



CLINICAL TRIAL CONSULTANTS AB

CONFIDENTIAL

## **Brief statistical report – Post hoc analyses**

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<b>Sponsor:</b>	<i>Swedish Match</i>
<b>Study code:</b>	<i>Post hoc analyses</i>
<b>CTC project no:</b>	<i>Post hoc SM</i>
<b>Study title:</b>	<i>Post hoc analyses of 17-01, 17-03 and 18-01</i>
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## STATISTICAL REPORT

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

<b>1</b>	<b>LIST OF ABBREVIATIONS .....</b>	<b>3</b>
<b>2</b>	<b>INTRODUCTION.....</b>	<b>4</b>
<b>3</b>	<b>POST HOC STUDY DETAILS.....</b>	<b>5</b>
3.1	Post hoc Objectives and Endpoints .....	5
<b>4</b>	<b>STATISTICAL AND ANALYTICAL PLANS .....</b>	<b>7</b>
4.1	Definition of Analysis Sets.....	7
4.1.1	Per Protocol Analysis Set.....	7
4.2	Definition of Baseline for Pharmacokinetic calculations .....	7
4.3	Summary Statistics .....	7
4.4	Significance Level .....	7
4.5	Multiple Comparisons/Multiplicity .....	7
4.6	Handling of Drop-outs, Missing Data and Outliers.....	7
<b>5</b>	<b>RESULT.....</b>	<b>8</b>
5.1	Hypothesis #1 .....	8
5.2	Hypothesis #2 .....	12
5.3	Hypothesis #3 .....	15
5.4	Hypothesis #4 .....	17
5.5	Hypothesis #5 .....	19
5.6	Hypothesis #6 .....	21
5.7	Hypothesis # 7 .....	37
5.8	Hypothesis #8 .....	38
<b>6</b>	<b>STATISTICAL DELIVERABLES .....</b>	<b>40</b>
<b>7</b>	<b>SOFTWARE.....</b>	<b>41</b>
<b>8</b>	<b>APPROVAL .....</b>	<b>42</b>

## STATISTICAL REPORT

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

### 1 LIST OF ABBREVIATIONS

Abbreviation of term	Explanation
G 8mg	General PSWL
G2 8mg	General PSWL*2
LH_N	Longhorn Natural
LH_W	Longhorn Wintergreen
ZYN 3mg	ZYN Smooth 3mg
ZYN_W 3mg	ZYN Wintergreen 3mg
ZYN_P 3mg	ZYN Peppermint 3mg
ZYN_S 3mg	ZYN Spearmint 3mg
ZYN 4.5mg	ZYN Smooth 4.5 mg
ZYN_W 4.5mg	ZYN Wintergreen 4.5 mg
ZYN 6mg	ZYN Smooth 6 mg
ZYN 8mg	ZYN Smooth 8 mg

## **STATISTICAL REPORT**

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

## **2 INTRODUCTION**

This brief statistical report gives the result from the Statistical Analysis Plan (SAP) for the post hoc analysis involving the following studies: SM17-01, SM17-03 and SM18-01.

## STATISTICAL REPORT

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

### 3 POST HOC STUDY DETAILS

#### 3.1 Post hoc Objectives and Endpoints

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## STATISTICAL REPORT

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

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## **4 STATISTICAL AND ANALYTICAL PLANS**

### **4.1 Definition of Analysis Sets**

#### **4.1.1 Per Protocol Analysis Set**

Only the Per Protocol Analysis set from each study was used.

### **4.2 Definition of Baseline for Pharmacokinetic calculations**

Pharmacokinetic parameters were calculated by non-compartmental analysis (NCA) according to the linear up- log down method using Phoenix WinNonlin ver. 8.1. The time for the pre-dose sample was set to 0 and plasma concentrations below the quantification limit was set to 0 before  $T_{max}$  and to missing thereafter. Baseline measurement was defined as the latest measurement prior to first dose of IMP.

Baseline adjustments were calculated according to the formula:

$$C(t)_{\text{adjusted}} = C(t)_{\text{observed}} - C(0)e^{-K_{el}(t)}$$

The elimination constant ( $K_{el}$ ) was calculated and the threshold for acceptance of regression was defined by:  $\geq 0.85$  for  $R^2_{\text{adj}}$ ,  $\leq 30\%$  for % residual AUC and  $\geq 1.0$  for the half-life span. The elimination constant for subjects not fulfilling all three acceptance criteria was calculated based on the mean calculated eliminations constants for the same subject at other dosing occasions. Subjects not fulfilling acceptable criteria for eliminations constant determination at any dosing occasion were excluded from the PK population.

### **4.3 Summary Statistics**

In general, all data collected were presented with summary statistics. Summary statistics includes at least number of patients, mean, standard deviation, median, minimum and maximum for continuous data and frequency and percentage for categorical data. Table with summary statistics was divided by treatment group.

### **4.4 Significance Level**

A significance level of 5% was applied for analyses.

### **4.5 Multiple Comparisons/Multiplicity**

No adjustment for multiple comparison/multiplicity were performed, all significant statistical findings, must be reviewed for medical relevance.

### **4.6 Handling of Drop-outs, Missing Data and Outliers**

Outliers were included in summary tables and were not handled separately in any analyses. No imputation of data was performed.

## STATISTICAL REPORT

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

## 5 RESULT

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## STATISTICAL REPORT

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

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Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB

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Study Code: Post-hoc analyses

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CLINICAL TRIAL CONSULTANTS AB

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Study Code: Post-hoc analyses

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CLINICAL TRIAL CONSULTANTS AB

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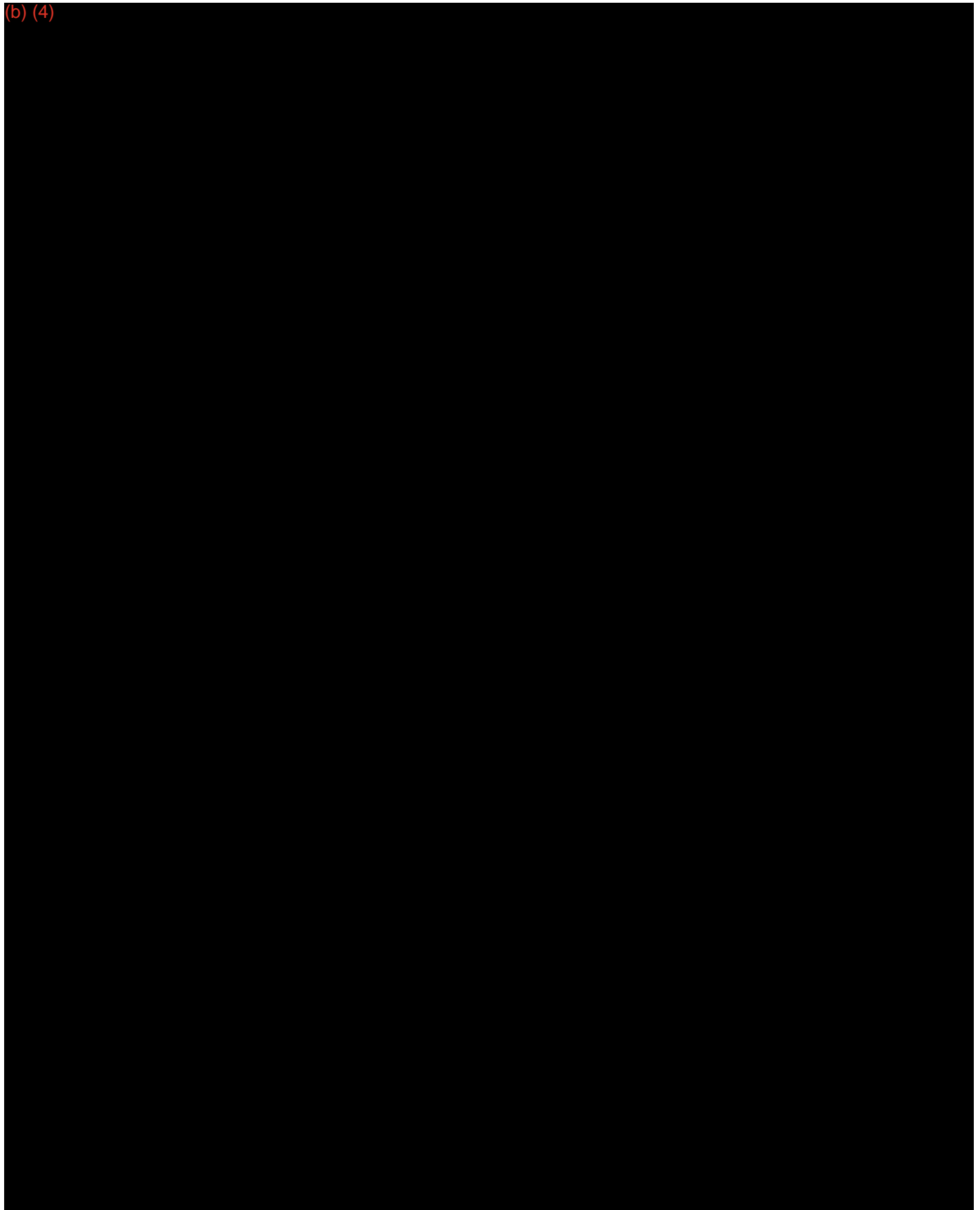
Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



CLINICAL TRIAL CONSULTANTS AB



(b) (4)

## STATISTICAL REPORT

Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

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CLINICAL TRIAL CONSULTANTS AB

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Study Code: Post-hoc analyses

CTC Project No: post hoc SM



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Protocol Version No: 1701, 1703 and 1801

Study Code: Post-hoc analyses

CTC Project No: post\_hoc\_SM



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