(III) Supplementary Efficacy Variables:

(1) **Mean change from baseline in subject evaluated total nasal symptom scores during the ragweed season (a.m. and p.m. combined), for days 1-15 (with days 1-7 and days 8-15 analyzed separately), days 16-30, days 31-45, days 46-61, days 61-71, and the endpoint visit (ITT population, Tables VII.-XI., SAS Datafiles). Refer to Attachment 1 for line listings.**

A review of the combined (a.m. and p.m. combined) mean change in the **total nasal symptom** scores as compiled from the SAS datafiles for the ITT population for all time intervals of study C93-215, indicates that at all 15 day time intervals after the start of the pollen season, with the exception of the day 31-45 and day 61-71 time intervals (which because of study design and a small subject number at these latter two time points, were non-estimable (N/E)), the mometasone treatment group demonstrated a statistically less significant increase in total nasal symptoms than the placebo treatment group ($p < .01$). Of note, the mometasone treatment group also demonstrated a statistically less significant increase in total nasal symptoms than the placebo treatment group (total nasal symptom score mometasone group=0.4, total nasal symptom score placebo group=0.7, $p<.01$; mean change in nasal score, mometasone group=0.1 (66%), mean change in nasal score, placebo group=0.3 (97.9%), $p=0.04$) during the prophylaxis period (Table VII.). The reason for this discrepancy is unclear, and although the 3 treatment populations were noted to have a similar severity of seasonal allergic rhinitis symptoms at baseline, the difference of the total nasal symptom scores between the mometasone group and placebo group was marginally statistically significant ($p=0.07$). Whether or not some subjects had underlying perennial rhinitis despite careful exclusion criteria to avoid enrolling subjects with active or anticipated active perennial rhinitis is also unclear. In summary, the mean scores increased in all treatment groups both before (the prophylaxis period) and after onset of the pollen season, however, for all 3 treatment groups, total nasal symptom scores were significantly greater after the onset of the pollen season.

Comparing the two active treatments, while not statistically significant, the mometasone treatment group demonstrated a numerically smaller increase in total nasal symptoms than the beclomethasone treatment group at all 15 day time intervals (Tables VII., VIII., IX., X., and XI.). For all 3 treatment groups and for all time periods, the standard deviation in the percent change in total nasal symptom scores was high, attesting to the high variability in subject nasal symptom scores.

Regarding the day 1-15 interval, the percent increase in total nasal symptoms in the mometasone treatment group was numerically smaller (total nasal symptom score=0.7, mean change in total nasal score=0.4 (86.6%) than the beclomethasone treatment group (total nasal symptom score=1.0, mean change in total nasal score=0.6 (216%), or the placebo group (total nasal symptom

score=2.0, mean change in total nasal score=1.6 (367%). In other words, mometasone pre-treated subjects had less severe worsening of SAR allergic symptoms during onset of the allergy season than did the other 2 treatment groups which was statistically significantly less severe when compared with placebo subjects but not when compared with beclomethasone subjects. Evaluation of subject diary scores for the day 1-15 interval separately for the a.m. and p.m. in order to assess duration of drug effect, failed to show a significant difference in raw total nasal symptom scores for either of the two active treatments but did show a greater change (% increase) in symptom scores during the p.m. in the mometasone treatment group (also noted for the beclomethasone group). These findings suggest that during the active ragweed season, no significant waning of effect of mometasone in decreasing SAR symptoms appears evident by 24 hours (mometasone group: 0.8=a.m. score (47.9% change) vs. 0.7=p.m. score (68% change). These results are summarized in Table VIII. of the review.

A separation of the day 1-15 interval into weekly intervals of day 1-7 and day 8-15 is presented in Tables IX. and X. of the review. Notable by week 2 of the pollen season (day 8-15), as compared with week 1, is a continued increase in total nasal symptoms for all 3 treatment groups. Nonetheless, the total nasal symptom score and mean change in total nasal symptom score for the mometasone treatment group was lower than the other 2 treatment groups (mometasone group: total nasal symptom score=0.9 and mean change in total nasal symptom score=0.5 (+125%)), and was statistically significantly lower than the placebo group. For the mometasone group per se, no significant difference in raw total nasal symptom scores was noted for the a.m. vs. p.m. scores during week 2 of treatment, although the p.m. score showed a slight increase in the percent change (week 2: a.m.= +75.4%, p.m.= +97.9% change).

Analysis of the day 16-30 interval during the ragweed season continued to demonstrate the greater efficacy of mometasone treatment in decreasing subject evaluated total nasal symptoms, as compared with the beclomethasone treatment group and placebo group, ((mometasone group: total nasal symptom score=1.2 and mean change in total nasal symptom score=0.8 (+184%), beclomethasone group (total nasal symptom score=1.4 and mean change in total nasal symptom score=1.0 (+225%), and placebo group, (total nasal symptom score=2.4 and mean change in total nasal symptom score=1.9 (+442%), $p < 0.01$ for mometasone vs. placebo and mometasone vs. beclomethasone for both raw total nasal symptom scores and the mean change in total nasal symptom score)).

Further analysis for days 31-45 and days 46-61 of the ragweed season required accounting for subject dropout at these later study timepoints, hence making it impossible to comment on the statistical significance of these findings. Nonetheless, the total nasal symptom scores for these two time intervals support conclusions for the day 1-15 and day 16-30 time points; namely that the mometasone treatment group had a smaller increase in total nasal symptoms as the ragweed season continued than either the beclomethasone treatment group or placebo (mometasone group: day 31-45: total nasal symptom score=1.4, mean

change in total nasal symptom score=1.0 (+173% increase), day 46-61: total nasal symptom score=1.4, mean change in total nasal symptom score=1.0 (+281%)). Total nasal symptom scores for the endpoint visit for all 3 treatment groups were similar to that of the day 16-30 interval. Of note, the total nasal symptom scores, the mean change in total nasal symptom scores, and the percent increase in scores did not uniformly increase for all treatment groups (namely, the mometasone group and placebo group) as the ragweed season advanced. The clinical implications of these findings are unclear but given the large standard deviation in subject symptom scores (refer to Table XI.), these findings most likely reflect large inter-subject and possibly intra-subject variability of symptom recording. A summary of the findings for these timepoints is provided in Table XI.

Reviewer's Note: As noted for the SAR studies of this NDA submission, the a.m. and p.m. scoring system represents an integration of the subject's symptoms over the previous 12 hours and does not represent a 'snap-shot' of the subject's clinical status at the particular time of symptom recording.

The majority of subjects in this study received mometasone prophylaxis for 4 weeks, however, of those who did not (primarily subjects at study sites -02 and -09, who received from 14-21 days of pre-treatment with mometasone (a total of 30 subjects) or one of the other treatments), shorter duration of pre-treatment with mometasone did not appear to change the trend in decreasing total nasal symptom scores (statistical comparison was not performed on these subjects because of low subject number and underpowering) [Response to FDA Request on Prophylaxis Studies, Schering Plough, Inc., 05/21/97, p. 58-84].

Furthermore, noted throughout this study for all supplementary efficacy variables was a significant decrease in study subject numbers (visit n values) for the % change in subject number (=n) for all subject evaluated symptom scores as the study progressed (total SAR, total nasal, total non-nasal, and individual nasal and non-nasal symptom scores). This decrease in subject number (=n) represented subjects who had 0 as a given symptom score with a resultant inability to compute the % change based on a denominator of 0. Acknowledging that the primary and secondary efficacy variables support the efficacy of mometasone in the prophylaxis of subjects with SAR, nonetheless the lack of incorporation of these subjects as data points into the supplementary efficacy variable analysis represents a study flaw which does not address symptom scores for all efficacy evaluable subjects.

Table VII.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Nasal Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION, [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARIS(A-B	A-C	
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-(
BASELINE																
--am & pm nasal	116	0.3	0.5	116	0.4	0.5	115	0.4	0.5	0.4	0.19	<.01	0.45	0.41	0.07	
--am nasal	116	0.4	0.5	115	0.5	0.6	115	0.5	0.6	0.5	0.49	<.01	0.34	0.39	0.25	
--pm nasal	116	0.3	0.5	115	0.3	0.4	115	0.4	0.6	0.8	0.08	<.01	0.67	0.53	0.03	
PROPHYLAXIS PERIOD																
--am & pm nasal																
RAW	116	0.4	0.7	115	0.6	1.0	115	0.7	0.9	0.8	0.05	<.01	0.62	0.14	<.01	
CHG	116	0.1	0.6	115	0.2	1.0	115	0.5	0.8	0.8	0.13	<.01	0.3	0.24	0.04	
%CHG	66	14.0	127	66	56.9	206	65	97.9	234							
--am nasal																
RAW	116	0.5	0.8	115	0.6	1.0	115	0.8	0.9	0.8	0.02	< .01	0.56	0.16	< .01	
CHG	116	0.1	0.7	115	0.2	1.1	115	0.3	0.9	0.8	0.09	< .01	0.2	0.37	0.03	
%CHG	63	2.4	124	57	0.5	140	60	106	272							
--pm nasal																
RAW	116	0.4	0.7	115	0.5	1.0	115	0.7	0.9	0.8	0.01	< .01	0.7	0.13	< .01	
CHG	116	0.1	0.6	115	0.2	1.0	115	0.3	0.8	0.8	0.23	0.03	0.47	0.26	0.09	
%CHG	43	1.1	135	43	54.9	161	52	87.0	227							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table VIII.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Nasal Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARISC A-B	A-C	B-
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-
BASELINE																
--am & pm nasal	116	0.3	0.5	115	0.4	0.5	115	0.4	0.6	0.4	0.19	<.01	0.46	0.41	0.07	
--am nasal	116	0.4	0.5	115	0.5	0.6	115	0.5	0.6	0.5	0.49	<.01	0.34	0.39	0.25	
--pm nasal	116	0.3	0.5	115	0.3	0.4	115	0.4	0.6	0.8	0.08	<.01	0.67	0.53	0.03	
DAYS 1-15 POLLEN (RAGWEED) SEASON																
--am & pm nasal																
RAW	114	0.7	1.0	111	1.0	1.3	109	2.0	2.0	1.6	<.01	<.01	0.01	0.1	<.01	
CHG	114	0.4	0.8	111	0.6	1.4	109	1.6	2.0	1.8	<.01	<.01	<.01	0.2	<.01	
%CHG	65	86.6	237	63	218	432	59	307	713							
--am nasal																
RAW	114	0.8	1.0	111	1.0	1.4	109	2.0	2.0	1.4	<.01	<.01	0.01	0.16	<.01	
CHG	114	0.4	0.9	111	0.6	1.4	109	1.5	2.1	1.5	<.01	<.01	<.01	0.26	<.01	
%CHG	62	47.9	174	55	115	355	55	307	622							
--pm nasal																
RAW	114	0.7	1.0	111	1.0	1.4	109	2.0	2.1	1.4	<.01	<.01	<.01	0.11	<.01	
CHG	114	0.4	1.0	111	0.7	1.4	109	1.6	2.1	1.5	<.01	0.01	<.01	0.17	<.01	
%CHG	42	68.0	203	42	168	382	47	282	511							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table IX.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Weekly Analysis of the Subject Evaluated Total Nasal Symptom Score: Supplementary Efficacy Variable--WEEK 1
Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARIS(A-B	A-C	
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	TXI	A-B	A-C	B-
BASELINE																
--am & pm nasal	116	0.3	0.5	118	0.4	0.6	115	0.4	0.6	0.4	0.18	<.01	0.44	0.41	0.07	
--am nasal	116	0.4	0.5	115	0.5	0.6	115	0.5	0.6	0.5	0.49	<.01	0.34	0.39	0.25	
--pm nasal	116	0.3	0.5	115	0.3	0.5	115	0.4	0.6	0.5	0.08	<.01	.67	0.53	0.03	
DAYS 1-7 POLLEN (RAGWEED) SEASON																
--am & pm nasal																
RAW	114	0.6	0.8	111	0.8	1.3	108	1.6	1.8	1.3	<.01	<.01	0.01	0.18	<.01	
CHG	114	0.2	0.8	111	0.4	1.3	109	1.2	1.8	1.3	<.01	<.01	0.01	0.19	<.01	
%CHG	65	42.9	197	63	173	3979	59	285	679							
--am nasal																
RAW	114	0.6	0.9	111	0.9	1.3	109	1.6	1.8	1.3	<.01	<.01	0.03	0.14	<.01	
CHG	114	0.2	0.8	111	0.4	1.3	109	1.1	1.9	1.4	<.01	<.01	.01	0.24	<.01	
%CHG	62	16.7	160	55	65.6	236	55	224	523							
--pm nasal																
RAW	114	0.5	0.8	111	0.8	1.3	109	1.6	1.9	1.3	<.01	<.01	,.01	0.11	<.01	
CHG	114	0.3	0.8	111	0.5	1.3	109	1.2	2.0	1.3	<.01	<.01	<.01	0.11	<.01	
%CHG	42	34.6	183	42	117	329	47	232	513							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table X.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Weekly Analysis of the Total Nasal Symptom Score: Supplementary Efficacy Variable--WEEK 2
Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARIS A-B	A-C	
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B
BASELINE																
--am & pm nasal	116	0.3	0.5	115	0.4	0.5	115	0.4	0.5	0.4	0.10	<.01	0.43	0.41	0.07	
--am nasal	116	0.4	0.5	115	0.5	0.6	115	0.5	0.6	0.5	0.49	<.01	0.34	0.39	0.25	
--pm nasal	116	0.3	0.5	115	0.3	0.5	115	0.4	0.6	0.5	0.08	<.01	.67	0.53	0.03	
DAYS 8-15 POLLEN (RAGWEED) SEASON																
--am & pm nasal																
RAW	114	0.9	1.2	108	1.2	1.5	105	2.2	2.3	1.8	<.01	<.01	<.01	0.18	<.01	
CHG	114	0.5	1.2	111	0.4	1.3	109	1.2	1.9	1.3	<.01	<.01	0.02	0.26	<.01	
%CHG	65	125	291	61	264	547	58	443	685							
--am nasal																
RAW	114	0.9	1.3	108	1.1	1.5	105	2.2	2.2	1.6	<.01	<.01	<.01	0.25	<.01	
CHG	114	0.5	1.2	108	0.7	1.6	105	1.7	2.3	1.6	<.01	<.01	<.01	0.34	<.01	
%CHG	62	75.4	211	53	166	510	55	380	734							
--pm nasal																
RAW	114	0.9	1.2	108	1.2	1.6	105	2.2	2.4	1.7	<.01	<.01	<.01	0.15	<.01	
CHG	114	0.6	1.3	108	0.8	1.7	105	1.8	2.5	1.7	<.01	<.01	<.01	0.2	<.01	
%CHG	42	97.9	243	40	231	542	47	327	545							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XI.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Nasal Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARISC A-B	A-C	E
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-(
BASELINE																
--am & pm nasal	116	0.3	0.5	116	0.4	0.5	115	0.4	0.6	0.4	0.19	<.01	0.32	0.41	0.07	
DAYS 16-30 POLLEN (RAGWEED) SEASON, am & pm nasal																
--am & pm nasal																
RAW	114	1.2	1.3	107	1.4	1.7	103	2.4	2.3	1.7	<.01	0.02	0.31	0.2	<.01	
CHG	114	0.8	1.3	107	1.0	1.8	103	1.9	2.3	1.8	<.01	0.13	0.06	0.42	<.01	
%CHG	65	184	322	60	228	369	58	442	856							
DAYS 31-45 POLLEN (RAGWEED) SEASON, am & pm nasal																
RAW	76	1.4	2.0	67	1.7	2.2	61	2.4	2.3	2.2	< .01	0.54	0.54	N/E	N/E	N/I
CHG	76	1.0	2.0	67	1.3	2.3	61	2.0	2.4	2.2	< .01	0.04	0.49	N/E	N/E	N/I
%CHG	40	173	361	33	223	611	30	404	880							
DAYS 46-61 POLLEN (RAGWEED) SEASON, am & pm nasal																
RAW	18	1.4	1.5	14	2.0	2.8	13	1.8	1.9	2.2	0.69	0.83	0.7	0.5	N/E	N/I
CHG	18	1.0	1.5	14	1.7	2.9	13	1.6	2.0	2.2	0.53	0.62	0.62	0.38	N/E	N/I
%CHG	11	281	384	8	602	1267	4	118	281							
ENDPOINT VISIT POLLEN (RAGWEED) SEASON, am & pm nasal																
RAW	116	1.2	1.7	115	1.5	1.9	115	2.6	2.5	2.0	< .01	0.02	0.08	0.26	< .01	
CHG	116	0.9	1.7	115	1.1	2.0	115	2.1	2.5	2.0	< .01	< .01	0.06	0.35	<.01	
%CHG	66	184	344	65	256	573	65	507	906							

SD= St' ' Deviation CHG=Change T X I = Treatment by Investigator interaction 'E=Non-estimable (due to small subject number)
# P-Va from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustm verall α level),

(III) Supplementary Efficacy Variables-cont:

(2) **Mean change from baseline ('baseline' defined as mean of the a.m. and p.m. symptom score from the subject diary for day 1/Visit 2 of the study plus the 3 prior consecutive days [179:35]) in total symptom scores during the ragweed season, as obtained from subject diaries (a.m. and p.m. combined) for: days 1-15 (with further separation into days 1-7 and days 8-15), days 16-30, days 31-45, days 46-61, and the endpoint visit. (ITT population, Tables XII.-XVI.). Refer to Attachment 1 for line listings.**

A review of the combined (a.m. and p.m. combined) mean change in the **total (nasal plus non-nasal) subject evaluated symptom** scores using the ITT population compiled from SAS datafiles for all time intervals of study C93-215, indicates that for all 15 day time intervals from the onset of the pollen season, with the exception of the prophylaxis period and the day 31-45 and day 61-71 time intervals (which because of study design and a small subject number at these latter two time points, were non-estimable (NE)), the mometasone treatment group demonstrated a statistically less significant increase in total symptoms than the placebo treatment group ($p < .01$). As was noted for the supplementary efficacy variable of the total nasal symptom score, the mean total symptom scores increased (as compared to baseline) in all treatment groups both before (the prophylaxis period) and after onset of the pollen season, with higher mean symptom score values recorded after the onset of the pollen season (Table XIII.). Again noted for the total symptom score during the prophylaxis period, and as discussed previously for the total nasal symptom score (prophylaxis period) was the numerically slightly smaller total symptom score for mometasone treatment subjects, as compared with the active treatment group and the placebo group. For the comparison of mometasone vs. the placebo group, these raw scores were statistically significant ($p=0.03$) but the mean differences were not ($p=0.2$).

Comparing the two active treatments, while not statistically significant, the mometasone treatment group demonstrated a numerically smaller increase in total symptom scores than the beclomethasone treatment group at all 15 day time intervals (Tables XIII.- XVI.). Evaluation of the first 15 day interval on a weekly basis revealed a numerically smaller increase in total symptom scores in the mometasone treatment group for week 1 (days 1-7) but not week 2 (days 8-15) of treatment.

Regarding the day 1-15 interval, the total SAR symptom score values and percent increase in total symptoms for the mometasone treatment group was numerically smaller (total SAR score=1.3, mean change=0.8 (208%) than the beclomethasone treatment group (total SAR score=1.7, mean change=1.1 (327%), and statistically significantly smaller than the placebo group (total SAR score=3.0, mean change=2.4 (428%), $p<.01$). Evaluation of subject diary scores for the day 1-15 interval separately for the a.m. and p.m. (Table XIII.) in order to assess

duration of drug effect, failed to show a significant difference in raw total symptom scores for either of the two active treatments but did show a greater change (% increase) in symptom scores during the p.m. in the mometasone treatment group (also noted for the beclomethasone group). Similar findings were demonstrated during analysis of the a.m. and p.m. scores for total nasal symptoms and again suggest that during the active ragweed season, no significant waning of effect of mometasone in decreasing total SAR symptoms appears evident by 24 hours post-dosing (mometasone group: 0.8=a.m. score (125% change) vs. 0.9=p.m. (95.2% change).

Separation of the day 1-15 interval into weekly intervals of day 1-7 and day 8-15 is presented in Tables XIV. and XV. of the review. Notable by week 2 of the pollen season (day 8-15), as compared with week 1, was a continued increase in total symptoms (a.m. and p.m. combined) for the mometasone treatment group, but no consistent increase in total symptoms for the beclomethasone or placebo treatment group. The clinical implications of this study finding are unclear, especially given the large standard deviations for each treatment group.

The raw total symptom score and percent change in symptom score for the mometasone treatment group was lower than the beclomethasone and placebo treatment groups for the first week of the ragweed season (mometasone group; raw score=1.0, mean change=0.5, % change=102% vs. the beclomethasone group; raw score=0.8, mean change=0.8, % change=267, and vs. the placebo group; raw score=2.3, mean change=1.8, % change=331; $p<.01$ for the mometasone group vs. placebo (Table XIV)). The raw total symptom score but not the percent change in symptom score for the mometasone treatment group was likewise lower than the beclomethasone and placebo treatment groups during the second week of the ragweed season ($p<.01$ for the mometasone group vs. placebo).

Analysis of the day 16-30 interval during the ragweed season demonstrated the continued greater efficacy of mometasone treatment in decreasing subject evaluated total symptoms, as compared with the beclomethasone treatment group and placebo group (mometasone group: total SAR symptom score=2.0, mean change=1.5 (279% increase in total symptoms), beclomethasone group: total SAR symptom score=2.5, mean change=2.0 (391% increase in total symptoms) and placebo group: total SAR symptom score=3.7, mean change=3.1, (574% increase in total symptoms (Table XVI)), $p<.01$ for mometasone vs. placebo and mometasone vs. beclomethasone)).

Analysis of the day 31-45 and day 46-61 study intervals reveal a mild steady increase in total SAR symptoms for the mometasone and beclomethasone treatment groups and a comparable plateauing of total SAR symptoms for the placebo group by day 31-45 (Table XVI.). Numerically, the total SAR symptom score was lower and % change in the total SAR symptom score for the mometasone group was smaller than that of the placebo or the beclomethasone groups, however, no conclusion could be based on these findings given the smaller number of subjects at these study points (i.e. study underpowering to derive a conclusion for these 2 time intervals). As was noted for the total nasal symptom

score, the total score for all three treatment groups at the endpoint visit was most similar to the day 16-30 interval.

(3) **Mean change from baseline ('baseline' defined as mean of the a.m. and p.m. symptom score from the subject diary for day 1/Visit 2 of the study plus the 3 prior consecutive days [179:35]) in total non-nasal symptom scores during the ragweed season, as obtained from subject diaries (a.m. and p.m. combined) for days 1-15, days 16-30, days 31-45, days 46-61, and the endpoint visit (ITT population, Tables XVII.-XIX.). Refer to Attachment 1 for line listings.**

Review of the combined (a.m. and p.m. combined) mean change in the **total non-nasal symptom** scores for the ITT population (using the primary SAS datafiles) for all time intervals of study C93-215, indicates that at all 15 day time intervals after onset of the pollen season (with the exception of the baseline period ($p=0.22$), the prophylaxis period ($p=0.96$) and the day 31-45 and 61-71 intervals--the latter secondary to a non-estimable p-value), the mometasone treatment group demonstrated a less statistically significant increase in total non-nasal symptoms than the placebo treatment group as noted in both the raw symptom score and the percent change from baseline in the total non-nasal score ($p<.01$).

Comparing the two active treatments, while not statistically significant, the mometasone treatment group demonstrated a numerically smaller increase in total non-nasal symptom scores than the beclomethasone treatment group at all 15 day intervals with the exception of the prophylaxis period (Tables XVII.-XIX.). Once again, for all 3 treatment groups and for all time periods, the large standard deviation in the percent change in the total nasal symptom score appears to confirm previous implications that subject SAR symptom scores have high variability.

In terms of the day 1-15 interval, the raw total non-nasal symptom score, the mean change in total non-nasal symptoms and the percent change in total non-nasal symptoms in the mometasone treatment group was statistically significantly smaller ($p<.01$) than the placebo group, but not so when compared with the beclomethasone group ($p=0.56$ for raw symptom score or $p=0.66$ for mean change in raw non-nasal symptom score). Evaluation of subject diary scores for the day 1-15 interval separately for the a.m. and the p.m. to assess duration of drug effect, failed to show a signficant difference in the raw non-nasal symptom score for the mometasone treatment group (mometasone group; raw score: a.m.=0.6 and p.m.=0.6, mean change in score: a.m.=0.4, p.m.=0.5). Similar findings of lack of waning of a duration effect on total non-nasal SAR symptoms were likewise noted for the beclomethasone treatment group and the placebo group for study C93-215 (Table XVIII.). Separation of the day 1-15 interval into weekly intervals of day 1-7 and day 8-15 in order to assess subject response from week 1 to week 2 of the ragweed season was not performed for the supplementary efficacy endpoint of total non-nasal symptoms.

Analysis of the day 16-30 interval (a.m. and p.m. scores combined) during the ragweed season demonstrated greater efficacy of the mometasone treatment group in decreasing total non-nasal symptom scores compared with placebo (p=0.01) and numerically (though not statistically) greater efficacy when compared with the beclomethasone treatment group (raw score comparison of mometasone vs. beclomethasone, p=0.17, comparison of the mean change in non-nasal symptom score for mometasone vs. beclomethasone, p=0.2).

Having taken into account subject dropouts, evaluation of the day 31-45 and day 46-61 interval of the ragweed pollen season nonetheless revealed a lower mean total non-nasal symptom score and smaller mean change in the non-nasal score in the mometasone group, as compared with placebo and the beclomethasone active control (Table XIX.). These findings are similar to those noted for subject total nasal and total SAR symptom scores. Total non-nasal symptom scores for the endpoint visit for all 3 treatment groups were similar to that of the day 16-30 interval. For the most part, the raw total non-nasal symptom scores and the percent increase in scores mildly but steadily increased for all treatment groups as the ragweed season advanced. Similar trends in data were noted for the prior 2 supplementary efficacy variables of total nasal and total SAR symptoms discussed previously. Given that the ragweed pollen counts were likely decreasing in at least several study centers (C93-215-02, -03, and -06) approximately 1 month after onset of the pollen season [179:175-183], the etiology of the increasing symptom scores in at least some study subjects (e.g. study site -02: subject 005, 017, 019, 020 (mometasone treatment group); study site -06: subject 041, study site -03 excluded because most subjects did not complete treatment beyond 30 days post-initiation of the ragweed season (efficacy evaluable population [179:122-123, 124-125, 130-131]): is not readily explained, although similar trends were observed for individual subjects in the beclomethasone and placebo treatment groups as well.

A summary of the statistical response of total nasal, total non-nasal, and total SAR (nasal plus non-nasal) seasonal allergic rhinitis symptoms for all 15 day study intervals is provided in Table XX. below.

Table XII.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARIS A-B	A-C	B
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-(
BASELINE																
--am & pm total	116	0.5	0.6	115	0.6	0.8	115	0.6	0.8	0.7	0.15	<.01	0.14	0.4	0.03	
--am total	116	0.6	0.7	115	0.7	0.9	115	0.7	0.9	0.7	0.54	<.01	0.14	0.42	0.29	
--pm total	116	0.4	0.6	115	0.5	0.8	115	0.6	0.9	0.7	0.05	<.01	0.31	0.46	0.02	
PROPHYLAXIS PERIOD																
--am & pm total symptom score																
RAW	116	0.7	1.0	115	0.9	1.6	115	1.1	1.5	1.3	0.09	<.01	0.49	0.23	0.03	
CHG	116	0.2	0.8	115	0.3	1.7	115	0.4	1.1	1.2	0.44	<.01	0.28	0.47	0.2	
%CHG	72	30.3	157	66	106	325	70	85.3	244							
--am total symptom score																
RAW	116	0.8	1.1	115	0.9	1.7	115	1.1	1.4	1.3	0.09	<.01	0.51	0.3	0.03	
CHG	116	0.2	1.0	115	0.3	1.8	115	0.5	1.2	1.3	0.26	<.01	0.2	0.54	0.1	
%CHG	70	25.6	148	61	19.1	133	63	120	297							
--pm total symptom score																
RAW	116	0.6	0.9	115	0.8	1.6	115	1.0	1.2	1.2	0.09	<.01	0.45	0.22	0.03	
CHG	116	0.2	1.6	115	0.3	1.7	115	0.4	1.1	1.3	0.65	0.01	0.27	0.42	0.42	
%CHG	50	23.8	67.8	50	67.8	189	58	74.4	217							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XIII.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARISC A-B	A-C	E
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-(
BASELINE																
--am & pm total	116	0.5	0.6	115	0.6	0.8	115	0.6	0.9	0.7	0.18	<.01	0.14	0.4	0.06	
--am total	116	0.6	0.7	115	0.7	0.9	115	0.7	0.9	0.7	0.54	<.01	0.14	0.42	0.29	
--pm total	116	0.4	0.6	115	0.5	0.8	115	0.6	0.9	0.7	0.05	<.01	0.31	0.46	0.02	
DAYS 1-15 POLLEN (RAGWEED) SEASON																
--am & pm total																
RAW	114	1.3	1.5	111	1.7	2.2	109	3.0	3.2	2.3	<.01	<.01	0.01	0.23	<.01	
CHG	114	0.8	1.5	111	1.1	2.2	109	2.4	3.3	2.3	<.01	<.01	<.01	0.06	<.01	
%CHG	71	208	542	65	327	839	64	486	1065							
--am total symptom score																
RAW	114	1.4	1.6	111	1.7	2.2	109	3.0	3.2	2.3	<.01	<.01	0.02	0.28	<.01	
CHG	114	0.8	1.5	111	1.0	2.3	109	2.4	3.3	2.3	<.01	<.01	0.01	0.39	<.01	
%CHG	69	125	296	58	191	400	58	459	938							
--pm total symptom score																
RAW	114	1.3	1.6	111	1.7	2.2	109	3.0	3.4	2.4	<.01	<.01	<.01	0.19	<.01	
CHG	114	0.9	1.6	111	1.2	2.2	109	2.5	3.4	2.4	<.01	<.01	<.01	0.27	<.01	
%CHG	49	95.2	176	49	229	432	52	307	572							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XIV.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARIS A-B	A-C	
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-
BASELINE																
--am & pm total	116	0.5	0.6	115	0.6	0.8	115	0.6	0.8	0.7	0.19	<.01	0.14	0.4	0.06	
--am total	116	0.6	0.7	115	0.7	0.9	115	0.7	0.9	0.7	0.54	<.01	0.14	0.42	0.29	
--pm total	116	0.4	0.6	115	0.5	0.8	115	0.6	0.9	0.7	0.05	<.01	0.31	0.46	0.02	
DAYS 1-7 POLLEN (RAGWEED) SEASON																
--am & pm total symptom score																
RAW	114	1.0	1.3	111	1.2	2.1	109	2.3	3.0	2.1	<.01	0.03	0.11	0.3	<.01	
CHG	114	0.5	1.3	111	0.8	2.1	109	1.8	3.0	2.1	<.01	0.02	0.02	0.36	<.01	
%CHG	71	102	270	65	267	903	84	331	750							
--am total symptom score																
RAW	114	1.1	1.3	111	1.3	2.1	109	2.3	2.8	2.1	<.01	0.04	0.11	0.3	<.01	
CHG	114	0.5	1.3	111	0.7	2.1	109	1.7	2.9	2.1	<.01	0.02	0.02	0.42	<.01	
%CHG	69	61.2	199	58	133	312	58	291	644							
--pm total symptom score																
RAW	114	1.0	1.3	111	1.3	2.1	109	2.4	3.1	2.2	<.01	0.02	0.01	0.22	<.01	
CHG	114	0.6	1.3	111	0.8	2.1	109	1.8	3.2	2.2	<.01	0.02	<.01	0.32	<.01	
%CHG	49	50.2	169	49	172	427	52	226	503							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XV.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARIS A-B	A-C	
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B
BASELINE																
--am & pm total	116	0.5	0.6	115	0.6	0.8	115	0.6	0.8	0.7	0.16	<.01	0.14	0.4	0.06	
--am total	116	0.6	0.7	115	0.7	0.9	115	0.7	0.9	0.7	0.54	<.01	0.14	0.42	0.29	
--pm total	116	0.4	0.6	115	0.5	0.8	115	0.6	0.9	0.7	0.05	<.01	0.31	0.46	0.02	
DAYS 8-15 POLLEN (RAGWEED) SEASON																
--am & pm total symptom score																
RAW	114	1.6	2.0	108	2.0	2.5	105	2.3	3.9	2.1	<.01	<.01	<.01	0.35	<.01	
CHG	114	1.1	2.0	108	0.5	2.1	105	1.8	3.9	2.1	<.01	<.01	<.01	0.34	<.01	
%CHG	71	298	870	65	267	503	64	351	750							
--am total symptom score																
RAW	114	1.6	2.0	108	1.9	2.4	105	3.4	3.9	2.7	<.01	<.01	<.01	0.35	<.01	
CHG	114	1.1	2.0	108	1.3	2.5	105	2.8	4.0	2.7	<.01	<.01	<.01	0.43	<.01	
%CHG	69	181	468	56	248	514	58	607	1248							
--pm total symptom score																
RAW	114	1.6	2.0	108	2.0	2.6	105	3.5	4.2	2.9	<.01	<.01	<.01	0.2	<.01	
CHG	114	1.2	2.1	108	1.5	2.6	105	3.0	4.3	2.9	<.01	<.01	<.01	0.27	<.01	
%CHG	49	136	215	47	291	496	52	226	503							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XVI.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARIS A-B A-C		
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-
BASELINE																
—am & pm total	116	0.5	0.6	115	0.5	0.6	115	0.6	0.6	0.7	0.15	<.01	0.74	0.4	0.06	[illegible]
DAYS 16-30 POLLEN (RAGWEED) SEASON, am & pm total symptom scores																
RAW	114	2.0	2.8	107	2.5	3.1	103	3.7	4.0	3.5	<.01	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
CHG	114	1.5	2.5	107	2.0	3.2	103	3.1	4.0	3.5	<.01	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
%CHG	71	279	464	62	301	642	63	574	859							
DAYS 31-45 POLLEN (RAGWEED) SEASON, am & pm total symptom scores																
RAW	76	2.3	3.5	67	2.9	4.0	61	3.6	4.2	3.9	0.02	0.19	0.72	N/E	N/E	N/
CHG	76	1.8	3.5	67	2.4	4.2	61	3.0	4.1	3.9	0.04	0.02	0.8	N/E	N/E	N/
%CHG	45	184	329	35	333	638	34	712	1716							
DAYS 46-61 POLLEN (RAGWEED) SEASON, am & pm total symptom scores																
RAW	18	2.4	2.8	14	2.9	5.8	13	2.5	2.6	4.0	0.77	0.8	0.67	0.63	N/E	N/
CHG	18	1.8	2.8	14	3.5	5.8	13	2.2	2.6	4.0	0.58	0.59	0.53	0.47	N/E	N/
%CHG	12	351	453	9	768	967	6	660	1200							
ENDPOINT VISIT POLLEN (RAGWEED) SEASON, am & pm total symptom scores																
RAW	116	2.0	3.0	115	2.6	3.5	115	3.9	4.3	3.5	<.01	<.01	0.06	0.16	<.01	
CHG	116	1.5	3.0	115	2.0	3.6	115	3.3	4.3	3.5	<.01	<.01	0.06	0.21	<.01	
%CHG	72	260	462	68	403	684	70	771	1582							

SD= Standard Deviation   CHG=Change   T X I = Treatment by Investigator interaction   N/E=Non-estimable (due to small subject number)
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XVII.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Non-Nasal Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARISC A-B	A-C	E
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-(
BASELINE																
--am & pm non-nasal	116	0.1	0.3	115	0.2	0.4	115	0.2	0.4	0.4	0.47	<.01	0.07	0.8	0.22	
--am non-nasal	116	0.1	0.3	115	0.2	0.4	115	0.2	0.4	0.4	0.85	<.01	0.04	0.66	0.59	
--pm non-nasal	116	0.1	0.3	115	0.2	0.4	115	0.2	0.5	0.4	0.21	<.01	0.2	0.57	0.08	
PROPHYLAXIS																
--am & pm non-nasal																
RAW	116	0.3	0.4	115	0.3	0.8	115	0.3	0.6	0.6	0.79	<.01	0.46	0.97	0.49	
CHG	116	0.1	0.4	115	0.1	0.8	115	0.1	0.4	0.4	0.99	<.01	0.47	0.91	0.66	
%CHG	33	132	429	26	91.1	264	37	207	384							
--am non-nasal																
RAW	116	0.3	0.5	115	0.3	0.8	115	0.3	0.7	0.6	0.73	<.01	0.64	0.75	0.44	
CHG	116	0.1	0.4	115	0.1	0.8	115	0.2	0.5	0.6	0.87	<.01	45	0.95	0.62	
%CHG	29	28.4	161	26	-30	81.0	29	22.0	140							
--pm non-nasal																
RAW	116	0.2	0.4	115	0.3	0.8	115	0.3	0.5	0.6	0.82	<.01	0.46	0.59	0.58	
CHG	116	0.1	0.4	115	0.1	0.9	115	0.1	0.5	0.6	0.73	0.02	0.42	0.88	0.55	
%CHG	21	-1.2	111	19	-43	58.3	32	-15	117							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XVIII.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Non-Nasal Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARISC A-B	A-C	E
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-(
BASELINE																
--am & pm non-nasal	116	0.1	0.3	115	0.2	0.4	115	0.2	0.4	0.4	0.47	<.01	0.01	0.5	0.22	
--am non-nasal	116	0.1	0.3	115	0.2	0.4	115	0.2	0.4	0.4	0.85	<.01	0.04	0.66	0.59	
--pm non-nasal	116	0.1	0.3	115	0.2	0.4	115	0.2	0.5	0.4	0.21	<.01	0.2	0.57	0.08	
DAYS 1-15 POLLEN (RAGWEED) SEASON																
--am & pm non-nasal																
RAW	114	0.6	0.8	111	0.7	1.0	109	1.0	1.6	1.1	<.01	0.02	0.1	0.09	<.01	
CHG	114	0.4	0.9	111	0.5	1.0	109	0.9	1.5	1.1	<.01	0.01	0.2	0.62	<.01	
%CHG	33	132	423	26	91.1	264	37	207	384							
--am non-nasal																
RAW	114	0.6	0.9	111	0.6	1.0	109	1.0	1.5	1.1	0.01	0.09	0.16	0.67	<.01	
CHG	114	0.4	0.9	111	0.5	1.0	109	0.9	1.40	1.1	<.01	0.03	0.05	0.75	<.01	
%CHG	29	71.8	256	24	35.9	187	25	149	358							
--pm non-nasal																
RAW	114	0.6	0.9	111	0.7	1.1	109	1.1	1.5	1.1	<.01	0.01	0.06	0.46	<.01	
CHG	114	0.5	0.9	111	0.5	1.1	109	0.9	1.5	1.1	0.01	<.01	0.08	0.58	<.01	
%CHG	21	-3.3	98.9	19	47.5	148	27	136	295							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XIX.
Efficacy of Mometasone vs. Beclomethasone vs. Placebo in the Treatment of SAR:
Subject Evaluated Total Non-nasal Symptom Scores
Supplementary Efficacy Variable--Intent-to-Treat (ITT) POPULATION [SAS Datafiles for NDA 20-762, Attachment 1]

	(A) Mometasone			(B) Beclomethasone			(C) Placebo			Pooled	ANOVA P-Values			PAIRWISE COMPARISC A-B	A-C	B-(
DAYS	N	Mean	SD	N	Mean	SD	N	Mean	SD	SD	TRT	INV	T X I	A-B	A-C	B-(
BASELINE																
-am & pm non-nasal	116	0.1	0.3	116	0.2	0.4	116	0.2	0.4	0.4	0.47	<.01	0.07	0.63	0.12	
DAYS 16-30 POLLEN (RAGWEED) SEASON, am & pm total non-nasal symptom scores																
RAW	114	0.8	1.3	107	1.1	1.7	103	1.3	2.0	1.6	0.03	<.01	0.08	0.17	0.03	
CHG	114	0.7	1.3	107	0.9	1.7	103	1.2	1.9	1.6	0.04	<.01	0.08	0.2	0.01	
%CHG	33	130	267	25	137	383	37	207	384							
DAYS 31-45 POLLEN (RAGWEED) SEASON, am & pm total non-nasal symptom scores																
RAW	76	0.9	1.7	67	1.2	2.0	61	1.2	2.1	1.9	0.26	0.06	0.91	N/E	N/E	N/I
CHG	76	0.8	1.8	67	1.1	2.1	61	1.0	2.0	1.9	0.41	0.01	0.96	N/E	N/E	N/I
%CHG	26	143	300	18	203	490	22	280	560							
DAYS 46-61 POLLEN (RAGWEED) SEASON, am & pm total non-nasal symptom scores																
RAW	18	1.0	1.5	14	1.9	3.1	13	0.7	1.0	2.1	1.9	0.26	0.06	0.91	N/E	N/I
CHG	18	0.8	1.5	14	1.8	3.0	13	0.7	1.0	2.0	0.69	0.6	0.37	0.63	N/E	N/I
%CHG	7	349	749	3	802	756	3	294	460							
ENDPOINT VISIT POLLEN (RAGWEED) SEASON, am & pm total non-nasal symptom scores																
RAW	116	0.8	1.5	115	1.1	1.8	115	1.4	2.1	1.8	0.04	<.01	0.06	0.13	0.01	
CHG	116	0.6	1.5	115	0.9	1.9	115	1.2	2.0	1.7	0.06	<.01	0.08	0.16	0.02	
%CHG	33	176	438	28	150	440	42	239	430							

SD= Standard Deviation CHG=Change T X I = Treatment by Investigator interaction N/E=Non-estimable (due to small subject number)
# P-Values are from 2-way analysis of variance and LSMeans pairwise comparisons (no adjustment for overall α level)

Table XX. Summary of Change in SAR Symptoms (a.m. and p.m. combined) with Mometasone Treatment
[SAS Datafiles for NDA 20-762, Attachment 1]

SAR SYMPTOM	*Statistical Response: Prophylaxis Period (Yes=Y/No=N)	*Statistical Response$_{DAY\ 1\text{-}15}$ (Yes=Y/No=N)	Statistical Response$_{DAY\ 16\text{-}30}$ (Y/N)	Statistical Response$_{DAY\ 31\text{-}45,\ DAY\ 46\text{-}61}$ (Y/N)	Statistical Response$_{Endpoint}$ (Y/N)
Total symptoms	No (^{2}p=0.2)	Yes	Yes	N/E	Yes
Total nasal symptoms	Yes	Yes	Yes	N/E	Yes
Total non-nasal symptoms	No (p=0.96)	Yes	Yes	N/E	Yes

* Statistical Response= Statistical response of mometasone treatment group, as compared with placebo.
N/E=non-estimable, based on inadequate subject numbers to maintain a power of 90%.
[2] p values were calculated based on the change in symptom score from baseline.

(III) Supplementary Efficacy Variables-cont.

(4) **Mean change from baseline ('baseline' defined as mean of the a.m. and p.m. symptom score from the subject diary for day 1/Visit 2 of the study plus the 3 prior consecutive days [179:35]) in individual nasal symptom scores during the ragweed season, as obtained from subject diaries (a.m. and p.m. combined) for days 1-15, days 16-30, days 31-45, days 46-61, and the endpoint visit (ITT population). Refer to Attachment 1 for line listings.**

Analysis of subject evaluated individual nasal symptom scores for each 15 day study interval subsequent to the onset of the pollen season included the following four nasal symptoms: rhinorrhea (nasal discharge), sneezing, nasal congestion, and nasal itch. Of note, the day 1-15 interval for the individual nasal symptom scores was not sub-analyzed by week 1 and week 2.

Evaluation of subject **rhinorrhea** (a.m. and p.m. combined) revealed that the mometasone treatment group had a lower mean rhinorrhea score than the placebo group at all 15 day time points with the marginal exception of the prophylaxis period (prophylaxis period rhinorrhea (raw) score: mometasone vs. placebo, p=0.03, mean change in score: mometasone vs. placebo, p=0.25) and which was statistically significant at day 1-15 (rhinorrhea score: mometasone group=0.2, % change=-1.6; rhinorrhea score: placebo=0.5, % change=55.2; p<.01 for both raw score and mean change) and day 16-30 (rhinorrhea score: mometasone group=0.3, % change=66.7; rhinorrhea score: placebo=0.6, % change=119; p<.01 for both raw score and mean change). While the mean rhinorrhea score for the mometasone group was numerically lower than that of the placebo group for the endpoint visit (rhinorrhea score: mometasone group=0.3, % change=84.0; rhinorrhea score: placebo=0.7, % change=74.0; p<.01 for both raw score and mean change), the mean % change in rhinorrhea increased for mometasone subjects. Rhinorrhea scores at day 31-45 and day 46-61 were lower for the mometasone treatment group than placebo but statistical significance was not assigned to these values because of study underpowering. Comparison of the mometasone treatment group with the active comparator, beclomethasone on this clinical endpoint revealed that in general, the mometasone treatment group had rhinorrhea scores numerically lower than or equal to the rhinorrhea scores of the beclomethasone treatment group for all 15 day study intervals. These differences were not statistically significant at any of the 15 day study intervals. Evaluation of rhinorrhea scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the rhinorrhea score at any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score. Post-hoc analysis of the a.m. vs. the p.m. scores was not performed, thus a significance level was not obtained for these values.

Evaluation of subject evaluated **sneezing** scores for the mometasone treatment group vs. placebo for all 15 day study intervals with the marginal

exception of the prophylaxis period (prophylaxis period sneezing (raw) score: mometasone vs. placebo, p=0.04, mean change in score: mometasone vs. placebo=0.2), revealed that sneezing scores and mean change in sneezing scores were statistically lower for the mometasone group than the placebo group ((day 1-15: sneezing score: mometasone group=0.2, % change=1.9; sneezing score: placebo=0.5, % change=120; p<.01 for both raw score and mean change and day 16-30: sneezing score: mometasone group=0.2, % change=62.6; sneezing score: placebo=0.5, % change=136; p<.01 for both the raw score and mean change)). While the mean sneezing score for the mometasone group was numerically lower than that of the placebo group for the endpoint visit (sneezing score: mometasone group=0.3, % change=120; sneezing score: placebo=0.6, % change=93.4; p<.01 for both the raw score and mean change), the mean % change in sneezing increased for mometasone subjects. Again, sneezing scores at day 31-45 and day 46-61 intervals were lower for the mometasone treatment group than placebo but statistical significance was not assigned to these values because of study underpowering. Comparison of the mometasone treatment group with the active comparator, beclomethasone with regard to the sneezing score revealed that in general, the mometasone treatment group had sneezing scores numerically lower than or equal to the sneezing scores of the beclomethasone treatment group for all 15 day study intervals. These differences were not statistically significant at any of the 15 day study intervals. Evaluation of sneezing scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the sneezing score at any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score.

Evaluation of subject evaluated **nasal congestion** scores for the mometasone treatment group vs. placebo for all 15 day study intervals, and including the prophylaxis period (prophylaxis period nasal congestion (raw) score: mometasone vs. placebo, p=0.01, mean change in score: mometasone vs. placebo, p=0.05), revealed that the nasal congestion scores and mean change in nasal congestion scores were statistically lower for the mometasone group than the placebo group (day 1-15: nasal congestion score: mometasone group=0.3, % change=19.0; nasal congestion score: placebo=0.7, % change=116; p<.01 and day 16-30: nasal congestion score: mometasone group=0.4, % change=46.9; sneezing score: placebo=0.8, % change=146; p<.01 for both raw score and mean change. While the mean nasal congestion score for the mometasone group was numerically lower than that of the placebo group for the endpoint visit: (nasal congestion score: mometasone group=0.3, % change=120; nasal congestion score: placebo=0.6, % change=93.4; p<.01 for both raw score and mean change), the mean % change in nasal congestion increased for mometasone subjects. Again, nasal congestion scores at day 31-45 and day 46-61 were lower for the mometasone treatment group compared with placebo but statistical significance was not assigned to these values because of study underpowering. Comparison of the mometasone treatment group with the active comparator, beclomethasone with regard to the nasal congestion score revealed that in general, the mometasone

treatment group had nasal congestion scores numerically lower than or equal to the nasal congestion scores of the beclomethasone treatment group for all 15 day study intervals. These differences were not statistically significant at any of the 15 day study intervals. Evaluation of nasal congestion scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the nasal congestion score at any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score.

Finally, evaluation of subject evaluated **nasal itch** scores for the mometasone treatment group vs. placebo for all 15 day study intervals, including the prophylaxis period (prophylaxis period nasal itch (raw) score: mometasone vs. placebo, p=0.01, mean change in score: mometasone vs. placebo=0.04), revealed that nasal itch scores and the mean change in nasal itch scores were statistically lower for the mometasone group than placebo ((day 1-15: nasal itch score: mometasone group=0.1, % change=10.1; nasal itch score: placebo=0.4, % change=73.1; p<.01 for both raw score and mean change; day 16-30: nasal itch score: mometasone group=0.2, % change=37.2; sneezing score: placebo=0.5, % change=126; p<.01 for both raw score and mean change, and the endpoint visit: nasal itch score: mometasone group=0.2, % change=22.3; nasal itch score: placebo=0.5, % change=160; p<.01 for both raw score and mean change) (again, nasal itch scores at day 31-45 and day 46-61 were lower for the mometasone treatment group than placebo but statistical significance was not assigned to these values because of study underpowering). Comparison of the mometasone treatment group with the active comparator, beclomethasone, with regard to the nasal itch score revealed that in general, the mometasone treatment group had nasal itch scores numerically lower than or equal to the nasal itch scores of the beclomethasone treatment group for all 15 day study intervals, although these differences were not statistically significant at any of the 15 day study intervals. Evaluation of nasal itch scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the nasal itch score at any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score.

In summary, review of the four nasal symptom scores showed that no single symptom disproportionately influenced the overall total nasal symptom score, although the nasal congestion score was higher for all treatment groups than either of the other 3 nasal symptoms analyzed in study C93-215. In contrast to the SAR pivotal trial C93-013 where a statistically significant decrease at all study intervals was only noted for the nasal congestion endpoint, prophylaxis with mometasone (also with beclomethasone) appeared to decrease all 4 nasal SAR symptoms in comparison with placebo. This may imply that prophylaxis with mometasone prior to onset of the pollen season may reduce nasal SAR symptoms to a greater degree than initiation of mometasone at the start of the pollen season but without head-to-head comparisons of a mometasone prophylaxis group vs. a mometasone treatment group where administration of drug began at the start of the pollen season (no prophylaxis), no firm conclusions can be made with regard to

the comparability of both treatment strategies in decreasing SAR symptoms. Furthermore, the clinical response from mometasone pretreatment may be indicative of a more general finding that applies to many, if not all nasal steroids when used prophylactically to treat SAR symptoms prior to onset of the allergy season.

No evidence of waning of mometasone action was noted for any of the 4 nasal symptoms over 24 hours, as noted in the a.m. vs. p.m. comparisons of drug efficacy. These findings support once a day dosing of mometasone for the prophylaxis of SAR symptoms in allergic subjects.

(5) **Mean change from baseline ('baseline' defined as mean of the a.m. and p.m. symptom score from the subject diary for day 1/Visit 2 of the study plus the 3 prior consecutive days [179:35]) in individual non-nasal symptom scores during the ragweed season, as obtained from subject diaries (a.m. and p.m. combined) for days 1-15, days 16-30, days 31-45, days 46-61, and the endpoint visit (ITT population). Refer to Attachment 1 for line listings.**

Analysis of subject evaluated **individual non-nasal symptom** scores for each 15 day study interval included the following four non-nasal symptoms: eye tearing, eye redness, eye itch, and ear/palatal itch. Of note, the day 1-15 interval for individual non-nasal symptom scores was not sub-analyzed by week 1 and week 2.

Evaluation of subject **eye tear** scores (a.m. and p.m. combined) revealed that the mometasone treatment group had statistically lower mean eye tear scores than the placebo group only at the day 1-15 interval (eye tear score: mometasone group=0.1, % change=-35; eye tear score: placebo=0.2, % change=19.7; p=.04 for both raw score and mean change) but had marginally statistically significantly lower eye tear scores at the day 16-30 interval (eye tear score: mometasone group=0.2, % change=47.6; eye tear score: placebo=0.3, % change=125; p=0.05 for raw score comparison between mometasone and placebo, p=0.06 for mean change in eye tear score for mometasone vs. placebo) and the endpoint interval (eye tear score: mometasone group=0.2, % change=70.2; eye tear score: placebo=0.3, % change=89.3; p=.07 for the raw eye tear score comparison of mometasone vs. placebo, p=0.1 for mean change in the eye tear score of mometasone vs. placebo). Eye tear scores at day 31-45 and day 46-61 intervals were similar between the mometasone and placebo group but were not consistently lower for the mometasone treatment group as compared with placebo (statistical significance was not assigned to these values because of study underpowering). Comparison of the mometasone treatment group with the active comparator, beclomethasone, on this clinical endpoint revealed that in general, the mometasone treatment group had eye tear scores numerically lower than the eye tear scores of the beclomethasone treatment group for all 15 day study intervals with the exception of the prophylaxis period. These differences were not statistically

significant at any of the 15 day study intervals. Evaluation of eye tear scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the eye tear score for any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score. As discussed in the analysis of individual nasal symptoms above, post-hoc analysis of the a.m. vs. the p.m. scores was not performed, and thus a significance level was not obtained for these values.

Evaluation of subject **eye redness** scores (a.m. and p.m. combined) revealed that the mometasone treatment group had lower mean eye redness scores than the placebo group at all 15 day time points with the exception of the prophylaxis period (eye redness (raw) score: mometasone vs. placebo, p=0.16, mean change in score: mometasone vs. placebo, p=0.34) and which were statistically significant at the day 1-15 (eye redness score: mometasone group=0.1, % change=-17; eye redness score: placebo=0.3, % change=12.3; p<.01 for both raw score and mean change comparisons between mometasone and placebo), the day 16-30 interval (eye redness score: mometasone group=0.2, % change=-22; eye redness score: placebo=0.3, % change=55.1; p=.03 for the raw score comparison between mometasone and placebo and p=0.02 for the mean change comparison between mometasone and placebo), and the endpoint visit (eye redness score: mometasone group=0.2, % change=-28; eye redness score: placebo=0.3, % change=42.7; p=.03 for the raw score comparison between mometasone and placebo and p=0.05 for the mean change comparison between mometasone and placebo). Eye redness scores for the mometasone group at day 31-45 and day 46-61 were lower than or equal to that of the placebo group, however statistical significance again was not assigned to these values because of study underpowering. Comparison of the mometasone treatment group with the active comparator, beclomethasone, with regard to eye redness, revealed that in general, the mometasone treatment group had eye redness scores numerically lower than or equal to the eye redness scores of the beclomethasone treatment group for all 15 day study intervals. These differences were not statistically significant at any of the 15 day study intervals. Evaluation of eye redness scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the eye redness score at any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score.

Evaluation of subject **eye itch** scores (a.m. and p.m. combined) revealed that the mometasone treatment group had statistically lower mean eye itch scores than the placebo group only at the day 1-15 interval (eye itch score: mometasone group=0.2, % change=-1.4; eye itch score: placebo=0.3, % change=22.6; p=.02 for the raw score comparison and p=0.04 for the mean change comparison in eye itch scores between mometasone and placebo) and the day 16-30 interval (eye itch score: mometasone group=0.3, % change=7.4; eye itch score: placebo=0.4, % change=22.9; p=0.03 for the raw score comparison, p=0.05 for mean change comparison between mometasone and placebo). Numerically lower but marginally statistically significantly lower eye itch scores were noted at the endpoint visit (eye

itch score: mometasone group=0.3, % change=-2.1; eye itch score: placebo=0.4, % change=29.6; p=.07 for the raw eye itch score comparison of mometasone vs. placebo, p=0.13 for mean change in the eye itch score of the mometasone group vs. placebo). Eye itch scores at the day 31-45 and day 46-61 intervals were the same for the mometasone and placebo group. Comparison of the mometasone treatment group with the active comparator, beclomethasone, with regard to eye redness revealed that the mometasone treatment group had eye itch scores numerically lower than the eye itch scores of the beclomethasone treatment group for all 15 day study intervals with the exception of the prophylaxis period. These differences were not statistically significant at any of the 15 day study intervals. Evaluation of eye itch scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the eye itch score for any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score.

Evaluation of subject **ear/palatal itch** scores (a.m. and p.m. combined) revealed that the mometasone treatment group had lower mean ear itch scores than the placebo group at all 15 day time points with the exception of the prophylaxis period (prophylaxis period ear/palatal itch (raw) score: mometasone vs. placebo, p=0.41, mean change in score: mometasone vs. placebo, p=0.98). Ear/palatal itch scores were statistically significantly lower for the mometasone group as compared with placebo at the day 1-15 interval (ear/palatal itch score: mometasone group=0.1, % change=-55; ear/palatal itch score: placebo=0.2, % change=64.2; p<.01 for both the raw score and mean change comparison in the ear/palatal itch scores between mometasone and placebo), the day 16-30 interval (ear/palatal itch score: mometasone group=0.1, % change=-16; ear/palatal itch score: placebo=0.3, % change=159; p<.01 for the raw score comparison between mometasone and placebo and p=0.01 for the mean change comparison in ear/palatal itch scores between mometasone and placebo), and the endpoint visit (ear/palatal itch score: mometasone group=0.1, % change=40.9; ear/palatal itch score: placebo=0.3, % change=124; p<.01 for the raw score comparison between mometasone and placebo and p=0.01 for the mean change comparison between mometasone and placebo). Ear/palatal itch scores for the mometasone group at day 31-45 and day 46-61 were lower than or equal to that of the placebo group, however statistical significance again was not assigned to these values because of study underpowering. Comparison of the mometasone treatment group with the active comparator, beclomethasone, with regard to ear/palatal itch, revealed that in general, the mometasone treatment group had ear/palatal itch scores numerically lower than or equal to the ear/palatal itch scores of the beclomethasone treatment group for all 15 day study intervals. These differences were not statistically significant at any of the 15 day study intervals. Evaluation of ear/palatal itch scores for the mometasone treatment group for the a.m. vs. the p.m. showed no significant difference in the ear/palatal itch score at any of the 15 day intervals (including the prophylaxis period) when the a.m. score was compared to the p.m. score.

Review of the four non-nasal symptom scores showed that no single symptom disproportionately influenced the overall total non-nasal symptom score, and in general, the numerical values for the non-nasal symptom scores were small and did not impact greatly on the total SAR score for study subjects. Importantly, in contrast to the SAR pivotal trial C93-013 where no statistically significant decrease in any non-nasal symptom score with mometasone treatment was noted at any study endpoint (day 1-15, day 16-30 and the endpoint visit), prophylaxis with mometasone (also with beclomethasone for some time intervals) appeared to decrease all 4 non-nasal SAR symptoms in comparison with placebo for the day 1-15 and day 16-30 interval. It should be noted however, that overall these symptom score differences, while statistically significant, were numerically very small (i.e. a 0.1-0.2 change in symptom scores) and unclear how relevant clinically. The non-nasal symptoms of eye redness and ear/palatal itching also appeared statistically significantly lower for the mometasone treatment group as compared with placebo for the endpoint visit. This was not the case for the symptoms of eye itching or eye tearing. Also of note, no statistically significant response of the mometasone treatment group compared with placebo for any of the 4 non-nasal symptoms was noted during the prophylaxis period. The efficacy results for both individual nasal and non-nasal SAR symptoms for study C93-215 are summarized in Table XXI.

No evidence of waning of mometasone action was noted for any of the individual (4) non-nasal symptoms over 24 hours, as noted in the a.m. vs. p.m. comparisons of drug efficacy. These findings support once a day dosing of mometasone for the prophylaxis of SAR symptoms in allergic subjects.

Table XXI. Change in Individual SAR Symptoms (a.m. and p.m. combined) with Mometasone Treatment

[SAS Datafiles for NDA 20-762, Attachment 1]

SAR SYMPTOM	*Statistical Response Prophylaxis Period (Yes=Y/No=N)	Statistical Response $_{DAY\ 1\text{-}15}$ (Yes=Y/No=N)	Statistical Response$_{DAY\ 16\text{-}30}$ (Y/N)	Statistical Response$_{DAY\ 15\text{-}45,\ DAY\ 46\text{-}61}$ (Y/N)	Statistical Response$_{Endpoint}$ (Y/N)
Nasal					
--Rhinorrhea	No ([2]p=0.25)	Yes	Yes	N/E	Yes
--Congestion	Yes (p=0.05)	Yes	Yes	N/E	Yes
--Itching	Yes	Yes	No (p=0.09)	N/E	Yes
--Sneezing	No (p=0.2)	Yes	No (p=0.11)	N/E	Yes
NON-Nasal					
--Eye Itching	No (p=0.52)	Yes	Yes (p=0.05)	N/E	No (p=0.13)
--Eye Tearing	No (p=0.67)	Yes	Yes	N/E	No (p=0.1)
--Eye Redness	No (p=0.34)	Yes	Yes	N/E	Yes (p=0.05)
--Ear/palate itching	No (p=0.98)	Yes	Yes	N/E	Yes

* Statistical Response= Statistical response of mometasone treatment group, as compared with placebo.
N/E=non-estimable, based on inadequate subject numbers to maintain a power of 90%.
[2] p values were calculated based on the change in symptom score from baseline.

III. Supplementary Efficacy Variables-cont.

(6) **All total (total SAR, total nasal, total non-nasal) and individual symptom scores, as determined by the physician (physician evaluations, ITT population) for study visits 3-9 (day 8, day 22, day 29, day 36, day 50, day 57, day 71, and the endpoint visit [180:389-403].**

An evaluation of total SAR, total nasal, total non-nasal symptom scores along with individual nasal and non-nasal symptom scores was performed at each study center visit by the principal investigator or designated study coordinator in order to provide an additional efficacy endpoint of subject response to mometasone treatment during both the prophylaxis (day 8, 22, 29) period and ragweed onset period (day 36, 50, 57, and 71).

Review of physician evaluated **total symptom scores** [180:389] for the three treatment groups showed that the mometasone treated subjects had statistically significantly lower total SAR symptoms compared with placebo at days 29, 36, 50, 57, and the endpoint visit ($p<.01$ for all study visits) and numerically lower but only marginally statistically significantly lower total SAR symptoms compared with the placebo group at day 22 (mometasone total SAR score=1.1 vs. placebo group total SAR score=1.6 ($p=0.05$); mometasone mean change in total SAR score=0.7 (35.4%) vs. placebo mean change in total SAR score=1.0 (64.9%), ($p=0.21$)), and day 71 ((mometasone total SAR score=3.0 vs. placebo group total SAR score=5.1 ($p=0.11$); mometasone mean change in total SAR score=2.3 (112%) vs. placebo mean change in total SAR score=4.5 (369%), ($p=0.09$)). No statistically significant differences were noted between the two active comparator groups, however the total SAR symptom scores for the mometasone group were numerically smaller than or equal to those of the beclomethasone group. Based on these pooled results, subjects treated with mometasone were found to experience less severe total SAR symptoms than the placebo group for much of the study duration, including at least part of the prophylaxis period.

Review of physician evaluated **total nasal symptom scores** [180:390] for the three treatment groups showed that, similar to the findings noted above for total SAR symptoms, the mometasone treated subjects had statistically significantly lower total nasal symptoms compared with the placebo group at days 29, 36, 50, 57, and the endpoint visit ($p<.01$ for all study visits) and numerically lower but only marginally statistically significantly lower total nasal symptoms compared with the placebo group at day 22 (mometasone total nasal score=0.7 vs. placebo group total nasal score=1.1 ($p=0.02$); mometasone mean change in total nasal score=0.4 (-14%) vs. placebo mean change in total nasal score=0.8 (-3.0%), ($p=0.07$)), and day 71 ((mometasone total nasal score=2.0 vs. placebo group total nasal score=3.5 ($p=0.04$); mometasone mean change in total nasal score=1.6 (11.1%) vs. placebo mean change in total nasal score=3.1 (250%), ($p=0.06$)). Additionally, some efficacy of mometasone in reducing the total nasal symptom

score was noted by day 8 (visit 3) of the study where the mometasone treatment group demonstrated a numerically smaller total symptom score compared with placebo which approached statistical significance (p=0.08) but whose mean change in total nasal score did not (p=0.42). Again, no statistically significant differences were noted between the two active comparator groups, however the total nasal symptom scores for the mometasone group were numerically smaller than or equal to those of the beclomethasone group. Based on these pooled results, subjects treated with mometasone were found to experience less severe total nasal symptoms than the placebo group for much of the study duration, including at least part of the prophylaxis period (day 29 and perhaps day 8 and day 22).

Interestingly, review of physician evaluated **total non-nasal symptom scores** [180:393] for the three treatment groups showed that the mometasone treated subjects did not have a statistically significantly lower total non-nasal symptom score compared with the placebo group at any study visit with the exception of the day 50 visit (mometasone total non-nasal symptom score=1.2 vs. placebo group total non-nasal symptom score=2.0 (p=0.01); mometasone mean change in total non-nasal symptom score=1.1 (15.8%) vs. placebo mean change in total non-nasal symptom score=1.8 (198%), (p=0.02)) and marginally, at the endpoint visit ((mometasone total non-nasal symptom score=0.9 vs. placebo group total non-nasal symptom score=1.5 (p=0.03); mometasone mean change in total non-nasal symptom score=0.8 (19.2%) vs. placebo mean change in total non-nasal symptom score=1.3 (87.5%), (p=0.06)). No statistically significant differences were noted between the two active comparator groups. The total non-nasal symptom scores for the mometasone group were numerically smaller than or equal to that of the beclomethasone group. Nonetheless, based on these pooled physician evaluated scores, one may not conclude statistically that subjects treated with mometasone experienced less severe total non-nasal symptoms than the placebo group for most of the study duration, with the exception of perhaps day 50 (visit 7) and the endpoint visit, although the overall trend in non-nasal symptom scores was for the mometasone treatment group to have numerically smaller non-nasal symptom scores than the placebo group at all study visits.

Evaluation of physician evaluated **individual nasal symptom scores** for all subject study visits indicates that for the 4 nasal symptoms of rhinorrhea, sneezing, nasal congestion, and nasal itch, subject symptom scores for the mometasone treated group were statistically smaller than those of the placebo group at the day 29, 36, 50, 57, and the endpoint visit [180:395-398]. Again, no statistically significant differences were noted for any of these 4 endpoints between the mometasone treatment group and the active comparator, beclomethasone.

Evaluation of physician evaluated **individual non-nasal symptom scores** for all subject study visits indicates that for the 4 non-nasal symptoms of eye tearing, eye redness, eye itch, and ear/palatal itch [180:395-403], the only statistically significant difference in symptoms between the mometasone group and placebo was noted for **eye tearing** at the endpoint visit (p=0.02 for the raw score comparison of mometasone vs. placebo or p=0.01 for the mean change in eye

tearing for mometasone vs. placebo), **eye itch** at the day 50 visit (p=0.04 for the raw score comparison of mometasone vs. placebo or p=0.05 for the mean change in eye itch for mometasone vs. placebo), and **ear/palatal itching** at the day 29 and day 50 visits (p≤.01). These inconsistent responses for non-nasal symptoms as evaluated by physician visits contrast with those of subject evaluated (diary) non-nasal symptom scores.

(7) The proportion of minimal symptom days (total nasal symptom score ≤ 2) during the prophylaxis period (Table V., ITT population) [179:223].

An analysis of the proportion of minimal symptom days during the prophylaxis period was conducted in order to ascertain that the majority of study subjects for all three treatment groups were minimally symptomatic with regard to their SAR symptoms and thereby improve the likelihood of detecting a true effect of the study drug mometasone in prophylaxing subjects against ragweed pollen effects compared with placebo. As shown in Table V., 95% of mometasone subjects were minimally symptomatic during the prophylaxis period, compared with 93% of beclomethasone subjects, and 88% of placebo subjects. The difference in the proportion of minimally symptomatic subjects between the mometasone and placebo group was statistically significant (p=0.01) and marginally statistically significant between the beclomethasone and placebo group (p=0.06). These findings suggest that all three groups were not equally symptomatic during the prophylaxis period, with the placebo group either having more SAR symptoms during this time interval than the other two groups, the three treatment groups having a component of PAR symptoms which for the two steroid treatment groups (but not placebo group) were receiving active treatment via intranasal steroids, or lastly, that the ragweed season began prematurely (prior to 1 month after initiation of treatment) for a number of study subjects and was only actively treated in the two steroid groups. Any of these three possibilities make it more difficult to quantify mometasone's effect on prophylaxis of SAR such as that due to ragweed allergen but actually represent a more 'real-life' situation of allergic disease and the possibility of overlap of SAR and PAR symptoms in any one individual.

(8) The proportion of days during the prophylaxis period when the total nasal symptom score=0 (i.e. the proportion of symptom-free days), Table VI., efficacy evaluable population [179:221].

Similar to (7) above, an analysis of the proportion of 'asymptomatic' symptom days during the prophylaxis period was conducted in order to ascertain that the majority of study subjects for all three treatment groups were not only minimally symptomatic but actually asymptomatic with regard to their SAR symptoms and thereby again, improve the likelihood of detecting a true effect of

the study drug mometasone in prophylaxing subjects against ragweed pollen effects compared with placebo.

As shown in Table VI., 67% of mometasone subjects were asymptomatic during the prophylaxis period, compared with 59% of beclomethasone subjects, and 53% of placebo subjects. The difference in the proportion of asymptomatic subjects between the mometasone and placebo group was statistically significant (p=0.01) and marginally statistically significant between the beclomethasone and placebo group (p=0.12). Interestingly, the difference in the proportion of asymptomatic days between the two active comparators, mometasone and beclomethasone, was also marginally statistically significant (p=0.09). Based on these findings, one may conclude that the three treatment groups were not equally symptomatic during the prophylaxis period of study C93-215, thus making any conclusions about the efficacy of mometasone in decreasing SAR symptoms (compared to the baseline) for any of the study endpoints potentially biased. As discussed in section 8.10.4.2 of this review ('Primary Efficacy Variable'), while it is not possible to include the prophylaxis period as a covariate for the analysis of the different time periods, subtraction of raw scores for the prophylaxis period was not noted to change the numerical advantage of mometasone treatment of placebo. Nonetheless, this discrepancy during the prophylaxis period between the different study groups must be considered when making concluding statements about the degree of efficacy of mometasone in SAR prophylaxis.

(9) The proportion of days during the <u>entire study</u> when the total nasal symptom score=0 (i.e. proportion of symptom-free days), Table VI, efficacy evaluable population [179:221].

The sponsor provided an analysis of the proportion of days during the entire study duration (from the onset of the prophylaxis period to the completion of the study) during which subjects reported being 'asymptomatic' with respect to their SAR symptoms. The purpose of this efficacy endpoint, while interesting perhaps in showing that the majority of mometasone subjects (55%) indeed were asymptomatic for the entire study duration, is of limited utility as a study endpoint. As shown in Table VI., 55% of mometasone subjects were asymptomatic for the entire study duration, compared with 48% of beclomethasone subjects, and 37% of placebo subjects. Both active drug groups had statistically significant differences in the proportion of asymptomatic days in terms of SAR symptoms, as compared to the placebo group (p<.01). A baseline proportion of asymptomatic days for each treatment group was not provided by the sponsor, hence it is more difficult to conclude that these differences are entirely due to active drug treatment with either mometasone or beclomethasone. Nonetheless, as noted in the reviewer's prior discussion of subject distribution by SAR severity at baseline (Section 8.10.4.1.C. of this review), similar baseline SAR scores would suggest that indeed the three study populations had a similar severity of total nasal and total SAR symptoms with a small but numerically greater symptom score for the beclomethasone and

placebo groups at baseline, when compared with the mometasone group.

Reviewer's Note: Summary of Efficacy Findings

Overall, mometasone was found to be effective in increasing the proportion of minimal symptom days during onset of the ragweed pollen season at a dose of 200 µg po qd, as related to prophylaxis of seasonal allergic rhinitis symptoms over the course of all study intervals. Mometasone administered at a dose of 200 µg po qd (once daily) was also found to statistically decrease total nasal symptom scores, total SAR scores and total non-nasal symptom scores, as compared to placebo. This effect of mometasone on decreasing non-nasal SAR symptoms was in contrast to those found in the SAR studies (e.g. C93-013) where mometasone was not administered prophylactically. Of note, this effect was also seen when the active comparator drug, beclomethasone, was administered prophylactically to study subjects, hence this effect may represent one which may be attributable to other nasal steroid preparations.

Mometasone did not demonstrate a significant waning of clinical efficacy based on separate a.m. and p.m. scoring of symptoms in subject diaries, a finding which supports once a day (qd) dosing of mometasone.

In terms of the primary efficacy variable, subset analysis by age, gender, and race revealed that mometasone treatment demonstrated similar efficacy in subjects age 12-17, 18-64, and > 64 years of age, and in males and females. Because the majority of study subjects for protocol C93-215 were Caucasian, no statistical conclusion can be reached regarding efficacy of mometasone in the small number of non-Caucasian subjects, however no significant difference in response was noted for non-Caucasian subjects compared with Caucasian subjects.

In summary, given a reasonable study design (and despite some study flaws which were previously addressed) to assess a therapeutic response in the treatment of seasonal allergic rhinitis when mometasone is given prophylactically before the onset of the pollen season, and reasonable clinical efficacy results, mometasone was found to be effective in decreasing the symptoms of SAR when used prophylactically, compared with placebo. Without a mometasone treatment arm in this study where subjects would have received mometasone at the onset of the pollen season, the additional degree of SAR symptom relief achieved by prophylaxis in contrast to initiation of treatment at the onset of the pollen season cannot be assessed.

Summary tables of all efficacy endpoints for study C93-215 (primary, secondary, and supplementary) are provided below (Table XXII., XXIII., and XXIV).

Table XXII. Primary Efficacy Variable of SAR and Treatment with Mometasone [179:223]

1° EFFICACY VARIABLE	STATISTICALLY SIGNIFICANT RESPONSE compared with PLACEBO: (Yes/No)
1. Proportion of minimal sx days during the pollen season (total nasal sx score ≤ 2)	*Yes

sx=Symptom

* Note: Statistically significant response for 1° efficacy variable carried by 2 of the 9 study centers (i.e. 7/9 centers had a statistically non-significant response.

Table XXIII. Secondary Efficacy Variables of SAR and Treatment with Mometasone [179:219, 223]

2° EFFICACY VARIABLE	STATISTICALLY SIGNIFICANT RESPONSE compared with PLACEBO: (Yes/No)
1. Proportion of minimal sx days during the first week of the pollen season (total nasal sx score ≤ 2)	Yes
2. Proportion of minimal sx days for the entire treatment period (total nasal sx score ≤ 2)	Yes
3. Proportion of asymptomatic days during the pollen season (total nasal sx score =0)	Yes
4. # of days from the start of the pollen season to the first occurrence of a non-minimal sx day (total nasal sx score > 2)	Yes
5. # of days from the start of treatment to the first occurrence of a non-minimal sx day (total nasal sx score > 2)	Yes

sx=Symptom, #=Number

Table XXIV. Supplementary Efficacy Variables of SAR and Treatment with Mometasone [179:221, 223, 180:389-403, SAS Datafiles, Attachment 1]

Supplementary EFFICACY VARIABLE		STATISTICALLY SIGNIFICANT RESPONSE compared with PLACEBO: (Yes/No)		
1.	Subject evaluated mean Δ in Total Nasal Sx Score DAY 1-15, DAY16-30, DAY 31-45, DAY 46-61, Endpoint Visit	Yes:	Day 1-15, Day 16-30, Endpoint Visit	
		*N/E:	Day 31-45, Day 46-61	
2.	Subject evaluated mean Δ in Total SAR Sx DAY 1-15, DAY16-30, DAY 31-45, DAY 46-61, Endpoint Visit	Yes:	Day 1-15, Day 16-30, Endpoint Visit	
		N/E:	Day 31-45, Day 46-61	
3.	Subject evaluated mean Δ in Total Non-nasal Sx DAY 1-15, DAY16-30, DAY 31-45, DAY 46-61, Endpoint Visit	Yes:	Day 1-15, Day 16-30, Endpoint Visit	
		N/E:	Day 31-45, Day 46-61	
4.	Subject evaluated individual nasal Sx DAY 1-15, DAY16-30, DAY 31-45, DAY 46-61, Endpoint Visit	Yes:	All 4 nasal sx: Day 1-15, Day 16-30, Endpoint Visit	
		N/E:	All 4 nasal sx: Day 31-45, Day 46-61	
5.	Subject evaluated individual non-nasal Sx DAY 1-15, DAY16-30, DAY 31-45, DAY 46-61, Endpoint Visit	Yes:	Eye Tearing:	Day 1-15
			Eye Redness:	Day 1-15, Day 16-30, Endpoint visit
			Eye Itch:	Day 1-15, Day 16-30
			Ear/Palatal Itch:	Day 1-15, Day 16-30, Endpoint Visit
		N/E:	Eye Redness:	Day 31-45, Day 46-61
			Ear/Palatal Itch:	Day 31-45, Day 46-61
6.	Physician evaluated total SAR, total nasal, total non-nasal, individual nasal and individual non-nasal sx	Yes:	Total SAR:	Day 29, 36, 50, 57, Endpoint Visit
			Total Nasal:	Day 29, 36, 50, 57, Endpoint Visit
			Total Non-nasal:	Day 50
			Individual Nasal	(all 4 sxs responded to mometasone): Day 29, 36, 50, 57, Endpoint Visit
			Individual Non-nasal:	Eye tearing: Endpoint Visit Eye Itch: Day 50 Ear/Palatal Itch: Day 29, 50
7.	Proportion of minimal sx days during the prophylaxis period	Yes		
8.	Proportion of asymptomatic days during the prophylaxis period	Yes		
9.	Proportion of asymptomatic days during the entire study	Yes		

Δ=Change, Sx=Symptom, Rx=Treatment

*N/E (Non-estimable): denotes numerically greater decrease in sx noted for the mometasone treatment group compared with placebo but p-value is non-estimable due to study underpowering.

8.9.4.3. SAFETY ANALYSIS:

A review of safety data was performed on the safety (intent-to-treat) population which consisted of all randomized subjects who received at least one post-baseline evaluation. For the safety population, 116 subjects each were treated with mometasone or beclomethasone and 115 subjects were treated with placebo.

Safety data consisted of clinical adverse events (further characterized as treatment emergent [179:67-71], treatment related (severe and non-severe) [179:75, 72-73], and treatment unrelated [183:3587-3829]), laboratory test values, vital signs, and pertinent physical exam findings such as nasal septal perforation or nasal candidiasis. A review of all safety parameters submitted by the sponsor by line listings was performed and those laboratory results, vital sign abnormalities, physical exam findings, and adverse events deemed by the medical reviewer to be clinically significant or pertinent negative results, are discussed in the sections below.

Overall, analysis of the safety data for protocol C93-215 indicates that mometasone was safe and well tolerated by subjects. Adverse events were similar to those observed with beclomethasone and in general, similar to those seen with nasal corticosteroid use. Unlike most studies reviewed in this NDA submission, the incidence of adverse events was found to be highest in the mometasone treatment group. No significant difference in adverse event rates was found based on age, gender, or race.

Adverse events were reported by 63% of subjects treated with mometasone, compared to 51% of subjects treated with beclomethasone, and 52% of subjects treated with placebo. The most frequently reported adverse events are summarized in Table 17 of the NDA submission (see below) [179:67]. For a complete listing of adverse events, please refer to [180:406-412].

Table 17 Incidence of Patients Reporting Frequent Treatment-Emergent Adverse Events[a] – Safety Population (Protocol No. C93-215).

	Number (%) of Patients[b]		
	MFNS (n = 116)	BDP (n = 116)	Placebo (n = 115)
Body As a Whole - General Disorders			
fatigue	1 (1)	0	3 (3)
headache	42 (36)	26 (22)	27 (23)
influenza-like symptoms	2 (2)	3 (3)	1 (1)
Central and Peripheral Nervous System Disorders			
dizziness	1 (1)	1 (1)	3 (3)
Gastro-Intestinal System Disorders			
nausea	2 (2)	0	3 (3)
Musculoskeletal System Disorders			
musculoskeletal pain	3 (3)	1 (1)	4 (3)
myalgia	2 (2)	4 (3)	3 (3)
Psychiatric Disorders			
insomnia	3 (3)	1 (1)	2 (2)
Reproductive Disorders, Female[c]			
dysmenorrhea	4 (6)	0	4 (8)
Resistance Mechanism Disorders			
infection, viral	3 (3)	7 (6)	3 (3)
Respiratory System Disorders			
coughing	3 (3)	3 (3)	5 (4)
epistaxis	5 (4)	3 (3)	5 (4)
nasal burning	3 (3)	1 (1)	2 (2)
nasal irritation	1 (1)	1 (1)	3 (3)
pharyngitis	7 (6)	12 (10)	6 (5)
rhinitis	1 (1)	1 (1)	4 (3)
sinusitis	2 (2)	3 (3)	2 (2)
sneezing	2 (2)	0	4 (3)
upper respiratory tract infection	7 (6)	3 (3)	1 (1)
Skin and Appendages Disorders			
insect bite	0	0	3 (3)
Special Senses Other, Disorders			
taste perversion	1 (1)	3 (3)	1 (1)

Headache was reported as the most frequent adverse event and was found to be present in 36% of subjects treated with mometasone, 22% of subjects treated with beclomethasone, and 23% of subjects treated with placebo [180:406]. All other adverse events were present in less than or equal to 10% of study subjects in either of the 3 treatment arms. The second most frequent adverse event was pharyngitis [180:410] (present in 6% of mometasone subjects, 10% of beclomethasone subjects, and 5% of placebo subjects), interestingly followed by dysmenorrhea [180:409, 183:3634-3635] (present in 6% of the mometasone group's female subjects, no beclomethasone subjects, and 8% of the placebo group's female subjects). Epistaxis, frequently cited as one of the more common adverse events in the SAR studies in this NDA submission was mild or moderate in severity, intermittent, and of short duration in all treatment groups. Epistaxis was recorded in 4% of mometasone and placebo subjects, respectively, and 3% of beclomethasone subjects [180:410]. No cases of nasal septal perforation or nasal ulceration were reported in any of the three treatment groups in this study [184:4450-4507]. One case of cataract formation in the left eye was reported in a subject in the beclomethasone treatment group who was struck by lightening (see below, C93-215-05, #26) and this was felt by the principal investigator to be unrelated to treatment [180:412, 183:3724, 3739]. No subject deaths were reported in this study [179:76], although a 22 year old male subject in the

beclomethasone treatment group (C93-215-05 #26) was struck by lightening and suffered a respiratory arrest with eventual full recovery and discharge from the hospital 4 days after the initial event [179:77, 183:3724].

Regarding associated infections, 6% of subjects treated with mometasone reported an upper respiratory tract infection, in contrast to 3% of subjects in the beclomethasone treatment group and 1% of subjects in the placebo group [180:410, 183:3728-3729, 3640-3641, 3658-3660, 3707-3709, 3796, 3820]. No cases of nasal or oral candidiasis were reported in any of the three treatment groups in this study [184:4450-4507]. One case of herpes simplex labialis in a 27 year old female (C93-215-05, #2) was reported for the mometasone treatment group during visits 6 and 7 of the study which was moderate in severity and thought to be unrelated to treatment by the investigator [180:409, 183:3636] along with one case of herpes zoster, reported in a 38 year old female (C93-215-01, #33) in the mometasone treatment group during visit 9 which was moderate in severity and also thought to be unrelated to treatment by the investigator [180:409, 183:3637]. In summary, the most frequent adverse events cited were symptoms known to be associated with seasonal allergic rhinitis itself, and not necessarily related to drug use per se.

Regarding significant laboratory tests abnormalities, one case of an elevated SGOT to 113 U/L (normal range 11-36 U/L) and SGPT to 75 U/L (normal range 6-43 U/L) was reported in a 28 year old male (subject C93-215-01 #043) during Visit 8 of the study, with repeat liver function tests measured 6 days later within normal range. The subject's presumed liver function test elevations were considered by the principal investigator to be a result of muscle damage from a 50 mile run 3 days prior to the Visit 8 blood test, and unrelated to study medication [179:76, 183:3624]. No other clinically relevant abnormal laboratory test results were reported in this study. Although there were scattered laboratory test values outside the normal ranges for several subjects, as assessed by shift tables, none were remarkable.

No clinically relevant changes in mean values from pretreatment were noted in any of the subjects' vital signs or body weight. Shift tables were similar among all 3 treatment groups. ECGs performed pretreatment and at endpoint failed to reveal any relevant abnormal findings.

Gender, race and age subgroup analyses of vital signs, body weight, laboratory data, and ECGs failed to reveal any differences between any of these subgroups and the overall subject population, although the number of non-Caucasian subjects and subjects between 12-17 years or > 64 years of age was too small to draw meaningful conclusions concerning these subgroups.

Regarding subject drop-outs due to adverse events, a total of 10 subjects (1 treated with mometasone, 5 treated with beclomethasone, and 4 treated with placebo) discontinued treatment because of adverse events [179:145-147]. The reason for discontinuation in the study for one subject in the mometasone treatment group (C93-215-06, #16) was bronchitis and sinusitis rated as moderate in severity and which was felt to be unrelated to treatment by the principal

investigator [179:76, 151]. Overall, for the 3 treatment groups, most subjects who discontinued treatment (7/10 subjects) did so for reasons 'unrelated' to the study drug [179:76, 149-153].

8.9.5. **Reviewer's Conclusion of Study Results:**

In this prophylaxis of SAR trial, 116 subjects received mometasone treatment, 116 subjects received the active comparator beclomethasone, and 115 subjects received placebo treatment.

With the exception of a greater percentage of subjects in the mometasone treatment group who were female, all 3 treatment arms were otherwise similar in demographic and clinical characteristics, including subject self-rated severity of SAR symptoms at baseline (0-3 score). The majority of subjects in this study received mometasone prophylaxis for 4 weeks, however, of those who did not (primarily subjects at study sites -02 and -09, who received from 14-21 days of pre-treatment with mometasone or one of the other treatments), shorter duration of pre-treatment with mometasone did not appear to change the trend in decreasing total nasal symptom scores (statistical comparison was not performed on these subjects because of low subject number and underpowering) [Response to FDA Request on Prophylaxis Studies, Schering Plough, Inc., 05/21/97, p. 58-84].

Results that Support Approval:

Mometasone administered at a dose of 200 μg qd intranasally was statistically better than placebo in increasing the proportion of minimal total nasal symptom days (based on subject self-rated total nasal symptom scores that were a composite of rhinorrhea, sneezing, nasal congestion, and nasal itch scores and were defined as being ≤ 2 to qualify as a 'minimal' symptom day) during the ragweed pollen season. Mometasone treatment increased the proportion of minimal symptom days to 84%, compared to a respective 63% increase in the proportion of minimal symptom days in the placebo treatment group (and as compared with a 79% increase in the beclomethasone treatment group). This statistically significant decrease in symptomatic days in mometasone treated subjects was likewise noted during the prophylaxis period, the first week of the pollen season, and more broadly, for the entire study treatment period, when compared to placebo. Mometasone treated subjects were statistically more likely to have a greater proportion of 'no' nasal symptoms ('asymptomatic' days) during the prophylaxis period, the pollen season and even the entire treatment period than the placebo treatment group. Additionally, the number of days from the start of treatment or start of the pollen season to the onset of a non-minimal nasal symptom day was more likely to be statistically significantly longer in subjects who were treated with mometasone than those receiving placebo.

Based on subject self-rated total SAR, total nasal, total non-nasal, and individual nasal and non-nasal symptom scores, mometasone treated subjects demonstrated statistically significantly lower symptom scores and a smaller

increase of symptoms with onset of the pollen season than the placebo treatment group. Because this relative decrease in symptoms in the mometasone treatment group already occurred during the prophylaxis period (a 4 week period), onset of action of mometasone in the prophylaxis setting appeared to occur sooner than 4 weeks, however based on the data provided by the sponsor, the approximate week of onset of action of mometasone cannot be more specifically defined. The physician evaluated subject symptom scores indicate that for almost all study parameters, treatment for at least 3-4 weeks (day 29 visit) was required before a statistically significant difference in symptoms was evident in mometasone treated subjects vs. placebo treated subjects.

Interestingly, and in contrast to the SAR studies reviewed in this NDA submission, the total and individual subject evaluated non-nasal symptom scores were found to be statistically significantly lower in the mometasone treatment group, as compared with placebo. This observation was likewise noted in the beclomethasone treatment group and implies that pretreatment with nasal steroids prior to onset of the pollen season in subjects with SAR may afford greater efficacy in decreasing other symptoms of SAR (non-nasal) in addition to nasal symptoms. Without a fourth study arm comparing mometasone pretreatment prior to onset of the pollen season with mometasone treatment at the onset of the pollen season, this question cannot be addressed definitively. Thus, based on the study design and efficacy results of trial C93-215, mometasone treatment appears to decrease SAR symptoms compared to placebo, however, it is not clear and not conclusive that pretreatment (prior to pollen season onset) with mometasone will statistically significantly decrease SAR symptoms compared with initiation of mometasone treatment at the time of pollen season onset.

Finally, physician rated subject total SAR, total nasal, total non-nasal, and individual nasal and non-nasal symptom scores indicate that for most study visits (exceptions noted below in the 'Results that did not support Approval' section), mometasone treated subjects had statistically better symptom scores than those subjects treated with placebo. A summary of all efficacy endpoints evaluated in study C93-215 is provided in Tables XXII.-XXIV.

Results that did not Support Approval:

Very few results from study C93-215 do not support approval of mometasone for the treatment of SAR. For the primary efficacy endpoint, one must note that only 2 of the 9 study centers had statistically significant differences between mometasone treatment and placebo and 3 additional centers (-01, [179:209], -04 [179:212], -07 [179:215]) approached statistical significance. In addition, several of the non-nasal symptoms were found to have a less consistent response in mometasone treated subjects, as compared with placebo. Notably, subject evaluated eye tearing scores on day 16-30 of the study were not found to be statistically different between the mometasone and placebo treated subjects. Of physician evaluated scores, the total and individual non-nasal symptom scores of mometasone treated subjects were overall not found to be consistently better than

those of placebo subjects. Given the lesser importance of non-nasal symptom scores in the assessment of SAR; these findings, while noted, are less critical in determining efficacy of mometasone treatment than nasal symptom scores.

Other Results:

Mometasone (200 µg qd) appeared to exert its effect at decreasing SAR symptoms (nasal and non-nasal) throughout the day, with similar subject self-rated total SAR, total nasal, total non-nasal, and individual nasal and non-nasal symptom scores achieved during the a.m. and p.m. measurements. Hence, mometasone administered as a 200 µg dose once a day demonstrated a reasonable 24 hour duration of effect in this study.

Safety:

Overall, mometasone was safe and well-tolerated administered as a once a day, 200 µg dose. No serious adverse events occurred in subjects treated with mometasone, nor were any deaths reported. Similar to placebo and similar to the SAR studies in this NDA submission, headache was the most common adverse event associated with mometasone use, followed by pharyngitis. The third most common adverse event, uniquely noted in this study, was dysmenorrhea in female subjects; however more female subjects comprised the mometasone treatment group, compared with the other two study arms. No nasal septal perforations or cases of nasal candidiasis were reported. While one case of cataract formation was reported in a beclomethasone treated subject, a scientific link between the subject's lightening strike and cataract formation was not provided by the sponsor. Because of study duration, this study did not specifically evaluate posterior subcapsular cataract formation or hypothalamic-pituitary-adrenal (HPA) axis suppression.

Summary:

Based on results of the seasonal allergic rhinitis prophylaxis trial C93-215, mometasone demonstrated adequate evidence of efficacy and safety compared with placebo in the treatment of symptoms of SAR. Based on study design, however, one cannot conclude that mometasone prophylaxis demonstrates superior efficacy in the treatment of SAR symptoms compared to mometasone treatment given at the time of onset of the allergy season.

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM & PM AVERAGED NASAL SYMPTON SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO				ANOVA P-VALUES @			PAIRWISE COMPARISONS @		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	POOLED SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.3	0.5	115	0.4	0.5	115	0.4	0.5	0.4	0.19	<.01	0.48	0.41	0.07	0.32
PRE	RAW	116	0.4	0.7	115	0.6	1.0	115	0.7	0.9	0.8	0.01	<.01	0.65	0.13	<.01	0.13
	CHG	116	0.1	0.6	115	0.2	1.0	115	0.3	0.8	0.8	0.12	<.01	0.32	0.29	0.04	0.32
	%CHG	66	14.0	127	65	56.6	206	65	97.9	234							
1-7	RAW	114	0.6	0.8	111	0.8	1.3	109	1.6	1.8	1.3	<.01	<.01	<.01	0.12	<.01	<.01
	CHG	114	0.2	0.8	111	0.4	1.3	109	1.2	1.9	1.3	<.01	<.01	<.01	0.19	<.01	<.01
	%CHG	65	42.9	197	63	173	397	59	285	579							
8-15	RAW	114	0.9	1.2	108	1.2	1.5	105	2.2	2.3	1.6	<.01	<.01	<.01	0.18	<.01	<.01
	CHG	114	0.5	1.2	108	0.8	1.6	105	1.8	2.3	1.6	<.01	<.01	<.01	0.25	<.01	<.01
	%CHG	65	125	291	61	264	547	59	443	885							
16-45	RAW	114	1.2	1.4	107	1.5	1.8	103	2.4	2.3	1.8	<.01	0.02	0.07	0.2	<.01	<.01
	CHG	114	0.8	1.4	107	1.1	1.8	103	2.0	2.3	1.8	<.01	<.01	0.05	0.26	<.01	<.01
	%CHG	65	187	330	60	243	426	58	466	689							
46-61	RAW	18	1.4	1.5	14	2.0	2.8	13	1.8	1.9	2.2	0.69	0.83	0.7	0.5	N/E	N/E
	CHG	18	1.0	1.5	14	1.7	2.9	13	1.6	2.0	2.2	0.53	0.62	0.62	0.38	N/E	N/E
	%CHG	11	281	384	8	602	1267	4	118	281							
ENDPT	RAW	116	1.2	1.4	115	1.6	1.9	115	2.6	2.4	1.9	<.01	0.01	0.03	0.11	<.01	<.01
	CHG	116	0.8	1.4	115	1.2	2.0	115	2.1	2.5	1.9	<.01	<.01	0.02	0.17	<.01	<.01
	%CHG	66	191	339	65	294	631	65	497	911							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
@ P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
PRE : PRE-SEASON TREATMENT INTERVAL -- OTHERS ARE DAYS POST-ONSET OF SEASON
@ SUM OF THE 4 NASAL SYMPTOMS FROM THE AVERAGED AM & PM DIARIES - RUNNY NOSE, STUFFINESS, SNEEZING AND ITCH
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF AM & PM DIARY BASELINE VALUES
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

NOTE: Data generated from SAS datafiles for ITT population (Dr. Jim Gebert, Biostatistics, HFD-570).

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM NASAL SYMPTON SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.4	0.5	115	0.5	0.6	115	0.5	0.6	0.5	0.49	<.01	0.34	0.39	0.25	0.77
PRE	RAW	116	0.5	0.8	115	0.6	1.0	115	0.8	0.9	0.8	0.02	<.01	0.56	0.16	<.01	0.14
	CHG	116	0.1	0.7	115	0.2	1.1	115	0.3	0.9	0.8	0.09	<.01	0.2	0.37	0.03	0.19
	%CHG	63	2.4	124	57	0.5	140	60	106	272							
1-7	RAW	114	0.6	0.9	111	0.9	1.3	109	1.6	1.8	1.3	<.01	<.01	0.03	0.14	<.01	<.01
	CHG	114	0.2	0.8	111	0.4	1.3	109	1.1	1.9	1.4	<.01	<.01	0.01	0.24	<.01	<.01
	%CHG	62	16.7	160	55	65.6	236	55	224	523							
8-15	RAW	114	0.9	1.3	108	1.1	1.5	105	2.2	2.2	1.6	<.01	<.01	<.01	0.25	<.01	<.01
	CHG	114	0.5	1.2	108	0.7	1.6	105	1.7	2.3	1.6	<.01	<.01	<.01	0.34	<.01	<.01
	%CHG	62	75.4	211	53	166	510	55	380	734							
16-45	RAW	114	1.2	1.4	107	1.5	1.8	103	2.4	2.3	1.8	<.01	0.01	0.1	0.18	<.01	<.01
	CHG	114	0.8	1.4	107	1.1	1.9	103	2.0	2.4	1.8	<.01	<.01	0.06	0.25	<.01	<.01
	%CHG	62	120	255	52	113	264	54	399	727							
46-61	RAW	18	1.4	1.6	14	2.2	3.1	13	1.8	2.1	2.4	0.58	0.8	0.57	0.41	N/E	N/E
	CHG	18	0.9	1.5	14	1.8	3.2	13	1.5	2.2	2.4	0.4	0.63	0.46	0.29	N/E	N/E
	%CHG	11	170	319	6	474	762	4	19.7	147							
ENDPT	RAW	116	1.2	1.4	115	1.6	2.0	115	2.6	2.4	1.9	<.01	<.01	0.06	0.1	<.01	<.01
	CHG	116	0.8	1.4	115	1.1	2.1	115	2.1	2.5	2.0	<.01	<.01	0.05	0.16	<.01	<.01
	%CHG	63	123	261	57	177	508	60	406	753							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
@ SUM OF THE 4 NASAL SYMPTONS FROM THE AM DIARY - RUNNY NOSE, STU FFINESS, SNEEZING AND ITCH
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 4 AM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO AND INCLUDING DAY 1
SYMPTONS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

PM NASAL SYMPTOM SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.3	0.5	115	0.3	0.5	115	0.4	0.6	0.5	0.08	<.01	0.67	0.53	0.03	0.12
PRE	RAW	116	0.4	0.7	115	0.5	1.0	115	0.7	0.9	0.8	0.01	<.01	0.7	0.13	<.01	0.14
	CHG	116	0.1	0.6	115	0.2	1.0	115	0.3	0.8	0.8	0.23	0.03	0.47	0.26	0.09	0.58
	%CHG	43	1.1	135	43	54.9	161	52	87.0	227							
1-7	RAW	114	0.5	0.8	111	0.8	1.3	109	1.6	1.9	1.3	<.01	<.01	<.01	0.11	<.01	<.01
	CHG	114	0.3	0.8	111	0.5	1.3	109	1.2	2.0	1.3	<.01	0.01	<.01	0.18	<.01	<.01
	%CHG	42	34.6	183	42	117	329	47	232	513							
8-15	RAW	114	0.9	1.2	108	1.2	1.6	105	2.2	2.4	1.7	<.01	<.01	<.01	0.15	<.01	<.01
	CHG	114	0.6	1.3	108	0.8	1.7	105	1.8	2.5	1.7	<.01	<.01	<.01	0.2	<.01	<.01
	%CHG	42	97.9	243	40	231	542	47	327	545							
16-45	RAW	114	1.2	1.4	107	1.5	1.7	103	2.4	2.4	1.8	<.01	0.04	0.06	0.23	<.01	<.01
	CHG	114	0.9	1.4	107	1.1	1.8	103	2.0	2.4	1.8	<.01	<.01	0.05	0.29	<.01	<.01
	%CHG	42	185	348	39	182	354	47	395	572							
46-61	RAW	18	1.4	1.4	14	1.8	2.6	13	1.7	1.9	2.1	0.83	0.73	0.86	0.62	N/E	N/E
	CHG	18	1.1	1.5	14	1.6	2.7	13	1.6	2.0	2.1	0.71	0.82	0.8	0.53	N/E	N/E
	%CHG	7	340	569	5	90.0	236	3	423	847							
ENDPT	RAW	116	1.2	1.4	115	1.5	1.9	115	2.6	2.5	1.9	<.01	0.02	0.02	0.14	<.01	<.01
	CHG	116	0.9	1.4	115	1.2	2.0	115	2.2	2.5	2.0	<.01	<.01	0.01	0.2	<.01	<.01
	%CHG	43	185	366	43	232	526	52	342	495							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LEHEANS FAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
@ SUM OF THE 4 NASAL SYMPTOMS FROM THE AM DIARY - RUNNY NOSE, STU FFINESS, SNEEZING AND ITCH
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 3 PM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO BUT NOT INCLUDING DAY 1
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM & PM AVERAGED TOTAL SYMPTOM SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES @			PAIRWISE COMPARISONS @		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.5	0.6	115	0.6	0.8	115	0.6	0.8	0.7	0.18	<.01	0.14	0.4	0.06	0.3
PRE	RAW	116	0.7	1.0	115	0.9	1.6	115	1.1	1.3	1.3	0.09	<.01	0.49	0.25	0.03	0.28
	CHG	116	0.2	0.9	115	0.3	1.7	115	0.4	1.1	1.2	0.44	<.01	0.22	0.47	0.2	0.58
	%CHG	72	39.3	157	68	106	325	70	95.3	244							
1-15	RAW	114	1.3	1.5	111	1.7	2.2	109	3.0	3.3	2.3	<.01	<.01	0.01	0.23	<.01	<.01
	CHG	114	0.8	1.5	111	1.1	2.2	109	2.4	3.3	2.3	<.01	<.01	<.01	0.32	<.01	<.01
	%CHG	71	208	542	65	327	539	64	486	1085							
16-30	RAW	114	2.0	2.3	107	2.5	3.1	103	3.7	4.0	3.1	<.01	0.01	0.05	0.15	<.01	<.01
	CHG	114	1.5	2.3	107	2.0	3.2	103	3.1	4.0	3.1	<.01	<.01	0.04	0.19	<.01	<.01
	%CHG	71	279	464	62	391	642	63	574	959							
31-45	RAW	76	2.3	3.5	67	2.9	4.0	61	3.6	4.2	3.9	0.02	0.19	0.72	N/E	N/E	N/E
	CHG	76	1.8	3.5	67	2.4	4.2	61	3.0	4.1	3.9	0.04	0.02	0.8	N/E	N/E	N/E
	%CHG	45	184	329	35	333	638	34	712	1716							
46-61	RAW	18	2.4	2.8	14	3.9	5.8	13	2.5	2.6	4.0	0.77	0.8	0.67	0.63	N/E	N/E
	CHG	18	1.8	2.8	14	3.5	5.8	13	2.2	2.6	4.0	0.58	0.59	0.53	0.47	N/E	N/E
	%CHG	12	351	453	9	760	967	6	660	1200							
ENDPT	RAW	116	2.0	3.0	115	2.6	3.5	115	3.9	4.3	3.5	<.01	<.01	0.06	0.16	<.01	<.01
	CHG	116	1.5	3.0	115	2.0	3.6	115	3.3	4.3	3.5	<.01	<.01	0.06	0.21	<.01	0.01
	%CHG	72	260	462	68	403	684	70	771	1582							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE

@ P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)

@ SUM OF THE 8 TOTAL SYMPTOMS FROM THE AVERAGED AM & PM DIARIES

BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF AM & PM DIARY BASELINE VALUES

SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE

SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED

SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES

ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM TOTAL SYMPTOM SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES @			PAIRWISE COMPARISONS @		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.6	0.7	115	0.7	0.9	115	0.7	0.9	0.7	0.54	<.01	0.14	0.42	0.29	0.8
PRE	RAW	116	0.8	1.1	115	0.9	1.7	115	1.1	1.4	1.3	0.09	<.01	0.51	0.3	0.03	0.25
	CHG	116	0.2	1.0	115	0.3	1.8	115	0.5	1.2	1.3	0.26	<.01	0.2	0.54	0.1	0.3
	%CHG	70	25.6	148	61	19.1	133	63	120	297							
1-15	RAW	114	1.4	1.6	111	1.7	2.2	109	3.0	3.2	2.3	<.01	<.01	0.02	0.28	<.01	<.01
	CHG	114	0.8	1.5	111	1.0	2.3	109	2.4	3.3	2.3	<.01	<.01	0.01	0.39	<.01	<.01
	%CHG	69	125	296	58	191	400	58	459	938							
16-30	RAW	114	2.0	2.4	107	2.6	3.1	103	3.7	4.0	3.1	<.01	0.01	0.04	0.12	<.01	<.01
	CHG	114	1.4	2.3	107	1.9	3.3	103	3.1	4.0	3.1	<.01	<.01	0.03	0.16	<.01	<.01
	%CHG	69	202	369	55	219	413	57	654	1349							
31-45	RAW	76	2.4	3.6	67	3.1	4.2	61	3.6	4.0	3.9	0.03	0.14	0.75	N/E	N/E	N/E
	CHG	76	1.7	3.6	67	2.4	4.4	61	2.9	3.9	3.9	0.05	0.01	0.81	N/E	N/E	N/E
	%CHG	45	139	277	33	218	404	30	366	757							
46-61	RAW	18	2.4	2.8	14	4.2	6.2	13	2.4	2.6	4.3	0.77	0.82	0.63	0.59	N/E	N/E
	CHG	18	1.6	2.8	14	3.7	6.3	13	2.1	2.7	4.2	0.57	0.61	0.5	0.43	N/E	N/E
	%CHG	12	256	413	7	707	649	5	91.8	199							
ENDPT	RAW	116	2.1	3.1	115	2.7	3.6	115	3.9	4.2	3.5	<.01	<.01	0.06	0.12	<.01	0.01
	CHG	116	1.5	3.0	115	2.1	3.8	115	3.3	4.2	3.5	<.01	<.01	0.06	0.16	<.01	0.02
	%CHG	70	192	371	61	232	428	63	613	1283							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
@ P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
@ SUM OF THE 8 TOTAL SYMPTOMS FROM THE AM DIARY
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 4 AM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO AND INCLUDING DAY 1
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

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PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

PM TOTAL SYMPTOM SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES @			PAIRWISE COMPARISONS @		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.4	0.6	115	0.5	0.8	115	0.6	0.9	0.7	0.05	<.01	0.31	0.46	0.02	0.09
PRE	RAW	116	0.6	0.9	115	0.8	1.6	115	1.0	1.2	1.2	0.09	<.01	0.45	0.22	0.03	0.34
	CHG	116	0.2	0.9	115	0.3	1.7	115	0.4	1.1	1.3	0.65	0.01	0.27	0.42	0.42	>.99
	%CHG	50	23.8	147	50	67.8	189	58	74.4	217							
1-15	RAW	114	1.3	1.6	111	1.7	2.2	109	3.0	3.4	2.4	<.01	<.01	<.01	0.19	<.01	<.01
	CHG	114	0.9	1.6	111	1.2	2.2	109	2.5	3.4	2.4	<.01	<.01	<.01	0.27	<.01	<.01
	%CHG	49	95.2	176	49	229	432	52	307	572							
16-30	RAW	114	2.0	2.3	107	2.5	3.1	103	3.7	4.2	3.1	<.01	0.01	0.06	0.19	<.01	<.01
	CHG	114	1.6	2.4	107	2.8	3.2	103	3.1	4.1	3.1	<.01	<.01	0.06	0.24	<.01	0.01
	%CHG	49	221	297	46	252	424	52	445	690							
31-45	RAW	67	2.4	3.6	56	3.2	4.1	54	3.5	4.4	4.0	0.3	0.24	0.96	M/E	M/E	M/E
	CHG	67	1.9	3.6	56	2.7	4.3	54	2.9	4.4	4.0	0.42	0.03	0.94	M/E	M/E	M/E
	%CHG	27	229	345	23	319	661	28	696	1347							
46-61	RAW	18	2.4	2.8	14	3.6	5.4	13	2.6	2.6	3.9	0.77	0.74	0.72	0.67	M/E	M/E
	CHG	18	1.9	2.8	14	3.3	5.4	13	2.4	2.6	3.8	0.6	0.53	0.57	0.53	M/E	M/E
	%CHG	8	359	553	6	485	587	5	552	632							
ENDPT	RAW	116	2.0	2.9	115	2.6	3.4	115	3.9	4.4	3.5	<.01	<.01	0.09	0.2	<.01	<.01
	CHG	116	1.6	2.9	115	2.1	3.5	115	3.3	4.3	3.5	<.01	<.01	0.12	0.27	<.01	0.01
	%CHG	50	239	367	50	290	528	58	519	976							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION M/E = NON-ESTIMABLE
@ P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
@ SUM OF THE 8 TOTAL SYMPTOMS FROM THE PM DIARY
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 3 PM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO BUT NOT INCLUDING DAY 1
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

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PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM & PM AVERAGED TOTAL SYMPTOM SCORE - POOLED DIARY DATA

	(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE	116	0.5	0.6	115	0.6	0.8	115	0.6	0.8	0.7	0.18	<.01	0.14	0.4	0.06	0.3
PRE RAW	116	0.7	1.0	115	0.9	1.6	115	1.1	1.3	1.3	0.09	<.01	0.49	0.25	0.03	0.28
CHG	116	0.2	0.9	115	0.3	1.7	115	0.4	1.1	1.2	0.44	<.01	0.22	0.47	0.2	0.58
%CHG	72	39.3	157	68	106	325	70	95.3	244							
1-7 RAW	114	1.0	1.3	111	1.3	2.1	109	2.3	2.9	2.1	<.01	0.03	0.03	0.25	<.01	<.01
CHG	114	0.5	1.3	111	0.8	2.1	109	1.8	3.0	2.1	<.01	0.02	0.01	0.35	<.01	<.01
%CHG	71	102	270	65	267	503	64	331	750							
8-15 RAW	114	1.6	2.0	108	2.0	2.5	105	3.5	4.1	2.7	<.01	<.01	<.01	0.26	<.01	<.01
CHG	114	1.1	2.0	108	1.4	2.5	105	2.9	4.1	2.7	<.01	<.01	<.01	0.33	<.01	<.01
%CHG	71	298	876	63	391	630	64	628	1522							
16-45 RAW	114	2.0	2.5	107	2.6	3.2	103	3.8	4.1	3.2	<.01	<.01	0.09	0.14	<.01	<.01
CHG	114	1.5	2.5	107	2.0	3.4	103	3.2	4.0	3.2	<.01	<.01	0.07	0.18	<.01	0.01
%CHG	71	278	458	62	407	650	63	635	1051							
46-61 RAW	18	2.4	2.8	14	3.9	5.8	13	2.5	2.6	4.0	0.77	0.8	0.67	0.63	N/E	N/E
CHG	18	1.8	2.8	14	3.5	5.8	13	2.2	2.6	4.0	0.58	0.89	0.53	0.47	N/E	N/E
%CHG	12	351	453	9	768	967	6	660	1200							
ENDPT RAW	116	2.0	2.5	115	2.7	3.4	115	4.0	4.1	3.2	<.01	<.01	0.01	0.08	<.01	<.01
CHG	116	1.5	2.5	115	2.1	3.6	115	3.3	4.1	3.3	<.01	<.01	0.01	0.12	<.01	0.01
%CHG	72	288	474	68	424	687	70	743	1562							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
@ SUM OF THE 8 TOTAL SYMPTOMS FROM THE AVERAGED AM & PM DIARIES
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF AM & PM DIARY BASELINE VALUES
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
%CHG PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
'DPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM TOTAL SYMPTON SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES @			PAIRWISE COMPARISONS @		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.6	0.7	115	0.7	0.9	115	0.7	0.9	0.7	0.54	<.01	0.14	0.42	0.29	0.8
PRE	RAW	116	0.8	1.1	115	0.9	1.7	115	1.1	1.4	1.3	0.09	<.01	0.51	0.3	0.03	0.25
	CHG	116	0.2	1.0	115	0.3	1.8	115	0.5	1.2	1.3	0.26	<.01	0.2	0.54	0.1	0.3
	%CHG	70	25.6	148	61	19.1	133	63	120	297							
1-7	RAW	114	1.1	1.3	111	1.3	2.1	109	2.3	2.8	2.1	<.01	0.04	0.11	0.3	<.01	<.01
	CHG	114	0.5	1.3	111	0.7	2.1	109	1.7	2.9	2.1	<.01	0.02	0.02	0.42	<.01	<.01
	%CHG	69	61.2	199	58	133	312	58	291	644							
8-15	RAW	114	1.6	2.0	108	1.9	2.4	105	3.4	3.9	2.7	<.01	<.01	<.01	0.35	<.01	<.01
	CHG	114	1.1	2.0	108	1.3	2.5	105	2.8	4.0	2.7	<.01	<.01	<.01	0.43	<.01	<.01
	%CHG	69	181	468	56	248	514	58	607	1248							
16-45	RAW	114	2.0	2.5	107	2.7	3.3	103	3.8	4.0	3.2	<.01	<.01	0.09	0.11	<.01	0.01
	CHG	114	1.5	2.5	107	2.0	3.5	103	3.2	4.0	3.2	<.01	<.01	0.07	0.15	<.01	0.01
	%CHG	69	202	367	55	231	415	57	665	1342							
46-61	RAW	18	2.4	2.8	14	4.2	6.2	13	2.4	2.6	4.3	0.77	0.02	0.63	0.59	N/E	N/E
	CHG	18	1.6	2.8	14	3.7	6.3	13	2.1	2.7	4.2	0.57	0.61	0.5	0.43	N/E	N/E
	%CHG	12	256	413	7	707	649	5	91.8	199							
ENDPT	RAW	116	2.0	2.5	115	2.8	3.5	115	4.0	4.1	3.3	<.01	<.01	0.01	0.06	<.01	0.01
	CHG	116	1.4	2.5	115	2.1	3.7	115	3.3	4.1	3.3	<.01	<.01	0.01	0.09	<.01	0.01
	%CHG	70	208	372	61	269	494	63	664	1391							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
@ P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
@ SUM OF THE 8 TOTAL SYMPTOMS FROM THE AM DIARY
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 4 AM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO AND INCLUDING DAY 1
SYMPTONS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
%E PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

PM TOTAL SYMPTOM SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.4	0.6	115	0.5	0.8	115	0.6	0.9	0.7	0.05	<.01	0.31	0.46	0.02	0.09
PRE	RAW	116	0.6	0.9	115	0.8	1.6	115	1.0	1.2	1.2	0.09	<.01	0.45	0.22	0.03	0.34
	CHG	116	0.2	0.9	115	0.3	1.7	115	0.4	1.1	1.3	0.65	0.01	0.27	0.42	0.42	>.99
	%CHG	50	23.8	147	50	67.8	189	58	74.4	217							
1-7	RAW	114	1.0	1.3	111	1.3	2.1	109	2.4	3.1	2.2	<.01	0.02	0.01	0.22	<.01	<.01
	CHG	114	0.6	1.3	111	0.8	2.1	109	1.8	3.2	2.2	<.01	0.02	<.01	0.32	<.01	<.01
	%CHG	49	50.2	169	49	172	427	52	226	503							
8-15	RAW	114	1.6	2.0	108	2.0	2.6	105	3.5	4.3	2.9	<.01	<.01	<.01	0.2	<.01	<.01
	CHG	114	1.2	2.1	108	1.5	2.6	105	3.0	4.3	2.9	<.01	<.01	<.01	0.27	<.01	<.01
	%CHG	49	136	215	47	291	496	52	378	694							
16-45	RAW	114	2.0	2.5	107	2.6	3.2	103	3.8	4.2	3.2	<.01	0.01	0.1	0.18	<.01	<.01
	CHG	114	1.6	2.5	107	2.1	3.3	103	3.2	4.1	3.2	<.01	<.01	0.1	0.23	<.01	0.01
	%CHG	49	227	308	46	263	460	52	498	768							
46-61	RAW	18	2.4	2.8	14	3.6	5.4	13	2.6	2.6	3.9	0.77	0.74	0.72	0.67	N/E	N/E
	CHG	18	1.9	2.8	14	3.3	5.4	13	2.4	2.6	3.8	0.6	0.53	0.57	0.53	N/E	N/E
	%CHG	8	359	553	6	485	587	5	552	632							
ENDPT	RAW	116	2.0	2.5	115	2.6	3.4	115	4.0	4.3	3.3	<.01	<.01	0.01	0.12	<.01	<.01
	CHG	116	1.6	2.5	115	2.1	3.5	115	3.4	4.2	3.3	<.01	<.01	0.01	0.17	<.01	0.01
	%CHG	50	232	349	50	302	523	58	428	680							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
@ SUM OF THE 8 TOTAL SYMPTOMS FROM THE PM DIARY
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 3 PM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO BUT NOT INCLUDING DAY 1
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
ONE PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

PM NON-NASAL EAR/PALATE ITCHING SCORE - POOLED DIARY DATA

	(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS	N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE	116	0.0	0.1	115	0.0	0.1	115	0.0	0.1	0.1	0.26	0.03	0.03	0.31	0.1	0.54
PRE RAW	116	0.0	0.1	115	0.0	0.2	115	0.1	0.1	0.2	0.67	0.37	0.74	0.61	0.37	0.71
CHG	116	0.0	0.1	115	0.0	0.2	115	0.0	0.1	0.2	0.97	0.55	0.24	0.84	0.8	0.96
%CHG	3	-58	44.3	6	-70	42.9	8	-41	96.2							
1-15 RAW	114	0.1	0.2	111	0.1	0.3	109	0.2	0.4	0.3	<.01	0.16	0.05	0.3	<.01	<.01
CHG	114	0.1	0.2	111	0.1	0.3	109	0.2	0.4	0.3	<.01	0.05	0.02	0.5	<.01	<.01
%CHG	3	-47	61.1	6	-50	74.6	7	-7.1	139							
16-30 RAW	114	0.1	0.3	107	0.2	0.5	103	0.3	0.5	0.4	0.02	0.68	0.18	0.32	<.01	0.06
CHG	114	0.1	0.3	107	0.1	0.5	103	0.2	0.5	0.4	0.03	0.54	0.12	0.46	0.01	0.06
%CHG	3	-2.1	100	6	-38	111	7	114	163							
31-45 RAW	67	0.1	0.3	56	0.2	0.5	54	0.3	0.6	0.5	0.14	0.25	0.8	N/E	N/E	N/E
CHG	67	0.1	0.3	56	0.2	0.5	54	0.2	0.6	0.4	0.17	0.19	0.7	N/E	N/E	N/E
%CHG	2	90.0	212	3	-64	62.5	5	139	157							
46-61 RAW	18	0.1	0.4	14	0.3	0.6	13	0.1	0.5	0.5	0.93	0.66	0.96	0.75	N/E	N/E
CHG	18	0.1	0.4	14	0.3	0.6	13	0.1	0.5	0.5	0.9	0.74	0.93	0.71	N/E	N/E
%CHG	2	170	382	2	-100	0.0										
ENDPT RAW	116	0.1	0.3	115	0.2	0.4	115	0.3	0.6	0.5	<.01	0.44	0.33	0.34	<.01	0.02
CHG	116	0.1	0.3	115	0.1	0.4	115	0.3	0.6	0.4	0.01	0.4	0.21	0.46	<.01	0.02
%CHG	3	80.0	312	6	-36	111	8	93.2	155							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 3 PM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO BUT NOT INCLUDING DAY 1
SYMPTOM IS SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

ATTACHMENT 4

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM & PM AVERAGED NASAL STUFFINESS SCORE - POOLED DIARY DATA

DAYS		(A) MFNS N	(A) MFNS MEAN	(A) MFNS SD	(B) VANCENASE N	(B) VANCENASE MEAN	(B) VANCENASE SD	(C) PLACEBO N	(C) PLACEBO MEAN	(C) PLACEBO SD	POOLED SD	ANOVA P-VALUES # TRT	ANOVA P-VALUES # INV	ANOVA P-VALUES # T X I	PAIRWISE COMPARISONS # A-B	PAIRWISE COMPARISONS # A-C	PAIRWISE COMPARISONS # B-C
BASELINE		116	0.2	0.3	115	0.2	0.3	115	0.2	0.3	0.3	0.71	<.01	0.54	0.84	0.43	0.85
PRE	RAW	116	0.2	0.3	115	0.3	0.4	115	0.3	0.4	0.3	0.02	<.01	0.33	0.03	0.01	0.63
	CHG	116	0.0	0.3	115	0.1	0.3	115	0.1	0.3	0.3	0.1	0.01	0.41	0.1	0.05	0.75
	%CHG	45	-17	88.7	47	17.7	108	49	34.5	121							
1-15	RAW	114	0.3	0.4	111	0.4	0.5	109	0.7	0.6	0.5	<.01	<.01	0.01	0.04	<.01	<.01
	CHG	114	0.1	0.4	111	0.2	0.5	109	0.5	0.6	0.5	<.01	0.17	0.01	0.11	<.01	<.01
	%CHG	45	19.0	144	46	78.6	207	45	116	238							
16-30	RAW	114	0.4	0.4	107	0.5	0.6	103	0.8	0.7	0.6	<.01	0.04	0.02	0.18	<.01	<.01
	CHG	114	0.2	0.5	107	0.3	0.6	103	0.6	0.7	0.6	<.01	0.01	0.02	0.25	<.01	<.01
	%CHG	45	46.9	166	43	66.7	172	44	146	260							
31-45	RAW	76	0.5	0.6	67	0.6	0.7	61	0.8	0.7	0.7	<.01	0.33	0.34	N/E	N/E	N/E
	CHG	76	0.3	0.6	67	0.5	0.8	61	0.6	0.8	0.7	<.01	0.05	0.27	N/E	N/E	N/E
	%CHG	28	66.8	235	23	97.7	207	19	136	279							
46-61	RAW	18	0.5	0.6	14	0.7	0.9	13	0.6	0.7	0.7	0.39	0.49	0.36	0.19	N/E	N/E
	CHG	18	0.3	0.6	14	0.6	0.9	13	0.5	0.7	0.7	0.18	0.8	0.1	0.11	N/E	N/E
	%CHG	7	225	399	5	211	241	2	222	346							
ENDPT	RAW	116	0.4	0.5	115	0.6	0.7	115	0.9	0.8	0.7	<.01	0.01	0.3	0.06	<.01	<.01
	CHG	116	0.3	0.6	115	0.4	0.7	115	0.6	0.8	0.7	<.01	<.01	0.28	0.15	<.01	0.01
	%CHG	45	52.3	200	47	78.4	189	49	162	253							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF AM & PM DIARY BASELINE VALUES
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM NASAL STUFFINESS SYMPTOM SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.2	0.3	115	0.2	0.4	115	0.2	0.3	0.3	0.99	<.01	0.6	0.96	0.93	0.89
PRE	RAW	116	0.2	0.3	115	0.3	0.4	115	0.4	0.4	0.3	0.03	<.01	0.43	0.06	0.01	0.47
	CHG	116	-0.0	0.4	115	0.1	0.4	115	0.1	0.4	0.4	0.03	<.01	0.47	0.08	0.01	0.41
	%CHG	48	-13	96.3	44	-16	86.2	47	22.9	104							
1-15	RAW	114	0.3	0.4	111	0.4	0.5	109	0.7	0.6	0.5	<.01	<.01	0.05	0.07	<.01	<.01
	CHG	114	0.1	0.4	111	0.2	0.5	109	0.5	0.7	0.5	<.01	0.02	0.05	0.09	<.01	<.01
	%CHG	47	-21	80.2	42	31.5	149	44	77.2	167							
16-30	RAW	114	0.4	0.5	107	0.6	0.6	103	0.8	0.7	0.6	<.01	0.01	0.04	0.17	<.01	<.01
	CHG	114	0.2	0.5	107	0.3	0.7	103	0.6	0.7	0.6	<.01	<.01	0.07	0.16	<.01	<.01
	%CHG	47	18.5	120	39	12.9	122	43	101	194							
31-45	RAW	76	0.5	0.6	67	0.7	0.8	61	0.8	0.7	0.7	<.01	0.17	0.41	N/E	N/E	N/E
	CHG	76	0.3	0.7	67	0.4	0.8	61	0.6	0.8	0.7	<.01	0.01	0.33	N/E	N/E	N/E
	%CHG	30	22.2	134	22	34.0	143	20	62.8	167							
46-61	RAW	18	0.5	0.6	14	0.8	0.9	13	0.6	0.7	0.7	0.27	0.39	0.29	0.13	N/E	N/E
	CHG	18	0.2	0.6	14	0.6	1.0	13	0.5	0.7	0.7	0.09	0.69	0.04	0.07	N/E	N/E
	%CHG	8	89.0	185	4	109	263	2	96.5	162							
ENDPT	RAW	116	0.5	0.6	115	0.6	0.7	115	0.9	0.8	0.7	<.01	<.01	0.39	0.08	<.01	<.01
	CHG	116	0.2	0.6	115	0.4	0.7	115	0.6	0.8	0.7	<.01	<.01	0.44	0.1	<.01	0.01
	%CHG	48	27.7	133	44	30.7	153	47	96.5	187							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 4 AM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO AND INCLUDING DAY 1
SYMPTOM IS SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

PM NASAL STUFFINESS SYMPTON SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.1	0.3	115	0.2	0.3	115	0.2	0.3	0.3	0.28	<.01	0.72	0.38	0.11	0.46
PRE	RAW	116	0.2	0.3	115	0.3	0.4	115	0.3	0.3	0.3	0.01	<.01	0.19	0.01	0.01	0.82
	CHG	116	0.0	0.3	115	0.1	0.3	115	0.1	0.3	0.3	0.2	0.16	0.15	0.09	0.2	0.67
	%CHG	24	-45	78.2	31	16.2	85.7	36	3.0	85.4							
1-15	RAW	114	0.3	0.4	111	0.4	0.5	109	0.6	0.6	0.5	<.01	<.01	<.01	0.04	<.01	<.01
	CHG	114	0.1	0.4	111	0.2	0.5	109	0.5	0.6	0.5	<.01	0.39	<.01	0.13	<.01	<.01
	%CHG	24	-28	79.7	30	56.7	149	32	56.6	124							
16-30	RAW	114	0.4	0.4	107	0.5	0.6	103	0.8	0.7	0.6	<.01	0.11	0.02	0.22	<.01	<.01
	CHG	114	0.3	0.5	107	0.4	0.6	103	0.6	0.7	0.6	<.01	0.05	0.01	0.36	<.01	<.01
	%CHG	24	2.0	106	27	57.1	137	32	92.7	151							
31-45	RAW	67	0.5	0.6	56	0.7	0.8	54	0.7	0.7	0.7	0.13	0.75	0.91	N/E	N/E	N/E
	CHG	67	0.3	0.6	56	0.6	0.8	54	0.6	0.8	0.7	0.34	0.35	0.85	N/E	N/E	N/E
	%CHG	11	0.7	119	13	138	204	15	40.8	111							
46-61	RAW	18	0.5	0.6	14	0.6	0.8	13	0.5	0.6	0.7	0.75	0.72	0.63	0.52	N/E	N/E
	CHG	18	0.5	0.7	14	0.6	0.8	13	0.5	0.7	0.7	0.45	0.8	0.3	0.37	N/E	N/E
	%CHG	2	50.0	212	2	200	0.0	1	-30	.							
ENDPT	RAW	116	0.4	0.5	115	0.6	0.7	115	0.8	0.8	0.6	<.01	0.06	0.12	0.09	<.01	<.01
	CHG	116	0.3	0.6	115	0.4	0.7	115	0.6	0.8	0.7	<.01	0.06	0.11	0.21	<.01	0.01
	%CHG	24	-5.3	105	31	78.5	170	36	89.6	148							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 3 PM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO BUT NOT INCLUDING DAY 1
SYMPTON IS SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM & PM AVERAGED NASAL DISCHARGE SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
DAYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.1	0.2	115	0.1	0.2	115	0.1	0.2	0.2	0.27	<.01	0.76	0.17	0.16	0.98
PRE	RAW	116	0.1	0.2	115	0.1	0.2	115	0.2	0.3	0.2	0.07	<.01	0.94	0.64	0.03	0.09
	CHG	116	0.0	0.2	115	0.0	0.3	115	0.1	0.3	0.2	0.24	0.08	0.78	0.61	0.25	0.1
	%CHG	17	-33	74.2	27	-25	105	26	15.6	149							
1-15	RAW	114	0.2	0.3	111	0.2	0.4	109	0.5	0.6	0.4	<.01	<.01	<.01	0.48	<.01	<.01
	CHG	114	0.1	0.3	111	0.1	0.4	109	0.4	0.6	0.4	<.01	0.01	<.01	0.78	<.01	<.01
	%CHG	17	-1.6	158	25	2.0	140	22	55.2	196							
16-30	RAW	114	0.3	0.4	107	0.4	0.5	103	0.6	0.7	0.5	<.01	0.04	0.03	0.31	<.01	<.01
	CHG	114	0.2	0.4	107	0.3	0.5	103	0.5	0.7	0.5	<.01	0.01	0.04	0.53	<.01	<.01
	%CHG	17	66.7	222	25	56.1	186	22	119	267							
31-45	RAW	76	0.4	0.6	67	0.4	0.6	61	0.7	0.7	0.6	<.01	0.76	0.42	N/E	N/E	N/E
	CHG	76	0.3	0.6	67	0.3	0.6	61	0.6	0.7	0.6	0.01	0.15	0.66	N/E	N/E	N/E
	%CHG	11	76.6	211	16	66.8	205	17	75.9	205							
46-61	RAW	18	0.4	0.5	14	0.5	0.7	13	0.6	0.7	0.7	0.32	0.5	0.44	0.28	N/E	N/E
	CHG	18	0.4	0.5	14	0.5	0.8	13	0.6	0.7	0.7	0.35	0.44	0.45	0.31	N/E	N/E
	%CHG	1	200	.	3	-6.7	90.2	2	-70	42.4							
ENDPT	RAW	116	0.3	0.5	115	0.4	0.5	115	0.7	0.8	0.6	<.01	0.05	0.04	0.68	<.01	<.01
	CHG	116	0.3	0.5	115	0.3	0.6	115	0.6	0.8	0.6	<.01	0.01	0.04	0.97	<.01	<.01
	%CHG	17	84.0	217	27	54.8	195	26	74.0	221							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF AM & PM DIARY BASELINE VALUES
SYMPTOMS ARE SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

AM NASAL DISCHARGE SYMPTOM SCORE - POOLED DIARY DATA

DAYS		(A) MFNS N	(A) MFNS MEAN	(A) MFNS SD	(B) VANCENASE N	(B) VANCENASE MEAN	(B) VANCENASE SD	(C) PLACEBO N	(C) PLACEBO MEAN	(C) PLACEBO SD	POOLED SD	ANOVA P-VALUES @ TRT	ANOVA P-VALUES @ INV	ANOVA P-VALUES @ T X I	PAIRWISE COMPARISONS @ A-B	PAIRWISE COMPARISONS @ A-C	PAIRWISE COMPARISONS @ B-C
BASELINE		116	0.1	0.2	115	0.1	0.2	115	0.1	0.2	0.2	0.19	<.01	0.76	0.08	0.2	0.62
PRE	RAW	116	0.1	0.3	115	0.1	0.2	115	0.2	0.3	0.3	0.04	<.01	0.02	0.77	0.02	0.04
	CHG	116	0.0	0.2	115	-0.0	0.3	115	0.1	0.3	0.3	0.09	0.14	0.34	0.3	0.24	0.03
	%CHG	18	-47	68.9	27	-40	76.8	24	-30	78.2							
1-15	RAW	114	0.2	0.4	111	0.2	0.4	109	0.4	0.6	0.4	<.01	<.01	0.01	0.71	<.01	<.01
	CHG	114	0.1	0.3	111	0.1	0.5	109	0.4	0.6	0.5	<.01	0.04	0.03	0.78	<.01	<.01
	%CHG	18	-28	77.9	25	-0.0	169	21	-8.4	103							
16-30	RAW	114	0.3	0.4	107	0.4	0.5	103	0.6	0.7	0.5	<.01	0.05	0.06	0.36	<.01	<.01
	CHG	114	0.2	0.4	107	0.2	0.6	103	0.5	0.7	0.6	<.01	0.01	0.09	0.77	<.01	<.01
	%CHG	18	4.6	102	25	36.3	155	21	40.0	149							
31-45	RAW	76	0.4	0.6	67	0.4	0.7	61	0.7	0.7	0.7	<.01	0.79	0.43	N/E	N/E	N/E
	CHG	76	0.3	0.6	67	0.3	0.7	61	0.5	0.7	0.7	0.02	0.1	0.72	N/E	N/E	N/E
	%CHG	11	8.1	97.7	15	62.5	220	16	29.0	128							
46-61	RAW	18	0.4	0.6	14	0.6	0.8	13	0.6	0.7	0.7	0.33	0.46	0.43	0.21	N/E	N/E
	CHG	18	0.3	0.5	14	0.6	0.9	13	0.5	0.8	0.7	0.37	0.36	0.43	0.23	N/E	N/E
	%CHG	2	150	70.7	2	35.6	34.6	3	-73	46.2							
ENDPT	RAW	116	0.3	0.6	115	0.4	0.6	115	0.7	0.7	0.6	<.01	0.05	0.05	0.55	<.01	<.01
	CHG	116	0.3	0.5	115	0.3	0.6	115	0.6	0.8	0.6	<.01	<.01	0.06	>.99	<.01	<.01
	%CHG	18	18.5	109	27	44.5	188	24	40.1	138							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE

@ P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LSMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)

BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 4 AM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO AND INCLUDING DAY 1

SYMPTOM IS SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE

SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED

SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES

ENDPT = LAST AVAILABLE POST-BASELINE VALUE FOR EACH SUBJECT

C93-215

PROPHYLACTIC TREATMENT OF SEASONAL ALLERGIC RHINITIS WITH MOMETASONE FUROATE AQUEOUS NASAL SPRAY

INTENT-TO-TREAT POPULATION

PM NASAL DISCHARGE SYMPTOM SCORE - POOLED DIARY DATA

		(A) MFNS			(B) VANCENASE			(C) PLACEBO			POOLED	ANOVA P-VALUES #			PAIRWISE COMPARISONS #		
AYS		N	MEAN	SD	N	MEAN	SD	N	MEAN	SD	SD	TRT	INV	T X I	A-B	A-C	B-C
BASELINE		116	0.0	0.2	115	0.0	0.2	115	0.1	0.2	0.2	0.33	<.01	0.75	0.79	0.16	0.25
HE	RAW	116	0.1	0.2	115	0.1	0.2	115	0.2	0.3	0.2	0.14	<.01	0.94	0.57	0.05	0.18
	CHG	116	0.1	0.2	115	0.1	0.2	115	0.1	0.3	0.2	0.65	0.11	0.78	0.7	0.36	0.59
	%CHG	9	-35	87.5	12	-3.1	86.2	15	-27	80.8							
-15	RAW	114	0.2	0.3	111	0.2	0.4	109	0.5	0.6	0.4	<.01	<.01	<.01	0.35	<.01	<.01
	CHG	114	0.1	0.3	111	0.2	0.4	109	0.4	0.6	0.4	<.01	<.01	<.01	0.36	<.01	<.01
	%CHG	9	-31	109	11	50.0	158	13	36.2	197							
16-30	RAW	114	0.3	0.4	107	0.4	0.5	103	0.6	0.7	0.5	<.01	0.05	0.02	0.29	<.01	<.01
	CHG	114	0.2	0.4	107	0.3	0.5	103	0.5	0.7	0.5	<.01	0.04	0.02	0.31	<.01	<.01
	%CHG	9	-15	102	11	76.5	153	13	42.3	221							
31-45	RAW	67	0.4	0.6	56	0.4	0.6	54	0.6	0.8	0.7	0.01	0.85	0.55	N/E	N/E	N/E
	CHG	67	0.3	0.6	56	0.4	0.6	54	0.5	0.8	0.7	0.03	0.23	0.61	N/E	N/E	N/E
	%CHG	6	4.2	82.7	7	84.0	208	8	85.9	301							
46-61	RAW	18	0.3	0.5	14	0.5	0.7	13	0.5	0.6	0.6	0.58	0.61	0.61	0.44	N/E	N/E
	CHG	18	0.3	0.5	14	0.4	0.7	13	0.5	0.6	0.6	0.62	0.43	0.58	0.5	N/E	N/E
	%CHG	1	200	.	2	-100	0.0										
ENDPT	RAW	116	0.3	0.5	115	0.3	0.5	115	0.7	0.8	0.6	<.01	0.11	0.08	0.52	<.01	<.01
	CHG	116	0.3	0.5	115	0.3	0.6	115	0.6	0.8	0.6	<.01	0.03	0.05	0.57	<.01	<.01
	%CHG	9	-14	93.0	12	42.2	179	15	50.2	229							

SD = STANDARD DEVIATION T X I = TREATMENT BY INVESTIGATOR INTERACTION N/E = NON-ESTIMABLE
# P-VALUES ARE FROM 2-WAY ANALYSIS OF VARIANCE AND LEMEANS PAIRWISE COMPARISONS (NO ADJUSTMENT FOR OVERALL ALPHA-LEVEL)
BASELINE FOR EACH SUBJECT WAS THE AVERAGE OF 3 PM DIARY ENTRIES - 3 CONSECUTIVE DAYS PRIOR TO BUT NOT INCLUDING DAY 1
SYMPTOM IS SCORED AS 0=NONE, 1=MILD, 2=MODERATE, 3=SEVERE
SUBJECTS WITHOUT BASELINE AND AT LEAST 1 POST-BASELINE VALUE WERE EXCLUDED
SOME PERCENT CHANGE VALUES MAY NOT BE AVAILABLE DUE TO 0 BASELINE VALUES
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