prepare and submit to the Senate Committee on Labor and Human Resources and the House Committee on Commerce a report that considers, among other things, the public health need for including devices and the adverse impact, if any, on device innovation and research if information on devices is publicly disclosed.

Sec. 809. Application of Federal Law to the Practice of Pharmacy Compounding.

Section 809 amends section 503 of the FFDCA by adding the new subsection (h). New subsection (h)(1) provides that sections 501(a)(2)(B) [Adulterated drug], 502(f)(1) [Misbranded drug], 502(1) [Antibiotic drug], 505 [New drugs], and 507 [Certification of antibiotics] shall not apply to a drug product that is compounded for an identified patient based on a medical need for a compounded product (1) by a licensed pharmacist in a State licensed pharmacy or Federal facility or licensed physician on the prescription order of a physician or other licensed practitioner authorized by State law to prescribe drugs; (2) by a licensed pharmacist or licensed physician in limited quantities, before receiving a valid prescription order for an identified individual if the compounding of the drug is based on a history of receiving valid orders that have been generated solely within an established relationship between the phar-

macist and the individual patient or the physician or other licensed practitioner who will write the prescription order.

The above noted sections of the FFDCE shall not apply to a drug product if the pharmacist or physician (1) compounds a drug product using bulk drug substances that meet the requirements of this section; (2) compounds a drug product using ingredients other than bulk drug substances that comply with an applicable U.S. Pharmacopeia monograph and the U.S. Pharmacopeia chapter on pharmacy compounding; (3) does no more than advertise or promote the compounding service and does not advertise or promote the compounding of a particular drug, class of drug or type of drug; (4) does not compound a drug product that appears on a list published by the Secretary of drug products that have been withdrawn or removed from market because it is unsafe or not effective; (5) does not compound a particular drug product that is identified by the Secretary in regulation as having demonstrable difficulties in being compounded that reasonably demonstrate an adverse affect on the safety and effectiveness of that drug product; and (6) does not distribute compounded drugs outside the State in which the pharmacy is located, unless the State agency of jurisdiction has entered into a memorandum of understanding (MOU) with the Secretary based on adequate regulation of compounding performed in the State, which provides for appropriate investigation of complaints by the State agency relating to compounded products distributed outside the State.

In cooperation with the National Association of Boards of Pharmacy, the Secretary is required to develop a standard MOU for use by States in complying with the subsection relating to distribution outside the State. Until 180 days after the standard MOU is developed or the date entered in the MOU, whichever is first, the subsection relating to distribution outside the State [new section 503(h)(2)(vi)] does not apply to a pharmacist or physician who does not distribute inordinate amounts of compounded drugs out of State.

Section 809(b) requires the Secretary, after consultation with the U.S. Pharmacopeia, to develop regulations limiting compounding to drug substances that are components of drug products approved by the Secretary and other substances identified by the Secretary. Sections 809 (c) and (d) state that new section 503(h)(1) shall not apply to compounded positron emission tomography drugs, as defined in section 202(jj), or radiopharmaceuticals.