

final rule modified the Class E airspace area at Omaha, NE.

**EFFECTIVE DATE:** 0901 UTC May 22, 1997.

**FOR FURTHER INFORMATION CONTACT:**

Kathy Randolph, Air Traffic Division, Operations Branch, ACE-530C, Federal Aviation Administration, 601 E. 12th Street, Kansas City, MO 64106; telephone (816) 426-3408.

**SUPPLEMENTARY INFORMATION:**

**History**

**Federal Register** Document 97-2419, Airspace Docket No. 96-ACE-21, published on January 31, 1997 (62 FR 4631), revised the descriptions of the Class E airspace area at Omaha, NE. A typographical error was discovered in the geographic coordinates. In addition, the Class E airspace area description is revised to remove the phrase "excluding that portion which lies within the Eppley Airfield and Offutt AFB Class E5 airspace". This action corrects those errors.

**Correction to Final Rule**

**§ 71.1 [Corrected]**

Accordingly, pursuant to the authority delegated to me, on page 4632, column 2, § 71.1, the geographic coordinates and airspace description of the Class E airspace area at Omaha, NE, as published in the **Federal Register** on January 31, 1997 (62 FR 4631) (**Federal Register** Document 97-2419) are corrected to read as follows:

**ACE NE E5 Omaha, NE [Corrected]**

Eppley Airfield, NE

(Lat 41°18'09" N., long. 95°53'39" W.)

Offutt AFB, NE

(Lat. 41°07'06" N. long. 95°54'45" W.)

Council Bluffs Municipal Airport, IA

(Lat 41°15'34" N., long. 95°45'36" W.)

That airspace extending upward from 700 feet above the surface within a 6.9-mile radius of the Eppley Airfield and within 3 miles each side of the Eppley Airfield ILS localizer course to Runway 14R extending from the 6.9-mile radius to 12 miles northwest of the airport and within a 7-mile radius of Offutt AFB and within 4.3 miles each side of the Offutt ILS localizer course extending from the 7-mile radius to 7.4 miles southeast of the AFB and within a 6.3-mile radius of the Council Bluffs Municipal Airport.

\* \* \* \*

Issued in Kansas City, MO on March 18, 1997.

**Herman J. Lyons, Jr.,**

Manager, Air Traffic Division, Central Region.  
[FR Doc. 97-12239 Filed 5-12-97; 8:45 am]

**BILLING CODE 4910-13-M**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Part 172**

[Docket No. 87G-0351]

**Food Additives Permitted for Direct Addition to Food for Human Consumption; 1,3-Butylene Glycol**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule.

**SUMMARY:** The Food and Drug Administration (FDA) is amending the food additive regulations to provide for the safe use of 1,3-butylene glycol as a formulation and processing aid in the manufacture of edible sausage casings. This action is in response to a petition filed by Teepak, Inc.

**DATES:** Effective May 13, 1997; written objections and requests for a hearing by June 12, 1997. The Director of the Office of the Federal Register approves the incorporation by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51 of a certain publication listed in new § 172.712, effective May 13, 1997.

**ADDRESSES:** Submit written objections to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** James C. Wallwork, Center for Food Safety and Applied Nutrition (HFS-215), Food and Drug Administration, 200 C St. SW., Washington, DC 20204-0001, 202-418-3078.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

In accordance with the procedures described in § 170.35 (21 CFR 170.35), Teepak, Inc., 915 North Michigan Ave., Danville, IL 61832-0597, submitted a petition (GRASP 7G0332) requesting that 1,3-butylene glycol be affirmed as generally recognized as safe (GRAS) for use in food as a formulation and processing aid, when used in accordance with current good manufacturing practice.

FDA published a notice of filing of this petition in the **Federal Register** of November 23, 1987 (52 FR 44936), and gave interested parties an opportunity to submit comments concerning the petition to the Dockets Management Branch (address above). FDA received no comments in response to that notice.

After the petition was filed, the petitioner amended the petition to limit

the scope of the requested GRAS affirmation. As amended, the petition asks FDA to affirm 1,3-butylene glycol as GRAS for use only as a formulation and processing aid in the manufacture of edible sausage casings.

**II. Standard for Evaluation of Petition**

Under § 170.30 (21 CFR 170.30), general recognition of safety may be based only on the views of experts qualified by scientific training and experience to evaluate the safety of substances added to food. The basis of such views may be either: (1) Scientific procedures, or (2) in the case of a substance used in food prior to January 1, 1958, experience based on common use in food (§ 170.30(a)). General recognition of safety based upon scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of the substance as a food additive and ordinarily is to be based upon published studies, which may be corroborated by unpublished studies and other data and information (§ 170.30(b)). In its petition, Teepak, Inc., has not claimed a history of common use in food before 1958, but rather has relied upon scientific procedures, primarily published scientific papers, to support its claim that 1,3-butylene glycol is GRAS.

In reviewing the data in the petition and other relevant material, FDA noted that the published studies on the safety of 1,3-butylene glycol are of varying quality. As discussed in section IV. of this document, the agency believes that the available data, taken together, establish the safety of 1,3-butylene glycol for the limited use requested in the petition. However, FDA does not believe that the data are sufficient to show that the basis for such a safety determination is generally recognized by experts in the field.

Thus, in accordance with 21 CFR 170.35(c)(5) and 170.38, the agency has determined that the requested use of 1,3-butylene glycol cannot be considered GRAS based upon scientific procedures and that the compound is a food additive subject to section 409 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348). FDA notified the petitioner of this conclusion and the firm agreed that 1,3-butylene glycol could be evaluated as a food additive rather than as a GRAS ingredient.

**III. Introduction**

**A. Identity**

1,3-Butylene glycol  
(CH<sub>2</sub>OHCH<sub>2</sub>CHOHCH<sub>3</sub>, CAS Reg. No.

107-88-0, and molecular weight 90.12) is the common name for 1,3-dihydroxybutane or 1,3-butanediol. It is a clear, colorless, hygroscopic, viscous liquid almost without odor.

#### *B. Regulated Food and Packaging Uses*

1,3-Butylene glycol is regulated for use under 21 CFR 173.220 *1,3-Butylene glycol* as a solvent for natural and synthetic flavoring substances, except where food standards preclude its use. Also, 1,3-butylene glycol is regulated for use in polyester formation under 21 CFR 175.320 *Resinous and polymeric coatings for polyolefin films* and as a reactant under 21 CFR 177.1680 *Polyurethane resins* in the preparation of resins for use in contact with dry bulk foods.

### **IV. Safety**

#### *A. Manufacturing Process*

1,3-Butylene glycol is produced through the controlled aldol condensation of acetaldehyde in the presence of dilute aqueous sodium hydroxide. The first reaction product, a trimer of acetaldehyde, is decomposed to a dimer, acetaldol (3-hydroxy-butyraldehyde), during the neutralization of the excess sodium hydroxide with dilute acetic acid. The unreacted acetaldehyde is removed by distillation. Acetaldol is then reduced to butylene glycol by hydrogenation in the presence of a nickel catalyst. 1,3-Butylene glycol thus produced is purified in a series of vacuum distillation towers. The product is manufactured to conform to the identity and specifications listed in the monograph entitled "1,3-Butylene Glycol" in the Food Chemicals Codex, 4th ed. (1996), p. 52.

#### *B. Proposed Use in Food*

The petition contains data demonstrating that 1,3-butylene glycol is effective in reducing breakage in manufactured sausage casings. The petition also contains data demonstrating that the petitioned substance is most effective at levels of 5 to 15 percent of the liquid phase of the casing (equivalent to 2 to 6 percent of the total casing weight). Included in the petition are data demonstrating that at levels higher than 6 percent, 1,3-butylene glycol sausage casings become more susceptible to breakage. Thus, the petition provides data demonstrating that the proposed ingredient is technologically self-limiting.

#### *C. Consumer Exposure*

Using sausage intake data from the Market Research Corp. of America (Ref. 1) and assuming from information

submitted with the petition that 1 percent of the weight of sausage is casing made with 6 percent 1,3-butylene glycol, FDA estimates that exposure to the proposed ingredient is 6.0 milligrams/person/day (mg/p/d) (mean) and 12 mg/p/d (90th percentile) for the 2+ years age group. For the 2- to 5-year-old age group subcategory, FDA estimates that exposure is 4.5 mg/p/d (mean) and 8.5 mg/p/d (90th percentile).

#### *D. Toxicology*

To provide evidence of the safety of 1,3-butylene glycol for the petitioned use, the petitioner provided published and unpublished reproduction and chronic feeding studies in rats and dogs, as well as a number of published short-term nutrition and metabolism studies. In addition, an agency-initiated literature search identified a reproduction study with 1,3-butylene glycol published in 1990.

A published 2-year dietary feeding study (Ref. 2) in beagle dogs reported no visible adverse effects on appearance, behavior, growth, food intake, urinalysis, hematology or serum biochemistry that could be attributed to treatment with 1,3-butylene glycol. The diets of male and female dogs were treated with the petitioned substance at 118, 228, and 613 mg/kilogram body weight/day (mg/kg bw/d) for males and 101, 228, and 732 mg/kg bw/d for females. Although microscopic lesions were observed in testes and lymph nodes of males after 1 and 2 years' treatment, FDA concludes that the lesions do not appear to be of pathological significance. Lesions of the type and severity observed are frequent incidental findings in dogs. Moreover, no significant difference in appearance between lesions in control and treated animals could be derived from the histopathological descriptions of the tissues examined. Therefore, the agency finds that the incidence of gross pathological lesions is unrelated to treatment and that this study supports a no-effect level of 700 mg/kg bw/d, the highest dose in the study.

The agency concludes that data from a published 2-year dietary feeding study (Ref. 2) in Sprague-Dawley rats cannot be used to establish the safety of 1,3-butylene glycol. The study had insufficient statistical power to detect an adverse response to 1,3-butylene glycol because an inadequate number of rats was used and widespread disease killed most of the rats during the second year of the study.

A published reproduction study (Ref. 3) in Long-Evans rats, treated by gavage with 1,3-butylene glycol (0, 706, 4,236, and 7,060 mg/kg bw/d) during days 6 to

15 of gestation, also reported no treatment-related effects on a variety of reproduction parameters (litter weight and size, crown-rump length, corpora lutea, implantation sites, sex distribution, intrauterine deaths, total malformed pups or incidence of litters with malformed pups). However, the researchers reported an increased incidence of low body weights and sternebral anomalies in pups from high-dose mothers, indicating a possible teratogenic effect from exposure to 1,3-butylene glycol. The full significance of the effects of the treatment of rats with 1,3-butylene glycol, though, cannot be determined from the available data. FDA finds that the data are insufficient to determine whether the observed anomalies were caused by the treatment-related reductions in birth weight or by a teratogenic effect of the additive. However, because the observed low body weights and sternebral anomalies occurred only in high-dose groups, the agency concludes that a no-effect level can be set from doses employed with mid-dose rats at 4,200 mg/kg bw/d.

A number of published and unpublished nutritional and metabolic studies with 1,3-butylene glycol were also provided (Refs. 4 through 21). Within the limited scope of those studies no significant toxicological effects were reported except in a human clinical study (Ref. 21). In that study, 1,3-butylene glycol fed to young male and female subjects (250 mg/kg bw/d in bread for four separate 7-day periods) was reported to significantly depress blood glucose (lowered by 12 percent relative to controls). The 1,3-butylene glycol-induced glucose reduction did not involve insulin or growth hormone, although its mechanism could not be determined. As discussed in section IV.D.1. of this section, the reduction in blood glucose would not be expected to occur at the low levels estimated for human dietary exposure from the proposed use of 1,3-butylene glycol.

Ordinarily, chronic studies in rodent and nonrodent species are needed to establish the safety of direct food ingredients (Ref. 22). Although the petitioner did not submit an acceptable chronic dietary rodent study, FDA concludes that the toxicological data submitted are adequate to establish the safety of the use of 1,3-butylene glycol in edible sausage casings, for the following reasons:

1. The metabolism of 1,3-butylene glycol is well understood. In the rat, 1,3-butylene glycol is metabolized in the liver cytosol in a manner similar to ethanol (Refs. 13 and 16). In the intact rat and in tissue slices, it is converted

to acetoacetate and  $\beta$ -hydroxybutyrate, which are normal intermediates in fat metabolism. In the kidney, 1,3-butylene glycol blocks gluconeogenesis at the conversion of 3-phosphoglycerate to glyceraldehyde-3-phosphate (Ref. 14). This metabolic blockage is responsible for the reduction in serum glucose that occurs when 1,3-butylene glycol is consumed at sufficiently high levels. At consumption levels that would be expected from the proposed use, however, 1,3-butylene glycol would not be expected to inhibit gluconeogenesis in the kidney. In addition, from an examination of the scientific literature on the metabolism of 1,3-butylene glycol, which is well understood and documented (Refs. 16 and 21), there is no indication that 1,3-butylene glycol would be expected to have any carcinogenic potential. Therefore, FDA concludes that a chronic rodent study is not necessary to support the safety of the proposed use of 1,3-butylene glycol.

2. To ensure an adequate margin of safety, FDA applied a 1,000-fold safety factor (rather than the normal 100-fold safety factor) to the no-effect level from the dog study (Ref. 2) to compensate for the lack of an acceptable chronic rodent study for 1,3-butylene glycol. Applying a 1,000-fold safety factor to the no-effect level from the dog study gives an acceptable daily intake (ADI) for 1,3-butylene glycol of 0.7 mg/kg bw. Although an adverse metabolic effect (decreased serum glucose) was reported in humans consuming 250 mg 1,3-butylene glycol/kg bw, it is unlikely that any such metabolic effects would be observed at the ADI, which is 350-fold lower. Furthermore, for 1,3-butylene glycol, the ADI (0.7 mg/kg bw) is greater than the daily exposure estimates of 0.1 mg/kg bw (mean) and 0.2 mg/kg bw (90th percentile) for adults, assuming a bw of 60 kg, and 0.3 mg/kg bw (mean) and 0.6 mg/kg bw (90th percentile) for 2- to 5-year-olds, assuming a body weight of 15 kg. Therefore, the agency concludes that the level of exposure resulting from the petitioned use of 1,3-butylene glycol is safe.

## V. Conclusion on Safety

FDA has evaluated the data in the petition and other relevant material regarding the use of 1,3-butylene glycol as a formulation and processing aid in sausage casings and concludes that the substance produces the intended technical effects and is safe under the proposed conditions of use. Therefore, the agency is amending the food additive regulations to provide for the requested use.

In accordance with § 171.1(h) (21 CFR 171.1(h)), the petition and the

documents that FDA considered and relied upon in reaching its decision to approve the petition are available for inspection at the Center for Food Safety and Applied Nutrition by appointment with the information contact person listed above. As provided in § 171.1(h), the agency will delete from the documents any materials that are not available for public disclosure before making the documents available for inspection.

## VI. Environmental Impact

The agency has carefully considered the potential environmental effects of this action. FDA has concluded that the action will not have a significant impact on the human environment, and that an environmental impact statement is not required. The agency's finding of no significant impact and the evidence supporting that finding, contained in an environmental assessment, may be seen in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

## VII. Objections

Any person who will be adversely affected by this regulation may at any time on or before June 12, 1997, file with the Dockets Management Branch (address above) written objections thereto. Each objection shall be separately numbered, and each numbered objection shall specify with particularity the provisions of the regulation to which objection is made and the grounds for the objection. Each numbered objection on which a hearing is requested shall specifically so state. Failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held. Failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Three copies of all documents shall be submitted and shall be identified with the docket number found in brackets in the heading of this document. Any objections received in response to the regulation may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

## VIII. References

The following references have been placed on display in the Dockets Management Branch (address above)

and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Memorandum from M. DiNovi, Chemistry Review Branch, to R. L. Martin, Direct Additives Branch, dated November 8, 1988.
2. Scala, R. A., and O. E. Paynter, "Chronic Oral Toxicity of 1,3-Butanediol," *Toxicology and Applied Pharmacology*, 10:160-164, 1967.
3. Mankes, R. F., V. Renak, J. Fieserher, and R. LeFevre, "Birthweight Depression in Male Rats Contiguous to Male Siblings in Utero Exposed to High Doses of 1,3-Butanediol During Organogenesis," *Journal of the American College of Toxicology*, 5:189-196, 1986.
4. Dymsha, H. A., "Nutritional Application and Implication of 1,3-Butanediol," *Federation Proceedings*, 34:2167-2170, 1975.
5. Giron, H. M., "Some Aspects of the Utilization of 1,3-Diols as Synthetic Dietary Energy Sources" (thesis for master of science degree), Massachusetts Institute of Technology, August 1968.
6. Food and Drug Research Laboratories, Inc., Morgareidge, K., "Utilization of 1,3-Butylene Glycol in Dogs," November 1, 1972.
7. Mehlman, M. A., "Synthetic Food Additives as a Source of Calories: 1,3-Butanediol," *Federation Proceedings*, 34:2166, 1975.
8. Miller, S. A., and H. A. Dymsha, "Utilization by the Rat of 1,3-Butanediol as a Synthetic Source of Dietary Energy," *Journal of Nutrition*, 91:79-88, 1967.
9. Stoewsand, G. S., H. A. Dymsha, M. A. Kilmore, and S. M. Swift, "Plasma Lipid Changes in Exercised Dogs Fed 1,3-Butanediol," *Federation Proceedings*, 25:608, 1966 (abstract).
10. Young, J. W., "Use of 1,3-Butanediol for Lactation and Growth in Cattle," *Federation Proceedings*, 34:2177-2181, 1975.
11. Mackerer, C. R., R. N. Saunders, J. R. Haettinger, and M. A. Mehlman, "Influence of 1,3-Butanediol on Blood Glucose Concentration and Pancreatic Insulin Content of Streptozotocin-Diabetic Rats," *Federation Proceedings*, 34:2191-2196, 1975.
12. Mehlman, M. A., R. B. Tobin, and J. B. Johnston, "Metabolic Control of Enzymes in Normal, Diabetic and Diabetic Insulin Treated Rats Utilizing 1,3-Butanediol" (undated).
13. Mehlman, M. A., R. B. Tobin, H. K. J. Hahn, V. DeVore, and L. Kleager, "Metabolic Fate of 1,3-Butanediol (BD) in the Rat," Omaha, NE (undated).
14. Mehlman, M. A., R. B. Tobin, and J. B. Johnston, "Influence of Dietary 1,3-Butanediol on Metabolites and Enzymes Involved in Gluconeogenesis and Lipogenesis in Rats," *Journal of Nutrition*, 100:1341-1346, 1970.
15. Mehlman, M. A., R. B. Tobin, and C. R. Mackerer, "1,3-Butanediol Catabolism in the Rat," *Federation Proceedings*, 34:2182-2185, 1975.
16. Nahapetian, A., "Metabolism in Vivo of 1,3-Butanediol in the Rat" (thesis for doctor of science degree), Massachusetts Institute of Technology, September 1971.
17. Parker, M. M. (under the supervision of Myron A. Mehlman), "Metabolic Effects of 1,3-Butanediol," Omaha, NE, August 1972.

18. Romsos, D. R., P. S. Belo, and G. A. Leveille, "Butanediol and Lipid Metabolism," *Federation Proceedings*, 34:2186-2190, 1975.

19. Tate, R. L., M. A. Mehlman, and R. B. Tobin, "The Metabolism of 1,3-Butanediol" (undated).

20. Tate, R. L., M. A. Mehlman, and R. B. Tobin, "Metabolic Fate of 1,3-Butanediol in the Rat: Conversion to  $\beta$ -Hydroxybutyrate," *Journal of Nutrition*, 101:1719-1726, 1971.

21. Tobin, R. B., M. A. Mehlman, C. Kies, H. M. Fox, and J. S. Soeldner, "Nutritional and Metabolic Studies in Humans With 1,3-Butanediol," *Federation Proceedings*, 34:2171-2176, 1975.

22. "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives Used in Food" in "Redbook," Center for Food Safety and Applied Nutrition, Food and Drug Administration, 1982. Available through National Technical Information Service (NTIS), 5285 Port Royal Rd., Springfield, VA 22161, order number PB-83-170696. Revised draft is available from the Office of Premarket Approval (HFS-206), 200 C St. SW., Washington, DC 20204-0001.

#### List of Subjects in 21 CFR Part 172

Food additives, Incorporation by reference, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs and redelegated to the Director, Center for Food Safety and Applied Nutrition, 21 CFR part 172 is amended as follows:

#### PART 172—FOOD ADDITIVES PERMITTED FOR DIRECT ADDITION TO FOOD FOR HUMAN CONSUMPTION

1. The authority citation for 21 CFR part 172 continues to read as follows:

**Authority:** Secs. 201, 401, 402, 409, 701, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 341, 342, 348, 371, 379e).

2. New § 172.712 is added to subpart H to read as follows:

##### § 172.712 1,3-Butylene glycol.

The food additive 1,3-butylene glycol (CAS Reg. No. 107-88-0) may be safely used in food in accordance with the following prescribed conditions:

(a) It is prepared by the aldol condensation of acetaldehyde followed by catalytic hydrogenation.

(b) The food additive shall conform to the identity and specifications listed in the monograph entitled "1,3-Butylene Glycol" in the Food Chemicals Codex, 4th ed. (1996), p. 52, which is incorporated by reference in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies are available from the Office of Premarket Approval, Center for Food

Safety and Applied Nutrition, 200 C St. SW., Washington, DC 20204-0001, or may be examined at the Center for Food Safety and Applied Nutrition's Library, Food and Drug Administration, 200 C St. SW., rm. 3321, Washington, DC, or at the Office of the Federal Register, 800 North Capitol St. NW., suite 700, Washington, DC.

(c) It is used in the manufacture of sausage casings as a formulation aid as defined in § 170.3(o)(14) of this chapter and as a processing aid as defined in § 170.3(o)(24) of this chapter.

Dated: April 14, 1997.

**Fred R. Shank,**

*Director, Center for Food Safety and Applied Nutrition.*

[FR Doc. 97-12461 Filed 5-12-97; 8:45 am]

BILLING CODE 4160-01-F

#### DEPARTMENT OF HEALTH AND HUMAN SERVICES

#### Food and Drug Administration

#### 21 CFR Part 812

#### Export Requirements for Medical Devices; Technical Amendment

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Final rule; technical amendment.

**SUMMARY:** The Food and Drug Administration (FDA) is amending its regulations for exporting devices for investigational use to correct the statutory reference. This action is being taken to reflect changes in the Federal Food, Drug, and Cosmetic Act (the act), and to ensure the accuracy and consistency of the regulations.

**EFFECTIVE DATE:** May 13, 1997.

**FOR FURTHER INFORMATION CONTACT:** Philip L. Chao, Office of Policy (HF-23), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20850, 301-827-3380.

**SUPPLEMENTARY INFORMATION:** At present, two statutory provisions in the act govern the export of devices that are not approved for marketing in the United States. The first provision, at section 801(e)(2) of the act (21 U.S.C. 381(e)(2)), became law as part of the Medical Device Amendments Act of 1976 (Pub. L. 94-295) and required FDA's approval of certain exports of unapproved devices.

The second provision, now codified as section 802 of the act (21 U.S.C. 382), was the result of the FDA Export Reform and Enhancement Act of 1996 (Pub. L. 104-134, and amended by Pub. L. 104-180) (the Export Act of 1996). The

Export Act of 1996 amended, among other things, sections 801 and 802 of the act. The Export Act of 1996 amended section 801(e)(2) of the act to state, in part, that export of an unapproved device may occur only if the agency determines that exportation of the device is not contrary to the public health and safety and has the approval of the country to which it is intended for export or "the device is eligible for export under section 802" of the act. Section 802 of the act, as amended, authorizes exports of unapproved drugs and devices if certain conditions or requirements are met. Under section 802(b)(1) of the act, an unapproved device may be exported to any country if the device complies with the laws of that country and has valid marketing authorization in Australia, Canada, Israel, Japan, New Zealand, Switzerland, South Africa, or in any country in the EU or the EEA (often referred to as the "listed countries"). At present, the EU countries are Austria, Belgium, Denmark, Germany, Greece, Finland, France, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. The EEA countries are the EU countries, plus Iceland, Liechtenstein, and Norway. As new countries join the EU or the EEA, they will automatically be treated as listed countries without any need for FDA action. Additionally, the Secretary of Health and Human Services may designate additional countries to be added to the list if certain requirements are met.

Other provisions of the Export Act of 1996 permit devices to be exported, without prior FDA approval, for investigational use in the listed countries and to be exported in anticipation of market authorization in the listed countries (section 802(c) and (d) of the act). Prior FDA approval is required for devices intended for use in the treatment of a tropical disease or a disease that is not of significant prevalence in the United States (section 802(e) of the act).

All devices exported under section 802 of the act are subject to certain requirements, under section 802(f) of the act. For example, the device must be manufactured, processed, packaged, and held in substantial conformity with current good manufacturing practice requirements or meet international standards as certified by an international standards organization recognized by the agency; must not be adulterated under section 501(a)(1), (2)(A), or (3) (21 U.S.C. 351(a)(1), (2)(A), or (3)) or section 501(c) of the act; and must comply with sections 801(e)(1)(A) through (D) of the act (which require the