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<p><b>For product information, please log-on to the web site</b> <a href="http://www.nasacort.com">www.nasacort.com</a> or contact one of our Medical Information Specialists at (800) 633-1610.</p>				
<p><b>Proprietary Drug Name:</b> NASACORT® AQ Nasal Spray</p>	<p><b>INN:</b> Triamcinolone Acetonide Nasal Spray</p>	<p><b>Therapeutic area and FDA approved indications:</b> For the treatment of nasal symptoms of seasonal and perennial allergic rhinitis in adults and children 6 years of age and older.</p>		
<p><b>Name of Sponsor/Company:</b> Aventis Pharmaceuticals, Inc., Member of the sanof-aventis group</p>				
<p><b>Title of Study:</b> (XRG5029C/4002) A Multicenter, Randomized, Double-blind, Cross-over Study of the Patient Preference and Sensory Attributes of Nasacort® AQ (Triamcinolone Acetonide Aqueous), Flonase® (Fluticasone Propionate) and Nasonex® (Mometasone Furoate Aqueous) Nasal Sprays in Patients with Allergic Rhinitis.</p>				
<p><b>Principal Study Investigators:</b></p> <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none;"> <p>Sandra Gawchik, D.O. Bernstein Clinical Research Center Presidents House 1 Presidents Dr. Upland-Chester, PA 19013</p> </td> <td style="width: 50%; border: none;"> <p>David Bernstein, M.D. Asthma &amp; Allergy Associates 8444 Winton Rd., Cincinnati, OH 45231</p> </td> </tr> </table>			<p>Sandra Gawchik, D.O. Bernstein Clinical Research Center Presidents House 1 Presidents Dr. Upland-Chester, PA 19013</p>	<p>David Bernstein, M.D. Asthma &amp; Allergy Associates 8444 Winton Rd., Cincinnati, OH 45231</p>
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<p><b>Study centre(s):</b> 6 centers in the USA</p>				
<p><b>Publication:</b> Stokes M, Amorosi SL, Thompson D, Dupclay L, Garcia J, Georges G. Evaluation of patients' preferences for triamcinolone acetonide aqueous, fluticasone propionate, and mometasone furoate nasal sprays in patients with allergic rhinitis. <i>Otolaryngol Head Neck Surg.</i> 2004 Sep;131(3):225-31.</p>				
<p><b>Study period (years): (date of first enrolment) (date of last completed):</b> August 16, 2001</p>	<p><b>Phase of development:</b> Phase IV</p>			

to October 8, 2001	
<p><b>Objectives:</b> To determine allergic rhinitis patients’ ratings of the sensory attributes of Nasacort® AQ, Flonase®, and Nasonex® and their preference for these individual products.</p>	
<p><b>Methodology:</b> This was a randomized, double-blind, cross-over study to determine patients’ ratings of the sensory attributes of triamcinolone acetonide, fluticasone propionate, and mometasone furoate aqueous nasal sprays, and their preference for these individual products. After administration of each of the products in a randomized order, patients evaluated each corticosteroid aqueous nasal spray by responding to questions given by a trained, independent interviewer blinded to the products. Products were administered according to a balanced design, allowing each product to be tested in each order position an equal number of times.</p>	
<p><b>Number of patients (planned and analyzed):</b> 106 planned/ 106 analyzed</p>	
<p><b>Diagnosis and main criteria for inclusion:</b> Male or non-pregnant, non-lactating females between the ages of 18 and 70 years, a two-year history of Allergic Rhinitis (seasonal or perennial), had AR symptoms at inclusion in the study, had a positive response to skin prick test or RAST (documented) for at least one allergen (perennial or seasonal) prevalent in the geographic area and environment, and to which patients had continuous exposure.</p>	
<p><b>Test product, dose and mode of administration, batch number:</b> Nasacort® AQ Nasal Spray 220 µg (=2 sprays/nostril) once daily batch # MN4689</p>	
<p><b>Duration of treatment:</b> 1 day- Patients were administered each test product in randomized order</p>	
<p>Reference therapy, dose and mode of administration, batch number: Flonase® Nasal Spray, 200 µg (=2 sprays/nostril), batch # CO25594 Nasonex® Nasal Spray 200 µg (=2 sprays/nostril), batch # OKTL128</p>	
<p><b>Criteria for evaluation:</b> <u>Patient preference</u> was assessed through two questionnaires measuring the acceptability of the product as well as sensory perceptions associated with the study agents:</p> <ol style="list-style-type: none"> <li>1. Nasal Spray Evaluation questionnaire (comfort, amount of medication run-down throat and nose, irritation, urge to sneeze, odor, taste, overall liking) was answered by the patient after administration of each product (3 questionnaires completed by the patient).</li> <li>2. Overall Nasal Spray Evaluation questionnaire was answered after the administration of the three products (1 questionnaire completed by the patient).</li> </ol> <p>The Nasal Spray Evaluation questionnaire included 14 items that were rated by the patient on a</p>	

100-point scale after the administration of each product. Ten items were rated immediately after product administration and four items were rated five minutes after product administration.

The Overall Nasal Spray Evaluation questionnaire included 2 questions answered by the patient after the administration of the three nasal sprays: the patient's preferred product to be prescribed, and the patient's expected compliance to each product.

Safety: Adverse event (AE) information collected at the clinic visit and baseline physical examination and vital signs.

**Statistical methods:** The mean score of the three Nasal Spray Evaluation questionnaires (one questionnaire was completed after each product administration) was summarized (n, mean, SD, median and range), by item and overall index, for each treatment group and overall.

Results were compared among the three nasal sprays (X, Y, Z) using an analysis of variance (ANOVA) of the cross-over design. Firstly, a 3-factors model (subject, treatment, and administration order) was used, including the interaction treatment x administration order. Only subject and treatment factors were kept (2-factors model) if all other effects (administration order and interaction) were non-significant.

The patient's preferred treatment to be prescribed was tabulated (n, %) by treatment (X, Y, Z) and overall, and compared among the three products by a Cochran-Mantel-Haenszel Test (preference frequencies by treatment controlling for subject).

The patient's expected compliance to treatment was tabulated (n, %) by treatment (X, Y, Z) and overall.

## SUMMARY – CONCLUSIONS

### PATIENT PREFERENCE RESULTS:

**Immediately following investigational product administration:** The statistically significant differences identified were in product odor and taste. Patients reported the odor of Nasacort® AQ to be less strong compared with Flonase® and Nasonex® [mean scores of 14.8 vs. 50.2 ( $p<0.0001$ ) and 53.2 ( $p<0.0001$ ), respectively]. Similarly, the taste of Nasacort® AQ was judged to be less strong than that of Flonase® and Nasonex® [mean scores of 14.4 vs. 21.6 ( $p=0.028$ ) and 28.9 ( $p<0.0001$ ), respectively]. Nasacort® AQ was rated more favorably for “liking taste” over Nasonex® (mean score of 76.0 vs. 65.7,  $p=0.005$ ).

In addition, immediately after administration Nasacort® AQ had a less bitter taste than Nasonex® (mean score of 9.2 vs. 16.7,  $p=0.014$ ). Also, patients perceived that less Nasacort® AQ ran down their nose and throat compared with Nasonex® (mean score of 25.9 vs. 32.3,  $p=0.038$ ); however, no statistically significant difference between treatments in medication run-off was found 5 minutes after administration.

In terms of differences between Flonase® and Nasonex®, Flonase® was rated as superior to Nasonex® for overall comfort during administration (mean score of 77.0 vs. 70.8,  $p=0.040$ ), strength of urge to sneeze (mean score of 12.8 vs. 19.1,  $p=0.030$ ), strength of taste (mean score of 21.6 vs. 28.9,  $p=0.026$ ), and bitter taste (mean score of 10 vs. 16.7,  $p=0.030$ ).

**Five minutes after administration:** Nasacort® AQ was rated as having less aftertaste than Nasonex® (mean score of 15.5 vs. 25.9,  $p=0.003$ ), and had significantly less irritation than Nasonex® (mean score of 19.2 vs. 26.3,  $p=0.022$ ). Also, Nasacort® AQ was rated higher for overall liking of product than Nasonex® (mean score of 67.5 vs. 55.6,  $p=0.0002$ ). Flonase® was rated as having significantly less irritation than Nasonex® (mean score of 17.8 vs. 26.3,  $p=0.005$ ). In addition, Flonase® was rated higher for overall product liking than Nasonex® (mean score of 63.6 vs. 55.6,  $p=0.017$ ). The differences between Nasacort® AQ and Flonase® for the amount of irritation and overall liking of the product were not statistically significant.

**Overall:** Patients indicated a preference (Total Preference Score 1) for Nasacort® AQ over both Flonase® and Nasonex® [mean scores of 76.9 vs. 73.4 ( $p=0.043$ ) and 68.7 ( $p<0.0001$ ), respectively]. The overall assessment of patient preference using the “Total Preference Score 2” score [the sum of the scores for the Nasal Spray Evaluation excluding patient’s overall liking (item 14)] had similar results, with Nasacort® AQ again ranked statistically significantly higher than either Flonase® (mean score of 77.8 vs. 74.3,  $p=0.035$ ) or Nasonex® (mean score of 77.8 vs. 69.9,  $p<0.0001$ ).

**SAFETY RESULTS:** Overall, Nasacort® AQ, Nasonex®, and Flonase® were safe and well tolerated in a single administration at a dose of 220 mcg, 200 mcg, and 200 mcg, respectively. When interviewed regarding any AEs that occurred following each nasal spray administration, of all 106 patients, 2 (1.9%) patients reported 2 AEs following Nasacort® AQ administration, one (0.9%) patient reported one AE following Nasonex® administration, and 5 (4.7%) patients reported 7 AEs following Flonase® administration. Most of the AEs reported during the study

were of mild intensity. All of the AEs were related to the study medication.

There were no deaths during the study. No patient prematurely discontinued from the study due to an AE.

**Date of the report:** 16 December, 2002