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Dietary Supplement and Nonprescription Drug Consumer Protection Act (P.L. 109-462)

Donna V. Porter, Domestic Social Policy Division

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Donna V. Porter
Specialist in Life Sciences
Domestic Social Policy Division

Summary

A bipartisan bill, the Dietary Supplement and Nonprescription Drug Consumer Protection Act (S. 3546) was introduced on June 21, 2006, and became law (P.L.109-462) on December 22, 2006. The law requires reports of serious adverse events to be submitted to the Food and Drug Administration (FDA) by manufacturers of dietary supplements and nonprescription drugs. Lawmakers were told of the limitations of data on adverse events attributed to dietary supplements during hearings on the dietary supplement ingredient ephedra held during several Congresses. This report provides background information on P.L.109-462 and summarizes its provisions. It will be updated as new action occurs.

On June 21, 2006, the Dietary Supplement and Nonprescription Drug Consumer Protection Act (S. 3546) was introduced by Senator Hatch, with Senators Durbin, Harkin, Enzi, and Kennedy as cosponsors. S. 3546 was referred to the Senate Committee on Health, Education, Labor, and Pensions (HELP), which ordered the measure reported on June 28, 2006. The committee report was printed on September 5, 2006.[1] The bill passed the Senate by unanimous consent on December 6, 2006, and passed the House under suspension of the rules on December 9. The law amends the Federal Food, Drug, and Cosmetic Act (FDCA) to require manufacturers of dietary supplements (DS) and over-the-counter (OTC) drugs[2] to report serious adverse events to the FDA. This report provides some background on dietary supplement regulation and adverse event reporting, and summarizes the law. Updates will be provided as additional action occurs.

[1] U.S. Congress, Senate Committee on Health, Education, Labor and Pensions, *Dietary Supplement and Nonprescription Drug Consumer Protection Act*, report to accompany S. 3546, 109th Cong., 2nd sess., S.Rept. 109-324 (Washington: GPO, 2006).

[2] The terms nonprescription and over-the-counter (OTC) drugs will be used interchangeably in this report.

Background

Prior to passage of the Dietary Supplement Health and Education Act of 1994 (DSHEA; P.L. 103-417), dietary supplements were regulated under the general food provisions of FDCA. DSHEA set out a separate regulatory framework for supplements for the first time. FDA promulgated regulations for most provisions of the new statute within several years of enactment, including definitions, safety, third-party literature, nutritional support statements, ingredient and nutrition labeling, and new dietary ingredients. DSHEA also created an Office of Dietary Supplements at the National Institutes of Health. The regulations on good manufacturing practices (GMPs) remain to be completed, although FDA has announced plans to publish the final rule by December 2006.

DSHEA established procedures for dietary supplements (DS) that differ from those that FDCA requires for prescription drugs. Under FDCA, a drug manufacturer must submit evidence of the safety and effectiveness of a product based on human clinical trials before the FDA can approve a drug for sale in the United States. Marketing of a supplement product, however, can begin without evidence of safety or effectiveness being submitted to the agency. DSHEA placed the burden of proof on the FDA to demonstrate that supplements were unsafe after they were on the market. This provision is different from the burden of proof placed on manufacturers of all other FDA-regulated products to demonstrate that products are safe before they are placed on the market.

Adverse event reporting was not part of the legislative debate when DSHEA was being considered. There was no requirement in either DSHEA or the implementing regulations for manufacturers to report adverse events to the agency. This issue came to the attention of Congress during hearings following media reports of consumers experiencing health problems after using ephedra.[3] In 1997, after receiving hundreds of reports of adverse events attributed to ephedra-containing supplements, the FDA proposed to restrict the dosage, prohibit formulations containing other stimulants and require warnings on ephedra-containing products. The FDA's proposed rule was criticized for the lack of scientific evidence to support it.[4] A Government Accountability Office (GAO) report that reviewed the scientific basis for the FDA ephedra proposal raised concerns about the process by which FDA had compiled the reports on the harmful effects of ephedra, and concluded that the agency lacked adequate data to set dosage levels.[5] When manufacturers were asked if they had any adverse event reports, some denied having any such information on their products. However, the FDA and Congress subsequently learned that some companies did have adverse event reports.

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[3] See CRS Report RL30750, *Dietary Supplements: Ephedra*, by Donna V. Porter.

[4] U.S Dept. of Health and Human Services (HHS), Food and Drug Administration, *Dietary Supplements Containing Ephedrine Alkaloids.* Proposed rule, *Federal Register,* v. 62, June 4, 1997, pp. 30678-30724.

[5] U.S. General Accounting Office, (now known as the Government Accountability Office,) *Dietary Supplements: Uncertainties in Analyses underlying FDA's Proposed Rule on Ephedrine Alkaloids,* GAO/HEHS/GGD-99-90, July 1999, p. 79.

Since 1972, mandatory reporting of adverse events to FDA has been required of prescription drug manufacturers when they learn that consumers have experienced undesirable effects from use of their products.[6] By regulation, prescription drug manufacturers must report all serious and unexpected adverse drug experiences that they become aware of to FDA within 15 days.[7] This postmarket reporting system allows the agency to determine whether there are patterns of adverse events in the general population using the drug that are serious enough to warrant focused study or some type of regulatory action. Drugs in clinical trials prior to FDA approval are tested in study populations that are much smaller than the number of anticipated potential users, so until a drug is on the market the agency has only limited evidence of side effects that may occur. These postmarket requirements for prescription drugs do not apply to nonprescription drug products.

In 1993, FDA expanded its postmarket surveillance capabilities by establishing a voluntary reporting system called MedWatch.[8] The agency designed the MedWatch program to facilitate its use by health professionals (i.e., physicians, nurses, pharmacists) and consumers through voluntary reporting of side effects and other health problems that they suspect are related to the use of prescription drugs and medical devices. The system also allows the reporting of adverse effects associated with the use of OTC drugs, dietary supplements, infant formulas and medical foods. When adverse events are reported to FDA, they are entered into the MedWatch's postmarketing surveillance database for further evaluation. The collected data are analyzed to assess whether the relationship between the use of a product and the reported adverse events might be causal. If a relationship is determined to be supported by the evidence in the database, the information is forwarded to the appropriate center officials to decide on further study, and whether public notification is needed.

Provisions of P.L.109-462

Definitions. For both OTC drugs and DS, a *serious adverse event* is defined as one that results in death, a life-threatening experience, inpatient hospitalization, a persistent or significant disability or incapacity, a congenital anomaly or birth defect, or requires medical or surgical intervention. The term *serious adverse event report* means a report that is required to be submitted to the Secretary under this act. The bill defines an *adverse event* for nonprescription drugs to mean any adverse health-related event associated with the use of an OTC drug, including an overdose (whether accidental or intentional), drug abuse, drug withdrawal or any failure of expected pharmaceutical action of the drug. For a dietary supplement (DS), an *adverse event* is defined as any health-related event associated with the use of a DS that is adverse. (The law does not outline the detail for DS that it does for OTC drugs.)

Reporting. For both OTC drugs and DS, the law would require a manufacturer, packer or distributor whose name appears on the label of the product (referred to as the responsible person) to submit to FDA any report received of a *serious adverse event*

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[6] See CRS Report RL30989, *The U.S. Drug Approval Process: A Primer*, by Blanchard Randall.

[7] 21 C.F.R. 314.80.

[8] Ibid.

associated with a OTC drug or DS product used in the United States, along with a copy of the label or information within the retail package of the product. Reports are to be submitted to FDA within 15 days of receipt by the manufacturer and any additional new medical information related to a case received within a year of the initial report is to be submitted within 15 days. The Secretary is to develop systems to ensure consolidation of reports for a single case. The Secretary is also to establish an exemption to the reporting requirements, if he determines that such an exemption would have no adverse effect on public health. Each serious adverse event report is to be submitted to the Secretary using a MedWatch form that has been modified for OTC drugs and DS, and may be accompanied by additional information. A manager's amendment on the bill, as adopted by the Senate HELP Committee, included a provision that would allow FDA to take action against foreign manufacturers that do not comply with these reporting requirements.

For DS, a retailer whose name appears on the label as a distributor may, through an agreement, authorize the DS manufacturer or packer to submit required reports to the Secretary, as long as the retailer provides to the manufacturer or packer notice of all adverse events associated with a DS that are reported to the retailer through the address or telephone number on the label. (The law contains no comparable provision on OTC drugs.)

Record Keeping. For both OTC drugs and DS, records for each adverse event report are to be maintained by the manufacturer for six years. The responsible person would be required to provide access to these records for a designated officer or employee of the Department of Health and Human Services (HHS) during a factory inspection. A serious event report including any new medical information, submitted to the Secretary, is to be considered a safety report. If it is released for public disclosure, the report may be accompanied by a statement that denies that the report or records constitute an admission that the product involved caused, or contributed to the adverse event. All personal identification information must be redacted from any record that is released under the Freedom of Information Act.

Preemption. For both OTC drugs and DS, no state or local government can establish or continue in effect any requirements related to a mandatory system for adverse event reports for OTC drugs or DS that are different from the provisions of this act. This provision does not affect the Secretary's authority to provide adverse event reports and information to any health, food or drug official or employee of any state, territory or political subdivision under a memorandum of understanding currently in effect. However, the personally identifiable information in adverse event reports provided by the Secretary to employees in other jurisdictions is not to be made public or otherwise disclosed without written consent of both the Secretary and the individual who submitted the report. A safety report may not be used to suggest that the information is an admission that the OTC drug or DS product caused or contributed to the adverse event.

Authorized Appropriations. For both OTC drugs and DS, the law would authorize appropriations of such sums as may be necessary to carry out the provisions on serious adverse event reporting.

Miscellaneous Provisions. For OTC drugs, the Secretary may modify requirements under the provisions of the act to maintain consistency with international harmonization efforts over time. (DS were exempted from all international harmonization efforts under provisions of the FDA Modernization Act of 1997.)

For both OTC drugs and DS, the labeling provisions would be amended to require that a product marketed in the United States bears the address or phone number of the person who is responsible for receiving any reports of a serious adverse event (e.g. the manufacturer). The amendments would take effect and apply to any OTC drug or DS product labeled on or after the date that is one year after the date of enactment. Within 270 days of enactment, the Secretary is to issue guidance on the minimum data elements that are to be included in a serious adverse event report.

Prohibition of Falsification of Reports. For OTC drugs and DS, the FDCA provisions would be amended to prohibit the falsification of a serious adverse event report submitted to a responsible person or the Secretary of HHS. This prohibition takes effect one year after the date of enactment.

Issues

Several earlier bills included provisions on mandatory reporting of adverse events for dietary supplements, but none saw any legislative action. A Senate amendment to the FY2006 Defense Appropriations legislation would have prohibited the sale of dietary supplements on military facilities unless there was mandatory reporting of adverse events. While that amendment was not adopted, interested parties in Congress and in the supplement industry and consumer community agreed to work on provisions that would achieve mandatory reporting by manufacturers. As a result, S. 3546, a bipartisan bill, was introduced on June 21, 2006, with the support of numerous trade associations and consumer groups, including the Consumers Union, the Center for Science in the Public Interest, the Consumer Health Care Products Association, the National Nutritional Foods Association, the Council for Responsible Nutrition, the American Herbal Products Association and the Utah Natural Products Association.

The requirements for mandatory reporting of serious adverse events for DS and OTC drugs would provide an opportunity for FDA to improve its ability to monitor and evaluate the potential adverse events associated with the use of these products. A single report of an incident alleged to be associated with a specific product is not necessarily indicative of a product with problems. However, the accumulation of numerous such reports attributed to a given product may indicate a trend for which the agency needs to take further action.

Information in a standard form received in a timely manner with identification to a specific product will also assist the agency. One problem that arose over the reports on ephedra was that they were incomplete, making it virtually impossible to successfully draw conclusions about what had occurred to individuals who allegedly had taken ephedra-containing products. The FDA's decision to regulate the sale of ephedra based on incomplete reporting of adverse events was cited in the 1999 GAO report, which subsequently led to the withdrawal of some provisions in the agency's proposed rule.

The mandatory reporting requirements of P.L.109-462 are similar to the regulatory requirements for the postmarketing surveillance system that FDA relies on for monitoring

the safety of prescription drugs. By comparison, MedWatch is a system that relies on health care professionals and consumers for voluntarily reporting concerns about products. A 2000 GAO study estimated that FDA receives reports on no more than 10% of all adverse drug events, providing data that is fragmentary and inconsistent.[9] A recent GAO drug safety report has suggested that FDA's postmarket decision-making and oversight process needed improvements.[10] Among its recommendations, GAO concluded that FDA needed to improve the process for establishing a mechanism for systematically tracking postmarket drug safety issues.

According to FDA, once it receives the data, whether from manufacturers or through the MedWatch program, the agency needs sufficient resources in terms of personnel with expertise to evaluate the data. In response to a question raised at the press conference when the bill was introduced, Senators indicated that the FDA has estimated that it would need $4 million to implement the bill's provisions, i.e., $2 million to implement the OTC drug provisions and $2 million to implement the DS provisions. The Congressional Budget Office estimates that implementing P.L.109-462 will result in additional discretionary outlays of $3 million in 2007 and $50 million over 2007-2011, assuming that the necessary funds are appropriated.[11] While the law authorizes such sums as are needed to implement the bill, it is unclear whether FDA will request or the Congress will appropriate such funding, now that the bill is enacted.

Finally, the law contains no provisions that address enforcement of mandatory serious adverse event reporting by manufacturers of OTC drugs and DS products. The ability of FDA to receive accurate data on adverse events would seem to require some type of enforcement mechanism or penalties. In the case of prescription drugs, failure to maintain records may result in FDA withdrawal of approval for marketing a drug. Such a provision could be applied to an OTC drug. However, no approval is needed for the marketing of dietary supplements, so this approach would not be useful.

Proponents say the surveillance of serious adverse events associated with OTC drugs and DS can only be successful if manufacturers, packers, distributors and retailers report to FDA when they receive information on events that may be linked to their products. A parallel system that requires information on every package with the intent to encourage health care professionals and consumers to report directly to the agency would also facilitate data collection, they say. In this view, providing MedWatch contact information on product packages, which the law does not do, might be an additional way to improve the agency's database on adverse events. Others observe that public education program, in conjunction with the MedWatch contact information on packaging, may be needed to promote voluntary reporting to the agency.

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[9] GAO *Adverse Drug Events: The Magnitude of Health Risk is Uncertain Because of Limited Incidence Data*, GAO/HEHS-0021, Jan. 18, 2000.

[10] GAO, *Drug Safety: Improvement Needed in FDA's Post Market Decision-making and Oversight Process*, March 2006, GAO-06-402, p. 67.

[11] CBO, S. 3546, *Dietary Supplement and Nonprescription Drug and Consumer Protection Act.* Cost Estimate. As reported by the Senate Committee on Health, Education, Labor and Pensions September 5, 2006, 8 p.