2. SYNOPSIS

| Title of Study: | SAFETY OF LORATADINE (SCH 29851) SYRUP IN CHILDREN 6 MONTHS TO 2 YEARS OLD |
| Investigator: | Jerry M. Herron, M.D. |
| Study Center: | Arkansas Research Medical Testing Center |
| Objective: | To characterize the safety of loratadine syrup (2.5 mL of 1 mg/mL syrup, orally QD [once daily]) compared to placebo in children 6 months to 2 years of age with a personal or strong family history of allergies. |
| Methodology: | Single-center, randomized, placebo-controlled, parallel-group, double-blind |
| Number of Subjects: | 221 |

### Diagnosis and Criteria for Inclusion:
- Subjects must have been 6 months to 2 years of age of either sex and of any race.
- Subjects must have had a documented personal or a strong family history (defined as either both parents and/or sibling with documented history of allergic disease) of allergies.
- Subjects must have been in general good health as confirmed by routine clinical evaluation.
- Subjects must have been free of any clinically significant disease, which would have interfered with the study evaluation.
- Parent/guardian of the subject must have given written informed consent and been able to adhere to dosing and visit schedules and met study requirements.

### Exclusion Criteria:
- Subjects who had a history of allergies to more than 2 classes of medication or who were allergic to or could not tolerate antihistamines.
- Subjects who had experienced an upper respiratory tract or sinus infection that required antibiotic therapy within 14 days prior to Screening, or who had experienced a viral upper respiratory infection within 7 days prior to Screening.
- Subjects who had used any investigational drug in the 30 days prior to Screening.
- Subjects who had a history of hypersensitivity to the study drugs or their excipients.
- Subjects who had family members working at the investigational study site.
- Subjects who were previously randomized into the study.
- Subjects who had current evidence of clinically significant hematopoietic, cardiovascular, hepatic, renal, neurological, psychiatric, autoimmune disease, or other disease that precluded the subject's participation in the study. Particular attention was to be given to subjects with conditions that would have interfered with the absorption, distribution, metabolism, or excretion of the study medication or with the parent/guardian's ability to reliably complete the diary card.
- Subjects who had a history of non-compliance with medications or treatment protocols.

### Test Product, Dose, Mode of Administration, Batch No(s):
Loratadine syrup (Batch Numbers 35274-078-A and 39554-060) 2.5 mL of 1 mg/mL syrup, administered orally, once daily. Subjects in the active treatment group whose subject numbers were between 1 and 167 received loratadine syrup from batch 35274-078-A. Subjects in the active treatment group whose subject numbers were between 168 and 240 received loratadine syrup from batch 39554-060.

### Duration of Treatment:
Once daily for 7 days.

### Reference Therapy, Dose, Mode of Administration, Batch No(s):
Matching placebo syrup (Batch Number 39554-052) was administered orally, once daily.

### Criteria for Evaluation:
Incidence of adverse events was the primary safety variable. Discontinue due to adverse events, changes from Baseline in vital signs, and changes from Baseline in electrocardiogram intervals were also summarized as safety evaluations.
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**Statistical Methods:** Analyses and summaries of safety data are based on all randomized subjects who received at least one dose of study medication. The frequency for the incidence of adverse events by treatment group and vital signs were tabulated. Adverse events were also summarized by age strata. The frequency of discontinuations due to adverse events and changes from Baseline in vital signs were tabulated and summarized. Changes in electrocardiogram (ECG) intervals were analyzed by analysis of variance (ANOVA) that extracts a source of variance due to treatment. Treatment comparisons were based on the least square means from the ANOVA, using a 5% (two-sided) significance level. In addition to the ANOVA of the ECG parameters, frequency tabulations of ECG data were done on the number of subjects, by treatment groups, in categories of percent change from Baseline as follows: < -20%, ≥ -20% to < -15%, ≥ -15% to < -10%, ≥ -10% to <+10%, ≥ +10% to <+15%, ≥ +15% to <+20%, ≥ +20%.

**SUMMARY – CONCLUSIONS:**

**RESULTS:** A total of 221 subjects (111 loratadine and 110 placebo) received study medication. Demographic and other Baseline characteristics were comparable between treatment groups. In both the loratadine treatment group and placebo treatment group, the mean age was approximately 16.4 months. The loratadine treatment group and placebo treatment group had similar proportions of subjects in each of the 2 age subgroups, ≥6 months to <1 year and ≥1 year to <2 years. Fifty-two percent of the subjects in the loratadine treatment group were female compared with 47% of subjects in the placebo group. In each treatment group, approximately half of the subjects were Caucasian and approximately half were Black; there was 1 subject of race other than Caucasian or Black in each treatment group. A total of 220 subjects completed the study; 1 subject discontinued for reasons not related to the assigned study medication.

**Safety:** Review of the safety data indicates that treatment with loratadine was well tolerated. The overall incidence of adverse events was lower for subjects treated with loratadine (8%) compared with placebo (11%). No adverse events were reported in >3% of subjects in either treatment group. The most frequently reported adverse events were fever (3% loratadine, 1% placebo), loose stools (2% loratadine, 3% placebo), vomiting (2% loratadine, 2% placebo), and somnolence (2% loratadine, 3% placebo). All of the reported adverse events were of mild or moderate severity. No serious adverse events were reported and no subjects discontinued from the study due to adverse events. Adverse events caused treatment interruption for 2 subjects (2%) in the loratadine group compared with 3 subjects (3%) in the placebo group. For all subjects in the study, ECGs remained normal and no clinically meaningful changes were observed. Mean changes in the PR, QRS, QT, and QTc intervals were examined. Both groups were comparable at Baseline and there were no statistically significant differences between treatment groups at the post-Baseline timepoint. No changes indicative of a treatment effect were observed in vital signs or physical examination findings.

**Efficacy:** Efficacy was not evaluated

**CONCLUSIONS:**

- Treatment with loratadine was well tolerated in young children, 6 months to 2 years of age; no unusual or unexpected adverse events or effects were reported or observed.

- No statistically significant differences in mean change from Baseline in ventricular rate, PR, QRS, QT, or QTc intervals were observed between treatment groups during the study.

**Date of the Report:** 3 February 2000