



B.F. ASCHER & COMPANY, INC. • *Pharmaceuticals • Consumer Products*

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Request for Information on OTC Drugs
FDA Docket No. 2003N-0539
68 Fed. Reg. 75585 (Dec. 31, 2003)
Submission of B.F. Ascher & Company

B.F. Ascher & Company hereby submits these comments in response to FDA's request for data and information regarding nasal moisturizers, in connection with the agency's review of over-the-counter (OTC) drug products, published in 68 Fed. Reg. 75,585 (Dec. 31, 2003). As a preliminary matter, B.F. Ascher wishes to thank the Agency for the opportunity to participate in this information collection effort.

B.F. Ascher manufactures and markets a wide range of pharmaceuticals and consumer products, including over-the-counter drugs and cosmetic products. For over twenty years, B.F. Ascher has marketed the Ayr® product line, an assortment of isotonic saline nasal sprays, mists, and drops, which are promoted by the Company as nasal moisturizers.

Summary

FDA's recent request for data and information declares that nasal moisturizer products containing sodium chloride and various saline buffer solutions are drugs, regardless of the claims made for the product.¹ With this call for data, the FDA appears to be ignoring its own prior holdings, based on the Federal Food, Drug, and Cosmetic Act ("FFDCA") and confirmed

¹ *OTC Drug Products: Safety and Efficacy Review*, 68 Fed. Reg. 75,585, 75,587 (Dec. 31, 2003). The published literature refers to such saline products as "isotonic," "balanced," "normalized," and "physiological".

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repeatedly by federal courts, that a product's intended use controls its regulatory status and that products intended to be used as cosmetics cannot be regulated as drugs by the agency. Indeed, the claims made for saline mists and similar products that are labeled as nasal moisturizers are solely cosmetic in nature. The products have been traditionally marketed and regulated as cosmetics and there is no valid legal basis for subjecting such products to an OTC monograph.

In the event that the labeling for such products includes claims that render them drug products from a regulatory perspective, which B.F. Ascher's products do not, there is adequate data to support the safety and effectiveness of isotonic saline nasal mists for use in relieving symptoms associated with rhinitis and other similar nasal conditions. I have attached to these comments several supporting studies, identified as Exhibits 1-10.

[NOTE: On May 10, 2004, the Cosmetic, Toiletry, and Fragrance Association ("CTFA") submitted comments in response to FDA's call for data. (FDA Docket 2003N-0539, Comment 1). To the extent CTFA's comments relate to the regulation of nasal moisturizers, B.F. Ascher endorses these comments and incorporates them by reference.]

Discussion

I. Intended Use of a Product is Determinative of Its Regulatory Status

A product's "intended use" is an essential element of its regulatory status. The Food, Drug, and Cosmetic Act defines "cosmetics" as "articles *intended to be* rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance," and components of such articles.² The term "drug" is defined as "articles *intended for use* in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals... [or]

² 21 U.S.C. § 321(i) (emphasis added).

intended to affect the structure or any function of the body of man or other animals” and components of these articles.³

Indeed, during the passage of the provisions discussed above, Congress explained that a manufacturer should have control over how its product was regulated, based on the product’s intended use as “clearly shown by the labeling and advertising” for the product.⁴ FDA explicitly adopted this position in its regulations defining “intended use” as “the objective intent of the persons legally responsible for the labeling...[and] is determined by such persons’ expression or may be shown by the circumstances surrounding the distribution of the article...[e.g.,] by labeling claims, advertising matter, or oral or written statements[.]”⁵

Moreover, specifically in the context of the OTC Monograph Rulemaking process, FDA has made clear that the “intended use” of a product, as set forth in the claims made on the product’s labeling, defines its regulatory status, and distinguishes drugs from cosmetic products.⁶ In addition, federal courts have consistently affirmed the position that the “intended use” of a

³ *Id.* § 321(g)(1) (emphasis added).

⁴ S. Rep. No. 361, 74th Cong., 1st Sess. 4 (1935).

⁵ 21 C.F.R. § 201.128 (2003).

⁶ *See, e.g., Sunscreen Drug Products for OTC Human Use; Final Monograph*, 64 Fed. Reg. 27,666, 27,669 (May 21, 1999) (“[I]f a product is intended solely to provide cosmetic effects on the skin...then the product may be marketed as a cosmetic,” and is not subject to regulation under the OTC monograph.) (“Sunscreen Final Monograph”); *Sunscreen Drug Products for OTC Human Use; Tentative Final Monograph*, 58 Fed. Reg. 28,194, 28,204-05 (May 12, 1993) (a product’s intended use determines its regulatory status; products intended to be used solely as cosmetics are not subject to OTC monograph) (“Sunscreen Tentative Final Monograph”); *Topical Antimicrobial Drug Products for OTC Human Use; Proposed Rulemaking for Diaper Rash Drug Products*, 55 Fed. Reg. 25,246, 25,253 (June 20, 1990) (product was not considered a drug because its intended use, as determined by its labeling, was not for the treatment or prevention of a disease); *External Analgesic Products for OTC Human Use; Skin Bleaching Drug Products for OTC Human Use; Tentative Final Monograph*, 47 Fed. Reg. 39,108, 39,114 (Sept. 3, 1982) (making distinction between drug and cosmetic claims because OTC drug monograph process only applies to drug products, while products with only cosmetic claims are not subject to OTC monograph). *See also Proposed Rulemaking for Diaper Rash Drug Products; Tentative Final Monograph*, 48 Fed. Reg. 5852, 5861-62 (Feb. 8, 1983) (claims in labeling that do not relate to a OTC product’s therapeutic characteristics are outside of the scope of the OTC drug review).

product, as evidenced by its labeling and promotional claims, is determinative of its regulatory status.⁷

Furthermore, because the claims made about a product or contained in its labeling are the dispositive factor in establishing a product's regulatory status as a drug or cosmetic, it is well established that the mere presence of an ingredient, such as saline buffer solution, does not, as FDA appears to be asserting, render a product a drug.⁸

II. Nasal Saline Mists Marketed as Nasal Moisturizers Are Not Drugs

Thus, FDA has long recognized that the OTC Drug Review does not extend to purely cosmetic products and labeling claims.⁹ Products such as Ayr® Saline Nasal Mist, which are intended for use as nasal moisturizers, have long been marketed to and used by consumers for purely cosmetic purposes such as moisturizing and cleansing nasal passages. Therefore, in the absence of claims that they are intended to prevent, mitigate, or treat a disease, or to affect the structure of function of the body, saline nasal moisturizers should be excluded from the OTC drug review process.

⁷ See, e.g., *United States v. Article Consisting of 216 Cartoned Bottles...Sudden Change*, 409 F.2d 734, 739, 742 (4th Cir. 1969) (the intended use of a product, as evidenced in its labeling and promotional claims, controls whether a product is subject to regulation as a drug) ("Sudden Change"); *United States v. Article of Drug Consisting of 36 Boxes... "Line Away Temporary Wrinkle Smoother, Coty"*, 415 F.2d 369, 371 (3rd Cir. 1969) (the promotional claims and labeling for a product are controlling in determining whether a product is a drug) ("Line Away"); *United States v. Article of Drug... "Helene Curtis Magic Secret"*, 331 F. Supp. 912, 915 (D. Md. 1971) (court did not consider the composition of the product, concluding that "it is the intended use [of the product] that controls.") ("Magic Secret").

⁸ See, e.g., *Magic Secret*, 331 F. Supp. at 915; *Sunscreen Tentative Final Monograph*, 58 Fed. Reg. at 28,205 (acknowledging that "a product may contain sunscreen ingredients and be a cosmetic and not a drug" if, among other reasons, it is not intended to be used as a drug and its labeling contains no claims that refer to the drug functions of the sunscreen ingredient). Cf. *Guidance for FDA Staff on Sampling or Detention Without Physical Examination of Decorative Contact Lenses (Import Alert #86-10)*; *Availability*, 68 Fed. Reg. 16,520, 16,521 (decorative contact lenses are classified as cosmetics, although similar contact lenses intended for corrective use are regulated as prescription devices).

⁹ See *supra* note 5.

Consistent with its intended use as a cosmetic product, the labeling for Ayr® nasal moisturizers includes claims that the product “[m]oisturizes and [s]oothes”, “restores critical moisture”, and can be used as a “nasal wash”. Although FDA has never specifically evaluated claims made about nasal moisturizer products, it has consistently held that OTC products that moisturize, lubricate, or relieve dryness are cosmetics and will not be regulated as drugs,¹⁰ a position that has been adopted by at least one federal court.¹¹ Similarly, in accordance with the statutory definition of “cosmetic”,¹² FDA also has deemed products other than soap that are intended solely to clean or cleanse the body (both internally and externally) to be cosmetics and excluded them from the OTC drug review process.¹³ Thus, based on the claims made by B. F. Ascher for its products, and under the FFDCAs and FDA’s own previous interpretations of the Act, Ayr® Saline Nasal Moisturizers and other similar products must be regulated as cosmetics and should not be subject to the OTC Monograph Rulemaking process.

III. There is Adequate Evidence to Establish the Safety and Efficacy of Nasal Saline Mists

In the event that FDA concludes that certain claims made for nasal saline mist products demonstrate that the products are intended be used as drugs, there is adequate evidence that

¹⁰ See, e.g., *Skin Protectant Drug Products for OTC Human Use; Final Monograph*, 68 Fed. Reg. 33,362, 33,364 (June 4, 2003) (use of skin protectants for “dryness” is a cosmetic claim.); *Sunscreens Final Monograph*, 64 Fed. Reg. at 27,669 (May 21, 1999) (products intended solely for moisturizing the skin are considered cosmetics); *Skin Protectant Drug Products for OTC Human Use; Tentative Final Monograph*, 48 Fed. Reg. 6,820, 6,826 (Feb. 15, 1983) (“The agency considers... ‘lubrication’ to be [a] cosmetic claim”).

¹¹ *Sudden Change*, 409 F.2d at 742 n.10 (acknowledging that claims that a product will “soften” or moisturize” are cosmetic claims).

¹² See also 21 U.S.C. § 321(i) (definition of cosmetics include products intended to cleanse the human body).

¹³ See, e.g., *Hair Grower and Hair Loss Prevention Drug Products for OTC Human Use*, 54 Fed. Reg. 28,772, 28,775 (July 7, 1989) (shampoo and scalp cleansers used solely for cleansing hair are cosmetics); *Skin Protectant Drug Products for OTC Human Use; Astringent Drug Products*, 54 Fed. Reg. 13,490, 13,495 (April 3, 1989) (“cleansing” and “drying” are considered cosmetic claims); *Vaginal Drug Products for OTC Human Use; Establishment of a Monograph*, 48 Fed. Reg. 46,694, 46,701 (Oct. 13, 1983) (vaginal douches intended to have a transitory effect by removal of secretions and bacteria are cosmetics, and claims for such products, including “cleansing”, “soothing”, and “refreshing” are cosmetic claims).

isotonic saline, used as a nasal mist or wash, is safe and effective for the relief of symptoms associated with sinonasal conditions, such rhinitis, sinorhinitis, and rhinosinusitis. The results of a number of clinical trials, which have been reported in peer reviewed medical journals, demonstrate the safety and efficacy of isotonic saline solutions used as nasal mists or washes. Further, the safety and efficacy of these products is widely accepted throughout the medical community as therapy for sinonasal conditions.

A. Reports of Clinical Trials

1. Spector, S.L. et al., Beneficial effects of propylene and polyethylene glycol and saline in the treatment of perennial rhinitis. *Clinical Allergy*, 1982, Volume 12, pages 187-196. ¹⁴

In this double-blind clinical trial studying the therapeutic use of saline nasal sprays and propylene and polyethylene glycol sprays as wetting agents in the treatment of perennial rhinitis, patients were evaluated over a two week baseline period and, during a four week treatment period, instructed to administer two sprays of saline¹⁵ or propylene and polyethylene glycol to each nostril four times daily. The therapeutic value of the nasal sprays was evaluated on the basis of a patient diary, in which subjects recorded how many hours per day symptoms of rhinitis were present, clinical assessments of the patient's status, a complete physical examination at the beginning and end of the study, a physical examination of the nose at regular intervals during the study, and laboratory examinations that included allergy skin tests, nasal smears, nasal biopsies, and nasal airflow measurements.

The authors of this study concluded that the use of a saline nasal spray was associated with "subjective and objective improvement [of symptoms of obstruction and inflammation] in

¹⁴ Copy attached as Exhibit 1.

¹⁵ The saline nasal spray was composed of "[p]hysiological saline 0.65% with benzyl alcohol as a preservative buffered and made isotonic with sodium bicarbonate." Ex. 1 at 188.

patients with perennial rhinitis.”¹⁶ This study also presents strong evidence of the safety of nasal saline mists. Indeed, the authors stated that side effects in this study were “almost non-existent;” the reported side effects were limited to occasional increases in nasal discharge with use of the nasal sprays.¹⁷

2. Nuutinen, J. et al., Balanced physiological saline in the treatment of chronic rhinitis. *Rhinology*, 24:265-269, 1986.¹⁸

This open-label clinical trial studied the effects of isotonic saline mist on nasal symptoms of patients with chronic rhinitis. Subjects were instructed to administer the saline solution *ad libitum* for one week and to record the number and frequency of the applications. At the conclusion of the study, patients completed a questionnaire about the effect of the solution on their symptoms and the effect of the saline spray on the efficacy of their ordinary nasal medications.¹⁹ Eighty-five (91%) of the ninety-three subjects reported that use of the saline solution relieved their symptoms of nasal obstruction.²⁰ Furthermore, twenty-two patients reported that the efficacy of their ordinary medications for nasal symptoms had improved.

Additionally, very few side effects were associated with the administration of nasal saline mist in this study. In fact, according to the questionnaires completed by the patients, a large majority (81%) of the patients experienced no side effects.²¹ Sixteen of the seventeen patients who reported side effects complained of “itching of the nose or sneezing.”²² One patient

¹⁶ Ex. 1 at 196.

¹⁷ Ex. 1 at 192.

¹⁸ Copy attached as Exhibit 2

¹⁹ Exhibit 2 at 266-67.

²⁰ Ex. 2 at 267.

²¹ Ex. 2 at 267.

²² *Id.*

reported bloody secretions from the nose; however, investigators were not clear whether this was attributable to the administration of saline or to the nasal steroids taken by this patient on a regular basis.²³

3. Pigret, D. and Jankowski, R., Management of post-ethmoidectomy crust formation: Randomized single-blind trial comparing pressurized seawater versus antiseptic/mucolytic saline. *Rhinology*, 34:38-40, 1996.²⁴

This randomized single-blind study compared the efficacy of nasal lavages with pressurized seawater to the efficacy of nasal irrigations with an antiseptic/mucolytic saline solution in post-operative care. In this clinical trial, the subjects, who had all undergone bilateral endoscopic nasal sphenoidectomies for nasal polyposis, were instructed to perform nasal lavages, with pressurized seawater²⁵ or a saline/antiseptic/mucolytic solution, for three weeks. During this time, the patients were asked to complete a diary to record on a ten-point scale common post-operative complaints, such as rhinorrhea and nasal obstruction. In addition, the solutions' efficacy at removing crusts and secretions were measured by weighing residual nasal crusts and residual secretions collected from the subjects' nostrils.

The authors of this study concluded that nasal lavages with pressurized seawater were "very useful in post-ethmoidectomy care."²⁶ Although this study does not directly address the use of saline mists in the treatment of rhinitis, this study provides evidence of the general safety of the administration of isotonic saline solutions to the nasal cavity.

B. Other references in medical and scientific literature

²³ *Id.*

²⁴ Copy attached as Exhibit 3.

²⁵ The seawater was sterilized by ultrafiltration and its sodium chloride concentration reduced by electrolysis. Ex. 3 at 39.

²⁶ Ex. 3 at 40.

Furthermore, it is clear from a wealth of articles in peer-reviewed journals, including treatment guidelines and research summaries, that the use of isotonic nasal sprays is a well-established treatment methodology for sinonasal conditions, such as rhinitis and rhinosinusitis, and is widely accepted as safe²⁷ and effective²⁸ by the medical community. In addition, although generally accepted as treatment for patients in all demographic groups, the use of nasal saline sprays has specifically been recommended in medical literature for use by women suffering from pregnancy-related rhinitis, due to its low risk profile,²⁹ and for use in infants to ease aspiration of dried nasal secretions by moisturizing sinuses.³⁰

Conclusion

By including saline nasal moisturizers in its most recent call for data and information, FDA is unfairly attempting to regulate as drugs products that have long been considered to be, and are marketed as, cosmetics. To include these cosmetic products in an OTC Monograph Rulemaking stands the drug review process on its head and should not be further pursued by the agency. However, if FDA decides to regulate saline nasal moisturizers as drugs, in derogation of the law and its own previous findings, there is sufficient evidence to establish that saline nasal mists are safe and effective in the management of sinonasal conditions.

²⁷ See, e.g., Klein, G.L., Acute Rhinosinusitis: Treatment Guidelines. *Infect. Med.* 15(10F):26-33, 1998 (Copy attached as Exhibit 4); Benninger, M.S. et al., The medical management of rhinosinusitis. *Otolaryngol Head Neck Surg* 117 (suppl 2):S41-S49, 1997 (Copy attached as Exhibit 5); Rambur, B., Pregnancy Rhinitis and Rhinitis Medicamentosa. *Journal of the American Academy of Nurse Practitioners*, 14(12):527-30, 2002 (Copy attached as Exhibit 6). See also Blake Papsin and Alison McTavish, Saline nasal irrigation: Its role as an adjunct treatment. *Canadian Family Physician*, 49:168-173, 2003 (Copy attached as Exhibit 7).

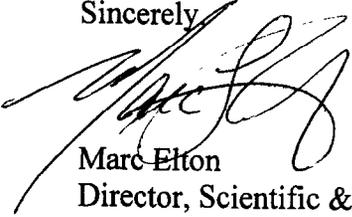
²⁸ See, e.g., Dykewicz, M.S. et al., Diagnosis and Management of Rhinitis: Complete Guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology, *Ann Allergy Asthma & Immun*, 81:478-518, 1998 (Copy attached as Exhibit 8); Karadag, A., Letter to Editor, *Pediatrics*, 109(1): 165, 2002 (Copy attached as Exhibit 9).

²⁹ See, e.g., Rambur, *supra* note 28; Dykewicz, M.S. et al., *supra* note 29.

³⁰ See, e.g., Dykewicz, M.S. et al., *supra* note 29; Pray, W.S., Treating Congestion in Children's Summer Colds. *US Pharmacist*, 27(2), 2002 (Copy attached as Exhibit 10).

Thank you for your consideration.

Sincerely



Marc Elton
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B.F. Ascher & Co., Inc.

Enclosures