Homepage using the RIMS link or the Energy Information Online icon. User assistance is available at 202–208–2222, or by E-mail to RimsMaster@ferc.fed.us.

Finally, the complete text on diskette in WordPerfect format may be purchased from the Commission's copy contractor, RVJ International, Inc. RVJ International, Inc., is located in the Public Reference Room at 888 First Street, NE, Washington, DC 20426.

The Federal Energy Regulatory Commission (Commission) is issuing this notice to update filing fees that the Commission assesses for specific services and benefits provided to identifiable beneficiaries. Pursuant to § 381.104 of the Commission's regulations, the Commission is establishing updated fees on the basis of the Commission's Fiscal Year 1998 costs. The adjusted fees announced in this notice are effective September 16, 1999. The Commission has determined with the concurrence of the Administrator of the Office of Information and Regulatory Affairs of the Office of Management and Budget, that this final rule is not a major rule within the meaning of section 251 of Subtitle E of SBREFA. [5 U.S.C. § 804(2)] The Commission is submitting this final rule to both Houses of Congress and to the Comptroller General.

The new fee schedule is as follows:

FEES APPLICABLE TO THE NATURAL GAS POLICY ACT	
1. Petitions for rate approval pursuant to 18 CFR 284.123(b)(2). (18 CFR 381.403)	$7,320
FEES APPLICABLE TO GENERAL ACTIVITIES	
1. Petition for issuance of a declaratory order (except under Part I of the Federal Power Act). (18 CFR 381.302(a))	14,710
2. Review of a Department of Energy remedial order: Amount in controversy	
$0–9,999. (18 CFR 381.303(b))	100
$10,000–29,999. (18 CFR 381.303(b))	600
$30,000 or more. (18 CFR 381.303(a))	21,470
3. Review of a Department of Energy denial of adjustment: Amount in controversy	
$0–9,999. (18 CFR 381.304(b))	100
$10,000–29,999. (18 CFR 381.304(b))	600
$30,000 or more. (18 CFR 381.304(a))	11,260
4. Written legal interpretations by the Office of General Counsel. (18 CFR 381.305(a))	4,220
FEES APPLICABLE TO NATURAL GAS PIPELINES	
1. Pipeline certificate applications pursuant to 18 CFR 284.224. (18 CFR 381.207(b))	1,000
FEES APPLICABLE TO COGENERATORS AND SMALL POWER PRODUCERS	
1. Certification of qualifying status as a small power production facility. (18 CFR 381.505(a))	12,650
2. Certification of qualifying status as a cogeneration facility. (18 CFR 381.505(a))	14,320
3. Applications for exempt wholesale generator status. (18 CFR 381.801)	1,460

List of Subjects in 18 CFR Part 381

Electric power plants, Electric utilities, Natural gas, Reporting and recordkeeping requirements.

By the Commission.

Thomas R. Herlihy,

Executive Director and Chief Financial Officer.

In consideration of the foregoing, the Commission amends Part 381, Chapter I, Title 18, Code of Federal Regulations, *as set forth below.*

PART 381—FEES

1. The authority citation for Part 381 continues to read as follows:

Authority: 15 U.S.C. 717–717w; 16 U.S.C. 791–828c, 2601–2645; 31 U.S.C. 9701; 42 U.S.C. 7101–7352; 49 U.S.C. 60502; 49 App. U.S.C. 1–85.

§ 381.302 [Amended]

2. In § 381.302, paragraph (a) is amended by removing ''$14,360'' and inserting ''$14,710'' in its place.

§ 381.303 [Amended]

3. In § 381.303, paragraph (a) is amended by removing ''$20,960'' and inserting ''$21,470'' in its place.

§ 381.304 [Amended]

4. In § 381.304, paragraph (a) is amended by removing ''$10,990'' and inserting ''$11,260'' in its place.

§ 381.305 [Amended]

5. In § 381.305, paragraph (a) is amended by removing ''$4,120'' and inserting ''$4,220'' in its place.

§ 381.403 [Amended]

6. Section 381.403 is amended by removing ''$7,140'' and inserting ''$7,320'' in its place.

§ 381.505 [Amended]

7. In § 381.505, paragraph (a) is amended by removing ''$12,340'' and inserting ''$12,650'' in its place and by removing ''$13,970'' and inserting ''$14,320'' in its place.

§ 381.801 [Amended]

8. Section 381.801 is amended by removing ''$1,620'' and inserting ''$1,460'' in its place.

[FR Doc. 99–21280 Filed 8–16–99; 8:45 am]

BILLING CODE 6717–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 96N–0144]

Over-the-Counter Drug Products Containing Colloidal Silver Ingredients or Silver Salts

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule establishing that all over-the-counter (OTC) drug products containing colloidal silver ingredients or silver

salts for internal or external use are not generally recognized as safe and effective and are misbranded. FDA is issuing this final rule because many OTC drug products containing colloidal silver ingredients or silver salts are being marketed for numerous serious disease conditions and FDA is not aware of any substantial scientific evidence that supports the use of OTC colloidal silver ingredients or silver salts for these disease conditions.

DATES: This regulation is effective September 16, 1999.

FOR FURTHER INFORMATION CONTACT: Bradford W. Williams, Center for Drug Evaluation and Research (HFD–310), Food and Drug Administration, 7520 Standish Pl., Rockville, MD 20855, 301–594–0063.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of October 15, 1996 (61 FR 53685), FDA published a proposed rule to declare that all OTC drug products containing colloidal silver ingredients or silver salts are not generally recognized as safe and effective, and are new drugs and misbranded within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)). Colloidal silver is a suspension of silver particles in a colloidal base. In recent years, colloidal silver preparations of unknown formulation have been appearing in retail outlets. These products are labeled for numerous disease conditions, many of which are serious diseases. The dosage form of these colloidal silver products is usually oral, but product labeling also contains directions for topical and, occasionally, intravenous use.

FDA has not approved a new drug application (NDA) for any colloidal silver product. None of the silver salts evaluated as part of FDA's OTC drug review was found to be generally recognized as safe and effective for its intended use(s). FDA is not aware of any substantial scientific evidence that supports the use of OTC colloidal silver ingredients or silver salts for disease conditions. The agency invited any interested parties to collect and submit any existing data and information that support the safety and effectiveness of colloidal silver ingredients or silver salts for any of the uses not already evaluated under the OTC drug review. Interested persons were invited to submit written comments on the proposed regulation and on the agency's economic impact determination by January 13, 1997.

In response to the proposal, the agency received 251 responses. Copies of these comments are on public display in the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Additional information that has come to the agency's attention since publication of the proposal is also on public display in the Dockets Management Branch.

Based on the information set forth in the proposed rule, and after consideration of the information submitted by the public comments (as summarized as follows), FDA is declaring that all OTC drug products containing colloidal silver ingredients or silver salts are not generally recognized as safe and effective, and are new drugs and misbranded within the meaning of section 201(p) of the act. Adequate safety and effectiveness data have not been provided to establish general recognition of the safety and effectiveness of colloidal silver or silver salt ingredients for any OTC drug uses. The data submitted did not include the required absorption, metabolism, tissue distribution, accumulation, excretion, and pharmacodynamics (effect of the drug at its action site) of silver in the body, both when taken internally and applied externally, and of the effect of the particle size of the silver on these systemic effects.

FDA is amending subpart E of part 310 (21 CFR part 310) to add § 310.548 for OTC drug products containing colloidal silver ingredients or silver salts. The agency has expanded proposed § 310.548(a) to include some additional silver ingredients.

II. Public Comments and the Agency's Response

A. General Comments

1. Many comments agreed with the proposed rule. One of these comments cautioned against the dangers of using untested drugs and recalled that Laetrile misled unsuspecting people in search of a quick cancer cure. Another comment provided personal experience as a victim of argyria who had been disfigured for 40 years as a result of using colloidal silver. This comment included an excerpt from a book that recorded 114 cases of argyria compiled in the 1930's. The comment contended that many marketers of colloidal silver deny the potential for harm and often misquote or distort the historical articles dealing with these products.

A physician, who was formerly a pharmacist, recounted his own experience in reviewing cases of argyria. The victims had ingested silver products in the 1940's and 1950's. The physician was concerned that a product that does not have any rational use would lead to the redevelopment of argryia as a clinical problem. Another physician/ophthalmologist commented that colloidal silver is dangerous quackery.

The agency appreciates these comments in support of its proposal.

B. Comments on Safety and Effectiveness

2. One comment expressed concern that many different silver products being marketed are inferior products and are not even true colloids. Another comment stated that the vast majority of silver products being sold are fraudulent products. The comment noted that it had tested a number of these products and found that several actually had no silver content, one did not contain the silver particle size as stated on the label, and only one product exceeded all stated purity and stability claims found on the label. The comment added that many of the products were only duplicates of older colloidal silver products. The comment considered these ''newer'' products as having the same dangers, intermittent effectiveness, and lack of stability as the older products. The comment contended that the vast majority of the colloidal silver products it tested are totally useless, some were dangerous to ingest, and some were possibly a threat to life. The comment stated that it is a major problem to keep off the market these so-called ''colloidal silver'' products that contain significant amounts of silver ions and silver salts. The comment suggested a revision of the United States Pharmacopeia (USP) specifications for these products.

Another comment stated that many of the colloidal silver products it analyzed are considered ''Bredig Sols'' (simple colloidal silver), referring to Bredig, Heidelberg, 1893. The comment added that a pure Bredig Sol is simply elemental silver in distilled water, while some Bredig Sols are mixed with saline to make them isotonic. The comment mentioned that the silver content in these products (a viable product could contain 0.005 percent silver) is many magnitudes less than the silver content of the products discussed by FDA in its safety and effectiveness evaluation (61 FR 53685 at 53686). The comment contended that the agency had not reviewed the Bredig Sols and disagreed with the agency's assumptions that there is an analogous comparison between colloidal silver proteins and other silver compounds to a simple Bredig Sol.

These comments highlight the existing problems in trying to establish whether any silver salts or colloidal silver ingredients can be generally recognized as safe and effective. Because of the acknowledged differences in silver content and particle size of the silver in various products, it is difficult to draw conclusions from clinical studies conducted on different silver products. The agency has minimal manufacturing controls information on these products. The agency does not have information that assures the strength, quality, purity, and potency of various silver products used in clinical studies and other reports included in the comments.

Concerning the comment suggesting a revision of USP specifications, the proposed rule stated that none of the formerly recognized colloidal silver preparations (e.g., colloidal silver iodide, strong (or mild) silver protein, ammoniacal silver nitrate solution) has been official in the USP or the National Formulary (N.F.) since 1975. It is industry's responsibility to have these silver ingredients reinstated in the USP or N.F. and to revise the specifications used in the former compendial monographs. Concerning ''Bredig Sols,'' the comment did not provide any specific safety and effectiveness data; thus, the agency is not able to establish that such products are generally recognized as safe and effective.

3. Several comments submitted information purporting to support the safety of colloidal silver and other silver ingredients. The comments contended that silver is nontoxic and has minimal side effects. One comment stated that silver is poorly absorbed and not readily retained in the body when taken orally. Another comment stated that colloidal silver is harmless to the liver, kidneys, other internal organs, human enzymes, and the eyes; contains no free radicals; and has no reaction with other medications. Several comments mentioned that argyria, a blue skin discoloration resulting from prolonged administration of silver compounds and accumulation in the body, is the main side effect that occurs. One comment explained that argyria occurs because a small amount of the silver compound is absorbed and deposited in the skin, where it is reduced by light to metallic silver; the resulting skin discoloration persisting almost indefinitely, although there are no associated toxic effects. The comment contended that colloidal silver is the only known form of silver that is not deposited under the skin even with large doses. Another comment added that most of the reported cases of argyria resulted from the use of silver nitrate, various ionic silver salts, or highly concentrated mild silver protein. The comment concluded that the dilute, mild silver protein products marketed today are similar to pre-1938 colloidal silver solutions and do not cause argyria. The comment also discussed the levels of silver in the majority of silver products marketed today and indicated that the amount of silver ingested from these products and the diet are within the Environmental Protection Agency's maximum daily exposure reference dose of 350 micrograms per day for a 70 kilogram (kg) adult.

Another comment presented the results of several animal (rat) studies involving acute or chronic administration of various amounts of colloidal silver (mild silver protein in colloidal suspension), approximately 1,500 parts per million (ppm), either by intravenous (IV) injection or in drinking water. The IV studies included an initial acute dose finding study followed by a chronic study (0.15 or 0.015 milligram (mg) per 1 milliliter (mL)). Two groups of four rats received each dosage; two rats served as controls and received 1 mL of physiological saline solution. Each rat received a total of 12 injections. The investigator reported that no abnormal clinical or behavioral signs were observed after 12 days of treatment. In another followup chronic IV rat study, three rats were injected with 1,500 ppm colloidal silver three times per week for 4 weeks (a total of 18 mg per 300 gram (g) rat), and three rats served as controls. All treated and control rats were weighed at the time of injection. At the completion of the study, there were no differences in body weight and no clinical signs or gross pathologic changes between the treated and control groups. The drinking water study involved 15 rats fed 1.5 ppm mild silver protein solution in their drinking water for 40 days. The rats showed no clinical signs of gross pathological changes at the end of the treatment period. Three rats received regular drinking water and served as controls. The investigator stated that the data do not provide information about the metabolic fate of the silver, but support safety if extrapolated to humans because a 60-kg person would have to be given 3,600 mg to receive an amount equivalent to the rats' highest dose (18 mg/300 g rat).

The agency does not consider this information adequate to establish general recognition of the safety of silver salts or colloidal silver ingredients for OTC drug use. The comments themselves indicate that ionic silver salts and highly concentrated mild silver protein clearly are not safe for OTC use. The animal data indicate that mild silver protein in colloidal suspension at low concentrations may be safe in rats when administered in specific concentrations for up to 40 days. Additional data are needed in humans on the absorption, metabolism, tissue distribution, accumulation, excretion, and pharmacodynamics of silver in the body, both when taken internally and applied externally, and of the effect of the particle size of the silver on these systemic effects. The agency concludes that a full pharmacologic profile that is relevant to human use is needed.

4. Several comments submitted information purporting to support the effectiveness of colloidal silver and other silver ingredients. One comment provided a partial list of the more than 650 diseases that colloidal silver has been used against and included a number of testimonials. Another comment stated that silver will kill 650 disease organisms, but it does not cure 650 diseases. The comment added that a Bredig Sol of silver at 30 ppm is an effective germicide for both gram-positive and gram-negative bacteria, fungi, yeasts, and viruses. Another comment noted the antimicrobial and bacteriostatic effects of diluted colloidal silver protein solutions. One comment provided a number of case reports involving the use of a colloidal silver (200 ppm) suspension with protein and distilled water and a mild silver protein cream to treat various conditions (e.g., rash, pain, and sore gums).

Another comment, from a physician, described a double-blind clinical study that he conducted using a commercial colloidal silver product (concentration not provided) in 22 men ages 50 to 82, with a mean age of 61.9 years. The physician obtained a brief medical history from each man and did a rectal examination. The men reported that nocturia (frequency of urination) ranged from one to five times a night. The physician assumed that the men had benign prostatic hypertrophy because of their age and the onset of symptoms in recent years. Of the 22 men, 15 took colloidal silver and 7 took placebo (colored water). The dose was 1 teaspoon (tsp) of the products morning and evening, and the duration of the study was from 19 to 23 days, with one exception of 10 days for a late entry. At the end of the study, four men (all on the colloidal silver) reported considerable improvement in the nocturia, with a reduction from 2 to 4 times to 1 time each night, while six other men (five on the colloidal silver) noted some improvement in the nocturia. Two men with a history of

transurethral resection of the prostate, who were on the colloidal silver, did not report any improvement.

Subsequently, all of the men continued on colloidal silver (1 tsp daily) for the next 8 weeks. The men were interviewed after about 4 more weeks, and each completed an American Urological Association (AUA) Symptom Index representing symptoms at the time of the interview. The men also completed an AUA index representing symptoms before starting the colloidal silver. The AUA index is based on answers to seven questions, graded from 0 (not at all) to 5 (almost always), with the score being a sum of the answers to the questions. The one man who reported improvement on placebo reported marked improvement on the colloidal silver, with his nocturia decreasing from 2 to 3 times to 1, and occasionally 0, time each night. His AUA index was 9+ at the beginning and improved to a 3 at the last interview. One man moved, and a followup was not obtained. Of the remaining 21 men, 16 reported improvement of varying degrees. All reported decreased nocturia, with five men recording an improvement of 2 or less on the AUA index and nine men reporting an improvement of 3 to 10 on the AUA index. One man reported that he had been taking a prescription drug for benign prostatic hypertrophy before starting the colloidal silver. The last two men had improvements of 14 and 18 on the AUA index, with nocturia decreasing by 3 and 2 times, respectively. Five men reported no improvement during the study. Two of these men had a history of transurethral resection of the prostate, one had been taking a prescription drug for this condition for the past 6 months and his nocturia had already improved to 1 time each night, and the other two had been having symptoms for 6 and 15 years, respectively, and had an enlarged prostate when the study began. The physician noted that because the four men with a tender prostate improved, it was reasonable to suggest that the beneficial action of the colloidal silver was due to its antibacterial activity. He hypothesized that there may be some subclinical prostatitis in many men with benign prostatic hypertrophy, and this might explain why the colloidal silver resulted in a remarkable reduction in the men's symptoms. The physician concluded that the results of this study merit further investigation by the medical community.

The physician also commented on some other observations from about 50 men who had taken colloidal silver (most for symptoms of prostatism) under his direction before, during, and after the study (a period of about 6 months). Six noted clearing of acne or other infectious lesions of the skin, three reported improvement of mucus in the throat and associated cough of long duration, two indicated that irritation around the anus had cleared, one stated that he had no summer colds for 3 months (which was unusual for him), eight reported improvement in nasal discharge and sinus trouble (especially when using colloidal silver in a nasal spray), two noted a reduction in upset stomach and abdominal pain, and two reported that their sexual enjoyment and performance had improved. The physician concluded that these observations suggested some areas that needed to be investigated further.

The agency finds that the previous studies are not adequate and well-controlled clinical studies of the type described in § 314.126 (21 CFR 314.126) that need to be conducted. The studies have major methodic flaws. There needs to be a clear statement of the objectives of the investigation and a protocol containing a specific study design, the method of subject selection (with inclusion and exclusion criteria), the method of assigning subjects to treatment and control groups, well-defined methods for measuring the subjects' responses, and methods for analysis of the study results. Adequate measures need to be taken to minimize bias on the part of the subjects, observers, and analysts of the data, which is done by adequate blinding. The agency is unable to determine the adequacy of the blinding in the physician's study because the placebo was described as ''colored water.'' The agency is not able to ascertain the degree of similarity or difference that existed in the appearance of the colloidal silver product and the placebo to determine how well the study was blinded. The studies need replication by other investigators and need to follow § 314.126. Likewise, the conditions described in the case reports provided by one comment need to be studied in adequate and well-controlled clinical trials. Finally, the information that silver will kill 650 disease organisms and that a Bredig Sol of silver at 30 ppm is an effective germicide for both gram-positive and gram-negative bacteria, fungi, yeasts, and viruses needs to be related to in vivo treatment for specific disease conditions. The agency concludes that the data and information submitted are not sufficient to establish general recognition of effectiveness for colloidal silver or other silver ingredients for any specific OTC condition.

C. The Grandfather Clauses of the Act

5. One comment claimed that the silver products marketed today are the same as the more dilute mild silver protein products marketed pre-1938 that did not cause argyria. The comment made the following recommendation: FDA should set guidelines of the acceptable levels of the solutions and the dosage based on current EPA safety standards and what was available pre-1938, so that a ''grandfathered'' standard is implemented. Another comment stated that not approving its colloidal silver product as a grandfathered colloidal silver would be to deprive the public of the use of an extremely safe and effective product already in use for 4 years.

The ''grandfather exemption'' was discussed in detail in the proposed rule (61 FR 53685 to 53686). None of the comments provided any evidence to show that the composition and the labeling of colloidal silver or silver salt drug products have remained unchanged since 1938 or 1962. Without such evidence, the products cannot qualify for either grandfather exemption, and there is no need to set any guidelines as requested by one comment.

D. Freedom of Choice

6. A number of comments included individual testimonials or expressions of belief that colloidal silver benefited their health and that of their family members or friends. A few comments mentioned benefits experienced by pets. Many of the comments stated that the proposed rule would deny them the freedom of choice to select their own drugs.

FDA's statutory mandate includes protection and promotion of the public health by ensuring that drugs are not only safe but also effective for their intended use. The Commissioner of Food and Drugs' decision on the status of Laetrile, published in the **Federal Register** of August 5, 1977 (42 FR 39788), expresses the agency's position on freedom of choice with respect to ensuring that drugs are not only safe, but also effective. That statement reads in part:

> In passing the 1962 Amendments to the act—the amendments that require that a drug be proved effective before it may be marketed—Congress indicated its conclusions that the absolute freedom to choose an ineffective drug was properly surrendered in exchange for the freedom from the danger to each person's health and well-being from the sale and use of worthless drugs * * *. To the extent that any freedom

has been surrendered by the passage of the legislation which bans from the marketplace drugs that have not been proven to be effective, that surrender was a rational decision which has resulted in the achievement of a greater freedom from the dangers to health and welfare represented by such drugs.

Agency regulations in 21 CFR 330.10(a)(4)(ii) state that the standards for effectiveness for an OTC drug that is generally recognized as effective include a requirement for controlled clinical investigations. Isolated case reports, random experience, and reports lacking the details that permit scientific evaluation are not considered adequate to establish effectiveness. Testimonials from consumers cannot be considered as adequate proof of effectiveness or safety. None of the comments presented any evidence of safety or effectiveness beyond personal experience.

In the absence of data demonstrating that the ingredients present in OTC drug products containing colloidal silver ingredients or silver salts are generally recognized as safe and effective, these ingredients cannot be included in an OTC drug product. After the effective date of the final regulation, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce (unless it is the subject of an approved NDA, of which there currently are none) that is not in compliance with this regulation will be subject to regulatory action.

E. The Dietary Supplement Health and Education Act (DSHEA)

7. Several comments, from consumers, stated that the specific product they used did not make any claims and might be considered a dietary supplement. None of the comments provided any labeling or specifics about the products they used.

This final rule addresses products marketed as OTC drugs. A product that is not intended for OTC ''drug'' use in accord with section 201(g)(1) of the act would not be subject to this final rule. A product containing silver could, under certain circumstances, be marketed as a dietary supplement if it meets the definition in section 201(ff) of the act and other applicable requirements. Among other things, such a product's label must state that the product is a dietary supplement and meet other labeling requirements of the act. (See, e.g., section 403(q), (r), and (s) of the act (21 U.S.C. 343(q), (r), and (s)).) It must also meet the safety requirements of the act. (See, e.g., 21 U.S.C. 342(a), (f), and (g).) FDA may take regulatory action against a product marketed as a dietary supplement when authorized to do so by the act.

A dietary supplement containing colloidal silver or silver salts may not be labeled in whole or in part for topical use. Section 201(ff)(2)(A)(i) of the act requires that a dietary supplement is a product that is ''intended for ingestion.'' The term ingestion has been addressed by the court in *United States* v. *Ten Cartons, Ener-B Nasal Gel,* 888 F. Supp. 393 (E.D.N.Y.), *aff'd,* 72 F.3d 285 (2d Cir. 1995). A topical product could not be a dietary supplement.

III. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities.

Title II of the Unfunded Mandates Reform Act (2 U.S.C. 1501 *et seq.*) requires that agencies prepare a written statement and economic analysis before proposing any rule that may result in an expenditure in any one year by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million (adjusted annually for inflation). As the agency stated in the proposed rule, this rulemaking is not expected to pose a significant impact on small business because only a limited number of products are affected (61 FR 53685 at 53687).

The agency believes that this final rule is consistent with the principles set out in the Executive Order and in these two statutes. The purpose of this final rule is to establish that all OTC drug products containing colloidal silver ingredients or silver salts for internal or external use are not generally recognized as safe and effective and are misbranded. The agency's Drug Listing System identifies a multitude of silver-containing products. These products may contain silver, silver ion, silver chloride, silver cyanide, silver iodide, silver oxide, or silver phosphate.

All of these manufacturers are considered small entities, using the U.S. Small Business Administration designation for this industry (750 employees).

Manufacturers will no longer be able to market OTC drug products containing any silver ingredients after the effective date of the final rule. While the manufacturers may incur a loss of revenue from some of these products, some silver products for internal use may be able to continue to be marketed as dietary supplements, provided they meet, among other regulatory requirements applicable to dietary supplements, the definition of dietary supplements in section 201(ff) of the act and meet the labeling requirements of section 403 of the act.

Manufacturers have been aware of the possible effects on the status of these OTC silver drug products since October 1996 and have not submitted adequate safety and effectiveness data to the agency. Since publication of the 1996 proposal and with the 30-day implementation date after publication of the final rule, manufacturers should have ample time to deplete most of their remaining stock of OTC drug products containing the affected ingredients.

The agency has considered a longer effective date for this final rule. However, manufacturers have not submitted the necessary data, and safety and effectiveness have not been established for the ingredients included in this final rule. Consumers will benefit from the removal from the marketplace of OTC drug products containing ingredients for which safety and effectiveness have not been established. If consumers purchase these products marketed as dietary supplements and if the product bears a statement claiming a benefit related to a classical nutrient deficiency disease and discloses the prevalence of such disease in the United States, describes the role of a nutrient or dietary ingredient intended to affect the structure or function of the body in humans, characterizes the documented mechanism by which a nutrient or dietary supplement acts to maintain such structure or function, or describes general well-being from consumption of a nutrient or dietary ingredient, then the labeling will have to inform them that ''This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.'' (See 21 U.S.C. 343(r)(6).)

While this final rule may cause manufacturers to discontinue marketing or reformulate or relabel some products, these manufacturers have known for some time that if adequate data were not submitted to support safety and effectiveness, cessation of marketing of the current OTC drug products would be required, in any event, when the final

rule was published and became effective.

The analysis shows that this final rule is not economically significant under Executive Order 12866 and that the agency has considered the burden to small entities. Thus, this economic analysis, together with other relevant sections of this document, serves as the agency's final regulatory flexibility analysis, as required under the Regulatory Flexibility Act. Finally, this analysis shows that the Unfunded Mandates Reform Act does not apply to the final rule because it would not result in an expenditure in any one year by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million.

IV. Paperwork Reduction Act of 1995

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

V. Environmental Impact

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 310

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 310 is amended as follows:

PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360b-360f, 360j, 361(a), 371, 374, 375, 379e; 42 U.S.C. 216, 241, 242(a), 262, 263b-263n.

2. Section 310.548 is added to subpart E to read as follows:

§ 310.548 Drug products containing colloidal silver ingredients or silver salts offered over-the-counter (OTC) for the treatment and/or prevention of disease.

(a) Colloidal silver ingredients and silver salts have been marketed in over-the-counter (OTC) drug products for the treatment and prevention of numerous disease conditions. There are serious and complicating aspects to many of the diseases these silver ingredients purport to treat or prevent. Further, there is a lack of adequate data to establish general recognition of the safety and effectiveness of colloidal silver ingredients or silver salts for OTC use in the treatment or prevention of any disease. These ingredients and salts include, but are not limited to, silver proteins, mild silver protein, strong silver protein, silver, silver ion, silver chloride, silver cyanide, silver iodide, silver oxide, and silver phosphate.

(b) Any OTC drug product containing colloidal silver ingredients or silver salts that is labeled, represented, or promoted for the treatment and/or prevention of any disease is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) for which an approved application or abbreviated application under section 505 of the act and part 314 of this chapter is required for marketing. In the absence of an approved new drug application or abbreviated new drug application, such product is also misbranded under section 502 of the act.

(c) Clinical investigations designed to obtain evidence that any drug product containing colloidal silver or silver salts labeled, represented, or promoted for any OTC drug use is safe and effective for the purpose intended must comply with the requirements and procedures governing the use of investigational new drugs as set forth in part 312 of this chapter.

(d) After September 16, 1999, any such OTC drug product containing colloidal silver or silver salts initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

Dated: July 14, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99–21253 Filed 8–16–99; 8:45 am]

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DEPARTMENT OF TRANSPORTATION

Coast Guard

33 CFR Part 165

[CGD01–99–135]

RIN 2115–AA97

Safety Zone Port of New York/New Jersey Annual Marine Events

AGENCY: Coast Guard, DOT.

ACTION: Final rule.

SUMMARY: The Coast Guard is removing a number of Safety Zone regulations for annual fireworks displays. This action is necessary to update the current regulations for Safety Zones. This action is intended to remove regulations for events that are now covered by other regulations.

DATES: This rule is effective August 17, 1999.

ADDRESSES: Documents as indicated in this preamble are available for inspection or copying at Coast Guard Activities New York, 212 Coast Guard Drive, room 205, Staten Island, New York 10305, between 8 a.m. and 3 p.m., Monday through Friday, except Federal holidays. The telephone number is (718) 354–4193.

FOR FURTHER INFORMATION CONTACT: Lieutenant J. Lopez, Waterways Oversight Branch, Coast Guard Activities New York (718) 354–4193.

SUPPLEMENTARY INFORMATION:

Regulatory History

Pursuant to 5 U.S.C. 553, a notice of proposed rulemaking (NPRM) was not published for this regulation. Good cause exists for not publishing an NPRM and for making this regulation effective less than 30 days after **Federal Register** publication. These procedures are unnecessary because this regulation is strictly administrative in nature. This final rule merely removes obsolete sections in 33 CFR part 165. The safety zones being removed have gone through notice and comment rulemaking and are included in the First Coast Guard District Fireworks list in 33 CFR 100.114.

Background and Purpose

One June 28, 1999, the First Coast Guard District published a Final rule in the **Federal Register** (64 FR 34543) updating the regulations for Fireworks displays within the First Coast Guard District (33 CFR 100.114). The following regulations for fireworks displays from 33 CFR part 165 were added to the list in § 100.114 and are no longer required in part 165:

1. § 165.161 Safety Zone; Annual ''Fireworks on the Navesink'' Fireworks Display Navesink River, Red Bank, New Jersey.

2. § 165.166 Safety Zone; Annual Burlington Independence Day Celebration Fireworks Display, Burlington Bay, Vermont.

3. § 165.167 Safety Zone; Annual Rensselaer Festival Fireworks Display, Hudson River, New York.

4. § 165.170 Safety Zone; Heritage of Pride Fireworks Display, Hudson River, New York.