DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 310 and 347

[Docket No. 78N–021A]

RIN 0905–AA06

Skin Protectant Drug Products for Over-the-Counter Human Use; Astringent Drug Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule in the form of a final monograph for over-the-counter (OTC) skin protectant drug products and establishing conditions under which OTC astringent drug products are generally recognized as safe and effective and not misbranded. FDA is issuing this final rule after considering public comments on the agency's proposed regulation, which was issued in the form of a tentative final monograph, and all new data and information on OTC astringent drug products that have come to the agency's attention. This final monograph is part of the ongoing review of OTC drug products conducted by FDA.

EFFECTIVE DATE: October 21, 1994.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD–810), Food and Drug Administration, 7520 Standish Place, Rockville, MD 20855, 301–594–5000.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of September 7, 1982 (47 FR 39412 and 39436), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), advance notices of proposed rulemaking for OTC external analgesic drug products and OTC skin protectant drug products. The agency also reopened the administrative records for these rulemakings to allow for consideration of the reports and recommendations on OTC astringent drug products prepared by the Advisory Review Panel on OTC Miscellaneous External Drug Products (Miscellaneous External Panel), which was the advisory review panel responsible for evaluating data on the active ingredients used as astringents. Interested persons were invited to submit comments by December 6, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by January 5, 1983.

In accordance with § 330.10(a)(10), the data and information considered by the Panel, after deletion of a small amount of trade secret information, were placed on display in the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

In the **Federal Register** of February 15, 1983 (48 FR 6820), the agency published a notice of proposed rulemaking for OTC skin protectant drug products. The agency issued this notice after considering the report and recommendations of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (Topical Analgesic Panel) and public comments on an advance notice of proposed rulemaking that was based on those recommendations. Interested persons were invited to submit comments by April 18, 1983, new data by February 15, 1984, and comments on the new data by April 16, 1984.

The agency's proposed regulation, in the form of a tentative final monograph, for OTC skin protectant drug products used as astringents was published in the **Federal Register** of April 3, 1989 (54 FR 13490). Interested persons were invited to file by June 2, 1989, written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs regarding the proposal. New data could have been submitted until April 3, 1990, and comments on the new data until June 4, 1990. Interested persons were invited to file comments on the agency's economic impact determination by August 1, 1989.

The agency stated in the proposal that it had determined that the external analgesic and skin protectant uses of OTC astringent drug products are so closely related that it would not serve the public interest to proceed with two separate rulemakings for the same ingredients. Accordingly, the agency proposed to combine the rulemakings for the external analgesic and skin protectant uses of OTC astringent drug products and to place the monograph for these products in the OTC skin protectant monograph. Final agency action occurs with the publication of this final monograph, which is a final rule establishing a monograph for OTC skin protectant drug products used as astringents.

The OTC drug procedural regulations (21 CFR 330.10) provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph. Accordingly, FDA does not use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage. In place of Category I, the term "monograph conditions" is used; in place of Categories II or III, the term "nonmonograph conditions" is used.

In the proposed regulation for OTC skin protectant drug products used as astringents (54 FR 13490), the agency advised that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication in the **Federal Register**. Therefore, on or after October 21, 1994, no OTC drug product that is subject to the monograph and that contains a nonmonograph condition, i.e., a condition that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless it is the subject of an application or abbreviated application (hereinafter called application) approved under section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) and 21 CFR part 314. Further, any OTC drug product subject to this monograph that is repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

In response to the proposed rule on OTC skin protectant drug products used as astringents, two manufacturers submitted comments. Copies of the comments are on public display in the Dockets Management Branch (address above). Any additional information that has come to the agency's attention since publication of the proposed rule is also on public display in the Dockets Management Branch.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to

the call-for-data notices published in the **Federal Register** of November 16, 1973 (38 FR 31697) and August 27, 1975 (40 FR 38179) or to additional information that has come to the agency's attention since publication of the notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch.

I. The Agency's Conclusions on the Comments

A. Comment on Ferric Subsulfate

1. One comment submitted information (Refs. 1 through 32) to support both OTC and professional use of ferric subsulfate solution (Monsel's Solution) as an astringent. The comment suggested consumer use as an astringent/hemostatic agent to arrest bleeding caused by minor surface cuts and grazes; professional use would be to arrest bleeding of superficial skin wounds resulting from minor surgical procedures, such as biopsies and curettage. The comment requested an oral hearing if the agency found the information to be inadequate.

The agency finds the information submitted by the comment insufficient to include ferric subsulfate solution in the final monograph as a topical astringent for either consumer or health professional use.

Most of the references provided refer to the use of ferric subsulfate solution as a hemostatic agent/styptic by medically trained health professionals in a clinical setting after biopsies, minor surgery, and other procedures causing minimal bleeding. None of the data provided suggest that a product containing ferric subsulfate as an astringent/hemostatic agent has ever been used or could be safely used by consumers. Further, the agency is not aware of any other data that show safety or effectiveness for OTC use by consumers. Therefore, the agency has no basis to include ferric subsulfate as an astringent for OTC consumer use in this monograph.

Regarding professional use, the references suggest that there are undesirable side effects and safety risks associated with using ferric subsulfate solution to arrest bleeding due to minor surgical procedures. Several references include reports of ferric subsulfate solution pigmenting the skin. Larson (Ref. 1) states that, although not common, pigmentation of the skin may result from sideroblast deposits or from stimulation of melanocytes. Larson adds that ferric subsulfate has a long-lasting cytotoxic effect that may make subsequent histologic examination of tissue difficult. Olmstead, Lund, and Leonard (Ref. 2) consider ferric subsulfate a histologic nuisance and discourage its use following biopsies of pigmented lesions or tumors that may present diagnostic difficulties. They claim ferric subsulfate promotes artifacts that can be troublesome to the pathologist if rebiopsy of a lesion is necessary, adding that ferric subsulfate may distort or obscure the basic pathologic process. Amazon, Robinson, and Rywlin (Ref. 3) describe the capacity of ferric subsulfate to produce ferrugination of collagen fibers, skeletal muscle, and perichondrium and to produce permanent discoloration of the skin. They state that when there is injury to skeletal muscle and other deep tissues by ferric subsulfate solution, an inflammatory reaction persists at these sites for weeks. They caution that clinicians should be aware that ferric subsulfate solution has demonstrable cytotoxic effects with long-lasting sequelae, and pathologists should be aware of the histopathologic findings that follow application of this solution. Wood and Severin (Ref. 4) suggest that ferric subsulfate may induce granulomas. These granulomas are rarely pigmented and must be differentiated histologically from pigmented neoplasms. Wood and Severin described a case in which a dermal nodule of atypical histiocytes (a macrophage present in connective tissue) developed at the site where ferric subsulfate solution had been applied to a wound 30 days earlier. Duray and Livolsi (Ref. 5) reported that the use of ferric subsulfate solution to achieve hemostasis at a biopsy site can also produce a clinically irregular area of hyperpigmentation accompanied by a pathologic pigmented and cellular dermal reaction. Davis, et al. (Ref. 6) mention the potential effect of ferric subsulfate solution obscuring the basic disease process in the uterine cervix.

Many uses of ferric subsulfate solution were discussed in the references submitted by the comment. However, questions remain concerning which procedures are safe and which are not. Standards for safety of OTC human drugs in § 330.10(a)(4)(i) (21 CFR 330.10(a)(4)(i)) include a low incidence of adverse reactions or significant side effects under adequate directions for use and warnings against unsafe use as well as low potential for harm that may result from abuse under conditions of widespread availability. If ferric subsulfate is cytotoxic as suggested by Larson (Ref. 1), the question of long-term adverse effects for the patient remains unanswered.

The agency finds that permitting the use of ferric subsulfate only in external dermatologic applications would also present difficulties. It is not clear from the references submitted how large a wound may be safely treated with ferric subsulfate solution. Although discoloration of the tissue sometimes results after using the product, there is no indication of the frequency or the severity of this problem. Without such information, the risk to the patient cannot be evaluated.

While ferric subsulfate solution has been in use for over 100 years, its iatrogenic effects (unfavorable response to medical intervention, induced by the intervention itself) have been recognized only recently (Refs. 2, 3, and 4). The agency does not have an adequate safety profile on this ingredient for the various uses suggested by the comment. The safety issues relevant to the product are not adequately addressed by the information provided.

The clinical effectiveness data provided were taken from the medical literature and involved situations where the product was applied by medically trained professionals (Refs. 7 through 32). The references do not provide any clinical information or data on which to base appropriate OTC drug labeling of the product for self-medication. Standards for effectiveness for OTC human drugs in § 330.10(a)(4)(ii) require controlled clinical investigations for proof of effectiveness, and specifically state that isolated case reports, random experience, and reports lacking the details which permit scientific evaluation will not be considered. Further, § 330.10(a)(4)(iii) requires the benefit-to-risk ratio of a drug to be considered in determining its safety and effectiveness.

The references include case reports of the uses of ferric subsulfate solution but do not include any controlled clinical studies to show effectiveness. Because other recognized safe astringent products are available for OTC human use and potential risks are associated with the use of ferric subsulfate solution, the benefit-to-risk ratio for ferric subsulfate solution for general consumer use is unfavorable based upon current information. While ferric subsulfate solution may have utility as an astringent/hemostatic when used by health professionals, substantive clinical data are necessary to establish the proper safe and effective conditions for use.

Accordingly, the agency concludes that the data provided are not sufficient to support monograph status for ferric subsulfate solution as an astringent for OTC topical use by consumers or by health professionals. Therefore, ferric subsulfate is not included in this final

monograph. The agency's detailed comments and evaluation of the data are on file in the Dockets Management Branch (Refs. 33 and 34).

Based on the lack of adequate safety and effectiveness data, the agency concludes that an oral hearing before the Commissioner is not warranted.

References

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(3) Amazon, K., M. J. Robinson, and A. M. Rywlin, "Ferrugination Caused by Monsel's Solution," *The American Journal of Dermatopathology*, 2:197–205, 1980.

(4) Wood, C., and G. L. Severin, "Unusual Histiocytic Reaction to Monsel's Solution," *The American Journal of Dermatopathology*, 2:261–264, 1980.

(5) Duray, P. H., and V. A. Livolsi, "Recurrent Dysplastic Nevus Following Shave Excision," *Journal of Dermatological Surgery and Oncology*, 10:811–815, 1984.

(6) Davis, J. R. et al., " Effects of Monsel's Solution in Uterine Cervix," *American Journal of Clinical Pathology*, 82:332–335, 1984.

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(9) Ferric Subsulphate Solution, *The National Formulary (IX)*, pp. 214–215, 1950.

(10) "Ferric Subsulphate Solution, N.F.," *U. S. Dispensatory*, 25th ed., p. 574, 1955.

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(20) Eyre, R. W., and G. G. Krueger, "Response to Injury of Skin Involved and Uninvolved with Psoriasis, and Its Relation to Disease Activity: Koebner and 'Reverse' Reactions," *British Journal of Dermatology*, 106:153–159, 1982.

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(33) Letter from W. E. Gilbertson, FDA, to D. B. DeVogel, American Dermal Corp., coded LET1, Docket No. 78N–021A, Dockets Management Branch.

(34) Letter from W. E. Gilbertson, FDA, to D. B. DeVogel, American Dermal Corp., coded LET6, Docket No. 78N–021A, Dockets Management Branch.

B. Comments on Hamamelis Water

2. One comment requested that FDA consider the use of specifically denatured alternative preservatives in the manufacture of Hamamelis water. The comment stated that by using its own aromatic and hamamelitannin ingredients as denaturants in the manufacture of Hamamelis water, the preparation would be in compliance with Hamamelis water National Formulary (N.F.) XI. The comment stated that the Bureau of Alcohol, Tobacco, and Firearms (BATF) should give it permission to use those alternative preservatives in the manufacture of Hamamelis water.

OTC drug monographs do not provide special exceptions to methods used to manufacture specific products. At the time that the tentative final monograph was published, Hamamelis water was not included in an official compendium. The agency's reference to "NF XI" in the tentative final monograph (54 FR 13490 at 13493) was intended to provide a standard for the preparation of Hamamelis water. Since that time, the United States Pharmacopeial Convention, Inc. (U.S.P.C.), has initiated development of a current compendial monograph for "Hamamelis water" (Refs. 1 and 2). The agency anticipates that a final monograph will be included in the United States Pharmacopeia (U.S.P.)—N.F. before the effective date of the final monograph for OTC astringent drug products. The proposed new U.S.P.—N.F. monograph is very similar to the former monograph in NF XI and provides a method of preparation. Accordingly, the final monograph for OTC astringent drug products in this document refers to the new U.S.P.—N.F. monograph for Hamamelis water.

The U.S.P.—N.F. provides under "General Notices" (Ref. 3) that a suitable formula of specially denatured alcohol may be substituted for alcohol in the manufacture of pharmacopeial preparations intended for internal or topical use, provided that the denaturant is volatile and does not remain in the finished product. It further states that a finished product that is intended for topical application to the skin may contain specially denatured alcohol, provided that the denaturant is either a normal ingredient or a permissible added substance. Any denatured alcohol used in the preparation of Hamamelis water would need to meet these requirements in order for the product to be marketed OTC in accordance with the final monograph in new part 347.

References

(1) "Pharmacopeial Forum," The United States Pharmacopeial Convention, Inc., Rockville, MD, p. 3855, September through October 1992.

(2) "Pharmacopeial Forum," The United States Pharmacopeial Convention, Inc., Rockville, MD, p. 5266, May through June 1993.

(3) "The United States Pharmacopeia XXII—The National Formulary XVII," The United States Pharmacopeial Convention, Inc., Rockville, MD, p. 3, 1989.

3. One comment requested that the agency reconsider and include in the final monograph several indications for use for Hamamelis water. The comment mentioned that these indications were not included in the agency's notice of proposed rulemaking, but had been recommended by the Miscellaneous External Panel in § 347.52(b)(2) of its advance notice of proposed rulemaking (47 FR 39436 at 39450 and 39451), as follows:

(i) "For use as an astringent for the treatment of bruises, contusions, and sprains."

(ii) "For protecting slight cuts and scrapes."

(iii) "For relieving muscular pains."

(iv) "For treating the pain and swelling of insect bites."

(v) "For use as an astringent for the treatment of skin irritation, sunburn, and external hemorrhoids."

The comment also requested an oral hearing if necessary.

As discussed in the proposed rule for OTC astringent drug products (54 FR 13490 at 13497), the agency is not aware of any data to support the use of Hamamelis water as an astringent for "bruises," "contusions," "sprains," "sunburn," or "relieving muscular pains." The comment did not submit any new data to substantiate any of these claims. Therefore, the agency has no basis for including any of these indications in this final monograph.

Claims for using Hamamelis water for external hemorrhoids are covered in the rulemaking for OTC anorectal drug products. Indications for Hamamelis water products for that use are included in § 346.50(b) of the final monograph for OTC anorectal drug products (21 CFR 346.50(b)). Claims for insect bites, minor cuts, and minor scrapes were proposed in § 347.52(b)(3) of the tentative final monograph (54 FR 13490 at 13497) and appear in new § 347.50(b)(3) of this final monograph. Because the comment did not submit any substantive or new information to support the indications not included in this final monograph, the agency concludes that an oral hearing is not warranted.

II. Summary of Changes From the Proposed Rule

1. In the tentative final monograph the agency proposed to identify Hamamelis water as "NF XI." Now that a new U.S.P. monograph has been established, the agency is identifying Hamamelis water as "U.S.P." (See comment 2.)

2. The definition for an astringent drug product proposed in § 347.3(c) appears in new § 347.3(a) of this final monograph. The active ingredients proposed in § 347.12 appear in new § 347.10 of this final monograph. The labeling of astringent drug products proposed in § 347.52 appears in new § 347.50 of this final monograph.

III. The Agency's Final Conclusions on OTC Astringent Drug Products

Based on available evidence, the agency is issuing a final monograph establishing conditions under which OTC skin protectant drug products used as astringents are generally recognized as safe and effective and not misbranded. Specifically, the agency has determined that the only ingredients that meet monograph conditions are aluminum acetate, aluminum sulfate, and Hamamelis water. All other ingredients considered in this rulemaking have been determined to be nonmonograph. These ingredients include, but are not limited to, acetone, alcohol, alum ammonium, alum potassium, aluminum chlorhydroxy complex (aluminum chloride hexahydrate), aromatics, benzalkonium chloride, benzethonium chloride, benzocaine, benzoic acid, boric acid, calcium acetate, camphor (gum camphor), clove oil (oil of cloves), colloidal oatmeal, cresol, cupric sulfate, eucalyptus oil (oil of eucalyptus), eugenol, ferric subsulfate (Monsel's Solution), honey, isopropyl alcohol, menthol, methyl salicylate (oil of wintergreen), oxyquinoline sulfate, p-t-butyl-m-cresol (para-tertiary-butyl-meta-cresol), peppermint oil (oil of peppermint), phenol (carbolic acid), polyoxyethylene laurate (polyoxyethylene monolaurate), potassium ferrocyanide, sage oil (oil of sage), silver nitrate, sodium borate (borax), sodium diacetate, talc, tannic acid, tannic acid glycerite, thymol, topical starch (starch), zinc chloride, zinc oxide, zinc phenolsulfonate, zinc stearate, zinc sulfate. All of these ingredients except ferric subsulfate (Monsel's Solution) were listed as nonmonograph in § 310.545(a)(18)(ii) (21 CFR 310.545(a)(18)(ii)) in a final rule published in the **Federal Register** of May 10, 1993 (58 FR 27636 at 27642). Ferric subsulfate is being included in that same section in this final rule. Accordingly, any skin protectant drug product labeled, represented, or promoted for use as an OTC astringent that contains any of the ingredients listed in § 310.545(a)(18)(ii) or that is not in conformance with this final monograph (new part 347) is considered a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)) and misbranded under section 502 of the act (21 U.S.C. 352) and may not be marketed for this use unless it is the subject of an approved application under section 505 of the act (21 U.S.C. 355) and 21 CFR part 314. An appropriate citizen petition to amend the monograph may also be submitted under 21 CFR 10.30 in lieu of an application. Any OTC skin protectant drug product for use as an astringent that is initially introduced or initially delivered for introduction into interstate commerce after the effective dates of § 310.545(a)(18)(ii) or this final rule that is not in compliance with the regulations is subject to regulatory action. Further, any OTC drug product subject to this monograph that is repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce.

No comments were received in response to the agency's request for specific comment on the economic impact of this rulemaking (51 FR 27346 at 27362, July 30, 1986). The agency has examined the economic consequences of this final rule in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this final rule for OTC skin protectant drug products used as astringents, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act (Pub. L. 96–354). That assessment included a discretionary regulatory flexibility analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC skin protectant drug products used as astringents is not expected to pose such an impact on small businesses. This final rule will require some relabeling of products containing monograph ingredients. Manufacturers will have 1 year to implement this new labeling. Nonmonograph ingredients except ferric subsulfate (Monsel's Solution) were addressed previously when § 310.545(a)(18)(ii) was published.

Therefore, the agency certifies that this final rule will not have a significant economic impact on a substantial number of small entities.

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

21 CFR Part 310

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

21 CFR Part 347

Labeling, Over-the-counter drugs.

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

PART 310—NEW DRUGS

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

Authority: Secs. 201, 301, 501, 502, 503, 505, 506, 507, 512–516, 520, 601(a), 701, 704, 705, 721 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 357, 360b-360f, 360j, 361(a), 371, 374, 375, 379e); secs. 215, 301, 302(a), 351, 354–360F of the Public Health Service Act (42 U.S.C. 216, 241, 242(a), 262, 263b-263n).

2. Section 310.545 is amended in paragraph (a)(18)(ii) by alphabetically adding the entry "Ferric subsulfate (Monsel's Solution)," by revising paragraph (d)(11), and by adding new paragraph (d)(22) to read as follows:

§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.

(a) * * *

(18) * * *

(ii) * * *

* * * * *

Ferric subsulfate (Monsel's Solution)

* * * * *

(d) * * *

(11) November 10, 1993, for products subject to paragraph (a)(18)(ii) of this section, except products that contain ferric subsulfate.

* * * * *

(22) April 21, 1993, for products subject to paragraph (a)(18)(ii) of this section that contain ferric subsulfate.

3. Part 347 is added as follows:

PART 347—SKIN PROTECTANT DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—Astringent Drug Products

Sec.

Authority: Secs. 201, 501, 502, 503, 505, 510, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 371).

Subpart A—Astringent Drug Products

§ 347.1 Scope.

(a) An over-the-counter skin protectant drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this part and each general condition established in § 330.1 of this chapter.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 347.3 Definitions.

As used in this part:

(a) *Astringent drug product* means a drug product that is applied to the skin or mucous membranes for a local and limited protein coagulant effect.

(b) [Reserved]

§ 347.10 Astringent active ingredients.

The active ingredient of the product consists of any one of the following within the specified concentration established for each ingredient:

(a) Aluminum acetate, 0.13 to 0.5 percent (depending on the formulation and concentration of the marketed product, the manufacturer must provide adequate directions so that the resulting solution to be used by the consumer contains 0.13 to 0.5 percent aluminum acetate).

(b) Aluminum sulfate, 46 to 63 percent (the concentration is based on the anhydrous equivalent).

(c) Hamamelis water, U.S.P.

§ 347.50 Labeling of astringent drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as an "astringent."

(b) *Indications.* The labeling of the product states, under the heading "Indications" any of the phrases listed in this paragraph (b), as appropriate. Other truthful and nonmisleading statements describing only the indications for use that have been established and listed in this paragraph (b) may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *For products containing aluminum acetate identified in § 347.10(a).* "For temporary relief of minor skin irritations due to" (select one or more of the following: "poison ivy," "poison oak," "poison sumac," "insect bites," "athlete's foot," or "rashes caused by soaps, detergents, cosmetics, or jewelry").

(2) *For products containing aluminum sulfate identified in § 347.10(b) for use as a styptic pencil.* "Stops bleeding caused by minor surface cuts and abrasions as may occur during shaving."

(3) *For products containing Hamamelis water identified in § 347.10(c).* (i) "For relief of minor skin irritations due to" (select one or more of the following: "insect bites," "minor cuts," or "minor scrapes").

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) "For external use only. Avoid contact with the eyes."

(2) *For products containing aluminum acetate identified in § 347.10(a) or hamamelis water identified in § 347.10(c).* "If condition worsens or symptoms persist for more than 7 days, discontinue use of the product and consult a" (select one of the following: "physician" or "doctor").

(3) *For products containing aluminum acetate identified in § 347.10(a) used as a compress or wet dressing.* "Do not cover compress or wet dressing with plastic to prevent evaporation."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) *For products containing aluminum acetate identified in § 347.10(a)*—(i) *For products used as a soak.* "For use as a soak: Soak affected area in the solution for 15 to 30 minutes. Discard solution after each use. Repeat 3 times a day."

(ii) *For products used as a compress or wet dressing.* "For use as a compress or wet dressing: saturate a clean, soft, white cloth (such as a diaper or torn sheet) in the solution, gently squeeze, and apply loosely to the affected area. Saturate the cloth in the solution every 15 to 30 minutes and apply to the affected area. Discard solution after each use. Repeat as often as necessary."

(2) *For products containing aluminum sulfate identified in § 347.10(b) for use as a styptic pencil.* "Moisten tip of pencil with water and apply to the affected area. Dry pencil after use."

(3) *For products containing hamamelis water identified in § 347.10(c).* "Apply to the affected area as often as necessary."

Dated: August 26, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

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