SIGNATURE PAGE

Document Name : TH1017 Clinical Study Report Final 12-Sep-2011.pdf

Document Title :

Document Version : 0.1; CURRENT; Most-Recent; For Approval

Date (GMT)	Signed by
25/Apr/2016 08:01:31	EmField
Justification	Clinical Approver

Justification	

Justification	

Justification	

Justification	

Justification	

Justification	

Reckitt Benckiser Healthcare International Limited

1 STUDY REPORT TITLE PAGE

EudraCT Number:	2010-024045-69.
Study Number:	TH1017
Protocol Title:	A multi centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.
Study Phase:	IV
Date First Patient Enrolled:	2nd February 2011
Date Last Patient Completed:	1st April 2011
Report Date:	Final 12th September 2011
Chief Investigator:	Dr. Damien McNally, Ormeau Health Centre, 120 Ormeau Road, Belfast BT7 2EB
Study Conduct Statement:	This study was conducted in accordance with ICH Good Clinical Practice and the ethical principles contained within the Declaration of Helsinki (South Africa, 1996), as referenced in EU Directive 2001/20/EC. Documents defined by ICH GCP as "essential documents" will be archived in the BHI company archive in Nottingham, NG90 6BH, UK

Reviewed and Agreed by:

Clinical Project Manager		Statistician:	
	15/9/11	Michael A Goulder	15-SEP-11
Miss Emma Field, BSc (Hons)	Date	Mr Michael A Goulder, BSc (Hons)	Date

Report Author			
C. Donaghy	15th Sept 11		
Mrs. Colette Donaghy BA (Hons) RGN, MSc	Date		

Reviewed and Approved by:

R&D Manager - Clinical (Healthcare)		Global Medical Director:	
	19/9/11		14th Sep 2011
Dr Sue Aspley BSc (Hons), PhD	Date	Dr P Berry MB ChB, MPH	Date

Study Sponsor: Reckitt Benckiser Healthcare UK Ltd, Dansom Lane, Hull, HU8 7DS

Reviewed and Agreed by:

Clinical Project Manager			Statistician:		
		14/9/11			
Miss Emma Field, BSc (Hons)		Date	Mr Michael A Goulder, BSc (Hons)		Date

Report Author					
Mrs. Colette Donaghy BA (Hons) RGN, MSc		Date			

Reviewed and Approved by:

R&D Manager - Clinical (Healthcare)			Global Medical Director:		
					14th Sep 2011
Dr Sue Aspley BSc (Hons), PhD		Date	Dr P Berry MB ChB, MPH		Date

Study Sponsor: Reckitt Benckiser Healthcare UK Ltd, Dansom Lane, Hull, HU8 7DS

2 SYNOPSIS

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	
Title of Trial: A multi centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.		
Investigator(s): Dr.Damien McNally. Dr. Paul Conn, Dr Malcolm McCaughey, Dr. Michael Redmond, Dr. Nigel Hart, Dr. Peter Ryan, Dr. Gerry McKeague, Dr. Sean Haigney		
Trial Centre(s): Multi Centre study in 8 GP Primary Care sites in Northern Ireland, UK		
Publication (reference): None.		
Studied Period: 3 months **Date first patient enrolled:** 2 February 2011 **Date last patient completed:** 1st April 2011		**Phase of Development:** IV
Objectives: The primary objective of the study was to determine the analgesic efficacy of Strepsils Plus and Strepsils Extra in patients with a sore throat due to upper respiratory tract infection (URTI) compared to a placebo lozenge. The analgesic properties were assessed by looking at the change in severity of throat soreness. Further objectives were to determine consumer acceptability of this product via responses to a consumer questionnaire (Appendix VIII).		

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

Methodology: Patients with a sore throat due to an upper respiratory tract infection either presented opportunistically or following a response to advertisements that had been placed in the Doctors surgery, local chemists and some local newspapers.

Patients were screened initially at the 8 primary care sites. Eligible patients that met the study inclusion and exclusion criteria were randomized to receive one of the three test products. Within 1 minute of the baseline assessments of Throat soreness (11-point scale) difficulty swallowing (100mm VAS) and Swollen throat (100mm VAS) and a two part consumer questionnaire, patients were blindfolded and dosed with the assigned trial medication according to their randomisation number (active or placebo lozenge). At 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose patients completed the throat soreness and difficulty swallowing scales along with a 7-point categorical sore throat relief scale, a 5-point categorical throat numbness scales and a 100mm VAS swollen throat scale. One question regarding speed of numbing sensation was completed at 1 minute post dose, one question concerning the soothing sensation was completed at 5 minutes, three questions concerning the strength, intensity and depth of numbing were completed at 20 minutes post dose and other relief and emotional questions were completed at 60 and 120 minutes post dose. In addition, an overall treatment rating and a global evaluation were completed 120 minutes by the patient. A practitioner's clinical assessment of the study medication was conducted at 120 minutes by the investigator.

Following completion of the two hour assessment, patients left the investigative site with a patient diary to record any concomitant medication or adverse events experienced up to 24 hours post dose of the study medication. A follow up telephone call by the site to the patient was made one to three days after completing the study to transcribe into the CRF any concomitant medications or adverse events recorded in the diary.

Number of Patients: **Planned:** 190

Analysed: 190 (Safety)
190 (Full analysis set)
174 (Per Protocol [PP])

Diagnosis and Main Criteria for Inclusion: Male and Female patients aged between 18 and 75 years of age with a sore throat due to an upper respiratory tract infection of onset not more than 4 days on the due day of treatment were eligible for randomisation to the study. Patients had to have objective findings that confirmed the presence of tonsillopharyngitis with a score of ≥5 on the expanded Tonsillopharyngitis Assessment (TPA) and a score of ≥6 on the throat soreness scale. Further inclusion criteria was a VAS score of >50mm on the difficulty swallowing and >33mm on the swollen throat scale at baseline.

Exclusion criteria excluded patients with conditions that could interfere with the assessment of sore throat analgesic activity and with any contraindications to any of the study medication.

Test Product: Strepsils Plus Lozenge (Batch No. 3EE2) and Strepsils Extra Blackcurrant Lozenge (Batch No. 4GG) x 1 Lozenge orally.

Each patient was blindfolded and dosed with one lozenge by a blinded member of staff and instructed to suck the lozenge slowly, moving the lozenge around the mouth until it dissolved and not to chew or crunch the lozenge.

Duration of Treatment: 2 hours

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

Reference Therapy: Non medicated sugar based placebo lozenge (Batch No. 2254653) x 1 lozenge orally

Criteria for Evaluation:

Efficacy: The Primary endpoint for this study was the change from baseline in severity of throat soreness (using the 11 point throat soreness scale) for the Strepsils Plus and Extra versus the placebo at 2 hours post dose

There were a number of secondary endpoints assessed. These were the AUC's from baseline to 2 hours for the change from baseline in difficulty swallowing, throat numbness and swollen throat. The change from baseline in difficulty in swallowing and swollen throat at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose was assessed as was throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. The total sum of pain relief ratings (TOTPAR), defined as the AUC from baseline to 2 hours post first dosing for sore throat relief, was assessed as was sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. Onset of analgesia defined as the times to first reporting 'moderate pain relief' (which is the midpoint on the 7-point sore throat relief scale) was assessed as was the Global evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) and Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at 2 hours. Responses to questions from the consumer questionnaire were also assessed.

Safety: Safety and tolerability of the lozenges were assessed in terms of the overall proportion of patients who reported adverse events (AEs) and serious adverse events (SAE's) during the 2 hours of observation and in the 24 hour period following administration of the lozenge when patients were asked to complete a patient diary. The information from the diary was obtained by a phone call to the patient by the nurse in a follow up period not exceeding 3 days post dose.

Statistical Methods: All efficacy variables were analysed using the full analysis dataset, which consisted of all patients who were randomised to the study and took study medication. The primary analysis and secondary analysis of the change from baseline in severity of throat soreness from 0 to 2 hours, AUC from baseline to 2 hours for the change from baseline of severity of throat soreness and difficulty in swallowing and the AUC from baseline to 2 hours for throat numbness and sore throat relief were repeated using a per-protocol set.

The primary efficacy variable was analysed using Analysis of Covariance (ANCOVA) with the baseline severity of throat soreness as a covariate and a factors for treatment group and centre.

The secondary AUC, changes from baseline and overall treatment rating variables were analysed using ANCOVA with baseline severity of throat soreness as a covariate and a factors for treatment group and centre. Covariates for swollen throat and difficulty swallowing were also added to the model for analysis of these variables. The time to onset of moderate pain relief was compared between treatment groups using the Cox-proportional hazards model. Consumer questionnaire responses were analysed using a proportional odds model (non-numeric data) or ANCOVA (numeric ordinal data).

Safety data were analysed using the safety set which included all patients who took study medication. The proportion of patients reporting treatment emergent adverse events was compared between treatment groups using the chi-square test.

Treatment group differences were presented with 95% confidence intervals. All AUC analyses were based on actual timings and were calculated using the trapezoidal rule.

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	
Concomitant medications ongoing at randomisation were coded using the ATC level 2 categories from the WHO dictionary Enhanced 3.11 Version. Adverse Events were listed and tabulated by treatment, severity, relationship to therapy and primary system organ class according to Version 13.1 of MedDRA.		

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

SUMMARY & CONCLUSIONS

Efficacy Results:

The treatment groups were matched for demographic variables with the age range being 18-73 years with a mean of 31.6 years. There was an imbalance in gender between the two Strepsils groups (33% male) and the placebo group 58% male with majority (98%) of patients being Caucasian. Strepsils Extra showed clear superiority with statistical significance over placebo for the primary variable of throat soreness and across all efficacy variables in the study. Strepsils Plus also achieved significant efficacy over Placebo at various time points for the efficacy measures and both Strepsils Lozenges showed statistically significant sore throat relief in comparison to placebo. Results for the primary efficacy variable are summarised in Table 1

TABLE 1
Primary Efficacy Variable - Change from baseline in throat soreness at 120 minutes post dose
Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore

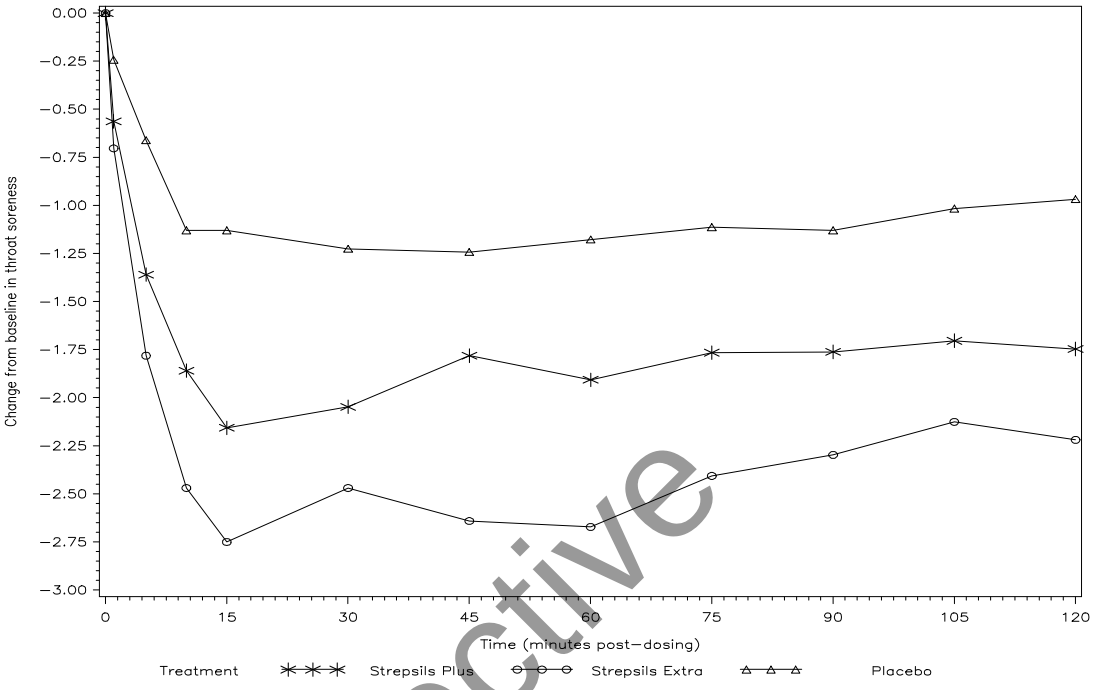
	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
FULL ANALYSIS SET			
N	64	64	62
Baseline (Mean±sd)	7.16±1.07	7.27±1.21	7.13±1.00
120 minutes post-dose (Mean±sd)	5.41±2.34	5.05±2.62	6.16±1.87
Change from baseline (Mean±sd)	-1.75±2.31	-2.22±2.66	-0.97±1.96
LS mean[a]	-1.78	-2.19	-1.03
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge V Placebo	-0.75	-1.54,0.04	0.06
Strepsils Extra lozenge V Placebo	-1.16	-1.95,-0.37	0.004 **
PER-PROTOCOL SET			
N	58	58	57
Baseline (Mean±sd)	7.10±1.00	7.40±1.12	7.25±0.93
120 minutes post-dose (Mean±sd)	5.48±2.31	5.12±2.62	6.26±1.89
Change from baseline (Mean±sd)	-1.62±2.09	-2.28±2.66	-0.98±2.03
LS mean[a]	-1.68	-2.22	-1.03
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.65	-1.47,0.18	0.12
Strepsils Extra lozenge – Placebo	-1.19	-2.01,-0.36	0.005 **

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A negative difference favours the first treatment against second treatment

Figure 1: mean change from baseline in throat soreness from 1-120 minutes post dose – Full analysis set

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

Throat soreness measured on an 11 point scale where 0=not sure, 10=very sore



Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

TABLE 11.4.3

Mean ± sd for change from baseline in throat soreness at 1, 5, 10, 15, 30, 45, 60, 75, 90 and 105 minutes post dose – Full analysis set

Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	7.20±1.12 (64)	7.27±1.21 (64)	7.13±1.00 (62)		
1	-0.56±1.21 (64)	-0.70±1.29 (64)	-0.24±0.82 (62)	ns	*
5	-1.36±1.73 (64)	-1.78±1.72 (64)	-0.66±1.01 (62)	*	***
10	-1.86±1.86 (64)	-2.47±2.01 (64)	-1.13±1.71 (62)	*	***
15	-2.16±2.07 (64)	-2.75±2.01 (64)	-1.13±1.61 (62)	**	***
30	-2.05±2.07 (64)	-2.47±1.97 (64)	-1.23±1.71 (62)	*	***
45	-1.78±2.11 (64)	-2.64±2.23 (64)	-1.24±1.91 (62)	ns	***
60	-1.91±2.10 (64)	-2.67±2.30 (64)	-1.18±1.93 (62)	ns	***
75	-1.77±2.14 (64)	-2.41±2.42 (64)	-1.11±1.92 (62)	ns	**
90	-1.76±2.16 (63)	-2.30±2.54 (64)	-1.13±1.94 (62)	ns	**
105	-1.70±2.24 (64)	-2.13±2.58 (64)	-1.02±2.00 (62)	ns	*

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

Source: Tables 14.2.3 to 14.2.12

Key secondary efficacy variable data are summarised in Table 2 - 6 – Full analysis set

Table 2

Mean ± sd (n) for change from baseline in difficulty in swallowing at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set

Difficulty in swallowing measured on 100mm VAS where 0mm = Not difficult, 100mm = Very difficult

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	72.5±10.5 (64)	73.6±12.1 (64)	70.8±11.9 (62)		
1	-8.0±13.7 (64)	-10.8±16.2 (64)	-4.1±11.4 (62)	ns	*
5	-15.1±17.2 (64)	-19.8±18.8 (64)	-6.4±11.6 (62)	**	***
10	-19.9±20.5 (64)	-25.6±21.3 (64)	-9.0±14.0 (62)	**	***
15	-21.8±21.9 (64)	-29.1±22.0 (64)	-10.1±13.8 (62)	***	***
30	-20.7±22.2 (64)	-28.6±22.2 (64)	-8.8±12.0 (62)	**	***
45	-18.6±21.7 (64)	-29.5±23.2 (64)	-8.7±12.7 (62)	**	***
60	-18.8±22.3 (64)	-29.7±24.2 (64)	-8.6±13.4 (62)	**	***
75	-19.3±23.2 (64)	-28.4±26.0 (64)	-7.4±13.1 (62)	**	***
90	-18.7±23.6 (64)	-26.9±27.4 (64)	-7.6±13.2 (62)	**	***
105	-19.8±23.6 (64)	-26.2±28.2 (64)	--7.4±13.9 (62)	**	***
120	-19.6±25.2 (64)	-27.0±30.2 (64)	-7.0±15.3 (62)	**	***

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

Table 3

Mean ± sd (n) for change from baseline in swollen throat at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set

Swollen throat measured on a 100mm VAS scale where 0mm = Not Swollen, 100mm = Very Swollen

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	66.1±16.3 (63)	68.3±18.1 (64)	66.7±15.2 (62)		
1	-2.8±13.1 (63)	-9.1±18.6 (64)	-1.9±11.8 (62)	ns	**
5	-8.3±16.2 (63)	-14.5±19.2 (64)	-4.3±13.4 (62)	ns	***
10	-13.4±18.6 (63)	-20.0±21.2 (64)	-6.7±15.5 (62)	*	***
15	-14.7±21.6 (63)	-23.0±21.9 (64)	-7.3±14.7 (62)	*	***
30	-15.8±20.5 (63)	-24.4±23.9 (64)	-6.2±15.2 (62)	**	***
45	-14.1±21.0 (63)	-24.3±24.0 (64)	-5.7±14.9 (62)	*	***
60	-14.3±21.7 (63)	-24.9±25.4 (64)	-7.1±19.0 (62)	ns	***
75	-14.8±23.1 (63)	-24.2±27.0 (64)	-5.6±15.9 (62)	*	***
90	-16.0±22.8 (63)	-22.8±28.9 (64)	-5.7±16.6 (62)	**	***
105	-15.5±24.1 (63)	-22.6±28.6 (64)	-5.5±17.0 (62)	*	***
120	-15.0±24.9 (63)	-23.1±29.6 (64)	-5.2±18.1 (62)	*	***

ns	Comparison not statistically significant
*	Comparison statistically significant at 5% level
**	Comparison statistically significant at 1% level
***	Comparison statistically significant at 0.1% level

Table 4

Mean ± sd (n) for sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post first dose – Full analysis set

Measured on a 7-point scale where 0 = No relief, 1 = Slight relief, 2 = Mild relief, 3 = Moderate relief, 4 = Considerable relief, 5 = Almost complete relief, 6 = Complete relief

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
1	1.13±1.29 (64)	1.03±1.05 (64)	0.37±0.71 (62)	***	***
5	1.83±1.30 (64)	1.83±1.11 (64)	0.76±1.00 (62)	***	***
10	2.20±1.37 (64)	2.41±1.28 (64)	0.98±1.22 (62)	***	***
15	2.28±1.34 (64)	2.66±1.39 (64)	1.00±1.20 (62)	***	***
30	2.17±1.50 (64)	2.63±1.41 (64)	0.97±1.06 (62)	***	***
45	1.98±1.52 (64)	2.52±1.53 (64)	0.92±1.11 (62)	***	***
60	1.86±1.55 (64)	2.42±1.64 (64)	0.82±1.02 (62)	***	***
75	1.78±1.59 (64)	2.33±1.75 (64)	0.76±0.99 (62)	***	***
90	1.66±1.60 (64)	2.08±1.78 (64)	0.71±1.03 (62)	***	***
105	1.63±1.65 (64)	1.97±1.80 (64)	0.71±1.12 (62)	***	***
120	1.66±1.64 (64)	1.95±1.89 (64)	0.68±1.11 (62)	***	***

ns	Comparison not statistically significant
*	Comparison statistically significant at 5% level
**	Comparison statistically significant at 1% level
***	Comparison statistically significant at 0.1% level

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

Table 5

Mean ± sd (n) for throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set

Throat numbness measured on a 5-point scale where 1 = None, 2 = Mild, 3 = Moderate, 4 = Considerable, 5 = Complete

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
1	2.08±0.99 (63)	1.84±0.74 (64)	1.63±0.93 (62)	*	Ns
5	2.40±1.04 (63)	2.38±0.90 (64)	1.80±0.98 (61)	***	**
10	2.54±1.08 (63)	2.70±0.91 (63)	1.84±0.97 (61)	***	***
15	2.63±1.03 (64)	2.69±1.05 (64)	1.84±0.96 (62)	***	***
30	2.33±1.11 (64)	2.56±0.97 (64)	1.77±0.80 (61)	**	***
45	2.17±1.09 (64)	2.48±1.15 (64)	1.74±0.85 (62)	*	***
60	2.08±1.19 (64)	2.27±1.22 (63)	1.64±0.78 (61)	*	**
75	1.95±1.12 (64)	2.19±1.22 (64)	1.58±0.80 (62)	*	**
90	1.91±1.16 (64)	2.09±1.28 (64)	1.52±0.78 (62)	*	**
105	1.92±1.17 (64)	2.05±1.28 (63)	1.48±0.78 (62)	*	**
120	1.92±1.21 (64)	2.03±1.36 (63)	1.45±0.76 (62)	*	**

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

Table 6 Summary of Additional Key Secondary Efficacy Variables – Full analysis set

Variable	**Strepsils Plus**	**Strepsils Extra**	**Placebo**
AUC fro baseline to 2 hours post dose in **difficulty swallowing** (measured on a 100mm VAS where 0mm=not difficult , 100mm = very difficult)			
N	64	64	62
Mean + SD	-19.1±20.0	-27.3±21.9	-8.0±11.6
LS mean[d]	-19.3	-27.2	-8.6
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus v placebo	-10.7	-17.1, -4.3	0.0012**
Strepsils Extra v placebo	-18.7	-25.1, -12.2	<0.0001***

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

Table 6 cont

Variable	**Strepsils Plus**	**Strepsils Extra**	**Placebo**
AUC from baseline to 2 hours post dose for the change in baseline in **swollen throat** (measured on a 100mm VAS where 0mm=not swollen, 100mm=very swollen)			
N	63	64	62
Mean + SD	-14.4±19.4	-22.8±23.3	-5.9±14.6
LS mean[e]	-14.9	-22.5	-6.2
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus v placebo	-8.8	-15.3, -2.2	0.009**
Strepsils Extra v placebo	-16.3	-22.9, -9.8	<0.0001***
AUC from baseline to 2 hours post dose for **sore throat relief (TOTPAR)** (measured on a 7 point scale where 0=no relief and 6 = complete relief)			
N	64	64	62
Mean + SD	1.86±1.33	2.28±1.41	0.81±0.95
LS mean[a]	1.90	2.31	0.84
Parameter estimates	LS mean[c]	95% CI	P
Strepsils Plus v placebo	1.06	0.62, 1.50	<0.0001***
Strepsils Extra v placebo	1.47	1.03, 1.91	<0.0001***
AUC from baseline to 2 hours post dose for the change in baseline in **throat numbness** (measured on a 5 point scale where 1= none and 5 = complete)			
N	64	64	62
Mean + SD	2.13±0.98	2.30±0.99	1.64±0.74
LS mean[a]	2.11	2.27	1.63
Parameter estimates	LS mean[c]	95% CI	P
Strepsils Plus v placebo	0.49	0.17,0.80	0.0024 **
Strepsils Extra v placebo	0.64	0.33,0.96	<0.0001 ***

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	Individual Trial Table Referring to Part of the Dossier	(For National Authority use only) Leave blank
Name of Finished Product: to be completed by Reg. Affairs	Volume: to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	Page: to be completed by Reg Affairs	

Table 6 Cont

Variable	Strepsils Plus	Strepsils Extra	Placebo
Consumer questionnaire: how would you rate this lozenge as a treatment for **sore throat** (asked at 2 hours post dose and measured on an 11 point scale where 0=poor and 10=excellent)			
N	64	64	62
Mean + SD	5.38±2.98	5.64±3.06	2.23±2.73
LS mean[a]	5.38	5.66	2.20
Parameter estimates	LS mean[c]	95% CI	P
Strepsils Plus v placebo	3.18	2.15,4.21	<0.0001 ***
Strepsils Extra v placebo	3.45	2.42,4.49	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A negative difference favours the first treatment against second treatment
c A positive difference favours the first treatment against second treatment
d Estimated from ANCOVA model with factors for treatment and centre and covariates for baseline throat soreness and baseline difficulty swallowing
e Estimated from ANCOVA model with factors for treatment and centre and covariates for baseline throat soreness and baseline swollen throat

The superiority of Strepsils Extra over placebo was evident with statistical significance achieved for all efficacy variables in the study. Strepsils Plus was also superior to placebo on all but the primary efficacy variable

Maximum reductions in throat soreness were evident at 15 minutes post dose for both Strepsils Lozenges compared to 45 minutes post dose for placebo.

Maximum mean throat numbness was obtained at 10 minute post dose for the Strepsils Extra lozenge and placebo and 15 minute post dose for Strepsils Plus.

Both Strepsils Lozenges showed statistically significant sore throat relief than placebo.

Maximum pain relief was observed at 15 minutes post dose for all 3 treatments

For the functional element of the consumer questionnaire statistically differences to placebo in favour of Strepsils Extra were obtained for improvements in talking (p=0.005) and swallowing (p=0.002) to one hour post dose. There was no significant improvement for Strepsils Plus v Placebo for any of the functional impairments.

There was a statistically significant difference in favour of both Strepsils Lozenges against placebo in patient reported outcomes of, how effective their lozenge was, the depth of numbing, intensity of the numbing, feeling their best overall and how happy they were with their throat. This significant difference was also reflected in the patient's response to feeling less distracted, making patients feel better than before and taking their minds of the pain. Both Strepsils Lozenges were found to offer highly significant soothing over placebo.

Both Strepsils Lozenges were rated highly statistically significantly better than placebo (p<0.0001) with respect to both the Practitioner Clinical assessment of the study medication and the Patient's Global evaluation of the medication.

Name of Sponsor/ Company: Reckitt Benckiser Healthcare	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)** Leave blank
Name of Finished Product: to be completed by Reg. Affairs	**Volume:** to be completed by Regulatory Affairs	
Name of Active Ingredient(s):	**Page:** to be completed by Reg Affairs	

SAFETY RESULTS: There were no statistically significant pair wise treatment differences between the treatment groups in the proportion of subjects reporting treatment emergent adverse events. There were a total of 7 adverse events reported by 6 patients. For the Strepsils Extra lozenge group, one (2%) patient reported two adverse events.

For the Strepsils Plus lozenge group, one (2%) patient reported one adverse event. The Placebo group had 4 (6%) patients report four adverse events

CONCLUSION: Strepsils Extra was more efficacious and achieved statistical significance over placebo for all the analgesic variables related to throat soreness, sore throat relief and difficulty in swallowing. Both Strepsils Lozenges demonstrated superiority over placebo consistently over the variables measured. Both Strepsils Lozenges were well tolerated.

Date of the report: Final 12th September 2011

3 TABLE OF CONTENTS

3.1 List of Tables and Figures Contained in the Body of the Report

3.2 List of Appendices

16.2.3 Patients excluded from the efficacy analysis

16.2.4 Demographic data

16.2.5 Compliance and/or drug concentration data

16.2.6 Individual efficacy response data

16.2.7 Adverse event listings (each patient)

16.2.8 Listing of other observations relating to safety

16.3 CASE REPORT FORMS

16.4 INDIVIDUAL PATIENT DATA LISTINGS (US ARCHIVAL LISTINGS)

4 LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Abbreviation in Full
ABPI	Association of the British Pharmaceutical Industry
AE	Adverse Event
AIDS	Acquired Immune Deficiency Syndrome
ANOVA	Analysis of variance
ANCOVA	Analysis of covariance
AR	Adverse Reaction
AUC	Area Under the Curve
BNF	British National Formulary
CFR	Code of Federal Regulations
CLIN	Practitioners Clinical Assessment of the Study Medication
CPM	Clinical Project Manager
CRF	Case Report Form
CRO	Contract Research Organisation
CTA	Clinical Trial Application
CV	Curriculum Vitae
DSS	Difficulty Swallowing Scale
EC	Ethics Committee
eCRF	Electronic Case Report Form
EU	European Union
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GLOBAL	Patient Global Evaluation of the Study Medication
GMP	Good Manufacturing Practice

Abbreviation	Abbreviation in Full
GP	General Practitioner
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
IEC	Independent Ethics Committee
IMSU	Investigational Material Supplies Unit
IND	Investigational New Drug
IRB	Institutional Review Board
ITT	Intent-to-treat
LS	Least square
NCR	No carbon required
NHS	National Health Service
NSAID	Non steroidal anti-inflammatory drug
PAIN	Practitioner's Assessment of Pharyngeal Inflammation
PIS	Patient Information Sheet
PK	Pharmacokinetic
QA	Quality Assurance
QC	Quality Control
RB	Reckitt Benckiser
R & D	Research and Development
SAE	Serious Adverse Event
SDV	Source Data Verification
SMO	Site Management Organisation
SOP	Standard Operating Procedure
TS	Throat Soreness Scale
SwoTS	Swollen Throat Scale
TOTPAR	Total Sum of Pain Relief Ratings
TPA	Tonsillopharyngitis Assessment
UK	United Kingdom (of Great Britain and Northern Ireland)
URTI	Upper Respiratory Tract Infection
US	United States (of America)
WCT	Worldwide Clinical Trials

5 ETHICS

5.1 Independent Ethics Committee (IEC) or Institutional Review Board (IRB)

The name and full address of the IEC consulted is provided in Appendix 16.1.3. The study Protocol, the Patient Information Sheet and Informed Consent Documents were submitted to Research Ethics Committee 1 on 30th November 2010 and a favourable opinion was given on 16th December 2010.

There were 2 Substantial Amendments and 5 Non Substantial Amendments submitted and approved/acknowledged as described below:

Substantial Amendment 1 (Protocol Amendment to remove 3 time points) submitted 19th January 2011 and Favourable opinion granted on 9th February 2011, Substantial Amendment 2 submitted 10th March 2011 (Removal of 2 back up sites and addition of 1 new back up site) and favourable opinion granted on 31st March 2011.

Non Substantial Amendment 1 (Administrative change, units of mass) submitted 6th January 2011 and acknowledged 10 January 2011, Non Substantial Amendment 2 (Administrative change to PIS and Informed Consent) submitted 25th January 2011 and acknowledged 26th January 2011, Non Substantial Amendment 3 (Display of Ethically Approved Posters on Surgery & Northern Ireland Science Park web sites) submitted 15th February 2011 and acknowledged 16th February 2011, Non Substantial Amendment 4 (Publishing of Ethically Approved Posters in Local Newspapers) submitted 3rd March 2011 and acknowledged 8th March 2011, Non Substantial Amendment 5 (increase of randomized number of patients to 190 from 180 submitted 16th March 2011 and acknowledged 21st March 2011).

5.2 Ethical Conduct of the Study

This study was conducted in accordance with the Declaration of Helsinki (South Africa, 1996), as referenced in EU Directive 2001/20/EC. It complied with International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) and applicable regulatory requirements.

5.3 Patient Information and Consent

During the course of the study 2 versions of a Patient Information and Consent Form were used with V2 replacing V1 as of the date of the former. Version 1 was dated the 29th November 2010 and Version 2 was dated the 16th March 2011, both versions were clearly identifiable via a unique footer on each page. The difference between the 2 versions is the total number of patients to be randomised as this increased from 180 (V1 29Nov10) to 190 (V2 16Mar11). Apart from the total number of randomised patients (and subsequently the total numbers allocated to each treatment group) both Patient Information and Consent Forms are identical in content. The increase in randomised patients was deemed a non-substantial amendment (number 5), was fully documented and accepted by the Research Ethics Committee. Copies of the patient information sheet and a blank consent form for both version 1 dated 29th November 2010 and version 2 dated 16th March 2011 are provided in Appendix 16.1.3 alongside a copies of the header and footers utilised to provide version control..

Patients who were considered by the Investigator to be suitable for entry into the study were given the opportunity to read the patient information sheet and consent form, and to ask questions. If they were happy with, and understood the information, they were asked to sign the consent form. The Investigator or Co investigator also signed the form. The patient was given a copy of the information sheet and signed consent form. No Protocol-related procedures were performed prior to the patient signing the consent form.

6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Appendix 16.1.4 contains a table listing the names and affiliations of the individuals whose participation materially affected the conduct of the study, together with their roles. The curriculum vitae (CV) of the Chief/Coordinating Investigator, Dr. Damien McNally and the Principal Investigator for each site are also included in the Appendix.

This study was carried out at 8 Primary Care sites in Northern Ireland led by the Principal Investigator at each site. All appropriate study related activities were delegated as appropriate at each site and this information is captured on the respective Site Signature Delegation log. Activities delegated in general were, consent of the patient to a sub investigator at the site, supervision of the patients to a trained research Nurse and CRF completion by trained members of the research team. The study was managed by Medevol Limited a Clinical Research Organisation. The Clinical Trial monitoring, Data management and statistical analysis were undertaken by Worldwide Clinical Trials in collaboration with Reckitt Benckiser. Study oversight and reporting of Adverse Events was managed by the Sponsor Reckitt Benckiser.

7. INTRODUCTION

The study was conducted to assess the efficacy of Strepsils Plus and Strepsils Extra in patients with a sore throat associated with acute URTI compared to placebo. The analgesic and numbing properties was assessed by comparing throat soreness, relief of sore throat and throat numbness over 2 hours following the first dose.

The assessment ratings related to analgesia i.e. throat soreness and sore throat relief are accepted validated analgesic assessment methodologies and have been used in previous clinical studies[1,2,,3] Because patients with sore throat also frequently complain of other qualities of pain (in particular, "difficulty swallowing", or dysphagia and a "swollen" sensation in the throat), these qualities of pain were measured using the Difficulty Swallowing Scale [4,16] and the Swollen Throat Scale [4,16]. This study was conducted using accepted and validated analgesic methodology in order to examine the hypothesis that Strepsils Plus and Extra provided analgesic benefits. Additional questions regarding consumer acceptability of the product to further understand the patients experience was assessed by completion of a consumer questionnaire.

8 STUDY OBJECTIVES

The primary objective of the study was to determine the analgesic efficacy of two Strepsils products in patients with a sore throat due to upper respiratory tract infection (URTI) compared to a placebo lozenge. The analgesic properties were also assessed by looking at the change in severity of throat soreness

Further objectives were to determine consumer acceptability of the product via responses to a consumer questionnaire (Appendix VIII).

9. INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan – Description

The study Protocol, Non Substantial Amendments No. 1-5 and 2 Substantial Amendments are included in Appendix 16.1. Unique Pages from the case report form (CRF) are included as Appendix 16.1.2.

This was a multi-centre, randomised, double blind, placebo controlled, single dose study to investigate the efficacy of two Strepsils lozenges (Plus and Extra) in the treatment of sore throat due to upper respiratory tract infection.

Patients with a sore throat due to an upper respiratory tract infection presented either opportunistically or in response to an advertisement to one of the 8 Primary care sites selected to conduct this study.

Of the 190 patients screened and randomized to the study, 174 were included in the per-protocol population.

Each Primary Care site received a Block of 33 study drug supplies and eligible patients (those who had met the inclusion and exclusion criteria) were randomly allocated to one of the 3 treatments below by the assignation of a number which was their randomization number. The site selected the number sequentially by starting from the lowest number to the highest number.

i. Strepsils Plus lozenge containing 0.6mg amylmetacresol BP, 1.2mg, 4-Dichlorobenzyl alcohol and 10mg Lidocaine Hydrochloride

ii. Strepsils Extra lozenge containing 2.4mg Hexylresorcinol

iii. Non-medicated sugar based placebo lozenge

In order to protect the blind for this study patients were blindfolded and were provided with the randomised lozenge in the clinic by an independent member of the investigational staff not involved in the study assessments. They were given the instruction to suck the lozenge slowly and move it around the mouth until it dissolved. The patients were asked not to chew or crunch the lozenge. An independent member of the investigational site staff observed the patients put the lozenge in their mouth. The blind fold was removed and patients completed self-assessment forms which consisted of validated throat soreness scores, a sore throat pain relief scale[1,2,3], a swollen throat scale[5,6], a difficulty swallowing scale[7] and a throat numbness scale[8]. Additional questions regarding consumer acceptability of the product were also contained in a consumer questionnaire. Efficacy assessments and consumer questions were recorded at protocol specified time-points over a 2 hour period. Once the 2 hour study assessment period was complete the patient left the clinic, taking a diary card to record any adverse events or medication taken over the next 24 hours. A member of the investigational team phoned the patient no less than 24 hours and no later than 3 days following the lozenge administration to check if the patient had taken any additional medication or experienced any adverse events.

No invasive procedures e.g. blood samples were required for the study.

There were a number of amendments to the study both substantial and non substantial and the details of these are listed in section 9.8 of this report.

9.2 Discussion of Study Design, Including the Choice of Control Groups

The methodology used to rate the analgesia according to throat soreness and sore throat relief is based on validated analgesic assessments used in previous clinical studies. (Ref TH0705[9] and TH0709[10]) Other indicators of pain such as difficulty in swallowing and a swollen sensation in the throat were also assessed by employment of the Difficulty Swallowing Scale [4,16] and the Swollen Throat Scale [4,16] .In order to discriminate between active and placebo treatment it was important to include patients with a sufficient degree of throat soreness at baseline and for this reason

patients needed to have a rating of 6 or more on the 11-point validated Throat Soreness Scale. They were also required to have a score of ≥ 5 on the Tonsillopharyngitis Assessment (TPA) (Schachtel[14,15]) .

A non-medicated sugar based lozenge was used as a placebo. The use of this lozenge provided a control for the demulcent effect caused by sucking any sugar based sweet. This placebo was matched for size and shape and was considered to be an adequate control. As the placebo was not colour matched to either of the 2 active lozenges it was necessary to blind fold the patients when taking the lozenge. Clinic staff that were not involved in any future supervision of the patient or their assessments gave the lozenge to the patients. This method ensured that both patients and staff, involved in efficacy assessments, remained blinded throughout the study.

9.3 Selection of Study Population

Patients with a sore throat due to a URTI presented to one of the 8 primary care sites either opportunistically or in response to an advertisement. They were randomised to the study if they met the following inclusion and exclusion criteria.

9.3.1 Inclusion Criteria

Only patients to whom all of the following conditions applied were included in the list of evaluable patients.

1) Age: ≥ 18 to ≤ 75 years.
2) Sex: male or female.
3) Primary diagnosis: Sore throat onset within the previous 4 days as a result of an upper respiratory tract infection.
4) Patients who had a sore throat (≥ 6) on the Throat Soreness Scale at baseline.
5) At least 1 symptom of URTI on the URTI questionnaire (e.g. sore throat).
6) Objective findings that confirmed the presence of tonsillopharyngitis (≥ 5 points on the expanded 21-point Tonsillopharyngitis Assessment).
7) Patients who had a difficulty swallowing score of >50mm on the Difficulty Swallowing Scale at baseline.
8) Patients who had a swollen throat score of >33mm on the Swollen Throat Scale at baseline.
9) The patient was willing to take 'nil by mouth' 10 minutes before the dose.
10) Patients who had given written informed consent.

9.3.2 Exclusion Criteria

Patients to whom any of the following conditions applied were excluded:

1) Any previous history of allergy or known intolerance to the study drug or the formulation active ingredients (AMC, DCBA, hexylresorcinol or lidocaine).

2) Woman of childbearing potential, who were pregnant or lactating, seeking pregnancy or failing to take adequate contraceptive precautions, (i.e. an oral or injectable contraceptive, an approved hormonal implant or topical patch, an intrauterine device, abstinence. A woman of childbearing potential was defined as any female who was less than 2 years post-menopausal or had not undergone a hysterectomy or surgical sterilisation, e.g. bilateral tubal ligation, bilateral ovariectomy (oophorectomy).
3) Those whose sore throat had been present for more than 4 days.
4) Those who had used any sore throat medication containing a local anaesthetic within the past 4 hours.
5) Those who had any disease that could have compromised breathing e.g. asthma, bronchospasm, bronchopneumonia.
6) The patient had any evidence of mouth-breathing.
7) Those who had evidence of severe coughing.
8) Those who could not tolerate fructose.
9) Those with a painful condition that may have distracted attention from sore throat pain (e.g. mouth ulcers, cough).
10) Those with a history of alcohol abuse or who consumed alcohol in excess of the recommended amounts (excessive alcohol >21 units per week for females and >28 units per week for males).
11) Those who had used an analgesic, antipyretic or cold medication (e.g. decongestant, antihistamine, antitussive or throat lozenge/spray) within the previous 8 hours.
12) Those who had used a longer acting or slow release analgesic during the previous 24 hours e.g. Piroxicam and Naproxen.
13) Those who had taken any medicated confectionary, throat pastille, spray, or any product with demulcent properties such as boiled sweets in the previous 2 hours.
14) Those with any history of renal or hepatic dysfunction.
15) Those previously randomised into the study.
16) Those who had participated in a clinical trial in the previous 30 days. Thirty days were calculated from time of last dosing in the prior trial to time of anticipated dosing in this trial.
17) Those unable in the opinion of the Investigator to comply fully with the study requirements.

9.3.3 Removal of Patients from Therapy or Assessment

The Investigator could withdraw patients from the study at any time. Reasons for removing a patient from the study included but were not limited to:

- adverse events that in the judgement of the Investigator could cause severe or permanent harm (significant clinical deterioration was an adverse event)
- violation of the study protocol
- in the Investigator's judgement, it was in the patient's best interest
- patient declined further study participation

The primary reason for withdrawal was documented as one of the following: adverse events; lack of efficacy; lost to follow-up; no further need for study medication (unless it was a study end point); protocol violation; death or other. The Investigator had to make reasonable attempts to contact patients who were lost to follow-up - a minimum of two documented telephone calls or a letter was considered reasonable.

If a patient was withdrawn prematurely from the study, the following assessments were carried out:

- Recording and review of all AE's.
- Review of the patient diary and check for AE's and concomitant medications.
- Female patients were asked if they were pregnant. No pregnancies were reported.
- Any other assessments deemed appropriate for the clinical care of the patient.

No patient's were withdrawn from the study.

9.4 Treatments

9.4.1 Treatments Administered

Patients were randomly allocated to one of three treatment groups. The following medications were supplied:

i. Strepsils Plus lozenge containing 0.6mg amylmetacresol BP, 1.2mg, 4-Dichlorobenzyl alcohol and 10mg Lidocaine Hydrochloride

ii. Strepsils Extra lozenge containing 2.4mg Hexylresorcinol

iii. Non-medicated sugar based placebo lozenge

Each patient was randomized to receive one of the 3 treatments by allocating them to an assigned number. Numbers were allocated in a sequential manner from lowest to highest at each site. Patients were given the instruction to suck the lozenge slowly and move it around the mouth until it dissolved. The patients were asked not to chew or crunch the lozenge. Patients completed self-assessment forms during the 2 hour observation period.

9.4.2 Identity of Investigational Product(s)

The identities of the medicines supplied in the study were:

Strepsils Plus Lozenge, containing 0.6mg amylmetacresol BP, 1.2mg, 4-Dichlorobenzyl alcohol and 10mg Lidocaine Hydrochloride PA 979/40/1, Batch No. 3EE2 x 1 lozenge orally.

Strepsils Extra Blackcurrant Lozenge, containing 2.4mg Hexylresorcinol, PL00063/0392, Batch No. 4GG x 1 lozenge orally.

Non-medicated sugar based Lozenge (Placebo) Batch No. 2254653 x 1 lozenge orally.

The two Strepsils lozenges and the non-medicated sugar based placebo lozenges were manufactured, primary packed, secondary packed and labelled to Good Manufacturing Practice by RB, Nottingham, NG90 2DB.

All drug supplies were re-packed into patient packs and labelled to GMP standards by the Investigational Material Supplies Unit (IMSU), Reckitt Benckiser Healthcare (UK) Ltd, Dansom Lane, Hull, HU8 7DS. This was a double-blind trial, therefore drug supplies needed to be blinded at site to the relevant staff and patients. They were shipped directly from the IMSU to the investigative site.

9.4.3 Method of Assigning Patients to Treatment Groups

Drug supplies were randomised by RB IMSU according to a computer-produced randomisation schedule. The randomisation schedule was checked by a statistician not involved in the analysis of the study. On entry, patients were allocated a unique patient number in numerical sequence. Issue of the study drug in this sequence ensured randomisation.

RB IMSU and the RB statistician held the master code for the randomisation schedule. The code was only to be broken for an individual patient in an emergency such as a serious adverse event that required knowledge of what study drug was taken in order that the SAE could be treated appropriately.

If the code for a patient was broken, the Investigator had to withdraw the patient from the study, document the details of the event in the patient's case report form and inform the RB Clinical Project Manager. The code was not required to be broken for any patients during the study.

The study monitor checked the randomisation codes on a regular basis at monitoring visits, to ensure the above procedures are being followed at the study site. All codes, whether sealed or opened, were returned to RB at the end of the study.

RB broke the code for analysis on 27th May 2011 only after all data queries had been answered and the database had been locked.

Each of the 8 sites had a specified Centre number. At screening, patients were allocated a unique patient (screening) number, and at randomisation study, patients were then allocated a randomisation number specific to the site in ascending numerical sequence. A listing linking patient number to randomisation number is provided in Appendix 16.2.3.1 and a summary of site and allocated randomisation numbers is in Table 9.4.1 below.

No patients withdrew from the study. 190 patients were enrolled to ensure that 174 evaluable patients completed the 2 hour assessment on Day 1.

Table 9.4.1 Randomisation numbers allocated by site

Centre Number	Principal Investigator	Randomisation numbers allocated
01	Dr Conn	034-066
02	Dr McNally	001-033
03	Dr McCaughey	232-264
04	Dr Redmond	133-165
05	Dr Hart	166-198
06	Dr Ryan	067-099
07	Dr McKeague	100-132
08	Dr Haigney	199-231

9.4.4 Selection of Doses in the Study

The dose selected was one lozenge (i.e. the normal non prescription dose) of either Strepsils Extra or Strepsils Plus lozenge. Placebo patients received one sugar coated non-medicated lozenge.

9.4.5 Selection of Timing of Dose for Each Patient

The timing of dosing for each patient was varied and was determined by the clinic staff. Only one Lozenge was taken during the study and this was taken as described in section 9.4.4.

9.4.6 Blinding

The lozenges were not colour matched and in order to maintain the double-blind, the dose was administered to the patient by an independent member of the Clinic staff that was not involved with any other study related procedures pre or post dosing. In addition each patient was blindfolded during dosing. This enabled both patient and staff supervising the efficacy and safety assessments to remain blinded.

9.4.7 Prior and Concomitant Therapy

Concomitant therapies are defined as prescribed medications, physical therapy, and over-the-counter preparations, including herbal preparations licensed for medicinal use, other than study medication and supplementary medication that the patient received during the course of the study.

The Investigator recorded any medications given for the treatment of adverse events on the concomitant medication page in the patient's case report form. Any medication taken by the patient during the course of the study was recorded on this form as was any change in concomitant therapy during the study, including cessation of therapy and initiation of therapy. Patients were given a patient diary and were asked to record any medications taken up to 24 hours post dose. This information was collected by a member of the study team by telephone contact up to 3 days after the study.

The use of the following treatments was not permitted during the study:

- The use of sore throat medication containing a local anaesthetic in the 4 hours before dosing (i.e. before the dosing day).
- Use of medicated confectionary, throat pastille, lozenge or any product with demulcent properties such as boiled sweets in the 2 hours before dosing.
- Use of analgesic, antipyretic or 'cold' medication (i.e. decongestant, antihistamine, antitussive or throat lozenge) in the 8 hours before dosing.
- Use of longer acting or slow release analgesic e.g. piroxicam and naproxen, in the 24 hours before dosing (before first dosing day).
- Use of antibiotic in the 14 days before enrolment into the study (before dosing) and throughout the study.
- No food or drink was permitted during the 2 hours assessment period.
- No smoking was permitted during the 2 hour assessment period.

9.4.8 Treatment Compliance

Compliance was assessed by study staff who watched the patient consume the medication while at the clinic on Day 1.

There was a mouth check to ensure the lozenge had been completely dissolved and each patient was observed to ensure they did not chew or crunch the lozenge.

9.5 Efficacy and Safety Variables

9.5.1 Efficacy and Safety Measurements Assessed and Flowchart

Table 9.5.1 Flowchart of Study Procedures

Study Period	Screening Pre dose	Treatment period Time (mins) after 1st dose (Day1)		Telephone Follow up (1-3 days post dose)
Study Day		0	1, 5, 10, 15, 30, 45, 60, 75, 90, 105, 120 mins	
Throat Descriptor Questionnaire	X			
Demographics	X			
Washout (if required)	X			
Pregnancy test (females)	X			
Medical History	X			
Concomitant Medication	X			X
Females: Pregnancy, fertility, contraceptive precaution questions				X*
Physical Examination	X			
PAIN	X			
TPA	X			
URTI		X	X (120 mins)	
Baseline assessments; TS DSS SwoTS		X		
Time of Dose		X		

Study Period	Screening Pre dose	Treatment period Time (mins) after 1st dose (Day1)		Telephone Follow up (1-3 days post dose)
Study Day		0	1, 5, 10, 15, 30, 45, 60, 75, 90, 105, 120 mins	
TS			X	
DSS			X	
SwoTS			x	
Throat numbness			X	
Sore Throat Relief			X	
Patient Global Evaluation of the study medication (GLOBAL)			X (120 mins post dose)	
Practitioners Clinical assessment of the study medication (CLIN)			X (120 mins post dose)	
Adverse Events		X (pre dose)	X (120 mins only)	X (up to 24 hours post dose)
Consumer questionnaire			X (1,5, 20, 60, 120 mins)	
Over all Treatment Rating			X (120 mins post dose)	
Telephone call to patient for review of Adverse Event and Concomitant Medication Diary				X

* Pregnancy question only

All assessments were conducted by the Investigator or delegated individual trained to conduct the relevant procedure.

9.5.1.1 Assessments for Screen, Efficacy and Safety

Demographic information: sex; race; date of birth; height (cm), weight (kg); smoking and alcohol history /use were collected at screening.

Medical history and current status: A medical history was noted at screening and the patient's current medical status was noted.

Medication and therapy history: At the screening visit the current and past medication was noted. Any medications or adverse events noted in the 24 hour

period following dosing was recorded by the patient in a diary and reported to the study team member when they phoned the patient no longer than 3 days post dose.

Female patients only: At the screening visit female patients were asked if they might be pregnant, if they were lactating or seeking pregnancy, or if they were taking adequate contraceptive precautions, or if they were at least two years post menopausal, or if they had been sterilised or had a hysterectomy**.**

Tonsillopharyngitis Assessment (TPA): At screening oral temperature, size of tonsils, oropharyngeal colour, number of oropharyngeal enanthems, size, number and tenderness of the anterior cervical lymph nodes were scored on a scale of 0-3. The sum of scores of the 7 separate features of tonsillopharyngitis provided the TPA with scores ranging from 0-21 points.

URTI Questionnaire: 1 minute pre- dose and at 120 minutes assessed the patient's eligibility to qualify for study inclusion as having an URTI. A minimum of one symptom (e.g. sore throat) was required.

Difficulty Swallowing Scale: up to 1 minute pre dose designated as 0, then at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. Patients were asked to swallow and place a line through the visual analogue scale in order to indicate how difficult it was for them to swallow, not difficult being at the left of the scale and very difficult being at the right end of the scale.

Throat Soreness Scale: up to 1 minute pre dose designated as 0, then at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. Patients were asked to swallow and circle on the 11-point ordinal scale how sore their throat was (0 being not sore and 10 being very sore).

Swollen Throat Scale: up to 1 minute pre dose designated as 0, then at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. Patients were asked to indicate on a 100mm visual analogue scale how swollen their throat was (0 being not swollen and 100mm being very swollen).

Sore throat Relief: 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. Patients were asked to assess sore throat relief on a 7-point scale (no relief, slight relief, mild relief, moderate relief, considerable relief, almost complete relief and complete relief).

Throat Numbness: 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose. Patients were asked to circle on a 5-point categorical Scale how numb their throat felt (none, mild, moderate, considerable, complete).

Consumer Questionnaire: Pre dose and 1, 5, 20, 60 and 120 minutes post dose. The patient was supervised throughout the 2 hour assessment period and the supervisor prompted the patient when to complete the relevant sections on this consumer questionnaire. Patients remained quiet and isolated from other patients in a designated area within the investigative site during the 2 hour assessment period.

Apart from the baseline score, the patients were unable to see their previous post-baseline scores.

Patient's Global Evaluation of study medication as a treatment of sore throat: 120 minutes post dose. Patients were asked to complete a grading for their medication using a standard 5-point category scale[10].

Practitioners Clinical Assessment of Study Medication as a treatment of sore throat: 120 minutes post dose. The investigator was asked to rate the patient's response to the study medicine on a 5-point category scale over the 2 hour observation period by considering the patient's response[10].

Overall Treatment Rating: 120 minutes post dose. Patients were asked how they would rate the lozenge as a treatment for sore throat by selecting a number between 0 (poor) and 10 (excellent) on an 11-point ordinal scale.

Adverse Events: 0,120 minutes and 24 hours post dose. Patients were asked at the intervals indicated if they had any symptoms other than a sore throat. These were recorded by the site staff during the in clinic period in the patient's case report form (CRF). In the follow up period outside the clinic the patient recorded these events in a patient diary and this information was obtained via a phone call to the patient by a member of the study team who recorded any such reports in the CRF.

The rating system used to determine the severity and relationship to study medication is given in Table 9.5.2

Table 9.5.2 Rating system used to determine Adverse Event Severity and Relationship to Study medication

Variable	Category	Definition
Severity		Severity was determined by the Investigator. For symptomatic AEs the following definitions were applied but medical experience and judgement was also be used in the assessment of severity.
	Mild	The AE did not limit usual activities; the patient may have experienced slight discomfort.
	Moderate	The AE resulted in some limitation of usual activities; the patient may have experienced significant discomfort.
	Severe	The AE resulted in an inability to carry out usual activities; the patient may have experienced intolerable discomfort or pain.
Relationship to study medication	Definite	An AE that followed an anticipated response to the study medication; and that was confirmed by both improvement upon stopping the study medication (dechallenge), and reappearance of the reaction on repeated exposure (rechallenge).
	Probable	An AE that followed a reasonable temporal sequence from administration of the study medication, that was an anticipated response to the study medication; and that could not be reasonably explained by the known characteristics of the patient's clinical state or concomitant therapy.
	Possible	An AE that followed a reasonable temporal sequence from administration of the study medicines; that may be an anticipated response to the study medication; but that could have been produced by the patient's clinical state or concomitant therapy.
	Unlikely	An AE that did not follow an anticipated response to the study medication; which may have been attributable to other than the study medication and that was more likely to have been produced by the patient's clinical state or concomitant therapy.
	None	An AE that was known beyond all reasonable doubt to be caused by the patient's state or concomitant therapy.

9.5.2 Appropriateness of Measurements

The assessments of analgesic efficacy were made using standard, widely used, published and reliable methodologies. Patient ratings included ordinal scales, 100mm VAS scales and categorical scales. Safety was assessed by using a standard AE reporting methodology.

9.5.3 Primary Efficacy Variable

The primary Efficacy Variable was the change from baseline in severity of throat soreness (using the 11-point throat soreness scale) for the Strepsils Plus and Extra versus the placebo at the 2 hours post dose.

9.5.4. Drug concentration Measurements

Drug concentrations were not measured in this study.

9.6 Data Quality Assurance

All data were entered onto the WCT NODES computer database by a member of the Data Management Section and then verified by repeat data entry by a further Section member. SAS Version 9.1[1] edit checks were used for consistency checks.

Before database lock, a database audit was performed which had three components.

Audit component 1: Consistency checking and query generation

Nineteen cases were selected to undergo full consistency checking where an error would be failure to issue a query when current procedure calls for data enquiry to be raised, or another failure to appropriately respond to a consistency check. A total of 5 queries were missed on 4 of the 19 cases. These were all for alterations not signed and dated.

Audit component 2: Transcription and annotation procedures

19 cases were selected for full assessment where errors could be either transcription or other failures with respect to standard procedures for annotating working copies. A total of 6 errors of one kind or another were found in 4 of the 19 cases. The total error rate was 6 per 7,417 fields or 0.08%. The error rate for 'significant data errors' was 1 per 7,417 fields or 0.01%. The acceptance level for the error rate in the final database quality assessment was the default error rate of 0.1%.

Audit component 3: Critical data fields

The critical fields were checked for 100% of cases. Any errors found were corrected. The fields were determined by the Study Statistician and Clinical Project Leader and were:

- Randomisation number
- Date and time of lozenge
- Time of assessments for all observations recorded from pre-dose to 120 minutes post dose
- All throat soreness, throat numbness, difficulty in swallowing and pain relief data recorded from pre-dose to 120 minutes post-dose
- All Adverse Event data

The findings of the audit indicated that data entry procedures have been followed carefully. No remedial actions were considered necessary.

The following aspects of this study were subject to a GCP compliance audit, conducted by appropriately trained and experienced personnel at WCT:

- Study database
- Statistical analyses
- Clinical Study Report

After database lock it was noted that the start date for paracetamol for patient number 255 (placebo) was incorrectly entered on the CRF as 15-Mar-10. The date should have been entered as 15-Mar-11 and therefore this medication started 9.75 hours after study medication dosing. All tables and listings in this report assume a start date of 15-Mar-11 for this medication.

9.7 Statistical Methods Planned in the Protocol and Determination of Sample Size

The statistical analysis was conducted by WCT on behalf of RB. A copy of the final statistical analysis plan is presented in Appendix 16.1.9.

All statistical tests performed were 2-tailed with significance determined by reference to the 5% significance level, unless otherwise stated. The null hypothesis at all times was the equality of the treatments being compared. All comparisons between the treatments were reported with 95% confidence intervals for the difference. For each statistical test, an observed significance level was quoted. Where this value was less than 0.05, 0.01 or 0.001, attention was drawn to the fact using the conventional "*", "**" or "***" annotation, respectively.

Normality assumptions were evaluated by an examination of the residual plots and the Shapiro-Wilk test of normality. Depending on the degree of departure from these assumptions, an alternate non-parametric approach could have been used for supportive purposes.

For any given variable, baseline was taken as the latest recorded assessment available prior to dosing with the study lozenge. All tabulations involving change from baseline data only included patients with cohort data i.e. with data at baseline and at follow-up.

All the area under curve analyses were based on actual rather than scheduled timings and was calculated using the trapezoidal rule. If the actual time was not recorded the scheduled time was used instead. Patients who withdraw prior to the 2-hour assessment had their last recorded score carried forward to 2 hours for each of the AUC calculations. For ease of interpretation the AUC value obtained was divided by the total time the scale is assessed for reporting purposes.

In the case where a patient recorded more than one score for any particular efficacy measure, the worst of the recorded scores were taken for analysis purposes.

All calculations and figures were produced using SAS Version 9.2[11].

For continuous variables, the mean, median, standard deviation, standard error of the mean, minimum, maximum and lower and upper 95% confidence limits for the mean for the population and for the individual treatment groups were given.

Categorical data were presented in contingency tables with cell frequencies and percentages for the patient population and for the individual treatment groups.

The comparability of treatment groups with respect to patient demographics and baseline characteristics were assessed in a descriptive manner, but no formal statistical testing was performed.

Concomitant medications ongoing at randomisation were coded using the ATC level 2 categories from the WHO dictionary Enhanced 3.11 Version.

9.7.1 Statistical and analytical Plan

9.7.1.1 Efficacy

The full analysis set and per-protocol (PP) populations were used in the analysis of efficacy, as described in Section 11.1.

Primary Endpoint

The primary efficacy endpoint for this study was the change from baseline in severity of throat soreness (using the 11-point throat soreness scale) for the Strepsils Plus and Extra versus placebo at 2 hours post dose.

The primary efficacy endpoint was analysed by analysis of covariance (ANCOVA) with baseline throat soreness severity as a covariate and factors for treatment group and centre. Treatment group differences were estimated using the mean square error from the ANCOVA and using Fisher's protected LSD method i.e. if the overall treatment effect in the ANCOVA model was significant at the 5% level, the comparisons of the Strepsils Plus and Strepsils Extra groups versus the placebo group were performed without any requirement to adjust the significance level for the pairwise comparisons. The 95% confidence interval for the difference in least square means was estimated using the mean square error from the ANCOVA.

Secondary Endpoints

All secondary endpoints and the supportive analyses were considered as descriptive evidence of efficacy and were analysed without any procedures to account for multiple comparisons.

The following variables were analysed using the same ANCOVA model as for the primary endpoint:

- AUC from baseline to 2 hours for the change from baseline in severity of throat soreness.
- Change from baseline in severity of throat soreness at 1, 5, 10, 15, 30, 45, 60, 75, 90, and 105 minutes post dose.
- AUC from baseline to two hours post-dose for sore throat relief (TOTPAR).
- Sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose.
- AUC from baseline to 2 hours for throat numbness.
- Throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes.
- Patient's Global Evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) at two hours.
- Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at two hours.
- Overall treatment rating at two hours.

The time taken for patients to first report at least moderate sore throat relief (i.e. onset of analgesia) was compared between treatment groups using a Cox proportional hazards model with factors for treatment group and centre and a covariate for baseline throat soreness severity. Patients not reporting at least moderate sore throat relief were censored at the time of their last recorded follow-up assessment.

The AUC for the change in the difficulty in swallowing from 0 to 2 hours and the change from baseline in difficulty in swallowing after 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose were analysed by ANCOVA with factors for treatment group and centre and covariates for baseline throat soreness and baseline difficulty in swallowing.

The AUC for the change in swollen throat from 0 to 2 hours and the change from baseline in swollen throat after 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose were analysed by ANCOVA with factors for treatment group and centre and a covariates for baseline throat soreness and baseline swollen throat.

The change from pre-dose to one hour post-dose in the functional impairment scale (each component and overall total score) was analysed by ANCOVA with factors for treatment group and centre and with covariates for the baseline throat soreness and the relevant baseline functional impairment score.

For the consumer questionnaire, questions on non-numeric ordinal scales were analysed using a proportional odds model[12] using PROC LOGISTIC in SAS with factors for treatment group and centre and a covariate for baseline throat soreness severity. Questions on numeric ordinal scales were analysed using the same ANCOVA model as the primary efficacy endpoint, except for the following two questions, viz: “How much do you feel like your best overall?” and “How happy are you, in relation to your throat?” both asked one and two hours post-dosing. These were analysed by ANCOVA with factors for treatment group and centre and with covariates for the baseline throat soreness and the relevant baseline score for the specific question.

Data from the URTI questionnaire at two hours was tabulated, but not formally analysed.

Mean profiles from baseline to two hours will be presented by treatment group for change from baseline in the following: throat soreness, difficulty in swallowing and swollen throat. Mean profiles by treatment group will also be presented for sore throat relief and throat numbness.

Exploratory analysis

Analyses of the primary efficacy endpoint were performed by key baseline characteristics. For each subgroup, the main effect and treatment-by-subgroup interaction terms were added to the standard model used in the primary endpoint analysis. Key variables of interest were centre, baseline throat soreness severity (≤median, >median), baseline difficulty in swallowing (≤median, >median), baseline swollen throat (≤median, >median), age at study entry (≤median, >median), gender and total score from tonsillo-pharyngitis assessment at baseline (≤median, >median). These models were used to estimate treatment comparisons within the subgroups that correspond with the sub-grouping factor. For the investigation of baseline throat soreness severity subgroup effect, the model fitted was analysis of variance (ANOVA) rather than ANCOVA as baseline throat soreness severity was considered a two-level factor rather than as a continuous covariate.

9.7.1.2 Safety

All treatment emergent adverse events were listed and tabulated by treatment, severity, relationship to therapy and primary system organ class according to MedDRA Version 13.1. In counting the number of events reported, a continuous event, i.e. reported more than once and which did not cease, were counted only once; non-continuous adverse events reported several times by the same patient were counted as multiple events. Events present immediately prior to the dose of study medication that did not worsen in severity, were not included. Events with start dates during follow-up (i.e. more than 24 hours after dosing) were not considered treatment emergent.

Pairwise differences between treatment groups in the proportion of patients reporting treatment emergent adverse events were compared via chi-square tests.

Concomitant medications commencing during the study were coded using the ATC level 2 categories from the WHO dictionary.

9.7.2 Determination of Sample Size

In a previous study conducted with Strepsils Original Lozenges[13] the difference in the change in throat soreness from baseline at 2 hours between Strepsils Original lozenge and placebo for patients with a TPA ≥ 5 and at least 6 on the 11-point throat soreness scale was -1.21 with a pooled standard deviation of 1.78. Assuming that the variability in this study will be similar, 57 patients per treatment arm would be sufficient to provide 95% power to detect a difference of -1.21 in the mean change from baseline in severity of throat soreness (using the 11-point throat soreness scale) using a 2 sample t-test at the 5% significance level.

In order to account for drop outs a total of 190 patients were recruited. The actual variability observed during the study was 2.24 (root mean square error from the ANCOVA model of the full analysis set) which was higher than predicted and as a consequence the study was power was less than expected. The difference of 1.16 between Strepsils Extra and placebo was statistically significant (p=0.004) whereas the difference of 0.75 between Strepsils Plus and placebo did not achieve statistical significance (p=0.06).

9.8 Changes in the Conduct of the Study or Planned Analysis

9.8.1 Changes in the Conduct of the Study

There were no changes in the conduct of the study

9.8.2 Changes in the Planned Statistical Analysis of the Study

There were no changes in the statistical analysis of the study

10 STUDY PATIENTS

10.1 Disposition of Patients

A total of 190 patients were randomised into the study (64 patients received Strepsils Extra lozenge, 64 patients received Strepsils Plus lozenge and 62 patients received placebo) between 2nd February 2011 and 31st March 2011. All patients completed the study.

Patients were recruited in eight centres and the number of patients randomised in each centre was as follows: Centre 1 (29), Centre 2 (33), Centre 3 (24), Centre 4 (30), Centre 5 (16), Centre 6 (13), Centre 7 (32) and Centre 8 (13).

10.2 Protocol Deviations

There were 16 patients excluded from the per-protocol dataset. Six patients (3.2%) patients reported difficulty in swallowing less than or equal to 50mm at screening; five patients (2.6%) patients reported swollen throat less than equal to 33mm at screening and four (2.1%) patients had throat soreness less than or equal to 6 at baseline. Five (2.6%) patients reported no symptoms on the URTI questionnaire at baseline. A further patient had assessments not performed within the admissible scheduled time interval. There were no treatment administration errors and no patients were taking inadmissible concomitant medication. Table 10.2.1 summarizes the major protocol deviations with further information within Appendix 16.2, Listing 16.2.2.1.

Table 10.2.1 Number (%) of patients with major protocol deviation

	Strepsils Plus lozenge (N=64)	Strepsils Extra lozenge (N=64)	Placebo (N=62)	Overall (N=190)
Number of patients reporting	5 (7.8%)	6 (9.4%)	5 (8.1%)	16 (8.4%)
Difficulty swallowing <=50mm at baseline	1 (1.6%)	2 (3.1%)	3 (4.8%)	6 (3.2%)
Swollen throat <=33mm at baseline	3 (4.7%)	2 (3.1%)	0	5 (2.6%)
Throat soreness <6 at baseline	0	2 (3.1%)	2 (3.2%)	4 (2.1%)
No symptoms on URTI questionnaire at baseline	1 (1.6%)	2 (3.1%)	2 (3.2%)	5 (2.6%)
Assessments not performed within admissible scheduled time interval	0	1 (1.6%)	0	1 (0.5%)
Treatment administration errors	0	0	0	0
Taking inadmissible concomitant medication	0	0	0	0

Patients could have more than one major protocol deviation
Source: Listing 16.2, Appendix 16.2.2.1

11 Efficacy

11.1 Data Sets Analysed

There were three analysis sets used in the analysis. These populations were defined as follows:

The **safety set** included all patients who take the study medication. The safety set was analysed as treated.

The analysis of efficacy data used two datasets.

Firstly the **full analysis set.** This analysis set consisted of all patients who were randomised to the study and took the study medication. Any patients with treatment administration errors were to be analysed according to the treatment to which they were randomised. This was the primary efficacy analysis population. For this study the full analysis and safety sets were identical. All efficacy variables were assessed using the full analysis set.

Secondly the **per-protocol set.** This analysis set is a subset of the full analysis set and consisted of all patients who satisfy all of the inclusion/exclusion criteria, who correctly receive the treatment to which they are randomised, and who successfully complete the treatment period up to the 2 hour assessment. All protocol deviations were assessed and documented on a case-by-case basis prior to the database lock, and any incidence of deviations considered having a serious impact on the efficacy results led to the relevant patient being excluded from the per-protocol analysis set. Major protocol deviations included:

- Treatment administration errors.
- Taking inadmissible concomitant medication (within the first 2 hours post-dosing or inadequate washout prior to randomisation).
- Inadmissible starting times of the follow-up assessments within the first 2 hours post dosing.
    - 1, 5, 10 and 15 minute assessment not performed within +/- 1 minutes of the scheduled times.
    - 30, 45, 60, 75, 90, 105 and 120 minute assessments not performed within +/- 5 minutes of the scheduled times.

The following were assessed using the per-protocol set

- Change from baseline in severity of throat soreness from 0 to 2 hours.
- AUC from baseline to 2 hours for change from baseline of severity of throat soreness and difficulty in swallowing.
- AUC from baseline to 2 hours for throat numbness and sore throat relief.

11.2 Demographic and Other Baseline Characteristics

A summary of patient demographics is presented in Tables 14.1.2 to 14.1.11. Summary statistics and frequency distributions are presented both overall and by treatment group. In general, the treatment groups were well balanced for the demographic variables.

Overall, the age ranged from 18 to 73 years, with a mean age of 31.6 years. There was an imbalance between the treatment groups with respect to gender; in each of the two active groups 21 (33%) patients were male whereas in the placebo group a total of 36 (58%) patients were male. The majority of patients, namely 186 (98%)

were Caucasian. A total of 136 (72%) patients drank alcohol, 60 (32%) were current smokers and 24 (13%) were former smokers. Mean duration of URTI was 2.11 days and mean duration of sore throat was 2.12 days.

Tables 14.1.2 and 14.1.3 presents full summary statistics of demographic variables.

TABLE 11.2.1 Demographics – Full analysis set

Variable	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo	Overall
Number of patients	64	64	62	190
Age (yr) (Mean ± sd)	32.4±15.8	30.9±12.8	31.5±11.7	31.6±13.5
Gender (Male)	21 (32.8%)	21 (32.8%)	36 (58.1%)	78 (41.1%)
Race (Caucasian)	64 (100%)	63 (98.4%)	59 (95.2%)	186 (97.9%)
Alcohol drinker (%)	44 (68.8%)	46 (71.9%)	46 (74.2%)	136 (71.6%)
Current smoker (%)	19 (29.7%)	21 (32.8%)	20 (32.3%)	60 (31.6%)
Former smoker (%)	9 (14.1%)	8 (12.5%)	7 (11.3%)	24 (12.6%)
Duration of sore throat (days) (Mean ± sd)	2.17±0.90	1.98±0.92	2.19±0.87	2.12±0.90
Duration of URTI (days) (Mean ± sd)	2.14±0.83	2.02±0.92	2.16±0.91	2.11±0.88

Source: Tables 14.1.2 and 14.1.3

Table 14.1.4 presents details of the throat descriptor questionnaire. Eighty-two (43%) patients had swollen/inflamed throats, 92 (48%) stated their sore throat made them feel “Disrupted - Help me to talk and swallow again”. In terms of which phrase best described their sore throat, 21 (33%) patients in the Strepsils Extra group had severe pain compared 12 (19%) in the other two treatment groups.

A total of 22 (12%) patients reported a previous medical condition (Table 14.1.5) and 93 (49%) patients reported an ongoing medical condition of which 41 (22%) patients had psychiatric conditions and 34 (18%) patients had conditions of the musculoskeletal system (Table 14.1.6).

The mean total score from the tonsillo-pharyngitis assessment at screening was 8.4 with a range of 5 to 17. With respect to the Practitioner's Assessment of Pharyngeal Inflammation, 16 (8%) patients had severe inflammation, 124 (65%) had moderate inflammation and 48 (25%) had mild inflammation. A further two (1%) patients had no data recorded for this scale (Table 14.1.7).

Table 14.1.8 presents details of the URTI Questionnaire at screening (symptoms over the past 24 hours) which contains 40 symptoms. The mean number of symptoms reported was 8.5 with a maximum number of symptoms of 24. The mean number of symptoms reported in Strepsils Extra group was 8.9 compared to 8.4 in the placebo group and 8.3 in the Strepsils Plus group. The most common symptoms reported were sore throat with 179 (94%) patients reporting, coughing with 111 (58%) patients reporting and throat tickle with 102 (54%) patients reporting. Four patients (numbers 046, 048, 049 and 050) reported no symptoms.

Table 14.1.9 presents details of the URTI Questionnaire at pre-dose (symptoms now) which contains 40 symptoms. The mean number of symptoms reported was 7.0 with a maximum number of symptoms of 24. The mean number of symptoms reported in Strepsils Extra group was 7.5 compared to 6.7 in the placebo group and 7.0 in the

Strepsils Plus group. The most common symptoms reported were sore throat with 179 (94%) patients reporting, coughing with 96 (51%) patients reporting and throat tickle with 89 (47%) patients reporting. Five patients (numbers 046, 048, 049, 050 and 203) reported no symptoms.

Table 14.1.10 presents a summary of the mean values of the efficacy variables recorded immediately before dosing. Table 11.2.2 below summarises these data. With respect to the functional impairment scale, of the four activities referenced, the sore throat was most affecting swallowing (mean score 7.11) and talking (mean score 5.67). The mean score for throat soreness was 7.20. For the pre-dose VAS for difficulty in swallowing the mean score was 72.3 mm (range 45, 100 mm). The mean score for swollen throat was 67.1 mm (range 1,100).

Patients in the Strepsils Plus group had lower mean scores than the other two treatment groups for both “How much do you feel like your best overall” and “How happy are you, in relation to your throat”.

TABLE 11.2.2 Mean ± sd for pre-dose efficacy variables – Full analysis set

Variable	Strepsils Extra lozenge	Strepsils Plus lozenge	Placebo	Overall
Number of patients	64	64	62	190
Functional Impairment Scale (How sore throat affected)				
Each activity measured on a 11-point scale where 0 = Would not interfere at all				
Talking	5.77±2.24	5.83±2.30	5.42±2.34	5.67±2.29
Swallowing	6.91±1.55	7.27±1.38	7.16±1.27	7.11±1.41
Concentrating	4.34±2.72	4.95±2.89	4.58±2.53	4.63±2.72
Reading	3.28±2.95	3.16±2.92	3.16±2.66	3.20±2.83
Total score (0 to 40)	20.3±7.4	21.2±7.2	20.3±6.7	20.6±7.1
Assessment of throat soreness on a 11-point scale (0 = Not Sore and 10 = Very Sore)	7.20±1.12	7.27±1.21	7.13±1.00	7.20±1.11
VAS of difficulty swallowing (0mm = Not difficult, 100mm = Very difficult)	72.5±10.5	73.6±12.1	70.8±11.9	72.3±11.5
VAS of swollen throat (0mm = Not swollen, 100mm = Very swollen)	66.1±16.3	68.3±18.1	66.7±15.2	67.1±16.5
How much do you feel like your best overall on a 11-point scale (0 = I feel at my very worst and 10 = I feel at my very best)	4.34±1.99	3.70±1.62	4.44±2.06	4.16±1.92
How happy are you, in relation to your throat (0 = Very unhappy with my throat, 100mm = Very happy with my throat)	3.38±2.19	2.56±1.75	3.35±2.13	3.09±2.06

Source: Table 14.1.10

There was an imbalance between the treatments in respect of the number of patients with medications ongoing at randomisation with 36 (56%) patients reporting in the Strepsils Plus group, 31 (48%) patients reporting in the Strepsils Extra group and 26 (42%) reporting in the placebo group. In terms of WHO ATC level 2 categories, the most commonly reported categories were sex hormones and modulators of the

genital system with 30 (16%) patients reporting and psychoanaleptics with 23 (12%) patients reporting (Table 14.1.11). Patient number 059 (Strepsils Plus group) was taking Etodolac once daily for rheumatoid arthritis (anti-inflammatory and anti-rheumatic products). Three patients were taking analgesics at baseline, all within the Strepsils Extra group. Patient number 144 was taking paracetamol three times daily for sore throat commencing 51.25 hours prior to dosing. Patient number 010 was taking Tramadol as required for arthralgia. Patient number 211 was taking paracetamol as required for foot pain.

11.3 Measurements of Treatment Compliance

All patients took their study medication dose in their respective clinic.

11.4 Efficacy results and tabulation of individual patient data

11.4.1. Analysis of Efficacy

Primary measures of efficacy

The primary endpoint was the change from baseline in throat soreness at 120 minutes post dose. All patients provided data for this measure, except for patient number 002 (Strepsils Plus group). In the ANCOVA model for the full analysis set (n=189), the terms for treatment (p=0.02) and baseline throat soreness (p=0.001) were statistically significant whereas the term for centre was not significant (p=0.24). The LS means reductions were -2.19 (Strepsils Extra lozenge), -1.78 (Strepsils Plus lozenge) and -1.03 (placebo). The pairwise differences between the Strepsils Extra and placebo were statistically significant (p=0.004). The pairwise difference between Strepsils Plus and placebo did not achieve statistical significance (p=0.06) (Table 14.2.1.1). A total of 16 (8%) patients were not included in the equivalent per-protocol analysis. The statistical conclusions were identical to those obtained with the full analysis set as described above. The LS means reductions were -2.22 (Strepsils Extra lozenge), -1.68 (Strepsils Plus lozenge) and -1.03 (placebo: Table 14.2.1.2). Table 11.4.1 below summarises these results.

TABLE 11.4.1 **Change from baseline in throat soreness at 120 minutes post dose**
Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
FULL ANALYSIS SET			
N	64	64	62
Baseline (Mean±sd)	7.16±1.07	7.27±1.21	7.13±1.00
120 minutes post-dose (Mean±sd)	5.41±2.34	5.05±2.62	6.16±1.87
Change from baseline (Mean±sd)	-1.75±2.31	-2.22±2.66	-0.97±1.96
LS mean[a]	-1.78	-2.19	-1.03
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.75	-1.54,0.04	0.06
Strepsils Extra lozenge – Placebo	-1.16	-1.95,-0.37	0.004 **
PER-PROTOCOL SET			
N	58	58	57
Baseline (Mean±sd)	7.10±1.00	7.40±1.12	7.25±0.93
120 minutes post-dose (Mean±sd)	5.48±2.31	5.12±2.62	6.26±1.89
Change from baseline (Mean±sd)	-1.62±2.09	-2.28±2.66	-0.98±2.03
LS mean[a]	-1.68	-2.22	-1.03
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.65	-1.47,0.18	0.12
Strepsils Extra lozenge – Placebo	-1.19	-2.01,-0.36	0.005 **

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A negative difference favours the first treatment against second treatment

Source: Tables 14.2.1.1 and 14.2.1.2

Secondary endpoints

For the area under the change from baseline curve (AUC) in severity of throat soreness, from baseline to 2 hours, the ANCOVA model for the full analysis set (n=190), the terms for treatment (p=0.0007) and baseline throat soreness (p=0.0002) were both highly statistically significant whereas the term for centre was not significant (p=0.42). The LS means reductions were -2.39 (Strepsils Extra lozenge), -1.85 (Strepsils Plus lozenge) and -1.18 (placebo). The pairwise differences between the two actives and placebo were both statistically significant (p=0.0001 for Strepsils Extra lozenge and p=0.03 for the Strepsils Plus lozenge) (Table 14.2.2.1). Sixteen (8%) patients were not included in the equivalent per-protocol analysis. The statistical conclusions were identical to those obtained with the full analysis set as described above except the difference between Strepsils Plus versus placebo comparison did not achieve statistical significance (p=0.07). The LS means reductions were -2.37 (Strepsils Extra lozenge), -1.74 (Strepsils Plus lozenge) and -1.17 (placebo: Table 14.2.2.2).

TABLE 11.4.2 **AUC from baseline to two hours post dose for the change from baseline in throat soreness**

Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
FULL ANALYSIS SET			
N	64	64	62
Mean±sd	-1.80±1.84	-2.38±1.94	-1.09±1.64
LS mean[a]	-1.85	-2.39	-1.18
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.66	-1.28,-0.05	0.03 *
Strepsils Extra lozenge – Placebo	-1.21	-1.82,-0.59	0.0001 ***
PER-PROTOCOL SET			
N	59	58	57
Mean±sd	-1.67±1.59	-2.38±1.91	-1.09±1.70
LS mean[a]	-1.74	-2.37	-1.17
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.58	-1.21,0.05	0.07
Strepsils Extra lozenge – Placebo	-1.20	-1.83,-0.57	0.0002 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A negative difference favours the first treatment against second treatment

Source: Tables 14.2.2.1 and 14.2.2.2

The individual changes from baseline in throat soreness at each follow-up are summarised in Table 11.4.3 below and presented in more detail in Tables 14.2.3 to 14.2.12. The comparisons between the Strepsils Extra lozenge and placebo were statistically significant at each time point and the Strepsils Plus lozenge versus placebo comparison was statistically significant between five and 30 minutes inclusive.

TABLE 11.4.3 **Mean ± sd for change from baseline in throat soreness at 1, 5, 10, 15, 30, 45, 60, 75, 90 and 105 minutes post dose – Full analysis set**

Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	7.20±1.12 (64)	7.27±1.21 (64)	7.13±1.00 (62)		
1	-0.56±1.21 (64)	-0.70±1.29 (64)	-0.24±0.82 (62)	ns	*
5	-1.36±1.73 (64)	-1.78±1.72 (64)	-0.66±1.01 (62)	*	***
10	-1.86±1.86 (64)	-2.47±2.01 (64)	-1.13±1.71 (62)	*	***
15	-2.16±2.07 (64)	-2.75±2.01 (64)	-1.13±1.61 (62)	**	***
30	-2.05±2.07 (64)	-2.47±1.97 (64)	-1.23±1.71 (62)	*	***
45	-1.78±2.11 (64)	-2.64±2.23 (64)	-1.24±1.91 (62)	ns	***
60	-1.91±2.10 (64)	-2.67±2.30 (64)	-1.18±1.93 (62)	ns	***
75	-1.77±2.14 (64)	-2.41±2.42 (64)	-1.11±1.92 (62)	ns	**
90	-1.76±2.16 (63)	-2.30±2.54 (64)	-1.13±1.94 (62)	ns	**
105	-1.70±2.24 (64)	-2.13±2.58 (64)	-1.02±2.00 (62)	ns	*

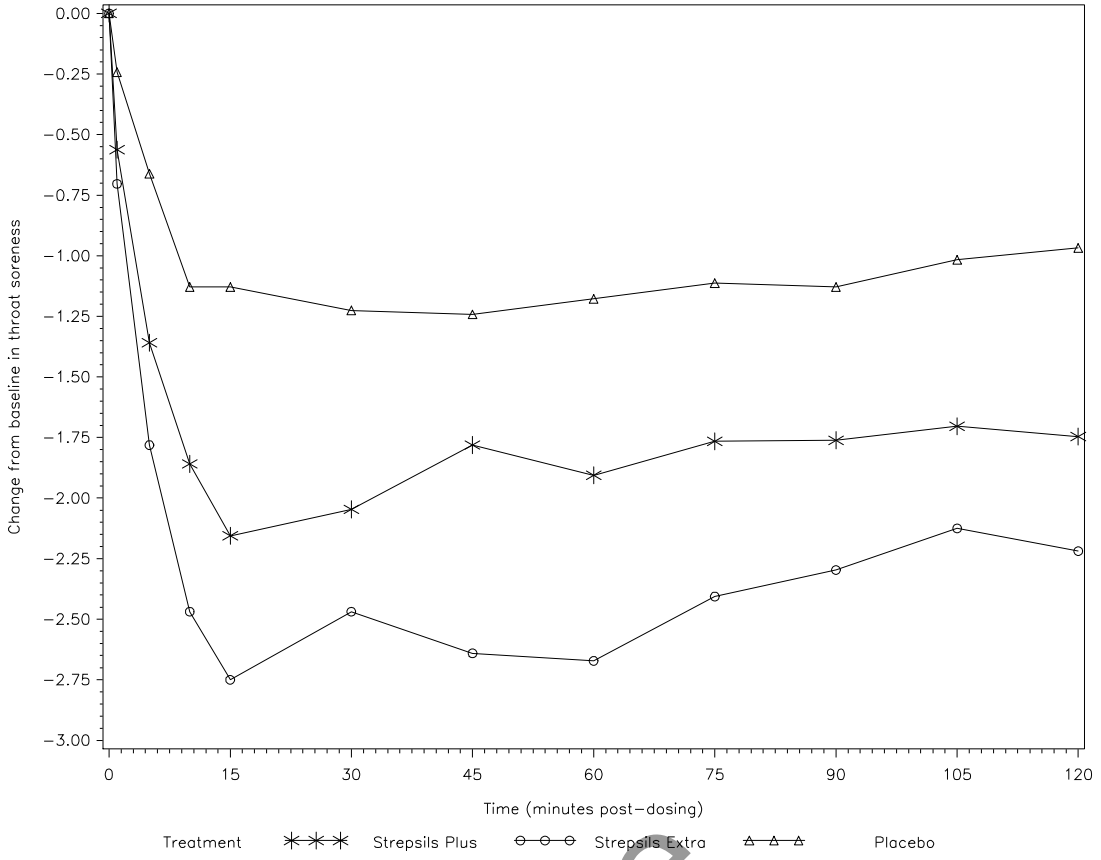
ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

Source: Tables 14.2.3 to 14.2.12

The maximum reductions in throat soreness were recorded at 15 minutes post-dose for both Strepsils lozenges, whereas the largest mean reduction for the placebo lozenge was at 45 minutes post-dose. The superiority of Strepsils Extra over placebo at all time points is clearly seen in Figure 11.4.1 below.

FIGURE 11.4.1 **Mean change from baseline in throat soreness from 1 to 120 minutes post first dose – Full analysis set**

Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore



The results of the analyses related to the AUC for sore throat pain relief (TOTPAR) from baseline to two hours post curve sore throat relief (TOTPAR) are given in Table 11.4.4 below. In the ANCOVA model for the full analysis set (n=190) the term for treatment was highly statistically significant (p<0.0001) whereas the terms for centre (p=0.51) and baseline throat soreness (p=0.41) were not statistically significant. The LS means were 2.31 (Strepsils Extra lozenge), 1.90 (Strepsils Plus lozenge) and 0.84 (placebo). The pairwise differences between the two actives and placebo were both highly statistically significant (p<0.0001) (Table 14.2.13.1).

Sixteen (8%) patients were not included in the equivalent per-protocol analysis. The statistical conclusions were identical to those obtained with the full analysis set as described above. The LS means reductions were 2.23 (Strepsils Plus lozenge), 1.81 (Strepsils Extra lozenge) and 0.82 (placebo: Table 14.2.13.2).

TABLE 11.4.4 **AUC from baseline to two hours post-dose for sore throat relief (TOTPAR)**
Measured on a 7-point scale where 0 = No relief, 1 = Slight relief, 2 = Mild relief, 3 = Moderate relief, 4 = Considerable relief, 5 = Almost complete relief, 6 = Complete relief

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
FULL ANALYSIS SET			
N	64	64	62
Mean±sd	1.86±1.33	2.28±1.41	0.81±0.95
LS mean[a]	1.90	2.31	0.84
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	1.06	0.62,1.50	<0.0001 ***
Strepsils Extra lozenge – Placebo	1.47	1.03,1.91	<0.0001 ***
PER-PROTOCOL SET			
N	59	58	57
Mean±sd	1.79±1.27	2.19±1.35	0.79±0.97
LS mean[a]	1.81	2.23	0.82
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	0.98	0.54,1.43	<0.0001 ***
Strepsils Extra lozenge – Placebo	1.41	0.96,1.85	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment
Source: Tables 14.2.13.1 and 14.2.13.2

The individual mean sore throat relief scores at each follow-up are summarised in Table 11.4.5 below and presented in more detail in Tables 14.2.14 to 14.2.24. The pairwise comparisons between both the Strepsils lozenges and placebo were highly statistically significant (p<0.001).

TABLE 11.4.5 **Mean ± sd (n) for sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post first dose – Full analysis set**
Measured on a 7-point scale where 0 = No relief, 1 = Slight relief, 2 = Mild relief, 3 = Moderate relief, 4 = Considerable relief, 5 = Almost complete relief, 6 = Complete relief

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
1	1.13±1.29 (64)	1.03±1.05 (64)	0.37±0.71 (62)	***	***
5	1.83±1.30 (64)	1.83±1.11 (64)	0.76±1.00 (62)	***	***
10	2.20±1.37 (64)	2.41±1.28 (64)	0.98±1.22 (62)	***	***
15	2.28±1.34 (64)	2.66±1.39 (64)	1.00±1.20 (62)	***	***
30	2.17±1.50 (64)	2.63±1.41 (64)	0.97±1.06 (62)	***	***
45	1.98±1.52 (64)	2.52±1.53 (64)	0.92±1.11 (62)	***	***
60	1.86±1.55 (64)	2.42±1.64 (64)	0.82±1.02 (62)	***	***
75	1.78±1.59 (64)	2.33±1.75 (64)	0.76±0.99 (62)	***	***
90	1.66±1.60 (64)	2.08±1.78 (64)	0.71±1.03 (62)	***	***
105	1.63±1.65 (64)	1.97±1.80 (64)	0.71±1.12 (62)	***	***
120	1.66±1.64 (64)	1.95±1.89 (64)	0.68±1.11 (62)	***	***

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level
Source: Tables 14.2.14 to 14.2.24

Maximum mean pain relief was obtained at 15 minutes post-dose for all three treatments, see Figure 11.4.2 below.

FIGURE 11.4.2
Mean sore throat relief from 1 to 120 minutes post first dose – Full analysis set
Measured on a 7-point scale where 0 = No relief, 1 = Slight relief, 2 = Mild relief, 3 = Moderate relief, 4 = Considerable relief, 5 = Almost complete relief, 6 = Complete relief

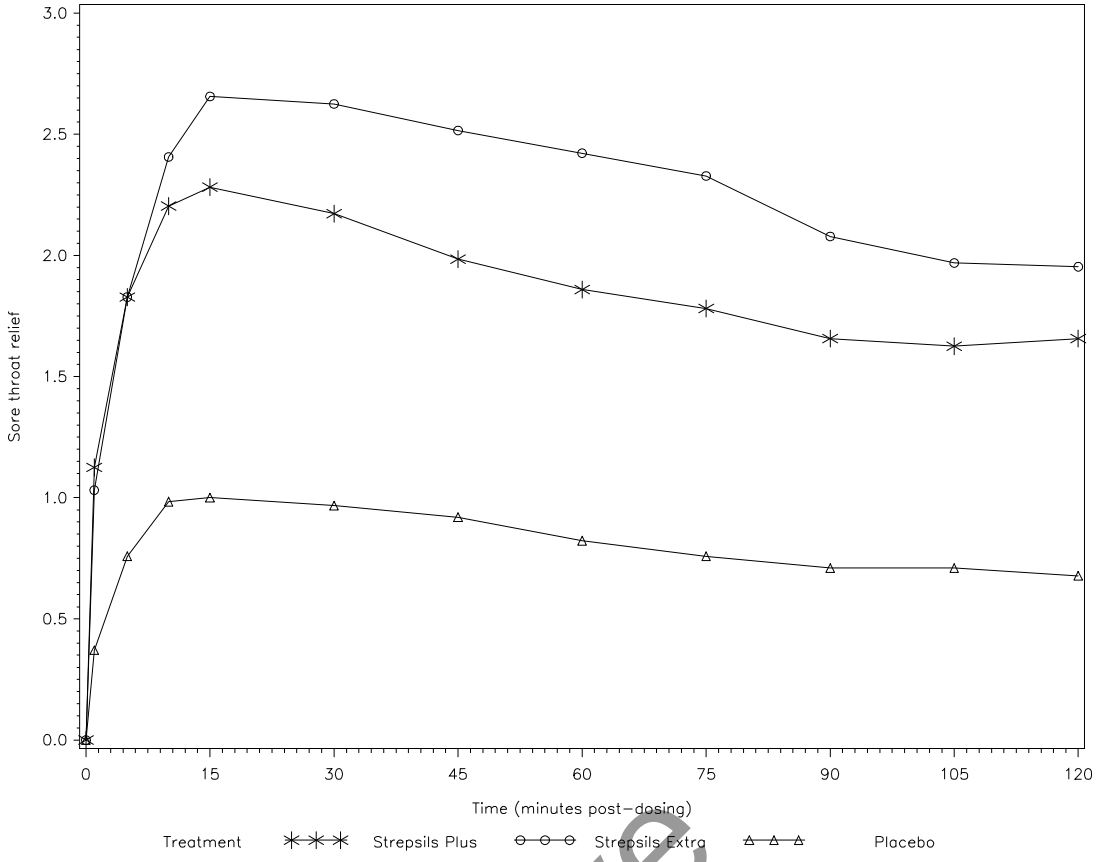


Table 14.2.25 gives the results of the analysis relating to the time taken for patients to be report moderate pain relief. In total, 46/64 (72%) reported moderate pain relief in the Strepsils Extra lozenge group, 39/64 (61%) reported moderate pain relief in the Strepsils Plus lozenge group and 13/62 (21%) in the placebo group. The pairwise comparisons between the Strepsils lozenges and placebo were highly statistically significant (p<0.0001) The Kaplan-Meier median time to reporting moderate pain relief was 12.5 minutes for Strepsils Extra patients and 30 minutes for Strepsils Plus patients.

The results of the analyses related to the AUC for the change from baseline to two hours post curve difficulty in swallowing are given in Table 11.4.6 below. In the ANCOVA model for the full analysis set (n=190) the term for treatment was highly statistically significant (p<0.0001) whereas the terms for centre (p=0.09), baseline score for difficulty swallowing (p=0.37) and baseline throat soreness (p=0.98) were not statistically significant. The LS means were -27.2 mm (Strepsils Extra lozenge), -19.3 mm (Strepsils Plus lozenge) and -8.6 mm (placebo). The pairwise differences between the two actives and placebo were both statistically significant (p<0.0001 for Strepsils Extra and p=0.0012 for Strepsils Plus) (Table 14.2.26.1).

Sixteen (8%) patients were not included in the equivalent per-protocol analysis. The statistical conclusions were identical to those obtained with the full analysis set as

described above. The LS means reductions were -27.8 mm (Strepsils Plus lozenge), -18.6 mm (Strepsils Extra lozenge) and -8.8 mm (placebo: Table 14.2.26.2).

TABLE 11.4.6 **AUC from baseline to two hours post first dose for the change in difficulty in swallowing**
Difficulty in swallowing measured on 100mm VAS where 0mm = Not difficult, 100mm = Very difficult

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
FULL ANALYSIS SET			
N	64	64	62
Mean±sd	-19.1±20.0	-27.3±21.9	-8.0±11.6
LS mean[a]	-19.3	-27.2	-8.6
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-10.7	-17.1,-4.3	0.0012 **
Strepsils Extra lozenge – Placebo	-18.7	-25.1,-12.2	<0.0001 ***
PER-PROTOCOL SET			
N	59	58	57
Mean±sd	-18.3±18.4	-27.7±22.0	-7.7±11.8
LS mean[a]	-18.6	-27.8	-8.8
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-9.8	-16.4,-3.3	0.004 **
Strepsils Extra lozenge – Placebo	-19.0	-25.7,-12.4	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and covariates for baseline throat soreness and baseline score for difficulty in swallowing
b A negative difference favours the first treatment against second treatment

Source: Tables 14.2.26.1 and 14.2.26.2

The individual mean reductions in difficulty in swallowing at each follow-up are summarised in Table 11.4.7 below and presented in more detail in Tables 14.2.27 to 14.2.37. The comparisons between the Strepsils Plus Extra and placebo were statistically significant at each timepoint and the Strepsils Plus lozenge versus placebo comparison was statistically significant from five minutes post-dose onwards.

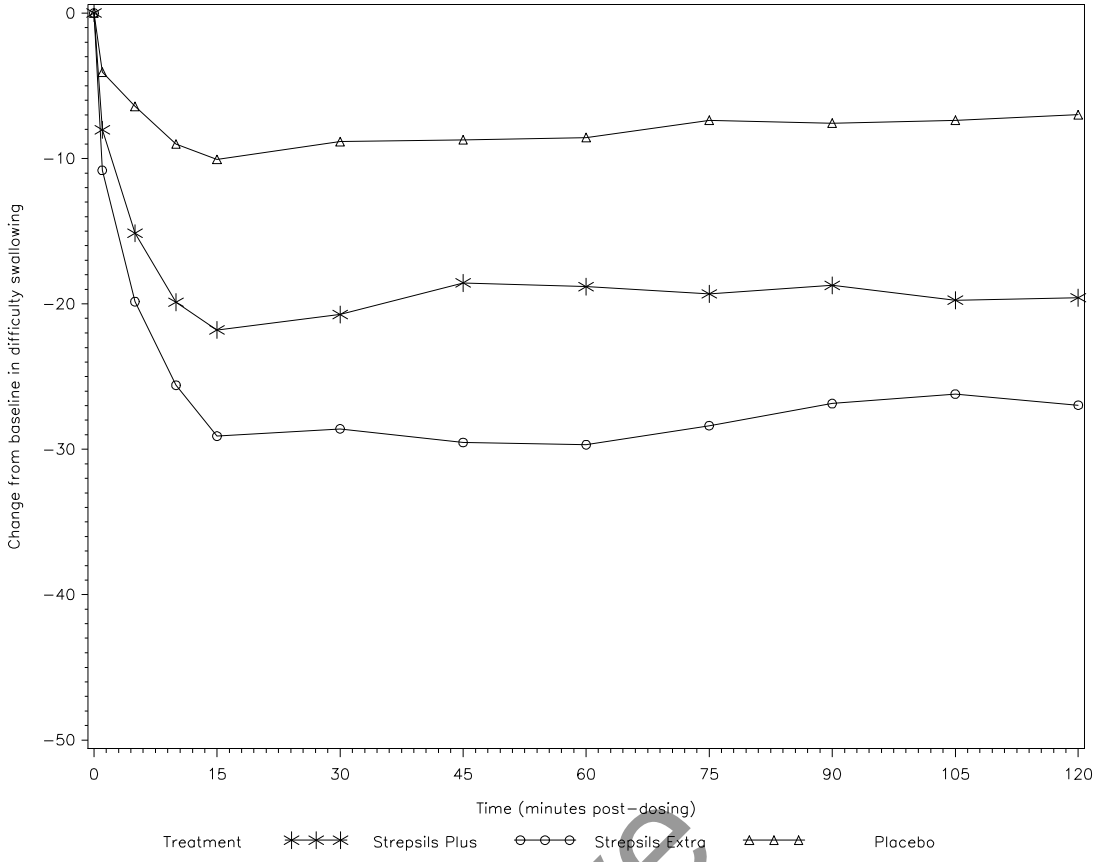
TABLE 11.4.7 **Mean ± sd (n) for change from baseline in difficulty in swallowing at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set**
Difficulty in swallowing measured on 100mm VAS where 0mm = Not difficult, 100mm = Very difficult

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	72.5±10.5 (64)	73.6±12.1 (64)	70.8±11.9 (62)		
1	-8.0±13.7 (64)	-10.8±16.2 (64)	-4.1±11.4 (62)	ns	*
5	-15.1±17.2 (64)	-19.8±18.8 (64)	-6.4±11.6 (62)	**	***
10	-19.9±20.5 (64)	-25.6±21.3 (64)	-9.0±14.0 (62)	**	***
15	-21.8±21.9 (64)	-29.1±22.0 (64)	-10.1±13.8 (62)	***	***
30	-20.7±22.2 (64)	-28.6±22.2 (64)	-8.8±12.0 (62)	**	***
45	-18.6±21.7 (64)	-29.5±23.2 (64)	-8.7±12.7 (62)	**	***
60	-18.8±22.3 (64)	-29.7±24.2 (64)	-8.6±13.4 (62)	**	***
75	-19.3±23.2 (64)	-28.4±26.0 (64)	-7.4±13.1 (62)	**	***
90	-18.7±23.6 (64)	-26.9±27.4 (64)	-7.6±13.2 (62)	**	***
105	-19.8±23.6 (64)	-26.2±28.2 (64)	--7.4±13.9 (62)	**	***
120	-19.6±25.2 (64)	-27.0±30.2 (64)	-7.0±15.3 (62)	**	***

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level
Source: Tables 14.2.27 to 14.2.37

The superiority of Strepsils Extra and Strepsils Plus lozenge in terms of changes from baseline in difficulty in swallowing versus Placebo can be seen in Figure 11.4.3 below.

FIGURE 11.4.3 **Mean change from baseline in difficulty in swallowing from 1 to 120 minutes post first dose – Full analysis set**
Difficulty in swallowing measured on 100mm VAS where 0mm = Not difficult, 100mm = Very difficult



Details of the analysis of the AUC for change from baseline in swollen throat from 0 to two hours post dose is presented in Table 11.4.8 below. In the ANCOVA model for the full analysis set (n=189) the terms for treatment (p<0.0001) and baseline score for swollen throat (p=0.0001) were highly statistically significant, whereas the terms for centre (p=0.19) and baseline throat soreness (p=0.33) were not statistically significant. The LS mean scores were -22.5 mm (Strepsils Extra lozenge), -14.9 mm (Strepsils Plus lozenge) and -6.2 mm (placebo). The pairwise differences between the two actives and placebo were both statistically significant (p<0.0001 for Strepsils Extra lozenge and p=0.009 for the Strepsils Plus lozenge) (Table 14.2.38).

TABLE 11.4.8 **AUC from baseline to two hours post first dose for the change in swollen throat – Full analysis set**
Swollen throat measured on a 100mm VAS scale where 0mm = Not Swollen, 100mm = Very Swollen

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	63	64	62
Mean±sd	-14.4±19.4	-22.8±23.3	-5.9±14.6
LS mean[a]	-14.9	-22.5	-6.2
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-8.8	-15.3,-2.2	0.009 **
Strepsils Extra lozenge – Placebo	-16.3	-22.9,-9.8	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A negative difference favours the first treatment against second treatment

Source: Tables 14.2.38

The individual mean reductions in swollen throat at each follow-up are summarised in Table 11.4.9 below and presented in more detail in Tables 14.2.39 to 14.2.49. The

comparisons between the Strepsils Extra lozenge and placebo were statistically significant at each timepoint ($p<0.01$) and the Strepsils Plus lozenge versus placebo comparison was statistically significant from 10 to 45 minutes post-dose inclusive and 75 to 120 minutes post-dose inclusive.

TABLE 11.4.9 **Mean ± sd (n) for change from baseline in swollen throat at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set**
Swollen throat measured on a 100mm VAS scale where 0mm = Not Swollen, 100mm = Very Swollen

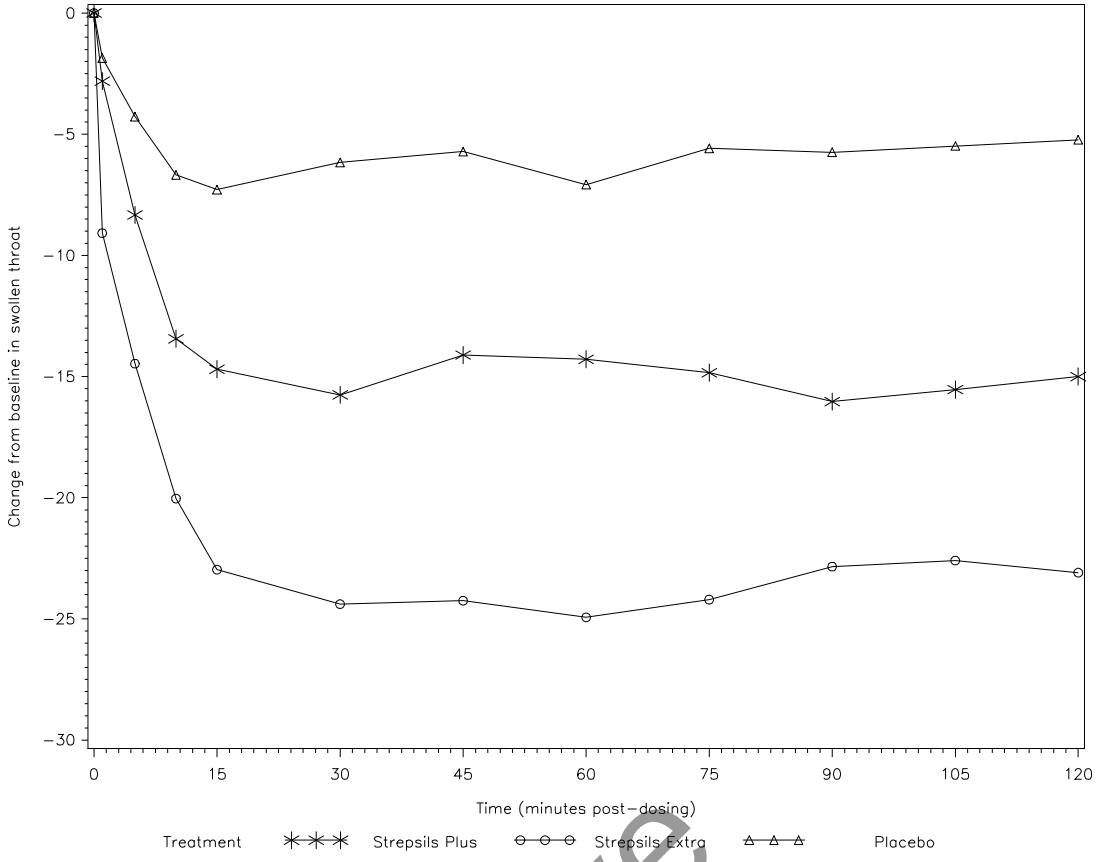
Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
0	66.1±16.3 (63)	68.3±18.1 (64)	66.7±15.2 (62)		
1	-2.8±13.1 (63)	-9.1±18.6 (64)	-1.9±11.8 (62)	ns	**
5	-8.3±16.2 (63)	-14.5±19.2 (64)	-4.3±13.4 (62)	ns	***
10	-13.4±18.6 (63)	-20.0±21.2 (64)	-6.7±15.5 (62)	*	***
15	-14.7±21.6 (63)	-23.0±21.9 (64)	-7.3±14.7 (62)	*	***
30	-15.8±20.5 (63)	-24.4±23.9 (64)	-6.2±15.2 (62)	**	***
45	-14.1±21.0 (63)	-24.3±24.0 (64)	-5.7±14.9 (62)	*	***
60	-14.3±21.7 (63)	-24.9±25.4 (64)	-7.1±19.0 (62)	ns	***
75	-14.8±23.1 (63)	-24.2±27.0 (64)	-5.6±15.9 (62)	*	***
90	-16.0±22.8 (63)	-22.8±28.9 (64)	-5.7±16.6 (62)	**	***
105	-15.5±24.1 (63)	-22.6±28.6 (64)	-5.5±17.0 (62)	*	***
120	-15.0±24.9 (63)	-23.1±29.6 (64)	-5.2±18.1 (62)	*	***

ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

Source: Tables 14.2.39 to 14.2.49

The superiority of Strepsils Extra and Strepsils Plus lozenge in terms of changes from baseline in swollen throat versus Placebo can be seen in Figure 11.4.4 below.

FIGURE 11.4.4 **Mean change from baseline in swollen throat from 1 to 120 minutes post first dose – Full analysis set**
Swollen throat measured on a 100mm VAS scale where 0mm = Not Swollen, 100mm = Very Swollen



Details of the analysis of the AUC from one minute to two hours post dose for throat numbness is presented in Table 11.4.10 below. In the ANCOVA model for the full analysis set (n=190) the term for treatment was highly statistically significant (p=0.0002) and term for centre was statistically significant (p=0.011) whereas the terms for baseline throat soreness (p=0.88) were not statistically significant. The LS mean scores for throat numbness were 2.27 (Strepsils Extra lozenge), 2.11 (Strepsils Plus lozenge) and 1.63 (placebo). The pairwise differences between the two actives and placebo were both statistically significant (p<0.0001 for Strepsils Extra lozenge and p=0.002 for the Strepsils Plus lozenge) (Table 14.2.50.1).

Sixteen (8%) patients were not included in the equivalent per-protocol analysis. The statistical conclusions were identical to those obtained with the full analysis set as described above. The LS mean scores for throat numbness were 2.23 (Strepsils Extra lozenge), 2.09 (Strepsils Plus lozenge) and 1.63 (placebo: Table 14.2.50.2).

TABLE 11.4.10 **AUC for throat numbness measurements from 1 to 120 minutes – Full analysis set**

Throat numbness measured on a 5-point scale where 1 = None, 2 = Mild, 3 = Moderate, 4 = Considerable, 5 = Complete

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
FULL ANALYSIS SET			
N	64	64	62
Mean±sd	2.13±0.98	2.30±0.99	1.64±0.74
LS mean[a]	2.11	2.27	1.63
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	0.49	0.17,0.80	0.0024 **
Strepsils Extra lozenge – Placebo	0.64	0.33,0.96	<0.0001 ***
	PER-PROTOCOL SET		
N	59	58	57
Mean±sd	2.11±0.93	2.24±0.96	1.64±0.77
LS mean[a]	2.09	2.23	1.63
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	0.46	0.14,0.78	0.005 **
Strepsils Extra lozenge – Placebo	0.60	0.28,0.92	0.0003 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.50.1 and 14.2.50.2

The individual mean throat numbness at each follow-up are summarised in Table 11.4.11 below and presented in more detail in Tables 14.2.51 to 14.2.61. The comparisons between the Strepsils Plus lozenge and placebo were statistically significant at each timepoint and the Strepsils Extra lozenge versus placebo comparison was statistically significant from five minutes post-dose onwards.

TABLE 11.4.11 **Mean ± sd (n) for throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose – Full analysis set**

Throat numbness measured on a 5-point scale where 1 = None, 2 = Mild, 3 = Moderate, 4 = Considerable, 5 = Complete

Minutes post-dose	Strepsils Plus lozenge (n)	Strepsils Extra lozenge (n)	Placebo (n)	Strepsils Plus versus Placebo	Strepsils Extra versus Placebo
1	2.08±0.99 (63)	1.84±0.74 (64)	1.63±0.93 (62)	**	ns
5	2.40±1.04 (63)	2.38±0.90 (64)	1.80±0.98 (61)	***	**
10	2.54±1.08 (63)	2.70±0.91 (63)	1.84±0.97 (61)	***	***
15	2.63±1.03 (64)	2.69±1.05 (64)	1.84±0.96 (62)	***	***
30	2.33±1.11 (64)	2.56±0.97 (64)	1.77±0.80 (61)	**	***
45	2.17±1.09 (64)	2.48±1.15 (64)	1.74±0.85 (62)	*	***
60	2.08±1.19 (64)	2.27±1.22 (63)	1.64±0.78 (61)	*	**
75	1.95±1.12 (64)	2.19±1.22 (64)	1.58±0.80 (62)	*	**
90	1.91±1.16 (64)	2.09±1.28 (64)	1.52±0.78 (62)	*	**
105	1.92±1.17 (64)	2.05±1.28 (63)	1.48±0.78 (62)	*	**
120	1.92±1.21 (64)	2.03±1.36 (63)	1.45±0.76 (62)	*	**

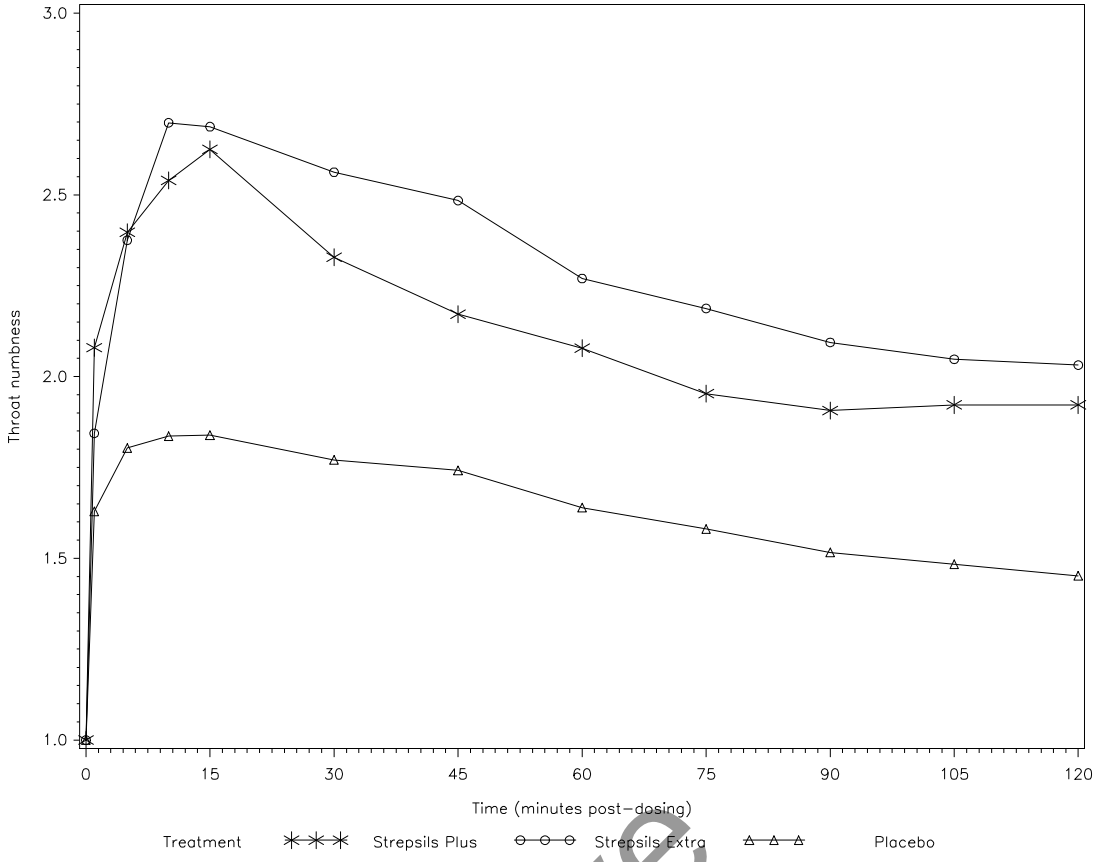
ns Comparison not statistically significant
* Comparison statistically significant at 5% level
** Comparison statistically significant at 1% level
*** Comparison statistically significant at 0.1% level

Source: Tables 14.2.51 to 14.2.61

Maximum mean throat numbness was obtained at 10 minutes post-dose for the Strepsils Extra lozenge and placebo lozenge and 15 minutes post-dose for the Strepsils Plus lozenge, see Figure 11.4.5 below.

FIGURE 11.4.5 **Mean throat numbness from 1 to 120 minutes post first dose – Full analysis set**

Throat numbness measured on a 5-point scale where 1 = None, 2 = Mild, 3 = Moderate, 4 = Considerable, 5 = Complete



Both Strepsils lozenges were rated highly statistically significantly better than placebo ($p<0.0001$) with respect to the Patient's Global Evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) recorded on an 5-point scale where 1 = Poor and 5 = Excellent. The LS mean scores estimated from the ANCOVA model were 2.81, 2.47 and 1.64 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Table 11.4.12 summarises these data, more detailed information is presented in Table 14.2.62.

TABLE 11.4.12 **Patient's Global Evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) at two hours – Full analysis set**

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
1 Poor	12 (18.8%)	8 (12.5%)	39 (62.9%)
2 Fair	21 (32.8%)	21 (32.8%)	10 (16.1%)
3 Good	19 (29.7%)	16 (25.0%)	7 (11.3%)
4 Very good	10 (15.6%)	11 (17.2%)	6 (9.7%)
5 Excellent	2 (3.1%)	8 (12.5%)	0 (0.0%)
Mean±sd	2.52±1.07	2.84±1.22	1.68±1.02
LS mean[a]	2.47	2.81	1.64
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	0.84	0.45,1.23	<0.0001 ***
Strepsils Extra lozenge – Placebo	1.17	0.78,1,56	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.62

Both Strepsils lozenges were rated highly statistically significantly better than placebo (p<0.0001) with respect to the Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) recorded on a 5-point scale where 1 = Poor and 5 = Excellent. The LS mean scores estimated from the ANCOVA model were 2.65, 2.50 and 1.59 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Table 11.4.13 summarises these data, more detailed information is presented in Table 14.2.63.

TABLE 11.4.13 **Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at two hours – Full analysis set**

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
1 Poor	12 (18.8%)	11 (17.2%)	40 (64.5%)
2 Fair	20 (31.3%)	18 (28.1%)	12 (19.4%)
3 Good	20 (31.3%)	21 (32.8%)	5 (8.1%)
4 Very good	11 (17.2%)	9 (14.1%)	4 (6.5%)
5 Excellent	1 (1.6%)	5 (7.8%)	1 (1.6%)
Mean±sd	2.52±1.04	2.67±1.16	1.61±1.00
LS mean[a]	2.50	2.65	1.59
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	0.91	0.53,1.28	<0.0001 ***
Strepsils Extra lozenge – Placebo	1.06	0.69,1.44	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.63

Both Strepsils lozenges were rated highly statistically significantly better than placebo (p<0.0001) with respect to the question asked at two hours concerning "how you would rate this lozenge as a treatment for sore throat" recorded on an 11-point scale where 0 = Poor and 10 = Excellent. The LS mean scores estimated from the ANCOVA model were 5.66, 5.38 and 2.20 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Table 11.4.14 summarises these data, more detailed information is presented in Table 14.2.64.

TABLE 11.4.14 **Overall treatment rating at two hours – Full analysis set**
Measured on an 11-point scale where 0 = Poor, 10 = Excellent

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Mean±sd	5.38±2.98	5.64±3.06	2.23±2.73
LS mean[a]	5.38	5.66	2.20
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	3.18	2.15,4.21	<0.0001 ***
Strepsils Extra lozenge – Placebo	3.45	2.42,4.49	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.64

Table 11.4.15 presents details of the changes from pre-dose to one hour post-dose in the functional impairment scale. Strepsils Extra had statistically significant improvements in talking (p=0.005) and swallowing (p=0.002) compared to placebo. For the overall score, Strepsils Extra lozenge achieved statistically significant reductions versus placebo (p=0.011) but the other pairwise comparison was not statistically significant. There were no statistically significant differences for concentrating and reading (Table 14.2.65).

TABLE 11.4.15 Change from pre-dose to one hour post-dose in the functional impairment scale (each component and overall total score)– Full analysis set
Each activity measured on an 11-point scale where 0 = Would not interfere at all, 10 = Would completely interfere

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
TALKING			
N	64	64	62
Mean±sd	-1.08±2.40	-1.69±2.33	-0.55±1.34
LS mean[a]	-1.02	-1.60	-0.60
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.42	-1.12,0.28	0.24
Strepsils Extra lozenge – Placebo	-1.00	-1.71,-0.30	0.005 **
SWALLOWING			
N	64	64	62
Mean±sd	-1.23±1.80	-1.91±2.56	-0.77±1.65
LS mean[a]	-1.27	-1.82	-0.72
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.55	-1.26,0.15	0.12
Strepsils Extra lozenge – Placebo	-1.10	-1.80,-0.40	0.002 **
CONCENTRATING			
N	64	64	62
Mean±sd	-1.00±2.30	-1.36±2.37	-0.95±1.77
LS mean[a]	-1.05	-1.22	-0.91
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.14	-0.84,0.57	0.71
Strepsils Extra lozenge – Placebo	-0.31	-1.02,0.41	0.40
READING			
N	63	64	62
Mean±sd	-0.76±2.49	-1.02±2.35	-0.60±1.49
LS mean[a]	-0.64	-0.92	-0.48
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-0.16	-0.84,0.52	0.64
Strepsils Extra lozenge – Placebo	-0.44	-1.12,0.24	0.20
TOTAL OF ALL FOUR RESPONSES			
N	64	64	62
Mean±sd	-4.2±6.8	-6.0±7.5	-2.9±4.5
LS mean[a]	-4.0	-5.6	-2.7
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	-1.3	-3.5,0.8	0.22
Strepsils Extra lozenge – Placebo	-2.9	-5.1,-0.7	0.011 *

a Estimated from ANCOVA model with factors for treatment and centre and covariates for baseline throat soreness and baseline score for the relevant variable
b A negative difference favours the first treatment against second treatment

Source: Table 14.2.6

Both Strepsils lozenges were judged statistically significantly faster (p<0.0001) than placebo with respect to “how quickly did you feel any numbing sensation”. The proportion of patients who reported a numbing sensation “Instantly as soon as I started to suck”, “Started after 1 to 5 seconds” or “Started after 6 to 10 seconds” were as follows: 12 (19%) for Strepsils Extra lozenge, 12 (19%) for Strepsils Plus lozenge and one (2%) for placebo. Table 11.4.16 summarises these data, more details are given in Table 14.2.66.

TABLE 11.4.16 Consumer questionnaire: How quickly did you feel any numbing sensation at one minute post-dose - Full analysis set

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Instantly as soon as I started to suck	2 (3.1%)	0 (0.0%)	0 (0.0%)
Started after 1 to 5 seconds	2 (3.1%)	7 (10.9%)	0 (0.0%)
Started after 6 to 10 seconds	8 (12.5%)	5 (7.8%)	1 (1.6%)
Started after 11 to 20 seconds	14 (21.9%)	7 (10.9%)	3 (4.8%)
Started after more than 20 seconds	11 (17.2%)	20 (31.3%)	8 (12.9%)
No numbing sensation (within the 1 minute)	27 (42.2%)	25 (39.1%)	50 (80.6%)
Parameter estimates[a]	Odds ratio[b]	95% CI	P
Strepsils Plus lozenge versus Placebo	7.07	3.19,15.66	<0.0001 ***
Strepsils Extra lozenge versus Placebo	6.63	2.99,14.70	<0.0001 ***

a Estimated from proportional odds model with factors for treatment and centre and a covariate for baseline throat soreness
b A value > 1 indicates the first treatment has quicker time to numbing sensation

Source: Table 14.2.66

Both Strepsils lozenges were rated highly statistically significantly better than placebo (p<0.0001) with respect to the question asked at five minutes post-dose concerning "how much do you think the lozenge soothed your throat" recorded on an 11-point scale where 0 = No soothing and 10 = Very soothing. The LS mean scores estimated from the ANCOVA model were 5.20, 4.80 and 2.01 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Table 11.4.17 summarises these data, more detailed information is presented in Table 14.2.67.

TABLE 11.4.17 Consumer questionnaire: How much do you think the lozenge soothed your throat at five minutes post-dose – Full analysis set
Measured on an 11-point scale where 0 = No soothing, 10 = Very soothing

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	63	62
Mean±sd	4.72±2.73	5.14±2.78	1.94±2.44
LS mean[a]	4.80	5.20	2.01
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	2.79	1.85,3.73	<0.0001 ***
Strepsils Extra lozenge – Placebo	3.19	2.24,4.13	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.67

Table 11.4.18 presents a summary of how deep down within the throat was the numbing felt at 20 minutes post-dose measured on an 11-point scale where 0 = No numbing and 10 = Very deep in the throat. There was highly statistically significantly more numbing (p<0.0001) for both Strepsils groups versus placebo. The LS mean scores estimated from the ANCOVA model were 4.75, 4.35 and 2.35 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Further details are presented in Table 14.2.68.

TABLE 11.4.18 Consumer questionnaire: How deep down within the throat was any numbing felt at 20 minutes post-dose - Full analysis set
Measured on an 11-point scale where 0 = No numbing, 10 = Very deep in the throat

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Mean±sd	4.22±2.68	4.66±2.55	2.24±2.67
LS mean[a]	4.35	4.75	2.35
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	2.00	1.10,2.90	<0.0001 ***
Strepsils Extra lozenge – Placebo	2.40	1.49,3.30	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Table 14.2.68

Table 11.4.19 presents a summary of the patients rating of the intensity of the numbing sensation at 20 minutes post-dose measured on an 11-point scale where 0 = No numbing and 10 = Very intense numbing There was highly statistically significantly more intense numbing (p<0.0001) for both Strepsils groups versus placebo. The LS mean scores estimated from the ANCOVA model were 4.80, 4.32 and 1.92 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Further details are presented in 14.2.69.

TABLE 11.4.19 **Consumer questionnaire: Intensity of any numbing sensation at 20 minutes post-dose – Full analysis set**
Measured on an 11-point scale where 0 = No numbing, 10 = Very Intense Numbing

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Mean±sd	4.25±2.78	4.77±2.52	1.87±2.43
LS mean[a]	4.32	4.80	1.92
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	2.40	1.50,3.30	<0.0001 ***
Strepsils Extra lozenge – Placebo	2.88	1.98,3.79	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.69

Table 11.4.20 presents a summary of the patients rating of the strength of the numbing sensation at 20 minutes post-dose measured on an 11-point scale where 0 = No numbing and 10 = Very strong numbing There was highly statistically significantly more strong numbing (p<0.0001) for both Strepsils groups versus placebo. The LS mean scores estimated from the ANCOVA model were 4.82, 4.15 and 1.81 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Further details are presented in 14.2.70.

TABLE 11.4.20 **Consumer questionnaire: Strength of any numbing sensation at 20 minutes post-dose – Full analysis set**
Measured on an 11-point scale where 0 = No numbing, 10 = Very Strong Numbing

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Mean±sd	4.11±2.71	4.83±2.54	1.79±2.42
LS mean[a]	4.15	4.82	1.81
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	2.33	1.44,3.22	<0.0001 ***
Strepsils Extra lozenge – Placebo	3.01	2.12,3.90	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.70

At one and two hours post-dose, patients who received Strepsils Extra lozenge had improved statistically significantly more than placebo-treated patients in “how much do you feel like your best overall” (p=0.0003 in both cases). Similarly at both assessments, patients who received Strepsils Plus lozenge had improved statistically significantly more than placebo-treated patients in this measure (p=0.002 in both cases). Further details are given in Table 14.2.71.

TABLE 11.4.21 Consumer questionnaire: Change from pre-dose in the 11-point scale for how much do you feel like your best overall - Full analysis set
Measured on a 11-point scale where 0 = I feel at my very worst, 10 = I feel at my very best

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
ONE HOUR			
N	64	64	62
Baseline (mean±sd)	4.34±1.99	3.70±1.62	4.44±2.06
One hour (mean±sd)	5.08±1.95	4.97±1.98	4.15±2.08
Change from baseline (mean±sd)	0.73±2.18	1.27±1.94	-0.29±2.06
LS mean[a]	0.76	0.95	-0.23
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	0.99	0.37,1.61	0.002 **
Strepsils Extra lozenge – Placebo	1.18	0.55,1.81	0.0003 ***
TWO HOURS			
N	64	64	62
Baseline (mean±sd)	4.34±1.99	3.70±1.62	4.44±2.06
Two hours (mean±sd)	5.13±2.11	5.13±2.28	4.00±1.99
Change from baseline (mean±sd)	0.78±2.58	1.42±2.45	-0.44±2.07
LS mean[a]	0.94	1.12	-0.22
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	1.16	0.44,1.87	0.002 **
Strepsils Extra lozenge – Placebo	1.34	0.62,2.06	0.0003 ***

a Estimated from ANCOVA model with factors for treatment and centre and covariates for baseline throat soreness and baseline score for the relevant variable
b A positive difference favours the first treatment against second treatment

Source: Table 14.2.71

At one and two hours post-dose, patients who received either of the Strepsils lozenges had improved statistically significantly more than placebo-treated patients in "how happy are you, in relation to your throat" (p≤0.009). Table 11.4.22 summarises these data, further details are given in Table 14.2.72.

TABLE 11.4.22 Consumer questionnaire: Change from pre-dose in the 11-point scale for how happy are you, in relation to your throat - Full analysis set
Measured on a 11-point scale where 0 = Very unhappy with my throat, 10 = Very happy with my throat

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
ONE HOUR			
N	64	64	62
Baseline (mean±sd)	3.38±2.19	2.56±1.75	3.35±2.13
One hour (mean±sd)	4.31±2.25	4.58±2.59	3.31±2.01
Change from baseline (mean±sd)	0.94±2.67	2.02±2.62	-0.05±2.08
LS mean[a]	1.12	1.71	0.12
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	0.99	0.25,1.74	0.009 **
Strepsils Extra lozenge – Placebo	1.59	0.83,2,34	<0.0001 ***
TWO HOURS			
N	64	64	62
Baseline (mean±sd)	3.38±2.19	2.56±1.75	3.35±2.13
Two hours (mean±sd)	5.02±2.45	4.66±2.82	3.26±1.92
Change from baseline (mean±sd)	1.64±2.79	2.09±3.03	-0.10±2.21
LS mean[a]	1.88	1.78	0.12
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Plus lozenge – Placebo	1.76	0.94,2.57	<0.0001 ***
Strepsils Extra lozenge – Placebo	1.66	0.83,2.49	0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and covariates for baseline throat soreness and baseline score for the relevant variable
b A positive difference favours the first treatment against second treatment

Source: Table 14.2.72

Both Strepsils lozenges were graded as making the patients feel statistically significantly less distracted than before they took the lozenge (p=0.003 for Strepsils Plus and p=0.0004 for Strepsils Extra) at two hours post-dose compared to placebo. The proportion of patients who reported agreed or strongly agreed with the phrase "I feel less distracted than before I took the lozenge" were as follows: 22 (34%) for

Strepsils Plus lozenge, 23 (37%) for Strepsils Extra lozenge and eight (13%) for placebo. Table 11.4.23 summarises these data.

TABLE 11.4.23 Thinking about this lozenge, how much do you agree or disagree with the phrase "I feel less distracted than before I took the lozenge" at two hours post-dose - Full analysis set

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	63	64	62
Agree strongly	6 (9.5%)	6 (9.4%)	0 (0.0%)
Agree	17 (27.0%)	16 (25.0%)	8 (12.9%)
Neither agree nor disagree	19 (30.2%)	27 (42.2%)	24 (38.7%)
Disagree	13 (20.6%)	9 (14.1%)	15 (24.2%)
Disagree strongly	8 (12.7%)	6 (9.4%)	15 (24.2%)
Parameter estimates[a]	Odds ratio[b]	95% CI	P
Strepsils Plus lozenge versus Placebo	2.64	1.38,5.04	0.0033 **
Strepsils Extra lozenge versus Placebo	3.21	1.68,6.17	0.0004 ***

a Estimated from proportional odds model with factors for treatment and centre and a covariate for baseline throat soreness
b A value > 1 indicates the first treatment is favoured

Source: Table 14.2.73

Both Strepsils lozenges were graded as making the patients feel statistically significantly better than before they took the lozenge (p=0.0002 for Strepsils Plus and p<0.0001 for Strepsils Extra) at two hours post-dose compared to placebo. The proportion of patients who reported agreed or strongly agreed with the phrase "I feel better than before I took the lozenge" were as follows: 31 (49%) for Strepsils Plus lozenge, 31 (49%) for Strepsils Extra lozenge and 12 (19%) for placebo. Table 11.4.24 summarises these data.

TABLE 11.4.24 Thinking about this lozenge, how much do you agree or disagree with the phrase "I feel better than before I took the lozenge" at two hours post-dose - Full analysis set

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	63	63	62
Agree strongly	6 (9.5%)	11 (17.5%)	2 (3.2%)
Agree	25 (39.7%)	20 (31.7%)	10 (16.1%)
Neither agree nor disagree	12 (19.0%)	9 (14.3%)	11 (17.7%)
Disagree	11 (17.5%)	18 (28.6%)	20 (32.3%)
Disagree strongly	9 (14.3%)	5 (7.9%)	19 (30.6%)
Parameter estimates[a]	Odds ratio[b]	95% CI	P
Strepsils Plus lozenge versus Placebo	3.44	1.80,6.60	0.0002 ***
Strepsils Extra lozenge versus Placebo	3.84	1.99,7.39	<0.0001 ***

a Estimated from proportional odds model with factors for treatment and centre and a covariate for baseline throat soreness
b A value > 1 indicates the first treatment is favoured

Source: Table 14.2.74

Both Strepsils lozenges had the effect of statistically significantly taking the patients mind off the pain (p<0.0001) at two hours post-dose compared to placebo. The proportion of patients who reported agreed or strongly agreed with the phrase "The lozenge took my mind off the pain" were as follows: 40 (63%) for Strepsils Plus lozenge, 48 (75%) for Strepsils Extra lozenge and 11 (18%) for placebo. Table 11.4.25 summarises these data.

TABLE 11.4.25 Thinking about this lozenge, how much do you agree or disagree with the phrase "The lozenge took my mind off the pain" at two hours post-dose - Full analysis set

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	63	64	60
Agree strongly	6 (9.5%)	13 (20.3%)	2 (3.3%)
Agree	34 (54.0%)	35 (54.7%)	9 (15.0%)
Neither agree nor disagree	6 (9.5%)	9 (14.1%)	7 (11.7%)
Disagree	11 (17.5%)	6 (9.4%)	25 (41.7%)
Disagree strongly	6 (9.5%)	1 (1.6%)	17 (28.3%)
Parameter estimates[a]	Odds ratio[b]	95% CI	P
Strepsils Plus lozenge versus Placebo	6.60	3.28,13.30	<0.0001 ***
Strepsils Extra lozenge versus Placebo	13.97	6.62,29.49	<0.0001 ***

a Estimated from proportional odds model with factors for treatment and centre and a covariate for baseline throat soreness
b A value > 1 indicates the first treatment is favoured

Source: Table 14.2.75

Both Strepsils lozenges were graded as making the patients feel statistically significantly happier than before they took the lozenge (p=0.006 for Strepsils Plus and p=0.0006 for Strepsils Extra) at two hours post-dose compared to placebo. The proportion of patients who reported agreed or strongly agreed with the phrase "I feel happier than before I took the lozenge" were as follows: 22 (37%) for Strepsils Plus lozenge, 26 (41%) for Strepsils Extra lozenge and 12 (20%) for placebo. Table 11.4.26 summarises these data.

TABLE 11.4.26 Thinking about this lozenge, how much do you agree or disagree with the phrase "I feel happier than before I took the lozenge" at two hours post-dose - Full analysis set

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	60	64	61
Agree strongly	3 (5.0%)	10 (15.6%)	1 (1.6%)
Agree	19 (31.7%)	16 (25.0%)	11 (18.0%)
Neither agree nor disagree	17 (28.3%)	16 (25.0%)	15 (24.6%)
Disagree	16 (26.7%)	18 (28.1%)	20 (32.8%)
Disagree strongly	5 (8.3%)	4 (6.3%)	14 (23.0%)
Parameter estimates[a]	Odds ratio[b]	95% CI	P
Strepsils Plus lozenge versus Placebo	2.51	1.31,4.82	0.006 **
Strepsils Extra lozenge versus Placebo	3.13	1.63,5.99	0.0006 ***

a Estimated from proportional odds model with factors for treatment and centre and a covariate for baseline throat soreness
b A value > 1 indicates the first treatment is favoured

Source: Table 14.2.76

Both Strepsils lozenges were highly statistically significantly targeting the throat pain (p<0.0001) at two hours post-dose compared to placebo. The proportion of patients who reported agreed or strongly agreed with the phrase "The lozenge targeted my throat pain" were as follows: 48 (75%) for Strepsils Plus lozenge, 41 (64%) for Strepsils Extra lozenge and 15 (24%) for placebo. Table 11.4.27 summarises these data.

TABLE 11.4.27 Thinking about this lozenge, how much do you agree or disagree with the phrase "The lozenge targeted my throat pain" at two hours post-dose - Full analysis set

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Agree strongly	11 (17.2%)	16 (25.0%)	2 (3.2%)
Agree	37 (57.8%)	25 (39.1%)	13 (21.0%)
Neither agree nor disagree	6 (9.4%)	7 (10.9%)	8 (12.9%)
Disagree	5 (7.8%)	12 (18.8%)	18 (29.0%)
Disagree strongly	5 (7.8%)	4 (6.3%)	21 (33.9%)
Parameter estimates[a]	Odds ratio[b]	95% CI	P
Strepsils Plus lozenge versus Placebo	7.47	3.74,14.91	<0.0001 ***
Strepsils Extra lozenge versus Placebo	7.14	3.59,14.23	<0.0001 ***

a Estimated from proportional odds model with factors for treatment and centre and a covariate for baseline throat soreness
b A value > 1 indicates the first treatment is favoured

Source: Table 14.2.77

Both Strepsils lozenges were highly statistically significantly soothing (p<0.0001) at two hours post-dose compared to placebo. The proportion of patients who reported agreed or strongly agreed with the phrase "The experience of this lozenge is soothing" were as follows: 47 (73%) for Strepsils Plus lozenge, 47 (73%) for Strepsils Extra lozenge and 19 (31%) for placebo. Table 11.4.28 summarises these data.

TABLE 11.4.28 Thinking about this lozenge, how much do you agree or disagree with the phrase "The experience of this lozenge is soothing" at two hours post-dose - Full analysis set

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Agree strongly	13 (20.3%)	14 (21.9%)	3 (4.8%)
Agree	34 (53.1%)	33 (51.6%)	16 (25.8%)
Neither agree nor disagree	6 (9.4%)	5 (7.8%)	8 (12.9%)
Disagree	6 (9.4%)	10 (15.6%)	16 (25.8%)
Disagree strongly	5 (7.8%)	2 (3.1%)	19 (30.6%)
Parameter estimates[a]	Odds ratio[b]	95% CI	P
Strepsils Extra lozenge vs. Placebo	6.46	3.24,12.86	<0.0001 ***
Strepsils Plus lozenge vs. Placebo	7.13	3.56,14.29	<0.0001 ***

a Estimated from proportional odds model with factors for treatment and centre and a covariate for baseline throat soreness
b A value > 1 indicates the first treatment is favoured

Source: Table 14.2.78

Table 11.4.29 presents a summary of how deep down within the throat was the relief felt at two hours post-dose measured on an 11-point scale where 0 = Not at all deep in the throat, 10 = Very deep in the throat. There was highly statistically significantly more deep down relief (p<0.0001) for both Strepsils groups versus placebo. The LS mean scores estimated from the ANCOVA model were 4.25, 4.52 and 1.97 for the Strepsils Extra lozenge, Strepsils Plus lozenge and placebo groups respectively. Further details are presented in 14.2.79.

TABLE 11.4.29 Consumer questionnaire: How deep down within the throat was the relief felt at two hours post-dose – Full analysis set
Measured on an 11-point scale where 0 = Not at all deep in the throat, 10 = Very deep in the throat

	Strepsils Plus lozenge	Strepsils Extra lozenge	Placebo
N	64	64	62
Mean±sd	4.45±2.48	4.20±2.76	1.90±2.53
LS mean[a]	4.52	4.25	1.97
Parameter estimates	LS mean[b]	95% CI	P
Strepsils Extra lozenge – Placebo	2.55	1.64,3.46	<0.0001 ***
Strepsils Plus lozenge – Placebo	2.28	1.38,3.19	<0.0001 ***

a Estimated from ANCOVA model with factors for treatment and centre and a covariate for baseline throat soreness
b A positive difference favours the first treatment against second treatment

Source: Tables 14.2.79

Table 14.2.80 presents details of the URTI Questionnaire at two hours post-dose. The mean number of symptoms reported was 6.2 in the placebo group, 5.5 in the Strepsils Extra group and 5.3 in the Strepsils Plus group. The proportion of patients reporting a sore throat was 90% in the placebo group compared to 77% in the Strepsils Plus group and 72% in the Strepsils Extra group.

11.4.2 Analytical Issues

Detailed documentation of statistical methods, as the final statistical analysis plan, is presented in Appendix 16.1.9.

There was some evidence of non-normality for the analyses involving the primary endpoint for the full analysis set. Transforming the data via the rank transformation did not alter the statistical conclusions from the model (analysis not reported), so it was decided to report the original planned model. The same was true for the equivalent per-protocol analysis of this variable which excluded four patients with baseline scores of less than 6.

There was also evidence of non-normality for a fair proportion of the secondary endpoints. Given that the degree of non-normality was minor and the very clear superiority of the two Strepsils formulations over placebo it was decided to appeal to the robustness of the F-test rather than perform additional non-parametric analyses.

11.4.2.1 Adjustments for Covariates

Pairwise treatment comparisons were made for each of the continuous efficacy variables using ANCOVA. All ANCOVA models included treatment group, centre and a covariate for baseline throat soreness and the baseline score for the relevant variable of interest if appropriate.

For the time to moderate pain relief, differences between the treatment groups were assessed using a Cox regression analysis with factors for treatment and centre and a covariate for baseline throat soreness.

In general, the terms for baseline scores were statistically significant in the statistical models. Patients with more severe symptoms had a greater scope for improvement and therefore mean reductions tended to be greater. In general, the term for centre was not statistically significant.

11.4.2.2 Handling of Dropouts or Missing Data

All incomplete dates were entered on the database as they were recorded in the CRF. Thereafter, the incomplete dates were completed using pre-defined rules. If a day or month was recorded as UNK or NA it was replaced by the first day of the month or January respectively, provided this does not contradict any other dates recorded. For missing adverse events and medications dates during the trial, the worst-case date was used (e.g. the end of the month for a stop date, the randomisation date for start of AE).

For all non-AUC analyses, missing data were not replaced.

Due to the lack of missing data no additional sensitivity analyses were performed on the primary efficacy endpoint.

11.4.2.3 Interim Analyses and Data Monitoring

No interim analyses or data monitoring were planned or performed; therefore this section is not applicable.

11.4.2.4 Multi-centre Studies

The statistical models included centre as a factor. There was no evidence to suggest that the results differed significantly between centres.

11.4.2.5 Multiple Comparison/Multiplicity

No attempt was made to adjust for the multiplicity for the secondary endpoints but there was for the Primary end points.

11.4.2.6 Use of an "Efficacy Subset" of Patients

The use of the Per Protocol (PP) population (defined in Section 11.1) was restricted to the primary efficacy endpoint (the change from baseline in severity of throat soreness at two hours) and the following variables

- Change from baseline in severity of throat soreness from 0 to 2 hours.
- AUC from baseline to 2 hours for change from baseline of severity of throat soreness and difficulty in swallowing.
- AUC from baseline to 2 hours for throat numbness and sore throat relief.

Sixteen patients were excluded from the PP set but the statistical conclusions drawn from this subset were qualitatively identical to those results obtained using the full analysis set.

11.4.2.7 Active-Control Studies Intended to Show Equivalence

This study was not designed to test equivalence; therefore this section is not applicable.

11.4.2.8 Examination of Subgroups

Analyses of the primary efficacy endpoint were performed by key baseline characteristics. For each subgroup, the main effect and treatment-by-subgroup interaction terms were added to the standard model used in the primary endpoint analysis. Key variables of interest were centre (Table 14.2.81), baseline throat soreness severity (≤median, >median; Table 14.2.82), baseline VAS for difficulty in swallowing (≤median, >median; Table 14.2.83), baseline VAS for swollen throat (≤median, >median; Table 14.2.84), age at study entry (≤median, >median; Table 14.2.85), gender (Table 14.2.86) and total score from tonsillo-pharyngitis assessment at baseline (≤median, >median; Table 14.2.87).

None of the treatment-by-subgroup interactions were statistically significant at the 10% level.

11.4.3 Tabulation of Individual Response Data

In addition to tables giving group data for efficacy variables, relevant individual patient data are presented in by-patient tabular listings in Appendix 16.2.

No individual response data are presented in the body of the report.

11.4.4 Drug Dose, Drug Concentration and Relationships to Response

This was not a dose response study and fixed doses of study medication were used; therefore this section is not applicable.

11.4.5 Drug-Drug and Drug-Disease Interactions

Drug/drug or drug/disease interactions were not examined in this study; therefore this section is not applicable.

11.4.6 By-Patient Displays

Group mean data represent the principal analysis in this study; therefore this section is not applicable.

11.4.7 Efficacy Conclusions

The superiority of Strepsils Extra was evident with statistical significance achieved for all efficacy variables in the study. Strepsils Plus also demonstrated superiority over placebo but failed to achieve statistical significance for the primary endpoint although there was a clear trend towards significance in the full analysis set (p=0.06).

For the Primary efficacy endpoint the change from baseline in throat soreness at 120 minutes post dose (using the 11-point Throat Soreness Scale) , LS mean reductions of -2.19, -1.78 and -1.03 were obtained for Strepsils Extra, Strepsils Plus and placebo respectively.

Maximum reductions in throat soreness were evident at 15 minutes post dose for both Strepsils Lozenges compared to 45 minutes post dose for placebo.

Both Strepsils lozenges showed statistically significant superiority in sore throat relief compared with placebo from 1 minute and over 2 hours and maximum pain relief was observed at 15 minutes post dose for all 3 treatments.

Both products produced statistically significant throat numbness over 2 hours which was statistically superior to placebo from 1 minute for Strepsils Plus and 5 minutes for Strepsils Extra. Maximum mean throat numbness was obtained at 10 minute post dose for the Strepsils Extra lozenge and placebo and 15 minute post dose for Strepsils Plus.

Both products were statistically significantly superior to placebo over 2 hours in relief of difficulty swallowing, with statistical significance from 1 minute for Strepsils Extra

and 5 minutes for Strepsils Plus. Both products were statistically significantly superior to placebo over 2 hours in relief of swollen throat, with significance from 1 minute for Strepsils Extra and from 10 to 45 minutes and 75 to 120 minutes for Strepsils Plus.

Overall both products showed significant relief across different patient reported outcomes previously proven to be independent[16] and were rated significantly superior to placebo in clinician and patient overall assessment ($p<0.0001$).

For the functional element of the consumer questionnaire statistically differences to placebo in favour of Strepsils Extra were obtained for improvements in talking ($p=0.005$) and swallowing ($p=0.002$) to one hour post dose.

There was a statistically significant difference in favour of both Strepsils Lozenges against placebo in patient reported outcomes of, how effective their lozenge was, the depth of numbing, intensity of the numbing, feeling their best overall and how happy they were with their throat. This significant difference was also reflected in the patient's response to feeling less distracted, making patients feel better than before they took the lozenge and taking their minds of the pain. Both Strepsils Lozenges were found to offer highly significant soothing over placebo with no difference observed between the two Strepsils Lozenges.

12 SAFETY EVALUATION

All patients who took at least one dose of study medication were included in the analysis of safety. The safety set was analysed as treated.

12.1 Extent of Exposure

Sixty-four patients received a single dose of Strepsils Extra, 64 patients received a single dose of Strepsils Plus and 62 patients received a single dose of placebo.

12.2 Adverse Events (AEs)

All treatment emergent adverse events for each patient are listed in Appendix 16.2, Listings 16.2.7.1 and 16.2.7.2, giving both preferred terms according to MedDRA (Version 13.1) and the original term used by the investigator.

12.2.1 Brief Summary of Events

Six patients reported a total of 7 treatment emergent events. Four (6%) patients reported at least one treatment emergent event in the placebo group compared to one (2%) patient in each of the two Strepsils groups. A total of four treatment emergent events were reported in the placebo group compared to two events in the Strepsils Extra lozenge group and one event in the Strepsils Plus lozenge group. The majority of events were of mild severity with one event classed as severe. None were considered to be definitely, probably or possibly related to the study medication.

12.2.2 Display of Adverse Events

Table 14.3.3 presents a summary of treatment emergent adverse events by primary system organ class. The most common class for events reported were nervous system disorders with three reports (two in the placebo group and one in the Strepsils Plus lozenge group).

Table 14.3.4 reports the number of patients reporting each preferred term. Two headaches were reported one in the Strepsils Plus group and one in the placebo group. There were single reports of the following five adverse events, ear pain (placebo group), dyspepsia (placebo group), nausea (Strepsils Extra group), pyrexia (Strepsils Extra group) and lethargy (one in the placebo group).

Table 14.3.5 presents a summary of treatment emergent adverse events by primary system organ class, preferred term, severity and relationship to study medication. All adverse events were graded as mild in severity except for patient 069 (placebo) who had a severe earache of the right ear. Five adverse events had no relationship to therapy and two had unlikely relationship (both in the placebo group).

More details about the severity and relationships of treatment emergent adverse events to study medication are given in Table 12.2.1 below.

TABLE 12.2.1 Severity and relationship of treatment emergent adverse events to therapy

Total	Strepsils Plus lozenge (n=64)		Strepsils Extra lozenge (n=64)		Placebo (n=62)	
Total	Number of patients reporting	Number of reports (% of total)	Number of patients reporting	Number of reports (% of total)	Number of patients reporting	Number of reports (% of total)
Total	1 (2%)	1	1 (2%)	2	4 (6%)	4
Severity:						
Mild	1 (2%)	1 (100%)	1 (2%)	2 (100%)	3 (5%)	3 (75%)
Moderate	-	-	-	-	-	-
Severe	-	-	-	-	1 (2%)	1 (25%)
Relationship:						
Definite	-	-	-	-	-	-
Probable	-	-	-	-	-	-
Possible	-	-	-	-	-	-
Unlikely	-	-	-	-	2 (3%)	2 (50%)
None	1 (2%)	1 (100%)	1 (1%)	2 (100%)	2 (3%)	2 (50%)

Source: Appendix 16.2. Listings 16.2.7.1 and 16.2.7.2

No events were reported during follow-up (i.e. more than 24 hours after dosing).

12.2.3 Analysis of Adverse Events

There were no statistically significant pairwise treatment differences between the treatment groups in the proportion of patients reporting treatment emergent adverse events. For the Strepsils Extra lozenge group, one (2%) patients reported two adverse events. For the Strepsils Plus lozenge group, one (2%) patient reported one adverse event. Within the placebo group, four (6%) patients reported four events.

12.3 Other Serious Adverse Events (SAEs) and other Significant Adverse Events.

There were no deaths, other serious or significant adverse events reported in this study.

12.4 Clinical Laboratory Evaluation

No laboratory data was recorded in this study.

12.5 Vital Signs, Physical Findings and other Observations Related to Safety

No other safety parameters were recorded during the study.

12.6 Safety Conclusions

There were no safety issues within this study.

There was no statistically significant difference between the treatment groups in relation to the proportion of patients reporting adverse events. There were no treatment emergent serious adverse events in this study and most likely to be related to the patient's upper respiratory tract infection such as headache and fever. The adverse events were varied and all but one of these was reported as being mild. There was one report of a severe earache in a patient treated with placebo.

13 DISCUSSION AND OVERALL CONCLUSIONS

13.1 Discussion

The primary objective of this study was to determine the analgesic properties of Strepsils Plus and Strepsils Extra throat lozenges in patients with a sore throat due to an Upper respiratory tract infection (URTI). Sample size and choice of primary endpoint were determined on the basis of limited previous clinical experience with the products. Both products are believed to achieve their analgesic efficacy through an anaesthetic action locally at the site of pain, so in addition to patient reported outcomes related to their throat condition, throat numbness was also evaluated.

Both products demonstrated efficacy in relieving sore throat through multiple independent patient reported outcomes with Strepsils Extra achieving statistically significant superiority across all measures. For Strepsils Plus, superiority was demonstrated but statistical significance was not consistent across all endpoints, particularly for the primary endpoint.

For the primary efficacy variable, the change 120 minutes post dose from baseline in throat soreness (using the 11-point Throat Soreness Scale) there were LS mean

reductions of -2.19 (Strepsils Extra), -1.78 (Strepsils Plus) and -1.03 (Placebo). The difference between the Strepsils Extra and placebo was statistically significant (P=0.004), this difference was not significant between Strepsils Plus and placebo (P=0.06) but very close to reaching significance at 0.05.

There was no significant centre differences observed for the primary endpoint and recruitment was capped at 33 patients at any one centre therefore it is unlikely that the centre contributed to the differences noted. 16 patients were excluded from the per-protocol analysis as they had not met the initial inclusion criteria and the decision was made to increase the total of patients randomized from 180 to 190 to give 174 evaluable patients. The actual variability observed during the study was 2.24 which was higher than predicted and as a consequence the study power was less than expected.

The minimal previous clinical experience was a major factor in the selection of primary endpoint and based on this study, was probably not the most representative candidate of product efficacy. As anaesthetic action is a major factor in efficacy and it is clear that the numbing effect for Strepsils Plus decreases over 2 hours (more so than Strepsils Extra), a primary endpoint selected at the end of the period of drug action (2 hours) should not be the only factor considered when evaluating the overall product efficacy. It is also conceivable that the ordinal Throat Soreness Scale represented a less defined descriptor of their pain than the more overt categorical sore throat relief scale.

There were a number of secondary endpoints assessed in the study, difficulty in swallowing, throat numbness, swollen throat and sore throat relief. Strepsils Extra and Strepsils Plus both demonstrated statistically significant efficacy over placebo which started within the first 1 to 10 minutes.

Strepsils Extra showed superiority over the placebo from baseline with regards to swollen throat with the Strepsils Plus showing greater efficacy to placebo at the majority of time points (from 10 to 45 minutes post dose and 75 to 120 minutes post dose). Why this efficacy is not seen at 60 minutes is not immediately apparent.

Both Strepsils Lozenges were rated significantly higher than placebo in the Global evaluation of the Study Medication as a Treatment of Sore Throat and the Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at 2 hours ($p<0.0001$). The benefits of both Strepsils Lozenges was very apparent in consumer questionnaire responses which reached statistical significance over all the patient reported outcomes of reported effectiveness, depth and intensity of numbing and how they felt overall in person and with their throat. Both Strepsils also showed a highly significant soothing effect over placebo.

The maximum reduction in throat soreness was evident at 15 minutes post dose for both active lozenges compared to placebo and the Kaplan-Meier time to moderate pain relief was estimated as 12.5 minutes for Strepsils Extra and 30 minutes for Strepsils Plus.

More adverse events were reported in the placebo group compared to the two active Strepsils groups (6% to 2%) but the events noted were mostly mild and were not thought to be related to the study medication.

13.2 Conclusion

Strepsils Extra was more efficacious and achieved statistical significance over placebo for all the analgesic variables related to throat soreness, sore throat relief, swollen throat and difficulty in swallowing. Strepsils Plus also showed efficacy across different patient reported outcomes despite not achieving statistical significance for the primary endpoint.

14 TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT

Table number	Table Title

14.1 Demographics Data

14.1.1	Details of withdrawal – Safety set
14.1.2	Demographics – Full analysis set
14.1.3	Primary diagnosis – Full analysis set
14.1.4	Throat descriptor questionnaire – Full analysis set
14.1.5	Relevant previous medical history – Full analysis set
14.1.6	Relevant ongoing medical history – Full analysis set
14.1.7	Screening assessments – Full analysis set
14.1.8	URTI Questionnaire at screening (symptoms over the past 24 hours) – Full analysis set
14.1.9	URTI Questionnaire at pre-dose – Full analysis set
14.1.10	Baseline efficacy assessments – Full analysis set
14.1.11	Concomitant medication ongoing at randomisation – Full analysis set

14.2 Efficacy Data

14.2.1.1	Primary efficacy endpoint - Change from baseline in throat soreness at 120 minutes post dose - Full analysis set
14.2.1.2	Primary efficacy endpoint - Change from baseline in throat soreness at 120 minutes post dose – Per-protocol set
14.2.2.1	AUC from baseline to two hours post dose for the change from baseline in throat soreness - Full analysis set
14.2.2.2	AUC from baseline to two hours post dose for the change from baseline in throat soreness – Per-protocol set
14.2.3	Change from baseline in throat soreness at 1 minute post dose - Full analysis set
14.2.4	Change from baseline in throat soreness at 5 minutes post dose - Full analysis set
14.2.5	Change from baseline in throat soreness at 10 minutes post dose - Full analysis set
14.2.6	Change from baseline in throat soreness at 15 minutes post dose - Full analysis set
14.2.7	Change from baseline in throat soreness at 30 minutes post dose - Full analysis set
14.2.8	Change from baseline in throat soreness at 45 minutes post dose - Full analysis set
14.2.9	Change from baseline in throat soreness at 60 minutes post dose - Full analysis set
14.2.10	Change from baseline in throat soreness at 75 minutes post dose - Full analysis set
14.2.11	Change from baseline in throat soreness at 90 minutes post dose - Full analysis set
14.2.12	Change from baseline in throat soreness at 105 minutes post dose - Full

	analysis set
14.2.13.1	AUC from baseline to two hours post-dose for sore throat relief (TOTPAR) - Full analysis set
14.2.13.2	AUC from baseline to two hours post-dose for sore throat relief (TOTPAR) – Per-protocol set
14.2.14	Sore throat relief at 1 minute post dose - Full analysis set
14.2.15	Sore throat relief at 5 minutes post dose - Full analysis set
14.2.16	Sore throat relief at 10 minutes post dose - Full analysis set
14.2.17	Sore throat relief at 15 minutes post dose - Full analysis set
14.2.18	Sore throat relief at 30 minutes post dose - Full analysis set
14.2.19	Sore throat relief at 45 minutes post dose - Full analysis set
14.2.20	Sore throat relief at 60 minutes post dose - Full analysis set
14.2.21	Sore throat relief at 75 minutes post dose - Full analysis set
14.2.22	Sore throat relief at 90 minutes post dose - Full analysis set
14.2.23	Sore throat relief at 105 minutes post dose – Full analysis set
14.2.24	Sore throat relief at 120 minutes post dose – Full analysis set
14.2.25	Onset of analgesia - Time to first reporting of moderate pain relief - Full analysis set
14.2.26.1	AUC from baseline to two hours post dose for the change from baseline in difficulty in swallowing - Full analysis set
14.2.26.2	AUC from baseline to two hours post dose for the change from baseline in difficulty in swallowing – Per-protocol set
14.2.27	Change from baseline in difficulty in swallowing at 1 minute post dose - Full analysis set
14.2.28	Change from baseline in difficulty in swallowing at 5 minutes post dose - Full analysis set
14.2.29	Change from baseline in difficulty in swallowing at 10 minutes post dose - Full analysis set
14.2.30	Change from baseline in difficulty in swallowing at 15 minutes post dose - Full analysis set
14.2.31	Change from baseline in difficulty in swallowing at 30 minutes post dose - Full analysis set
14.2.32	Change from baseline in difficulty in swallowing at 45 minutes post dose - Full analysis set
14.2.33	Change from baseline in difficulty in swallowing at 60 minutes post dose - Full analysis set
14.2.34	Change from baseline in difficulty in swallowing at 75 minutes post dose - Full analysis set
14.2.35	Change from baseline in difficulty in swallowing at 90 minutes post dose - Full analysis set
14.2.36	Change from baseline in difficulty in swallowing at 105 minutes post dose - Full analysis set
14.2.37	Change from baseline in difficulty in swallowing at 120 minutes post dose - Full analysis set
14.2.38	AUC from baseline to two hours post dose for the change from baseline in swollen throat - Full analysis set
14.2.39	Change from baseline in swollen throat at 1 minute post dose - Full analysis set

14.2.40	Change from baseline in swollen throat at 5 minutes post dose - Full analysis set
14.2.41	Change from baseline in swollen throat at 10 minutes post dose - Full analysis set
14.2.42	Change from baseline in swollen throat at 15 minutes post dose - Full analysis set
14.2.43	Change from baseline in swollen throat at 30 minutes post dose - Full analysis set
14.2.44	Change from baseline in swollen throat at 45 minutes post dose - Full analysis set
14.2.45	Change from baseline in swollen throat at 60 minutes post dose - Full analysis set
14.2.46	Change from baseline in swollen throat at 75 minutes post dose - Full analysis set
14.2.47	Change from baseline in swollen throat at 90 minutes post dose - Full analysis set
14.2.48	Change from baseline in swollen throat at 105 minutes post dose - Full analysis set
14.2.49	Change from baseline in swollen throat at 120 minutes post dose - Full analysis set
14.2.50.1	AUC from baseline to two hours post-dose for throat numbness - Full analysis set
14.2.50.2	AUC from baseline to two hours post-dose for throat numbness – Per-protocol set
14.2.51	Throat numbness at 1 minute post dose - Full analysis set
14.2.52	Throat numbness at 5 minutes post dose - Full analysis set
14.2.53	Throat numbness at 10 minutes post dose - Full analysis set
14.2.54	Throat numbness at 15 minutes post dose - Full analysis set
14.2.55	Throat numbness at 30 minutes post dose - Full analysis set
14.2.56	Throat numbness at 45 minutes post dose - Full analysis set
14.2.57	Throat numbness at 60 minutes post dose - Full analysis set
14.2.58	Throat numbness at 75 minutes post dose - Full analysis set
14.2.59	Throat numbness at 90 minutes post dose - Full analysis set
14.2.60	Throat numbness at 105 minutes post dose - Full analysis set
14.2.61	Throat numbness at 120 minutes post dose - Full analysis set
14.2.62	Patient's Global Evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) at two hours - Full analysis set
14.2.63	Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at two hours - Full analysis set
14.2.64	Overall treatment rating at two hours - Full analysis set
14.2.65	Consumer questionnaire: Change from baseline in the individual and total scores from Functional Impairment Scale at one hours post-dose - Full analysis set
14.2.66	Consumer questionnaire: How quickly did you feel any numbing sensation at one minute post-dose - Full analysis set
14.2.67	Consumer questionnaire: How much do you think the lozenge soothed your throat at five minutes post-dose - Full analysis set
14.2.68	Consumer questionnaire: How deep down within the throat was any

numbing felt at 20 minutes post-dose - Full analysis set

14.2.69 Consumer questionnaire: Intensity of any numbing sensation at 20 minutes post-dose - Full analysis set

14.2.70 Consumer questionnaire: Strength of any numbing sensation at 20 minutes post-dose - Full analysis set

14.2.71 Consumer questionnaire: Change from baseline in how much the patient felt like their best overall at one and two hours post-dose - Full analysis set

14.2.72 Consumer questionnaire: Change from baseline in degree of happiness in relation to their throat at one and two hours post-dose - Full analysis set

14.2.73 Thinking about this lozenge, how much do you agree or disagree with the phrase “I feel less distracted than before I took the lozenge” at two hours post-dose - Full analysis set

14.2.74 Thinking about this lozenge, how much do you agree or disagree with the phrase “I feel better than before I took the lozenge” at two hours post-dose - Full analysis set

14.2.75 Thinking about this lozenge, how much do you agree or disagree with the phrase “The lozenge took my mind off the pain” at two hours post-dose - Full analysis set

14.2.76 Thinking about this lozenge, how much do you agree or disagree with the phrase “I feel happier than before I took the lozenge” at two hours post-dose - Full analysis set

14.2.77 Thinking about this lozenge, how much do you agree or disagree with the phrase “The lozenge targeted my throat pain” at two hours post-dose - Full analysis set

14.2.78 Thinking about this lozenge, how much do you agree or disagree with the phrase “The experience of this lozenge is soothing” at two hours post-dose - Full analysis set

14.2.79 Consumer questionnaire: How deep down within the throat was the relief felt at two hours post-dose - Full analysis set

14.2.80 URTI Questionnaire at two hours - Full analysis set

14.2.81 Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by centre - Full analysis set

14.2.82 Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by baseline throat soreness severity - Full analysis set

14.2.83 Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by baseline difficulty in swallowing - Full analysis set

14.2.84 Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by baseline swollen throat - Full analysis set

14.2.85 Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by age at study entry - Full analysis set

14.2.86 Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by gender - Full analysis set

14.2.87 Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by total score from tonsillo-pharyngitis assessment at baseline - Full analysis set

14.3 Safety Data

14.3.1	Extent of exposure to study medication - Safety set
14.3.2	Summary of treatment emergent adverse event reporting – Safety set
14.3.3	MedDRA Summary of treatment emergent adverse events by primary system organ class – Safety set
14.3.4	MedDRA Summary of treatment emergent adverse events by primary system organ class and preferred term – Safety set
14.3.5	MedDRA Summary of treatment emergent adverse events by primary system organ class, preferred term, severity and relationship to study medication – Safety set
14.3.6	Concomitant medication commencing during the study – Safety set

15 REFERENCES

(1) Watson N, Nimmo WS, Christian J, Charlesworth A, Speight J and Miller K. Relief of sore throat with the anti-inflammatory throat lozenge flurbiprofen 8.75mg: a randomised double blind placebo controlled study of efficacy and safety. International Journal of Clinical Practice 2000 54 (8): 490-496

(2) Benrimoj SI, Langford JH, Christian J, Charlesworth A and Steans A. Efficacy and Tolerability of the anti-inflammatory throat lozenge flurbiprofen 8.75mg in the treatment of sore throat. Clin Drug Invest. 2001 21 (3): 183-193

(3) Blagden M, Christian J, Miller K and Charlesworth A. Multidose flurbiprofen 8.75mg lozenges in the treatment of sore throat a randomised double blind, placebo controlled study in the UK General Practice Centres. International Journal of Clinical Practice 2002 56 (2): 95-100

(4) Schachtel BP, Sore throat pain. In: Max MB, Portnoy RK, and Laska EM, eds. The Design of Analgesic Clinical Trials (Advances in pain research and therapy; Vol. 18). New York: Raven Press, 1991: 393-406

(5) Schachtel BP, Homan HD, Gibb IA, Christian J. Demonstration of dose-response of flurbiprofen lozenges with the sore throat pain model. Clin Pharmacol Ther. 2002;71: 375-80

(6) Schachtel BP. Sore throat pain. In: Max MB, Portnoy RK, and Laska EM, Eds. The Design of Analgesic Clinical Trials (Advances in pain research and therapy; Vol. 18). New York: Raven Press, 1991: 393-406

(7) Schachtel BP, Fillingim JM, Beiter DJ, Lane AC, Schwartz LA. Rating scales for analgesics in sore throat. Clin Pharmacol Ther. 1984;36: 151-6

(8) McNally D, Simpson M, Morris C, Shephard A, Goulder M. Rapid relief of acute sore throat with AMC/DCBA throat lozenges: randomised controlled trial. Int J Clin Pract. 2010 Jan; 64 (2): 194-207. Epub 2009 Oct 22.

(9) TH0709. Clinical Study Report, Reckitt Benckiser, Healthcare, Data on File.

(10) TH0901. Clinical Study Report, Reckitt Benckiser, Healthcare. Data on File.

(11) SAS Institute Inc. The SAS System, Version 9.2. Cary, NC, SAS Institute Inc.2009.

(12) McCullagh P. “Regression models for ordinal data (with discussion)”. Journal of the Royal Statistical Society, Series B, 1980:42 (2), 109-142

13) Wade AG. A randomized double-blind, parallel group, placebo-controlled, multiple-dose study of the efficacy of Strepsil lozenges in the relief of acute sore throat. Oxford JS ed. 2008 - This is Boots Healthcare International 1996. Research Report BH5013R

14) Burnett I, Schachtel B, Sanner K, Bey M, Grattan T and Little John S. Onset of Analgesia of Paracetamol Tablet containing Sodium Bicarbonate: A Double-Blind, Placebo-controlled study in Adult Patients with Acute Sore Throat. Clin Ther. 2006; 28: 1273-1278

15) Schachtel BP, Fillingim JM, Thoden WR, lane AC and Baybutt RI. Sore throat pain in evaluation of mild analgesics. Clin Pharmacol Ther. 1988; 44 (6): 704-711

16) Schachtel BP, McCormick CG and Giefer EE. Patient –Reported Outcomes (PROs) in the Pharyngitis Pain Model. Abstract PM035, 13th World Congress on Pain, Montreal 2010.

APPENDICES

APPENDIX 16.1 STUDY INFORMATION

This Appendix contains the following sections:

16.1.1 Protocol and Protocol amendments

16.1.2 Sample case report form (unique pages only)

16.1.3 List of IECs or IRBs

16.1.4 List and description of Investigators and other important participants in the study.

16.1.5 Signatures of principal or chief/coordinating Investigator(s)

16.1.6 Listing of patients receiving test drug(s) from specific batches, where more than one batch was used.

16.1.7 Randomisation scheme and codes (patient identification and treatment assigned).

16.1.8 Audit certificates

16.1.9 Documentation of statistical methods.

16.1.10 Documentation of inter-laboratory standardisation methods and quality assurance procedures.

16.1.11 Publications based on the study.

16.1.12 Important publications referenced in the report – copies of papers.

APPENDIX 16.1.1 PROTOCOL AND PROTOCOL AMENDMENTS

This appendix contains:

- Final Protocol, dated: 29th November 2010 (64 pages)
- Protocol Administrative change No. 1 dated 30th November 2010 (3 pages)
- Protocol Amendment 1, dated 30th November 2010 (3 pages)
- Protocol Amendment 2 dated 6th March 2011 (2 pages)

APPENDIX 16.1.2 SAMPLE CASE REPORT FORM (UNIQUE PAGES ONLY).

This appendix contains (35 pages):

- Demography
- Medical history
- Physical examination
- Screening assessments (Part 1)
- Screening assessments (Part 2)
- Inclusion & Exclusion criteria
- Inclusion & Exclusion criteria
- Pre-dose: part 1
- Pre-dose: part 2
- Pre-dose: part 3
- Dosing
- 1 minute assessment
- 1 minute assessment (Continued)
- 5 minute assessment
- 5 minute assessment (Continued)
- 10 minute assessment
- 15 minute assessment
- 20 minute assessment
- 30 minute assessment
- 45 minute assessment
- 60 minute assessment
- 60 minute assessment (Continued)
- 75 minute assessment
- 90 minute assessment
- 105 minute assessment
- 120 minute assessment
- 120 minute assessment (Continued)
- 120 minute assessment (Continued)
- Discharge

- Post Study Follow-up Telephone Call
- Final Evaluation Form
- Signature Page
- Unscheduled visit
- Concomitant Medication and Therapies
- Adverse Events

APPENDIX 16.1.3 LIST OF IECs OR IRBs

This appendix contains:

- List of name and address of the ethics committee used in the study.

Office for Research Ethics Committees in Northern Ireland (ORECNI), Research Ethics Committee 1, 1-4 Haslem's Lane, Lisburn, BT28 1TW

- Representative written information for Patient and sample consent form version 1 dated 29th November 2010 (13 pages in total).
- Representative written information for Patient and sample consent form version 2 dated 16th March 2011 (13pages in total).

Both Patient Information and Consent Forms were clearly identified by a header on each printed page:

Participant information sheet and consent form for Protocol No: TH1017 Eudract N°: 2010-024045-69

But with a different version and dated footer on each printed page as shown below:

Patient Information and Consent Form V1 dated 29th November 2010

<<PRINT ONTO GP PRACTICE HEADED PAPER>>

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Strepsils Plus and Strepsils Extra Efficacy study

Study Title:	A multi centre,, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.

Invitation to take part

We would like to invite you to take part, voluntarily in our research study. The study is looking at two treatments, Strepsils Plus lozenge containing 0.6mg amylmetacresol BP , 1.2 mg 4-Dichlorobenzyl alcohol (a mild antiseptic) and 10mg Lidocaine Hydrochloride (a mild anaesthetic) and Strepsils Extra Lozenge containing 2.4mg Hexylresorcinol (a mild antiseptic and anaesthetic) which are currently indicated for the relief of symptoms that may accompany mouth and throat infection. Before you decide if you would like to take part or not, we would like you to understand why the research is being done and what it will involve for you. Please take the time to read the following information carefully. Ask your study doctor if there is anything that is not clear or if you would like information. Talk to others about the study if you wish. Take time to decide whether or not you want to take part. If you do decide to take part in the study after reading this information you will be asked to complete, sign and date the attached consent form and to keep it as a useful reference.

This information sheet is split into two parts.

Part 1 tells you the purpose of the study and what will happen to you if you take part

Part 2 gives you more information on the conduct of the study.

PART 1

What is the purpose of the study?

A sore throat can be caused by a virus or bacterial infection and will generally cause inflammation of the tonsils and the surrounding area that cause the symptoms we associate with sore throats.

The primary aim of this study is to determine the pain-relieving effect of two different Strepsils lozenges in patients with a sore throat due to an upper respiratory tract infection compared to a placebo lozenge (A placebo is commonly called a 'dummy pill' as it contains no active ingredients. It's purpose is to act as a control, and in the case of this study will account for the lubricating effects on a sore throat of sucking a sugar based sweet). This study will also provide additional information on the acceptability of the two lozenges from questionnaires about the lozenges.

The study will require a 2 hour stay in the GP surgery following your initial appointment. A Follow up phone call will take place 1-3 days after you have taken the lozenge to check if you had any adverse effects and if you needed to take any additional treatment. There will be a total of 180 patients recruited into this study, all of which will be recruited in Northern Ireland.

Why have I been invited?

You have been invited to take part in the study because you are aged between 18 and 75 and you have a sore throat which started within the past 4 days. You may be responding to a poster you have seen in the pharmacy or your own GP clinic. There is a list of reasons why you may not be suitable to enter the study. If you are not suitable for the study, the reasons will be discussed with you by the clinic staff either on the phone or at the GP clinic.

Do I have to take part?

Taking part in this study is entirely voluntary. It is up to you to decide whether or not to take part. If you agree to take part we will ask you to sign a consent form. You are free to withdraw from the study at any time without giving a reason. This will not affect the standard of care you receive. You will also be given a copy of this information sheet and consent form to keep. If you agree, your GP may be informed that you have agreed to take part in the study

What will happen to me if I take part?

Your participation in the study may be a maximum of 5 days (from initial visit to follow up phone call if your initial visit is not the day you are eligible to enter the study) .However, if your initial visit and study entry occur on the same day, your maximum participation time will be 3 days. The first visit will take around 2.5 hours depending on your medical history and the time the study nurse will take to instruct you on how to complete the study questionnaires. The follow up phone call will take around 7-10 minutes. We plan to complete the study by April 2011.

This is a "randomised study" which means you will be randomly assigned to one of the 3 treatment groups below. To find out which treatment is best for giving pain relief we need to make comparisons. We put people into groups and give each group a different treatment by chance. A total of 180 patients will be randomly allocated into one of three treatment groups as follows:

- One group of patients (60 patients) will receive a Strepsils Plus lozenge only.
- One group of patients (60 patients) will receive a Strepsils Extra lozenge only.
- One group of patients (60 patients) will receive placebo (dummy) lozenge. (A dummy treatment which contains no active ingredient).

The study is also "double blind". This means that neither you nor your study doctor will know which treatment group you are in (although, if your study doctor needs to find out they can do so).

Screening

If you have responded to an advertisement or have seen a poster in your local pharmacy you will have been asked some questions over the phone already by a trained representative to see if you may meet the requirements for the study.

Screening / Day 1 Visit

At this visit you will now be asked to read the patient information sheet and ask any questions you may have and then if you wish to take part in the study you will be asked to sign the consent form before any study assessments can be performed. Your doctor will ask you about your medical history and current medical status. If you are female and able to have children, you will be asked some questions about the possibility of pregnancy and contraception and you will have a pregnancy test performed using a sample of urine. All this information will help determine if you are suitable for the study. The doctor will examine your throat and check for symptoms of an upper respiratory tract infection and how long you have had a sore throat. You will be asked to describe the nature of your sore throat by answering specific questions and the doctor will also conduct a physical examination of the eyes, ears,

nose, mouth and lungs and complete an assessment of your sore throat called a Tonsillo-Pharyngitis Assessment (TPA). The completion of the TPA ensures that only patients with acute tonsillopharyngitis are recruited into the study. The doctor will ask you whether you have taken any prohibited therapies such as sore throat treatments, or boiled sweets earlier that day. If you have answered yes to this, the doctor or nurse may ask you to return to the clinic at a later time in order that the effects of any prior treatment have worn off. This is called a washout period. The specific washout period for this study will depend on when you last took a treatment that is not allowed. These are as follows:

Washout period of 2 hours if you have taken: Medicated sweets, pastilles, spray or any product with a soothing property such as boiled sweets

Washout period of 4 hours if you have taken: Sore throat medication containing a local anaesthetic

Washout period of 8 Hours if you have taken: Any analgesic (pain relieving), antipyretic (fever relieving e.g. paracetamol) or cold medication (e.g. hot drink remedies or throat lozenges)

Washout period of 24 hours if you have taken: Any longer acting or slow release medications (eg Piroxicam and Naproxen, both anti-inflammatory treatments during the previous 24 hours:

If you are suitable to take part in the study you will be asked to sit in a quiet area in the clinic during the treatment and follow up time. You will be asked to answer questions about your throat and the lozenge and you will complete 5 rating scales at various time points over the 2 hours. You will also be asked to complete 2 questionnaires at these same time points over the 2 hour period. The clinic staff will instruct you on how to complete these questionnaires and they will remain with you at all times. You will be asked to remain quiet to ease your throat and also not to discuss your lozenge treatment with any other patients who may also be in the study at the same time. You can ask any questions you want during this time to the trained study team nurse. You will not be allowed to consume any food, drinks, throat lozenges (aside from the trial medication), sweets, chewing gum or any other medication during this 2 hour period. No smoking will be allowed during this visit.

Administration of Study Medication

The lozenges used in this study will not be matched for colour and therefore in order to ensure neither the patient, the doctor or the nurse who stays with you during the treatment visit knows which lozenge you receive you will be asked to wear a blindfold at the time you take your lozenge. You will be provided with one lozenge in the clinic by a member of the clinical team that will not be involved in helping you complete any of the study assessments. They will observe you putting the lozenge into your mouth. Once the lozenge is placed in your mouth you may remove the blindfold. You will be asked to suck the lozenge slowly and move it round your mouth until it dissolves. You should not chew or crunch your lozenge. You will be asked to swallow and then complete 5 rating scales one minute before taking the lozenge and then at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes after receiving your first lozenge. You will be asked to complete a consumer questionnaire at 1, 5, 20, 60 and 120 minutes and an overall treatment rating questionnaire at 120 minutes after you have taken the lozenge. The rating scales/questionnaires include the following:

- **Throat Soreness Scale:** You will be asked by the study nurse to swallow and then circle a number on the scale that shows how sore your throat is when you swallow.
- **Throat Numbness:** You will be asked to circle the phrase that best describes the numbness of your throat.
- **Sore throat relief:** You will be instructed by the study nurse to 'Tick the phrase that best describes the relief of your sore throat'.
- **Swollen Throat Scale using the visual analogue scale:** You will be asked to swallow and place a line through the scale to indicate how swollen your throat is (not swollen on the left and very swollen on the right of the scale)
- **Difficulty in swallowing using the visual analogue scale:** You will be asked by the study nurse to swallow and place a line through the scale to indicate the degree of difficulty you are experiencing with swallowing, a line to the left means it is not swollen and a line to the right hand end means it is very swollen.
- **Consumer Questionnaire:** You will be asked set questions about the effect of the lozenge at 5 intervals after taking the lozenge
- **Overall treatment rating:** You will be asked to complete this rating scale 2 hours after receiving your lozenge to indicate how effective the lozenge was for your sore throat.

You will also be asked about the presence of any symptoms or complaints e.g. side effects, during this 2 hour visit and these will be recorded by the study nurse/doctor. You will be given a patient diary to record symptoms or complaints and any medication taken up to 24 hours after taking the lozenge. You will leave the clinic after the 2 hour visit with your patient diary and you will be advised to take care over the next two hours with cold and hot food and drink to prevent any possible burns as you may have received the lozenge that contains lidocaine, the local anaesthetic.

Follow-up Telephone Call

One of the trained study team members will phone you 1-3 days after you have taken the lozenge. They will review your patient diary with you and ask you if you have recorded any symptoms (other than having a sore throat) or complaints since your last visit and whether you have recorded taking any medication. Any information you have recorded will be transferred by the study team member into the case report form (CRF) during the telephone call.

Expenses and Payments

You will receive an inconvenience payment of £50 when both the study visit and the study follow up phone call have been fully completed. This will cover travel costs and any other expenses you may incur as a result of taking part in this study.

What will I have to do?

If you take part in this study you must agree to take your medication as instructed by the clinic staff.

What is the drug being tested?

Strepsils Plus and Strepsils Extra are being tested to see if one works better than the other. Strepsils Plus lozenge containing 0.6mg amylmetacresol BP, 1.2 mg 4-Dichlorobenzyl alcohol have antiseptic properties, and 10mg Lidocaine Hydrochloride (a local anaesthetic) and Strepsils Extra Lozenge containing 2.4mg Hexylresorcinol (which has antiseptic and anaesthetic properties).

It is important that you tell the clinic staff if you are already taking part in any other studies. If so, you will not be allowed to take part in this study. It is important that you tell your study doctor what medications (prescribed or over the counter), or herbal products you are taking. You must not take any other experimental (research) drugs during the study.

It is important that you are available for the follow up phone call from the study team member 1-3 days after you have taken the lozenge.

You will be given an emergency card. It will be the size of a credit card and it will contain information that is needed in the event of an emergency. It will indicate you are a patient taking part in a study. You should carry this with you at all times. Please

ensure that you show this card during any visit to your GP (if he/she is not your study doctor), pharmacist, hospital clinic or any Accident and Emergency (A&E) department.

In the event of an emergency appropriate action will be taken by the study doctor in liaison with the company organising and sponsoring this study (Reckitt Benckiser Healthcare (RB), UK Limited)

What are the alternative treatments?

There are other preparations treatments available to treat sore throats. Your study doctor can discuss these treatments with you.

What are the possible disadvantages of taking part?

Possible side-effects that have been noted from some people who received Strepsils lozenges include occasional hypersensitivity reactions e.g. allergic reactions. You should not take part in the study if you are allergic to the product or any of the ingredients in the product. Your study doctor will discuss the product and the ingredients with you and if become concerned while taking part in the study you should contact your doctor.

It is possible that no therapeutic or other direct health benefits may result during or following completion of this study.

Women of childbearing potential must be using an effective form of contraception in order to participate in this study (e.g. the contraceptive pill, hormonal implant or topical patch or an intrauterine device). Pregnant and breastfeeding women, or women planning to get pregnant should not take part in this study. And will be required to take a pregnancy test before they take part.

If you do become pregnant during the course of the study, you must tell your study doctor **immediately** so appropriate action can be discussed. The company carrying out this trial may wish to follow up your pregnancy until its completion, should you fall pregnant during the course of the study. .

What are the side effects of any treatment received when taking part?

There are no known side effects from the treatments apart from a possible allergic reaction mentioned above.

Harm to the unborn child

There is a lack of evidence of safety of the lozenges in pregnancy, however the lozenges have been in use for many years and no ill consequences have been noted. However as with all medications caution should be taken during pregnancy and breastfeeding and for this reason we are not including these women in the study.

What are the possible benefits of taking part?

This study is being carried out to assess the efficacy (effectiveness) of Strepsils Plus and Strepsils Extra in patients with sore throat associated with an upper respiratory tract infection. We cannot promise the study will help you but the information we get from this study may help improve the treatment of people with sore throats.

What happens when the research study stops?

Sometimes during research new things are found out about the research medicine. If this occurs, your study doctor or the study sponsor, Reckitt Benckiser may withdraw you from the study at any time if it is thought unsafe or inappropriate for you to continue or if you find it difficult to follow the study instructions. Your future medical treatment will not be affected. After study participation has ended,

Serious medical events may be followed up and reported for a period of time. Once the study is complete, arrangements for your care will be discussed with you and will not differ from the usual standard care you receive.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

<u>This completes Part 1</u>

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

PART 2

What if relevant new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your study doctor will tell you about it and discuss with you whether you should continue in the study. If you decide not to carry on, your study doctor will make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an agreement outlining the discussion you have had.

On receiving new information your study doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What will happen if I don't want to carry on with the study?

You will be free to withdraw from the study at any time. As this is a very short study this will not have any impact for you with regards to follow up.

What if there is a problem?

Complaints:

If you have a concern about any aspect of this study, you should contact your Study Doctor or alternatively the Practice Manager, Tel: xxx xxxxxxxx who will do his/her best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the GP practice.

Harm:

The Sponsor will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

The sponsor will pay compensation where the injury probably resulted from:-

- A drug being tested or administered as part of the trial protocol
- Any test or procedure you received as part of the trial

Any payment would be without legal commitment (please ask if you require more information on this).

We would not be bound by these guidelines to pay compensation where (amongst other reasons):

- The injury resulted from a drug or procedure outside the trial protocol
- The protocol was not followed

Will my taking part in this study be kept confidential?

All personal information collected during the study will be kept strictly confidential, coded, protected and stored in accordance with the Data Protection Act 1998. It will be used only for the research and for submission to Regulatory Authorities in an anonymous form i.e. they will not be able to identify you. Your information will be identified by a number, possibly your initials and date of birth, but not your full name. All information about you which leaves the study site will not be traced back to you. The study doctor is the only one that holds a list to link the subject identity to the data collected. Any transfer of this information will be done according to the rules and regulations protecting personal information.

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the company sponsoring the study and the company organizing the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty. Clinical data may also be sent to Reckitt Benckiser Healthcare and to its associated companies some of which are based outside the European Union (EU) where data protection laws are not as comprehensive but the company will take all reasonable steps to protect your privacy.

You have a right to see and copy your personal health information related to the research study for as long as the research institution holds this information. You have the right to obtain updated information about what data is recorded as well as the right to require corrections of errors. However, to ensure the scientific integrity of the study you will not be able to review some of your personal health information related to the study, until after the study has been completed.

As a matter of course, your G.P. will be informed that you are taking part in this study unless you request otherwise.

What will happen to the results of the research study?

Reckitt Benckiser analyse the clinical data during and after the trial to assess the medication and to produce reports. If you withdraw consent from the study, no new data will be added to the database, however all data collected up to that time point will be used. The results may be published in the scientific press and may be submitted to government authorities. Any information about you, which leaves the

clinic, may include your initials and date of birth but not your full name or address. The study may be published in a medical journal in an anonymised form.

Who is organising and funding the research?

Reckitt Benckiser, the healthcare company that makes Strepsils, are sponsoring this study. They are based in Hull, UK. All the costs of the study (medicines, visits, tests) will be paid for by the Sponsor. The clinic involved in the study will receive these funds as necessary to cover the cost of carrying out the study.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by the xxx Ethics Committee based in Northern Ireland.

Further Information and contact details

Should you have additional questions about this study or advice as to whether you take part or not please contact your study doctor or nurse.

If you are unhappy about the study please contact the practice manager/manageress.

In an emergency please contact the number given below.

Study Doctor:	
Study Nurse:	
Practice Manager/Manageress	
GP Practice Address and telephone number:	
Emergency contact number:	

Thank you for reading this information sheet

<<PRINT ONTO GP PRACTICE HEADED PAPER>>

CONSENT FORM

Study Title:	A multi centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.
Protocol Number:	TH1017
Patient Identification number	
Name of Research Doctor and site	
Contact telephone number:	

Please read the following statements and initial each box against each statement and sign and date this page.

Please Initial Box

1. I confirm that I have read and understood the information sheet Version 1 Dated 29th November 2010 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by individuals from Reckitt Benckiser Healthcare, from regulatory authorities or from the HSC Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. I agree that data about me relating to this study may be sent to countries that do not have data protection laws similar to those in the UK.	

5. I agree to my GP being informed of my participation in the study.	
6. I have received a copy of this Participant Information Sheet and Consent Form to keep and I agree to take part in the above study.	

……..	.....	.....
Name of PATIENT (Please Print)	Date	Signature

…….	……..	……..……....
Name of INVESTIGATOR (Please Print)	**Date**	Signature

When completed, one copy of this document will be given to the patient; one copy will be kept in the patients' medical notes and the original document will be retained in the study site file.

Patient Information and Consent Form V2 dated 16th March 2011

<<PRINT ONTO GP PRACTICE HEADED PAPER>>

PARTICIPANT INFORMATION SHEET AND CONSENT FORM

Strepsils Plus and Strepsils Extra Efficacy study

Study Title:	A multi centre,, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.

Invitation to take part

We would like to invite you to take part, voluntarily in our research study. The study is looking at two treatments, Strepsils Plus lozenge containing 0.6mg amylmetacresol BP , 1.2 mg 4-Dichlorobenzyl alcohol (a mild antiseptic) and 10mg Lidocaine Hydrochloride (a mild anaesthetic) and Strepsils Extra Lozenge containing 2.4mg Hexylresorcinol (a mild antiseptic and anaesthetic) which are currently indicated for the relief of symptoms that may accompany mouth and throat infection. Before you decide if you would like to take part or not, we would like you to understand why the research is being done and what it will involve for you. Please take the time to read the following information carefully. Ask your study doctor if there is anything that is not clear or if you would like information. Talk to others about the study if you wish. Take time to decide whether or not you want to take part. If you do decide to take part in the study after reading this information you will be asked to complete, sign and date the attached consent form and to keep it as a useful reference.

This information sheet is split into two parts.

Part 1 tells you the purpose of the study and what will happen to you if you take part

Part 2 gives you more information on the conduct of the study.

PART 1

What is the purpose of the study?

A sore throat can be caused by a virus or bacterial infection and will generally cause inflammation of the tonsils and the surrounding area that cause the symptoms we associate with sore throats.

The primary aim of this study is to determine the pain-relieving effect of two different Strepsils lozenges in patients with a sore throat due to an upper respiratory tract

infection compared to a placebo lozenge (A placebo is commonly called a 'dummy pill' as it contains no active ingredients. It's purpose is to act as a control, and in the case of this study will account for the lubricating effects on a sore throat of sucking a sugar based sweet). This study will also provide additional information on the acceptability of the two lozenges from questionnaires about the lozenges.

The study will require a 2 hour stay in the GP surgery following your initial appointment. A Follow up phone call will take place 1-3 days after you have taken the lozenge to check if you had any adverse effects and if you needed to take any additional treatment. There will be a total of 190 patients recruited into this study, all of which will be recruited in Northern Ireland.

Why have I been invited?

You have been invited to take part in the study because you are aged between 18 and 75 and you have a sore throat which started within the past 4 days. You may be responding to a poster you have seen in the pharmacy or your own GP clinic. There is a list of reasons why you may not be suitable to enter the study. If you are not suitable for the study, the reasons will be discussed with you by the clinic staff either on the phone or at the GP clinic.

Do I have to take part?

Taking part in this study is entirely voluntary. It is up to you to decide whether or not to take part. If you agree to take part we will ask you to sign a consent form. You are free to withdraw from the study at any time without giving a reason. This will not affect the standard of care you receive. You will also be given a copy of this information sheet and consent form to keep. If you agree, your GP may be informed that you have agreed to take part in the study

What will happen to me if I take part?

Your participation in the study may be a maximum of 5 days (from initial visit to follow up phone call if your initial visit is not the day you are eligible to enter the study) .However, if your initial visit and study entry occur on the same day, your maximum participation time will be 3 days. The first visit will take around 2.5 hours depending on your medical history and the time the study nurse will take to instruct you on how to complete the study questionnaires. The follow up phone call will take around 7-10 minutes. We plan to complete the study by April 2011.

This is a "randomised study" which means you will be randomly assigned to one of the 3 treatment groups below. To find out which treatment is best for giving pain relief we need to make comparisons. We put people into groups and give each group a

different treatment by chance. A total of 190 patients will be randomly allocated into one of three treatment groups as follows:

- One group of patients (third of total patients) will receive a Strepsils Plus lozenge only.
- One group of patients (third of total patients) will receive a Strepsils Extra lozenge only.
- One group of patients (third of total patients) will receive placebo (dummy) lozenge. (A dummy treatment which contains no active ingredient).

The study is also "double blind". This means that neither you nor your study doctor will know which treatment group you are in (although, if your study doctor needs to find out they can do so).

Screening

If you have responded to an advertisement or have seen a poster in your local pharmacy you will have been asked some questions over the phone already by a trained representative to see if you may meet the requirements for the study.

Screening / Day 1 Visit

At this visit you will now be asked to read the patient information sheet and ask any questions you may have and then if you wish to take part in the study you will be asked to sign the consent form before any study assessments can be performed. Your doctor will ask you about your medical history and current medical status. If you are female and able to have children, you will be asked some questions about the possibility of pregnancy and contraception and you will have a pregnancy test performed using a sample of urine. All this information will help determine if you are suitable for the study. The doctor will examine your throat and check for symptoms of an upper respiratory tract infection and how long you have had a sore throat. You will be asked to describe the nature of your sore throat by answering specific questions and the doctor will also conduct a physical examination of the eyes, ears, nose, mouth and lungs and complete an assessment of your sore throat called a Tonsillo-Pharyngitis Assessment (TPA). The completion of the TPA ensures that only patients with acute tonsillopharyngitis are recruited into the study. The doctor will ask you whether you have taken any prohibited therapies such as sore throat treatments, or boiled sweets earlier that day. If you have answered yes to this, the doctor or nurse may ask you to return to the clinic at a later time in order that the effects of any prior treatment have worn off. This is called a washout period. The specific washout period for this study will depend on when you last took a treatment that is not allowed. These are as follows:

Washout period of 2 hours if you have taken: Medicated sweets, pastilles, spray or any product with a soothing property such as boiled sweets

Washout period of 4 hours if you have taken: Sore throat medication containing a local anaesthetic

Washout period of 8 Hours if you have taken: Any analgesic (pain relieving), antipyretic (fever relieving e.g. paracetamol) or cold medication (e.g. hot drink remedies or throat lozenges)

Washout period of 24 hours if you have taken: Any longer acting or slow release medications (eg Piroxicam and Naproxen, both anti-inflammatory treatments during the previous 24 hours:

If you are suitable to take part in the study you will be asked to sit in a quiet area in the clinic during the treatment and follow up time. You will be asked to answer questions about your throat and the lozenge and you will complete 5 rating scales at various time points over the 2 hours. You will also be asked to complete 2 questionnaires at these same time points over the 2 hour period. The clinic staff will instruct you on how to complete these questionnaires and they will remain with you at all times. You will be asked to remain quiet to ease your throat and also not to discuss your lozenge treatment with any other patients who may also be in the study at the same time. You can ask any questions you want during this time to the trained study team nurse. You will not be allowed to consume any food, drinks, throat lozenges (aside from the trial medication), sweets, chewing gum or any other medication during this 2 hour period. No smoking will be allowed during this visit.

Administration of Study Medication

The lozenges used in this study will not be matched for colour and therefore in order to ensure neither the patient, the doctor or the nurse who stays with you during the treatment visit knows which lozenge you receive you will be asked to wear a blindfold at the time you take your lozenge. You will be provided with one lozenge in the clinic by a member of the clinical team that will not be involved in helping you complete any of the study assessments. They will observe you putting the lozenge into your mouth. Once the lozenge is placed in your mouth you may remove the blindfold. You will be asked to suck the lozenge slowly and move it round your mouth until it dissolves. You should not chew or crunch your lozenge. You will be asked to swallow and then complete 5 rating scales one minute before taking the lozenge and then at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes after receiving your first lozenge. You

will be asked to complete a consumer questionnaire at 1, 5, 20, 60 and 120 minutes and an overall treatment rating questionnaire at 120 minutes after you have taken the lozenge. The rating scales/questionnaires include the following:

- **Throat Soreness Scale:** You will be asked by the study nurse to swallow and then circle a number on the scale that shows how sore your throat is when you swallow.
- **Throat Numbness:** You will be asked to circle the phrase that best describes the numbness of your throat.
- **Sore throat relief:** You will be instructed by the study nurse to 'Tick the phrase that best describes the relief of your sore throat'.
- **Swollen Throat Scale using the visual analogue scale:** You will be asked to swallow and place a line through the scale to indicate how swollen your throat is (not swollen on the left and very swollen on the right of the scale)
- **Difficulty in swallowing using the visual analogue scale:** You will be asked by the study nurse to swallow and place a line through the scale to indicate the degree of difficulty you are experiencing with swallowing, a line to the left means it is not swollen and a line to the right hand end means it is very swollen.
- **Consumer Questionnaire:** You will be asked set questions about the effect of the lozenge at 5 intervals after taking the lozenge
- **Overall treatment rating:** You will be asked to complete this rating scale 2 hours after receiving your lozenge to indicate how effective the lozenge was for your sore throat.

You will also be asked about the presence of any symptoms or complaints e.g. side effects, during this 2 hour visit and these will be recorded by the study nurse/doctor. You will be given a patient diary to record symptoms or complaints and any medication taken up to 24 hours after taking the lozenge. You will leave the clinic after the 2 hour visit with your patient diary and you will be advised to take care over the next two hours with cold and hot food and drink to prevent any possible burns as you may have received the lozenge that contains lidocaine, the local anaesthetic.

Follow-up Telephone Call

One of the trained study team members will phone you 1-3 days after you have taken the lozenge. They will review your patient diary with you and ask you if you have recorded any symptoms (other than having a sore throat) or complaints since your last visit and whether you have recorded taking any medication. Any information you have recorded will be transferred by the study team member into the case report form (CRF) during the telephone call.

Expenses and Payments

You will receive an inconvenience payment of £50 when both the study visit and the study follow up phone call have been fully completed. This will cover travel costs and any other expenses you may incur as a result of taking part in this study.

What will I have to do?

If you take part in this study you must agree to take your medication as instructed by the clinic staff.

What is the drug being tested?

Strepsils Plus and Strepsils Extra are being tested to see if one works better than the other. Strepsils Plus lozenge containing 0.6mg amylmetacresol BP, 1.2 mg 4-Dichlorobenzyl alcohol have antiseptic properties,and 10mg Lidocaine Hydrochloride (a local anaesthetic) and Strepsils Extra Lozenge containing 2.4mg Hexylresorcinol (which has antiseptic and anaesthetic properties).

It is important that you tell the clinic staff if you are already taking part in any other studies. If so, you will not be allowed to take part in this study. It is important that you tell your study doctor what medications (prescribed or over the counter), or herbal products you are taking. You must not take any other experimental (research) drugs during the study.

It is important that you are available for the follow up phone call from the study team member 1-3 days after you have taken the lozenge.

You will be given an emergency card. It will be the size of a credit card and it will contain information that is needed in the event of an emergency. It will indicate you are a patient taking part in a study. You should carry this with you at all times. Please ensure that you show this card during any visit to your GP (if he/she is not your study doctor), pharmacist, hospital clinic or any Accident and Emergency (A&E) department.

In the event of an emergency appropriate action will be taken by the study doctor in liaison with the company organising and sponsoring this study (Reckitt Benckiser Healthcare (RB), UK Limited)

What are the alternative treatments?

There are other preparations treatments available to treat sore throats. Your study doctor can discuss these treatments with you.

What are the possible disadvantages of taking part?

Possible side-effects that have been noted from some people who received Strepsils lozenges include occasional hypersensitivity reactions e.g. allergic reactions. You should not take part in the study if you are allergic to the product or any of the ingredients in the product. Your study doctor will discuss the product and the ingredients with you and if become concerned while taking part in the study you should contact your doctor.

It is possible that no therapeutic or other direct health benefits may result during or following completion of this study.

Women of childbearing potential must be using an effective form of contraception in order to participate in this study (e.g. the contraceptive pill, hormonal implant or topical patch or an intrauterine device). Pregnant and breastfeeding women, or women planning to get pregnant should not take part in this study. And will be required to take a pregnancy test before they take part.

If you do become pregnant during the course of the study, you must tell your study doctor **immediately** so appropriate action can be discussed. The company carrying out this trial may wish to follow up your pregnancy until its completion, should you fall pregnant during the course of the study.

What are the side effects of any treatment received when taking part?

There are no known side effects from the treatments apart from a possible allergic reaction mentioned above.

Harm to the unborn child

There is a lack of evidence of safety of the lozenges in pregnancy, however the lozenges have been in use for many years and no ill consequences have been noted. However as with all medications caution should be taken during pregnancy and breastfeeding and for this reason we are not including these women in the study**.**

What are the possible benefits of taking part?

This study is being carried out to assess the efficacy (effectiveness) of Strepsils Plus and Strepsils Extra in patients with sore throat associated with an upper respiratory

tract infection. We cannot promise the study will help you but the information we get from this study may help improve the treatment of people with sore throats.

What happens when the research study stops?

Sometimes during research new things are found out about the research medicine. If this occurs, your study doctor or the study sponsor, Reckitt Benckiser may withdraw you from the study at any time if it is thought unsafe or inappropriate for you to continue or if you find it difficult to follow the study instructions. Your future medical treatment will not be affected. After study participation has ended,

Serious medical events may be followed up and reported for a period of time. Once the study is complete, arrangements for your care will be discussed with you and will not differ from the usual standard care you receive.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in this study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

<u>This completes Part 1</u>

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

PART 2

What if relevant new information becomes available?

Sometimes we get new information about the treatment being studied. If this happens, your study doctor will tell you about it and discuss with you whether you should continue in the study. If you decide not to carry on, your study doctor will

make arrangements for your care to continue. If you decide to continue in the study you will be asked to sign an agreement outlining the discussion you have had.

On receiving new information your study doctor might consider it to be in your best interests to withdraw you from the study. He/she will explain the reasons and arrange for your care to continue.

If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What will happen if I don't want to carry on with the study?

You will be free to withdraw from the study at any time. As this is a very short study this will not have any impact for you with regards to follow up.

What if there is a problem?

Complaints:

If you have a concern about any aspect of this study, you should contact your Study Doctor or alternatively the Practice Manager, Tel: xxx xxxxxxxx who will do his/her best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the GP practice.

Harm:

The Sponsor will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

The sponsor will pay compensation where the injury probably resulted from:-

- A drug being tested or administered as part of the trial protocol
- Any test or procedure you received as part of the trial

Any payment would be without legal commitment (please ask if you require more information on this).

We would not be bound by these guidelines to pay compensation where (amongst other reasons):

- The injury resulted from a drug or procedure outside the trial protocol

- The protocol was not followed

Will my taking part in this study be kept confidential?

All personal information collected during the study will be kept strictly confidential, coded, protected and stored in accordance with the Data Protection Act 1998. It will be used only for the research and for submission to Regulatory Authorities in an anonymous form i.e. they will not be able to identify you. Your information will be identified by a number, possibly your initials and date of birth, but not your full name. All information about you which leaves the study site will not be traced back to you. The study doctor is the only one that holds a list to link the subject identity to the data collected. Any transfer of this information will be done according to the rules and regulations protecting personal information.

If you join the study, some parts of your medical records and the data collected for the study will be looked at by authorised persons from the company sponsoring the study and the company organizing the research. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and we will do our best to meet this duty. Clinical data may also be sent to Reckitt Benckiser Healthcare and to its associated companies some of which are based outside the European Union (EU) where data protection laws are not as comprehensive but the company will take all reasonable steps to protect your privacy.

You have a right to see and copy your personal health information related to the research study for as long as the research institution holds this information. You have the right to obtain updated information about what data is recorded as well as the right to require corrections of errors. However, to ensure the scientific integrity of the study you will not be able to review some of your personal health information related to the study, until after the study has been completed.

As a matter of course, your G.P. will be informed that you are taking part in this study unless you request otherwise.

What will happen to the results of the research study?

Reckitt Benckiser analyse the clinical data during and after the trial to assess the medication and to produce reports. If you withdraw consent from the study, no new data will be added to the database, however all data collected up to that time point will be used. The results may be published in the scientific press and may be

submitted to government authorities. Any information about you, which leaves the clinic, may include your initials and date of birth but not your full name or address. The study may be published in a medical journal in an anonymised form.

Who is organising and funding the research?

Reckitt Benckiser, the healthcare company that makes Strepsils, are sponsoring this study. They are based in Hull, UK. All the costs of the study (medicines, visits, tests) will be paid for by the Sponsor. The clinic involved in the study will receive these funds as necessary to cover the cost of carrying out the study.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and approved by the Research Ethics Committee based in Northern Ireland.

Further Information and contact details

Should you have additional questions about this study or advice as to whether you take part or not please contact your study doctor or nurse.

If you are unhappy about the study please contact the practice manager/manageress.

In an emergency please contact the number given below.

Study Doctor:	
Study Nurse:	
Practice Manager/Manageress	
GP Practice Address and telephone number:	

Emergency contact number:	

Thank you for reading this information sheet

<<PRINT ONTO GP PRACTICE HEADED PAPER>>

CONSENT FORM

Study Title:	A multi centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.
Protocol Number:	TH1017
Patient Identification number	
Name of Research Doctor and site	
Contact telephone number:	

Please read the following statements and initial each box against each statement and sign and date this page.

Please Initial Box

1. I confirm that I have read and understood the information sheet Version 2 Dated 16th March 2011 for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by individuals from Reckitt Benckiser Healthcare, from regulatory authorities or from the HSC Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. I agree that data about me relating to this study may be sent to countries that do not have data protection laws similar to those in the UK.	
5. I agree to my GP being informed of my participation in the study.	
6. I have received a copy of this Participant Information Sheet and Consent Form to keep and I agree to take part in the above study.	

……..	.....	.....
Name of PATIENT (Please Print)	Date	Signature

…….	……..	……..……..
Name of INVESTIGATOR (Please Print)	**Date**	Signature

When completed, one copy of this document will be given to the patient; one copy will be kept in the patients' medical notes and the original document will be retained in the study site file.

APPENDIX 16.1.4 LIST AND DESCRIPTION OF INVESTIGATORS AND OTHER IMPORTANT PARTICIPANTS IN THE STUDY

This appendix contains:

- Curriculum vita (CV) of:
  - Chief Investigator (1 page)
  - Principal Investigator(s) (7 pages)

- Table listing the names and affiliations of the individuals whose participation materially affected the conduct of the study, together with their role (2 pages).

Curriculum Vitae

Name:	Dr Damien McNally
Present Position: (Job title, department and organisation)	GP Partner, Ormeau Health Centre
Address: (Full work address)	Ormeau Health Centre 120 Ormeau Road Belfast BT7 2EB
Telephone number: Fax number: e-mail address	02890 320030 02890 278380 damienmcnally@doctors.org.uk
Qualifications:	MB, BCh, BAO, MRCGP, DRCOG, Diploma in Mental Health (QUB)
Professional registration: (Name of body, registration number and date of registration.)	GMC Registration – 4045760 Aug 1993
Previous Appointments/Experience: (Include previous appointments and other current appointments.)	Aug 93 - Aug 94: Pre Registration House Officer, Lagan Valley Hospital, Lisburn Aug 94 – Aug 96: SHO – A&E / General Surgery, Ards Hospital, Newtownards. Aug 96 – Feb 96: SHO – Medicine / Coronary Care, Ards Hospital, Newtownards Feb 96 – Aug 96: SHO – Obstetrics & Gynae, Downe Hospital, Downpatrick Aug 96 – Feb 97: SHO – Psychiatry, Ards Hospital, Newtownards Feb 97 – Aug 97: SHO – Paediatrics, Ulster Hospital, Dundonald Aug 97 – Aug 98: GP Registrar, North Parade Medical Centre, Belfast Aug 1998 –Jul 2003: GP Locum July 2003 – **present:** GP Principal, Ormeau Health Centre
Clinical Trial Experience and Training: (Summary of research experience, including the extent of your involvement. Refer to therapeutic areas rather than reference to specific sponsors or drugs. Detail any relevant training)	I have acted as a Principal Investigator on clinical trials, covering the following therapeutic areas COPD, Asthma, Hypertension, Diabetes, Cardiovascular Disease, Gastroenterology, Paediatric Dermatitis, Vaccines, Obesity and Winter Ailments. All clinical trials completed have been phase II, III & IV and all have been for blue chip pharmaceutical companies. I have acted as Chief Investigator in a Winter Ailment clinical trial – study paper published – Int J Clin Pract, January 2010, 64,2. 194-207 I have completed training on all aspects of clinical research i.e. ICH/GCP, study procedures, patient recruitment and consenting procedures, drug accountability and storage. Most recent GCP training – 15.7.2010 "INFORM" – EDC training – 10.7.2008. "RAVE" – EDC training – 25.11.2009.
Company/Regulatory Audits:	No company or regulatory audits to date, frequent and varied general practice audits conducted on an ongoing basis.
Date: __/__/____ (Day / Month / Year)	Signature:

Curriculum Vitae

Name:	Dr Paul Conn
Present Position: *(job title, department, organisation, start date)*	General Practitioner, Principal Oct 1988 - present
Address: (Full work address) **Email:**	Ballygomartin Group Practice 17 Ballygomartin Road Belfast BT13 3BW paulconn@doctors.org.uk
Telephone number:	028 90 716333
Qualifications:	MB, BCh, BAO, DRCOG, MRCGP, MRCPGP
Professional registration: *(Name of body, registration number and date of registration.)*	2832607
Previous Appointments/ Experience: *(Include all start/ end dates)*	Aug 1983 – Aug 1984 CHO, RVH, Belfast Aug 1984 – Jul 1987 SHO, RVH, Belfast Aug 1987 – Jul 1988 GP Registrar, Dunmurry Jul 1988 – Oct 1988 GP locum, various locations Oct 1988 -date GP partner, Ballygomartin Group Practice
Clinical Trial Experience and Training: *(Summary of research experience, including the extent of your involvement. Refer to therapeutic areas rather than to specific sponsors or drugs. Detail any relevant training and insert (most recent date of GCP Training)*	I have completed training on all aspects of clinical research i.e. ICH/GCP, study procedures, patient recruitment and consenting procedures, drug accountability and storage. The date on my most recent GCP training certificate is 8th Oct 2009
Company/Regulatory Audits:	Audit completed 6th-8th April 2009.
Date: 08/06/11 Day Month Year	**Signature:**

Template CV

Curriculum Vitae

Name:	Dr Malcolm McCaughey
Present Position: *(Job title, department, and organisation.)*	GP Principal, Randalstown Medical Practice Commenced Sept 1974
Address: (Full work address)	5 Neilsbrook Road Randalstown Co. Antrim BT41 3AE
Telephone number:	028 94 472575
Qualifications:	MB BCH, BAO, DRCOG, MRCGP, MICGP
Professional registration: *(Name of body, registration number and date of registration.)*	GMC No: 1373758 MDU No: 102084E Royal College No: 26430 BMA No: 1212583
Previous Appointments/Experience: *(Include previous appointments, current appointments and all start and end dates.)*	Aug 1972 – Aug 1974 JHO & SHO Craigavon Area Hospital Medicine, Surgery, Obstetrics & Gynaecology, Psychiatry, Geriatrics, Paediatrics and Cardiology
Clinical Trial Experience and Training: *(Summary of research experience, including the extent of your involvement. Refer to therapeutic areas rather than reference to specific sponsors or drugs. Detail any relevant training and include most recent date of GCP Training)*	Investigator in many studies since 1996 including OA studies, asthma study, diabetic studies, COPD, children's vaccination study, eczema study and IBS study. Attendance at various study specific training days. Completed training on all aspects of clinical research i.e. ICH/GCP, study procedures patient recruitment and consenting procedures, drug accountability and storage GCP training update completed: 19-Mar-09, previous GCP training was DEC2007 by Kristina Brown on behalf of Johnson& Johnson.
Company/Regulatory Audits:	Frequent and varied general practice audits conducted on an ongoing basis and Company audits x 3. MHRA GCP Inspection- May 2008
Date: 23 / 06 / 09 Day Month Year	**Signature:**

Curriculum Vitae

Name:	Dr Michael Redmond
Present Position: *(Job title, department, organisation, start date)*	GP Principal 1996 – present
Address: (Full work address)	Broughshane medical Practice 76 Main Street Broughshane BT42 4JP
Email:	bmptrial@hotmail.com
Telephone number:	02825 861214
Qualifications:	MBChB 1991 DRCOG 1993
Professional registration: *(Name of body, registration number and date of registration.)*	GMC Registration- 3560048
Previous Appointments/Experience: *(Include all start and dates)*	GP Training Lochgilphead Surgery Argyl, Scotland Aug 1994-July 1995 GP Training scheme West of Scotland. July 1992-Aug 1994 6 Months post in the following clinical areas. Obs & Gynae Lale of Leven Hospital Alexander, Scotland A&E Lale of leven Hospital Alexander, Scotland General Medicine County Hospital Oban, Scotland Psychiatry Argyll & Bute Hospital Lochgilphead Scotland
Clinical Trial Experience and Training: *(Summary of research experience, including the extent of your involvement. Refer to therapeutic areas (alike) that is specific substance or drugs. Detail only relevant training with most recent date of GCP Training)*	I have also participated in the Medevol GP research training program which includes training on all aspects of clinical research i.e. ICHGCP, study procedures, patient recruitment and consenting procedures. ICHGCP training completed: 22nd June 2010
Company/Regulatory Audits:	No company or regulatory audits to date, frequent and varied general practice audits conducted on an ongoing basis.
Date: 11/11/2011 Day Month Year	**Signature:**

Template CV

Curriculum Vitae

Name:	Nigel Hart
Present Position: *(Job title, department, organization, start date)*	General Practitioner (Partner) 2.7.2007 – present
Address: *(Full work address)*	Crossgar Surgery James Street Crossgar. BT30 9JU
Email:	n.hart@qub.ac.uk
Telephone number:	028 44830202
Qualifications:	MMedSc 2010, MD 2006, MRCGP 2003, DRCOG 2001, DCH 2001, MB BCH BAO 1999, BSc 1990.
Professional registration:	GMC 4618723
Previous Appointments/Experience: *(include all start and dates)*	Dec 07 – Current (Alongside GP Role in Crossgar Surgery) Senior Lecturer, Queen's University Belfast Nov 06 – Jun 07 Prison Medical Officer (Northern Ireland Prison Service) Aug 06 – Jun 07 Locum General Practitioner Aug 06 – Nov 07 Research Clinician Nov 05 – Current out of hours trainer for GP registers (North and West Urgent Care) Jan 05 – Current regular locum out of hours sessions (North and West Urgent Care) Nov 03 – Sep 06 Clinical Research Fellow (Dept of General Practice, Queen's University Belfast Aug 02 – Oct 03 Research Registrar (Dept of General Practice, Queen's University Belfast) Aug 00 – Jul 02 SHO post, Obs & Gynae, Paediatrics, Care of the elderly and A&E (Royal Group of Hospitals, Belfast)
Clinical Trial Experience and Training: *(Summary of research experience, including the extent of your involvement. Refer to therapeutic areas rather than to specific compounds or drugs. Detail any relevant training and insert most recent date of GCP Training)*	PI in 2 Clinical Trials covering the following Therapeutic Areas: Hypertension & CVD Primary Care Researchor Development Award from National R&D (November 2003) General Practice and Research Training (GPARTs) Award. R&D Northern Ireland (August 2002) Participant in application to R&D for funding of local Research Network in Stroke Medicine under the umbrella of Clinical Research Collaboration in Primary Care, 2005-06 I have completed training on all aspects of clinical research i.e. ICH/GCP, study procedures, patient consenting and recruitment procedures, drug accountability and storage. Date completed: 8th October 2008
Company/Regulatory Audits:	No company or regulatory audits to date, frequent and varied general practice audits conducted on an ongoing basis.
Date: 16/2/10 Day Month Year	**Signature:**

Template CV

Curriculum Vitae

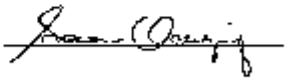
Name:	Dr Peter Stephen John Ryan
Present Position: *(Job title, department, organization, start date)*	GP Principal, Cherryvalley Group Practice 1 Apr 2003 - present
Address: *(Full work address)* **Email:**	Kings Square Kings Road Belfast BT5 7BP Peter.ryan@cvgp.gp.n-i.nhs.uk
Telephone number:	028 90 401 844
Qualifications:	MB BCh BAO MRCGP DRCOG DCH
Professional registration: *(Name of body, registration number and date of registration.)*	GMC Registration – 4331081 01 Aug 1997
Previous Appointments/Experience: *(Include all start/ end dates)*	2001-2003: Locum GP 2000-2001: GP Registrar, Belfast 1997-2000: General Practice Training, Whiteabbey Hospital, Antrim Area Hospital. Coleraine Hospital, Whiteabbey. Holywell 1996-1997: PRHO, Belfast City Hospital, Downe Hospital
Clinical Trial Experience and Training: *(Summary of research experience, including the extent of your involvement. Refer to therapeutic areas rather than to specific sponsors or drugs. Detail any relevant training and insert most recent date of GCP Training)*	I have completed training on all aspects of clinical research i.e. ICH/GCP, study procedures patient recruitment and consenting procedures, drug accountability and storage. The date on my most recent GCP training certificate is: 8th October 2009 Previous Clinical Trial experience - Principal Investigator in 4 Cardiovascular Trials (Hypertension, Angina/ Ischemic Heart disease. & CVD Prevention).
Company/Regulatory Audits:	No company or regulatory audits to date, frequent and varied general practice audits conducted on an ongoing basis.
Date: 13/12/09 Day Month Year	**Signature:**

Curriculum Vitae

Name:	Gerry McKeague
Present Position: *(plus title, department, organisation, start date)*	GP Partner, UHCQ Apr 2009 - present
Address: *(Full work address)* **Email:**	University Health Centre at Queen's 5 Lennoxvale Belfast BT9 5BY g.mckeague@hotmail.com
Telephone number:	028 9097 5551
Qualifications:	MB, BAO, BCh, MRCGP, DCH
Professional registration: *(Name of body, registration number and date of registration.)*	GMC 4118693 July 1997
Previous Appointments/ Experience: *(Include all start/ end dates)*	GP in Australia – Victoria, July 2003 – Sept 2005 Locum GP in Northern Ireland Jan 2006 – Dec 2006 Salaried GP, University Health Centre at Queen's Sept 2007 – Mar 2009 University Health Centre at Queen's GP Partner, Apr 2009 - present
Clinical Trial Experience and Training: *(Summary of research experience, including the extent of your involvement. Refer to therapeutic areas rather than to specific sponsors or drugs. Detail any relevant training and insert most recent date of GCP Training)*	I have completed training on all aspects of clinical research i.e. ICH/GCP, study procedures, patient recruitment and consenting procedures, drug accountability and storage. The date on my most recent GCP training certificate is 5th May 2010
Company/Regulatory Audits:	As per practice
Date: 12 / 6 / 2011 Day Month Year	**Signature:**

Template CV

Curriculum Vitae

Name:	Dr Sean Haigney
Present Position: *(Job title, department, organization, start date)*	GP, Mount Oriel Medical Centre June 2000- present
Address: (Full work address) **Email:**	Mount Oriel Medical Centre 2 Mount Oriel Belfast BT8 7HR sean.haigney@yahoo.co.uk
Telephone number:	02890701653
Qualifications:	MB BAO BCH MRCGP DCH DRCOG
Professional registration: *(Name of body, registration number and date of registration.)*	4108249
Previous Appointments/Experience: *(Include all start/ end dates)*	**1994- 1995:** JHO, Newtownards Hospital **1995- 1997:** SHO, 2 year GP Rotation, Daisy Hill Hospital, Newry **1997- 1998:** GP Registrar Church Street Surgery, Newtownards **1998- 2000:** GP Locum Mount Oriel and South East Belfast Doctors on Call. **Oct 2000- Dec 2005:** Research Physician, Bio-Kinetic Europe Ltd
Clinical Trial Experience and Training: *(Summary of research experience, including the extent of your involvement. Refer to therapeutic areas rather than to specific sponsors or drugs. Detail any relevant training and insert most recent date of GCP Training)*	I have considerable clinical research experience working as a co-investigator over a five year period in a regional phase 1 CRO unit. I have experience in several therapeutic areas including analgesia, rheumatoid arthritis, virology, diabetes, hypertension, cardiovascular and HRT. I have completed training on all aspects of clinical research i.e. ICH/GCP, study procedures, patient consenting and recruitment procedures, drug accountability and storage. The date on my most recent GCP training certificate is: 8th October 2008
Company/Regulatory Audits:	I was involved in a number of regulatory inspections and sponsor audits when I acted as co-investigator. I am currently involved in a number of frequent and varied general practice audits conducted on an ongoing basis.
Date: 12 | 1 | 12 | 09 | Day Month Year	**Signature:** 

Template CV

Names and Affiliations of Key Individuals in the Study

Title and Name	Qualifications	Job Title	Work Address	Study Role
Ms. Emma Field	BSc (Hons)	Clinical Project Manager	Reckitt Benckiser, Healthcare UK Ltd, Dansom Lane, Hull, HU8 7DS	Clinical Project Manager
Dr. Phil Berry	MB, ChB, MPH	Global Medical Director	Reckitt Benckiser, Healthcare UK Ltd, Dansom Lane, Hull HU8 7DS	Study Physician
Dr. Sue Aspley	BSc (Hons), PhD	R&D Manager, Clinical Health Care	Reckitt Benckiser, Healthcare UK Ltd, Dansom Lane, Hull HU8 7DS	Senior Statistician
Mr. Mike A Goulder	BSc (Hons)	Senior Statistician	World Wide C,inical Trials, Newton Centre, Nottingham Science and Technology Park, Nottingham	Senior Statistician
Mrs. Colette Donaghy	BA (Hons), RGN, MSc	Chief Operating Officer	Medevol Ltd, The Innovation Centre, NI Science Park, Belfast BT3 9DT	CRO representative/ Report Author
Dr. Damien Mc Nally	MB, BCh, BAO, MRCGP, DRCOG, Diploma in Mental Health (QUB)	General Practitioner	Ormeau Health Centre, 120 Ormeau road, Belfast, BT7 2EB	Chief Investigator
Dr. Paul Conn	MB, BCh, BAO, DRCOG, MRCGP, MRCPGP	General Practitioner	Ballygomartin Group Practice, 17 Ballygomartin Road, Belfast, BT13 3BW	Principal Investigator
Dr. Malcolm	MB BCH, BAO, DRCOG, MRCGP,	General Practitioner	Randalstown Medical Practice, 5 Neillsbrook	Principal Investigator

Mc Caughey	MICGP		Road, Randalstown, BT41 3AE	
Dr. Michael Redmond	MBChB, DRCOG	General Practitioner	Broughshane Medical Practice, 76 Main Street, Broughshane, Ballymena BT42 4JP	Principal Investigator
Dr. Nigel Hart	MD,MRCGP,DRCOG, DCH,MB BCH,BAO BSc	General Practitioner	Crossgar Surgery,James Street, Crossgar, BT30 9JU	Principal Investigator
Dr. Peter Ryan	MB BCh BAO MRCGP DRCOG DCH	General Practitioner	Cherryvalley Group Practice, Kings Square, Kings Road, Belfast BT5 7BP	Principal Investigator
Dr. Gerry Mc Keague	MB, BAO, BCh, MRCGP, DCH	General Practitioner	University Health Centre at Queen's, 5 Lennoxvale, Belfast, BT9 5BY	Principal Investigator
Dr. Sean Haigney	MB BAO BCH, MRCGP DCH DRCOG	General Practitioner	Mount Oriel Medical Centre,2 Mount Oriel, Belfast BT8 7HR	Principal Investigator

APPENDIX 16.1.5 SIGNATURE OF CO-ORDINATING INVESTIGATOR

Reckitt Benckiser

PRINCIPAL INVESTIGATOR'S SIGNATURE

Study Number: TH1017

Report Title: A multi centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.

Phase: IV

Principal Investigator:

By my signature below, I hereby state that I have read this report and confirm that, to the best of my knowledge, it accurately describes the conduct and results of the study. I agree its conclusions and do not wish to make an additional statement regarding the safety of the product under test.

Damien McNally — 15th Sept 2011

Dr. Damien McNally — Date

MB,BCh,BAO, MRCGP,DRCOG,Diploma in Mental Health

Principal in General Practice

Ormeau Health Centre, 120 Ormeau Road, Belfast BT7 2EB

Tel no: - 028 90326030

APPENDIX 16.1.6 LISTING OF PATIENTS RECEIVING TEST DRUG(S) FROM SPECIFIC BATCHES, WHERE MORE THAN ONE BATCH WAS USED.

This appendix is not relevant for the present study because only one batch of each study medication was used.

APPENDIX 16.1.7 RANDOMISATION SCHEME AND CODES (PATIENT IDENTIFICATION AND TREATMENT ASSIGNED)

Randomization Method

Drug supplies were randomised by RB IMSU according to a computer-produced randomisation schedule. The randomisation schedule was checked by a statistician not involved in the analysis of the study. On entry, patients were allocated a unique patient number in numerical sequence. Issue of the study drug in this sequence ensured randomisation.

RB IMSU and the RB statistician held the master code for the randomisation schedule. The code was only to be broken for an individual patient in an emergency such as a serious adverse event that required knowledge of what study drug was taken in order that the SAE could be treated appropriately.

Table of Randomization Codes (8 pages)

- see next page

Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

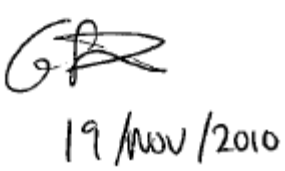
Centre 1	
Patient number	**Treatment**
001	X
002	Z
003	X
004	Y
005	Y
006	Z
007	Z
008	Y
009	X
010	Y
011	X
012	Z
013	Y
014	X
015	X
016	Z
017	Z
018	Y
019	Z
020	Y
021	X
022	Z
023	X
024	X
025	Z
026	Y
027	Y
028	X
029	Z
030	Y
031	X
032	Z
033	Y
Page 1 of 8	

19/NOV/2010

Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

Centre 2	
Patient number	**Treatment**
034	Z
035	X
036	Y
037	X
038	Z
039	Y
040	X
041	Z
042	Y
043	Y
044	Z
045	X
046	X
047	Y
048	Z
049	Y
050	X
051	Z
052	Z
053	Y
054	X
055	Y
056	X
057	Z
058	Y
059	Z
060	X
061	Z
062	Y
063	X
064	Y
065	X
066	Z
Page 2 of 8	



Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

Centre 3	
Patient number	**Treatment**
067	Y
068	Z
069	X
070	Z
071	Y
072	X
073	X
074	Z
075	Y
076	Y
077	Z
078	X
079	Z
080	X
081	Y
082	Z
083	Z
084	X
085	Y
086	Y
087	X
088	Z
089	Y
090	Y
091	Z
092	X
093	X
094	X
095	Z
096	Y
097	Z
098	Y
099	X
Page 3 of 8	

GR
19/Nov/2010

Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

Centre 4	
Patient number	**Treatment**
100	X
101	Y
102	Z
103	X
104	X
105	Y
106	Z
107	Y
108	Z
109	Z
110	Z
111	Y
112	X
113	Y
114	X
115	Z
116	X
117	Z
118	X
119	Y
120	Y
121	X
122	Y
123	Z
124	Y
125	Z
126	X
127	Z
128	Z
129	Y
130	Y
131	X
132	X
Page 4 of 8	

Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

Centre 5	
Patient number	**Treatment**
133	Z
134	Y
135	X
136	X
137	Y
138	Z
139	X
140	Z
141	Y
142	Z
143	X
144	Y
145	Y
146	X
147	Z
148	Z
149	X
150	X
151	Z
152	Y
153	Y
154	Z
155	X
156	Z
157	X
158	Y
159	Y
160	X
161	Z
162	Y
163	Z
164	Y
165	X
Page 5 of 8	

19/NOV/2010

Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

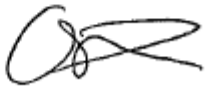
Centre 6	
Patient number	**Treatment**
166	X
167	Z
168	X
169	Y
170	Y
171	Z
172	Z
173	Y
174	X
175	Z
176	X
177	Y
178	X
179	Y
180	Z
181	Z
182	Z
183	X
184	Y
185	Y
186	X
187	X
188	Z
189	Y
190	Y
191	Z
192	X
193	Y
194	X
195	Z
196	X
197	Z
198	Y
Page 6 of 8	

19/NOV/2010

Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

Centre 7	
Patient number	**Treatment**
199	Y
200	Z
201	X
202	X
203	Y
204	Y
205	Z
206	Z
207	X
208	Y
209	Z
210	X
211	Y
212	Z
213	X
214	Y
215	Z
216	X
217	X
218	Y
219	Z
220	X
221	Y
222	Z
223	X
224	Z
225	Z
226	Y
227	Y
228	X
229	Y
230	X
231	Z
Page 7 of 8	



19/NOV/2010

Project Lance (TH1017) **19 November 2010**

RANDOMISATION LIST

Centre 8	
Patient number	**Treatment**
232	Z
233	Y
234	X
235	Z
236	Y
237	X
238	Y
239	Z
240	X
241	X
242	X
243	Z
244	Y
245	Z
246	Y
247	X
248	Y
249	Z
250	Y
251	Z
252	X
253	Y
254	Z
255	X
256	X
257	Y
258	Z
259	X
260	Y
261	Z
262	Y
263	Z
264	X
Page 8 of 8	

19/NOV/2010

APPENDIX 16.1.8 AUDIT CERTIFICATES

This appendix is not appropriate for this study as no audits have been conducted.

APPENDIX 16.1.9 DOCUMENTATION OF STATISTICAL METHODS

WORLDWIDE CLINICAL TRIALS

STATISTICAL ANALYSIS PLAN

TH1017

A multi centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.

Ref: TH1017/SAP/1.0

Final Version

Date effective: 27-Apr-11

SUMMARY OF SECTIONS

1. INTRODUCTION

1.1 Objectives

This document details the statistical analysis that will be performed for the Reckitt Benckiser Healthcare (UK) Limited (RB) study TH1017.

The primary objective of the study is to determine the analgesic efficacy of two Strepsils products in patients with a sore throat due to upper respiratory tract infection (URTI) compared to a placebo lozenge. The analgesic properties are also assessed by the change in severity of throat soreness.

Further objectives are to determine consumer acceptability of the product via responses to a consumer questionnaire.

1.2 Design

The study is a multi-centre, randomised, double-blind, placebo-controlled, single-dose study to investigate the efficacy of two Strepsils lozenges (Plus and Extra) in the treatment of sore throat due to upper respiratory tract infection.

The study population consists of patients who have a sore throat due to URTI that attend the study centre or respond to advertisements.

In order to discriminate between active and placebo treatment, it is important to include patients with a sufficient degree of throat soreness at baseline, therefore patients are asked to assess their throat soreness using the Throat Soreness Scale (TSS) Ratings a validated 11-point scale which indicates the degree of throat soreness on swallowing, this is marked between 0 (not sore) and 10 (very sore). Patients with a score of 6 or more then undergo a Tonsillopharyngitis Assessment (TPA), performed by the investigator or designated sub-investigator. A score of $\geq$5 is required to confirm the presence of tonsillopharyngitis and endorse entry into the study. This assessment ensures that only patients with acute tonsillopharyngitis, the condition causing sore throat, (not chronic, recurrent tonsillitis or laryngitis) are recruited into the study. A non-medicated, sugar based placebo lozenge is used in this study. The aim of the placebo is to control the demulcent effect seen with sucking any sugar based sweet. The lozenges are not colour matched and in order to maintain the double blind patients are blindfolded during dosing and be independently dosed with the lozenge by a member of staff who then has no further involvement in the study. This enables both patient and staff supervising the assessments to remain blinded.

Patients with a sore throat due to upper respiratory tract infections who are eligible to take part in the study receive a lozenge in the clinic. Patients complete self-assessment forms which consist of validated throat soreness scores, a sore throat pain relief scale, a swollen throat scale, a difficulty swallowing scale and a throat numbness scale. Additional questions regarding consumer acceptability of the product are also contained in a consumer questionnaire. Efficacy assessments and consumer questions are recorded at regular intervals over two hours. Once the 2-hour study assessment period is complete the patient leaves the clinic, taking with them a diary card to record any adverse events over the remaining 24 hours.

Prior to randomisation, potential patients are asked the following screening questions:

- How long have you had a sore throat? (to identify onset in the past 4 days).
- How would you describe your pain: mild pain, moderate pain, or severe pain? (to identify mild, moderate or severe pain).

Patients who meet the criteria for entry into the study are then asked to read the Informed Consent Form and ask any questions they may have.

After giving consent, patients have Baseline procedures performed.

Patients who are eligible for the study are asked to describe their sore throat on the self-administered Throat Descriptor Questionnaire:

1. How would you describe your sore throat? Select one

    a. Dry and scratchy

    b. Sharp and stabbing pain

    c. Swollen and inflamed

2. Which one description best fits how your sore throat makes you feel?

    a. Anxious – I don't want it to get worse

    b. Distracted – I just want to carry on

    c. Disrupted – Help me to talk and swallow again

3. Which phrase best describes your throat *now* when you swallow?

    (no pain, mild pain, moderate pain, severe pain)

(This categorical pain intensity scale is the Throat Pain Scale.)

The following baseline assessments are conducted/recorded:

Demographic data

- sex
- race
- date of birth
- height (cm)
- weight (kg)

Medical history and current status.

- primary diagnosis (pharyngitis)
- current symptoms of upper respiratory tract infection (URTI Questionnaire)

- duration of sore throat
- medical history (including smoking) and current status

Medication and therapy history

- current medication usage

Physical examination for URTI, throat examination and tests

- physical examination concentrating on eyes, ears, nose, mouth, lungs
- Tonsillo-Pharyngitis Assessment (TPA)
- PAIN (Practioner's Assessment of Pharyngeal Inflammation)

A washout period, if required, is permitted before the baseline assessment, in order to allow patients who have taken prohibited therapies such as other throat pastilles, boiled sweets etc, to be considered for entry. The washout period is determined by the type of prohibited therapy taken by the patient.

Baseline assessments are made no more than one minute before the first dose.

The URTI Questionnaire (Symptoms over Past 24 Hours, Symptoms Now, Symptoms at 2 Hours) is filled in.

This index (presented to the patient as a list of "Symptoms") consists of nominal scales for common symptoms of upper respiratory tract infection (URTI), such as sore throat, stuffy nose, runny nose, cough, sneezing, feverishness, achiness, headache, head fullness, tiredness, inability to sleep, loss of appetite, earache, ear fullness, phlegm, swollen glands, etc. The URTI Questionnaire is then repeated at two hours to identify any analgesic effects of the study medication. (The Questionnaire also contains symptoms that can be ascribed to URTI or medications, such as upset stomach, nausea, headache, making this instrument also useful in the interpretation of "adverse non-drug related events.") Thus the patient is asked to identify all symptoms experienced over the past 24 hours, all current symptoms at Baseline (now), and all symptoms present at 2 hours after the first dose.

The patient must have a minimum of one URTI symptom at Baseline (e.g., sore throat due to pharyngitis) to qualify for study inclusion as having URTI.

Further Baseline assessments are Throat Soreness Scale, Difficulty Swallowing and Swollen Throat Scale.

The 5 ratings assessments are completed at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose.

The 5 rating scales are as follows:

1. Difficulty Swallowing: using a 100mm VAS scale with endpoints of 'not difficult' on the left side and 'very difficult' on the right side.

2. **Throat Soreness Scale:** assessed on an 11-point ordinal scale, patients are asked to swallow and then circle the number on the scale that shows how sore their throat is. Ratings on this 0 to 10 ordinal scale are marked with 0=not sore and 10=very sore.

3. Swollen Throat Scale: using a 100mm VAS scale, patients are asked to swallow and evaluate how swollen their throat feels using endpoints of 'not swollen' and 'very swollen'.

4. **Sore throat Relief:** assessed on a 7-point scale. Scores on the 7-point categorical scale (no relief, slight relief, mild relief, moderate relief, considerable relief, almost complete relief, complete relief) represent a direct assessment of pain relief and will be used to compare treatment effects.

5. **Throat Numbness:** using a 5-point categorical scale, patients are asked to circle the phrase which best describes the numbness of their throat now (none, mild, moderate, considerable, complete).

Consumer Questionnaire: The patient also completes the consumer questions at 1, 5, 20, 60 and 120 minutes post-dose. Full details are given in the study protocol.

Patient Global Evaluation of study medication as a treatment of sore throat: At 120 minutes post dose the patients are asked by the study nurse/personnel "How do you rate the study medicine as a treatment for sore throat?"

The patients grade the study medication as a treatment for sore throat using a standard 5-category scale (poor, fair, good, very good, excellent).

Practitioners Clinical Assessment of Study medication as a treatment of sore throat: At 120 minutes post dose the Investigator is asked by the study nurse/personnel "Considering the patient's response to the study medicine over the past 2 hours, how do you rate the study medicine as a treatment for sore throat?"

The Investigator grades the study medication as a treatment for sore throat using a standard 5-category scale.

Overall Treatment Rating: At 120 minutes post-dose the patients are asked by the study nurse/personnel to provide an overall rating of the lozenge. 'How would you rate this lozenge as a treatment for sore throat?' The patient then selects a number from 0 (poor) to 10 (excellent) on an 11 point ordinal scale.

Adverse Event Assessment: Patients are asked if they have any untoward signs or symptoms (other than symptoms of a sore throat) at the pre-dose time point, at the end of the 2 hour assessment and 24 hours post dose.

Patient Diary: Each patient is given a diary to act as an 'aide memoire' to record adverse events and concomitant medication up to 24 hours post dose. Patients record the time the AE started, reason/nature of the AE and the time it ended, they also record what action was taken.

Discharge: Patients are discharged after the 2 hour in-clinic evaluation period with their adverse event /concomitant medication diary card and are followed up by a trained representative of the investigative site by telephone at any time from 1-3 days post dose.

A total of 180 patients (60 in each treatment group) are randomized into the study.

1.3 Time Course

The last patient's last visit is scheduled for April 2011. The first draft of the report will be available during the second quarter of 2011.

1.4 Responsibilities

Worldwide Clinical Trials (WCT) on behalf of the Sponsor (Reckitt Benckiser Healthcare (UK) Limited) will conduct the statistical analysis. The analysis will be co-ordinated by Michael Goulder. The Statistics Section of the Final Study Report will be written by WCT following the guidelines in the ICH E3 document.

2. ELABORATION OF STUDY PROTOCOL

2.1 Study Populations

The **all patient set** will include all patients who are enrolled into the study (i.e. consented). This analysis set will be used to report patient disposition.

The **safety set** will include all patients who take the study medication. The safety set will be analysed as treated.

The analysis of efficacy data will use two datasets:

The **full analysis set.** This analysis set will consist of all patients who are randomised to the study and take the study medication. Any patients with treatment administration errors will be analysed according to the treatment to which they were randomised. This is the primary efficacy analysis population.

The **per-protocol set.** This analysis set will be a subset of the full analysis set and will consist of all patients who satisfy all of the inclusion/exclusion criteria, who correctly receive the treatment to which they are randomised, and who successfully complete the treatment period up to the 2 hour assessment. All protocol deviations will be listed and summarised in the clinical study report. These will be assessed and documented on a case-by-case basis prior to the database lock, and any incidence of deviations considered having a serious impact on the efficacy results will lead to the relevant patient being excluded from the per-protocol analysis set. Major protocol deviations include:

- Treatment administration errors.
- Taking inadmissible concomitant medication (within the first 2 hours post-dosing or inadequate washout prior to randomisation).
- Inadmissible starting times of the follow-up assessments within the first 2 hours post dosing.
    - 1, 5, 10 and 15 minute assessment not performed within +/- 1 minutes of the scheduled times.
    - 30, 45, 60, 75, 90, 105 and 120 minute assessments not performed within +/- 5 minutes of the scheduled times.

All efficacy variables will be assessed using the full analysis set. The following will also be assessed using the per-protocol analysis

- Change from baseline in severity of throat soreness from 0 to 2 hours
- AUC from baseline to 2 hours for change from baseline of severity of throat soreness and difficulty in swallowing
- AUC from baseline to 2 hours for throat numbness and sore throat relief.

2.2 Primary Endpoints

The primary efficacy endpoint for this study is the change from baseline in severity of throat soreness (using the 11 point throat soreness scale) for the Strepsils Plus and Extra versus the placebo at the 2 hours post dose.

2.3 Secondary Endpoints

The secondary endpoints for this study are:

- AUC from baseline to 2 hours for the change from baseline in severity of throat soreness.
- Change from baseline in severity of throat soreness at 1, 5, 10, 15, 30, 45, 60, 75, 90, and 105 minutes post dose.
- Total sum of pain relief ratings (TOTPAR): defined as the AUC from baseline to 2 hours post first dosing for sore throat relief.
- Sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose.
- Onset of analgesia defined as the times to first reporting 'moderate pain relief' (which is the mid-point on the 7-point sore throat relief scale).
- AUC from baseline to 2 hours for the change from baseline in difficulty swallowing.
- Change from baseline in difficulty in swallowing at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose.
- AUC from baseline to 2 hours for the change from baseline in swollen throat.
- Change from baseline in swollen throat at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose.
- AUC from baseline to 2 hours for the change from baseline in throat numbness.
- Throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose.
- Global evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) and Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at 2 hours.
- Responses to the questions from the consumer questionnaire.

2.4 Safety Analysis

Safety and tolerability will be assessed in terms of the overall proportion of patients with adverse events (AEs) and serious adverse events (SAEs). All adverse events reported are recorded within the case record form. Events will be coded using the latest version of MedDRA available at the time of database lock. Coding will include lower level term, preferred term and primary system organ class. Tabulations will be provided including severity and relationship to therapy.

The number of patients who withdraw from the study will be presented. The timings and reasons for withdrawal will be tabulated.

2.5 Sample size

In a previous study conducted with Strepsils Original Lozenges[1] the difference in the change in throat soreness from baseline to 2 hours between Strepsils Original lozenge and placebo for patients with a TPA ≥ 5 and at least 6 on the 11-point throat soreness scale was -1.21 with a pooled standard deviation of 1.78. Assuming that the variability in this study will be similar, 57

patients per treatment arm will be sufficient to provide 95% power to detect a difference of -1.21 in the mean change from baseline in severity of throat soreness (using the 11-point throat soreness scale) using a 2 sample t-test at the 5% significance level.

In order to account for drop outs a total of 180 patients (60 per treatment arm) will be recruited.

2.6 Interim Analyses

No interim analyses are planned.

3. STATISTICAL METHODS

3.1 General

All statistical tests performed will be 2-tailed with significance determined by reference to the 5% significance level, unless otherwise stated. The null hypothesis at all times will be the equality of the treatments being compared. All comparisons between the treatments will be reported with 95% confidence intervals for the difference. For each statistical test, an observed significance level will be quoted. Where this value is less than 0.05, 0.01 or 0.001, attention will be drawn to the fact using the conventional "*", "**" or "***" annotation, respectively.

All incomplete dates will be entered on the database as they were recorded in the CRF. Thereafter, the incomplete dates will be completed using pre-defined rules. If a day or month is recorded as UNK or NA it will be replaced by the first day of the month or January respectively, provided this does not contradict any other dates recorded. For missing adverse events and medications dates/times during the trial, the worst-case date will be used (e.g. the end of the month for a stop date and 23:59 for the stop time, the randomisation date for start of AE).

Normality assumptions will be evaluated by an examination of the residual plots and the Shapiro-Wilk test of normality. Depending on the degree of departure from these assumptions, an alternate non-parametric approach may be used for supportive purposes.

For any given variable, baseline is taken as the latest recorded assessment available prior to dosing with the study lozenge. All tabulations involving change from baseline data will only include patients with cohort data i.e. with data at baseline and at follow-up.

All the area under curve analyses will be based on actual rather than scheduled timings and will be calculated using the trapezoidal rule. If the actual time is not recorded the scheduled time will be used instead. Patients who withdraw prior to the 2-hour assessment will have their last recorded score carried forward to 2 hours for each of the AUC calculations. For ease of interpretation the AUC value obtained will be divided by the total time the scale is assessed for reporting purposes.

For all non-AUC analyses, missing data will not be replaced.

In the case where the patient records more than one score for any particular efficacy measure, the worst of the recorded scores will be taken for analysis purposes.

All calculations and figures will be produced using SAS Version 9.2[2].

3.2 Data Summaries

The data will be summarized in tabular form by treatment. Graphical presentations of the data will also be provided where appropriate.

3.3 Continuous

For continuous variables, the mean, median, standard deviation, standard error of the mean, minimum, maximum and lower and upper 95% confidence limits for the mean for the population and for the individual treatment groups will be given.

3.4 Categorical

Categorical data will be presented in contingency tables with cell frequencies and percentages for the patient population and for the individual treatment groups.

4. ANALYSIS PLAN

4.1 Introduction

All summaries and analyses documented below will be presented in the final integrated statistical/clinical report and tables that will be based on the E3 guidelines published by ICH. However, it is noted here that no analysis plan prepared in advance of the data can be absolutely definitive and so the final report may contain additional tables or statistical tests if warranted by the data obtained. The justification for any such additional analyses will be fully documented in the final report.

4.2 Baseline Comparability

4.2.1 Intent

The comparability of treatment groups with respect to patient demographics and baseline characteristics will be assessed in a descriptive manner, but no formal statistical testing will be performed. Any clinically significant difference will be accounted for in the subsequent analysis by adding the relevant variable(s) to the analysis of covariance (ANCOVA) model for the primary endpoint as an exploratory analysis.

4.2.2 Variables Considered

Standard continuous or categorical variable summaries will be presented for the following variables based on the Safety population.

Demography (Table 14.1.2)

- Centre
- Age at screening visit (years)

- Gender (Male, Female)
- Race (Caucasian, Asian, Afro-Caribbean, Other)
- Alcohol drinker (Yes, No). If yes, number of units per week
- Smoking status (Never, Former, Current)
- If former or current smoker, whether smoked cigarettes or cigars and number per day

Primary Diagnosis (Tables 14.1.3)

- Duration of URTI (days)
- Duration of sore throat (days)

Throat Descriptor Questionnaire (Table 14.1.4)

- How would you describe your sore throat (Dry/scratchy, Sharp/Stabbing pain, Swollen/Inflamed)
- Which one description best fits how your sore throat makes you feel? (Anxious – I don't want it to get worse, Distracted – I just want to carry on, Disrupted – Help me to talk and swallow again)
- Which phrase best describes your throat now when you swallow? (No pain, Mild pain, Moderate pain, Severe pain)

Medical History (Tables 14.1.5 and 14.1.6)

- Relevant previous and ongoing medical history (Yes/No). Ongoing conditions will not include sore throat and URTI.

Separate tabulations will be produced for previous and ongoing conditions within each of the following categories:

- Cardiovascular
- Respiratory
- Gastrointestinal
- Urogenital

- Endocrine/metabolic
- Musculoskeletal
- Neurological
- Dermatological
- Haematology
- Surgery
- Allergies/drug sensitivity
- Eyes
- Ears
- Nose/throat
- Autoimmune
- Psychiatric
- Other

Screening assessments (Table 14.1.7)

- Total score from tonsillo-pharyngitis assessment
- Practioner's Assessment of Pharyngeal Inflammation (No Inflammation, Mild Inflammation, Moderate Inflammation, Severe Inflammation)

URTI Questionnaire at screening and baseline (Tables 14.1.8 and 14.1.9)

- What are your symptoms over the past 24 hours
  - Runny nose (Yes, No)
  - Sneezing (Yes, No)
  - Headache (Yes, No)

- Head Fullness (Yes, No)
- Stuffy Nose (Yes, No)
- Sore Throat (Yes, No)
- Throat-Clearing (Yes, No)
- Coughing (Yes, No)
- Ear Ache (Yes, No)
- Mouth-Breathing (Yes, No)
- Wheezing (Yes, No)
- Chest Tightness (Yes, No)
- Throat Tickle (Yes, No)
- Crackling Ears (Yes, No)
- Clogged Ears (Yes, No)
- Phlegm (Yes, No)
- Ear Fullness (Yes, No)
- Post-Nasal Drip (Yes, No)
- Burning Ears (Yes, No)
- Sweating (Yes, No)
- Achiness (Yes, No)
- Lack of Energy (Yes, No)
- Loss of Appetite (Yes, No)
- Inability to Sleep (Yes, No)
- Drowsy (Yes, No)

- Watery Eyes (Yes, No)
- Sinus Pressure (Yes, No)
- Sinus Pain (Yes, No)
- Heartburn (Yes, No)
- Upset Stomach (Yes, No)
- Acid Indigestion (Yes, No)
- Nausea (Yes, No)
- Pressure Around the Eyes (Yes, No)
- Dizzy (Yes, No)
- Feverish (Yes, No)
- Chills (Yes, No)
- Garbled Speech (Yes, No)
- Tender Neck Glands (Yes, No)
- Swollen Neck Glands (Yes, No)
- Other (specify) (Yes, No)
- Number of symptoms reported

- What are your symptoms now
  - Runny nose (Yes, No)
  - Sneezing (Yes, No)
  - Headache (Yes, No)
  - Head Fullness (Yes, No)
  - Stuffy Nose (Yes, No)

- Sore Throat (Yes, No)
- Throat-Clearing (Yes, No)
- Coughing (Yes, No)
- Ear Ache (Yes, No)
- Mouth-Breathing (Yes, No)
- Wheezing (Yes, No)
- Chest Tightness (Yes, No)
- Throat Tickle (Yes, No)
- Crackling Ears (Yes, No)
- Clogged Ears (Yes, No)
- Phlegm (Yes, No)
- Ear Fullness (Yes, No)
- Post-Nasal Drip (Yes, No)
- Burning Ears (Yes, No)
- Sweating (Yes, No)
- Achiness (Yes, No)
- Lack of Energy (Yes, No)
- Loss of Appetite (Yes, No)
- Inability to Sleep (Yes, No)
- Drowsy (Yes, No)
- Watery Eyes (Yes, No)
- Sinus Pressure (Yes, No)

- Sinus Pain (Yes, No)
- Heartburn (Yes, No)
- Upset Stomach (Yes, No)
- Acid Indigestion (Yes, No)
- Nausea (Yes, No)
- Pressure Around the Eyes (Yes, No)
- Dizzy (Yes, No)
- Feverish (Yes, No)
- Chills (Yes, No)
- Garbled Speech (Yes, No)
- Tender Neck Glands (Yes, No)
- Swollen Neck Glands (Yes, No)
- Other (specify) (Yes, No)
- Number of symptoms reported

Baseline efficacy assessments (Table 14.1.10)

- Assessment of throat soreness on an 11-point ordinal scale where 0 = “Not Sore” and 10 = “Very Sore”.
- Assessment of difficulty in swallowing on a 100 mm VAS with “Not Difficult” on the left hand side of the 100 mm line and “Very Difficult” on the right hand side.
- Swollen Throat Scale on a 100mm VAS scale, patients are asked to swallow and evaluate how swollen their throat feels using endpoints of ‘Not Swollen’ and ‘Very Swollen’.
- Individual and total scores from Functional Impairment Scale each recorded on 11-point ordinal scales where 0 = “Would not interfere at all and 10 = “Would completely interfere”.

- How much do you feel like your best overall on an 11-point ordinal scale where 0 = “I feel at my very worst”, 10 = “I feel at my very best”.

- How happy are you, in relation to your throat on an 11-point ordinal scale where 0 = “Very unhappy with my throat”, 10 = “Very happy with my throat”.

Concomitant medications (Table 14.1.11)

Concomitant medications ongoing at randomisation will be coded using the ATC level 2 categories from the WHO dictionary.

4.3 Primary Endpoint

The primary efficacy endpoint for this study is the change from baseline in severity of throat soreness (using the 11-point throat soreness scale) for the Strepsils Plus and Extra versus the placebo at the 2 hours post dose.

4.3.1 Principal Analysis

The primary efficacy endpoint will be analysed by analysis of covariance (ANCOVA) with baseline throat soreness severity as a covariate and factors for treatment group and centre. Treatment group differences will be estimated using the mean square error from the ANCOVA and using Fisher’s protected LSD method i.e. if the overall treatment effect in the ANCOVA model is significant at the 5% level, the comparisons of the Strepsils Plus and Strepsils Extra groups versus the placebo group will be performed without any requirement to adjust the significance level for the pairwise comparisons. The 95% confidence interval for the difference in least square means will be estimated using the mean square error from the ANCOVA (Tables 14.2.1.1 and 14.2.1.2).

4.3.2 Sensitivity Analysis

Depending on the degree and distribution of missing data additional sensitivity analyses may be performed on the primary efficacy endpoint using multiple imputation techniques and replacing missing values by the worst possible score.

4.4 Secondary Endpoints

All secondary endpoints and the supportive analyses will be considered as descriptive evidence of efficacy and will be analysed without any procedures to account for multiple comparisons.

The following variables will be analysed using the same ANCOVA model as for the primary endpoint:

- AUC from baseline to 2 hours for the change from baseline in severity of throat soreness (Tables 14.2.2.1 and 14.2.2.2).
- Change from baseline in severity of throat soreness at 1, 5, 10, 15, 30, 45, 60, 75, 90, and 105 minutes post dose (Tables 14.2.3 and 14.2.12).
- AUC from baseline to two hours post-dose for sore throat relief (TOTPAR) (Tables 14.2.13.1 and 14.2.13.2).
- Sore throat relief at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose (Tables 14.2.14 to 14.2.24).
- AUC from baseline to 2 hours for throat numbness (Tables 14.2.50.1 and 14.2.50.2).
- Throat numbness at 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose (Table 14.2.51 to 14.2.61).
- Patient's Global Evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) at two hours (Table 14.2.62).
- Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at two hours (Table 14.2.63).
- Overall treatment rating at two hours (Table 14.2.64).

The time taken for patients to first report at least moderate sore throat relief (i.e. onset of analgesia) will be compared between treatment groups using a Cox proportional hazards model with factors for treatment group and centre and a covariate for baseline throat soreness severity. Patients not reporting at least moderate sore throat relief will be censored at the time of their last recorded follow-up assessment (Table 14.2.25).

The AUC for the change in the difficulty in swallowing from 0 to 2 hours (Tables 14.2.26.1 and 14.2.26.2) and the change from baseline in difficulty in swallowing after 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose (Tables 14.2.27 to 14.2.37) and the will be analysed by ANCOVA with factors for treatment group and centre and covariates for baseline throat soreness and baseline difficulty in swallowing.

The AUC for the change in swollen throat from 0 to 2 hours (Table 14.2.38) and the change from baseline in swollen throat after 1, 5, 10, 15, 30, 45, 60, 75, 90, 105 and 120 minutes post dose (Tables 14.2.39 to 14.2.49) will be analysed by ANCOVA with factors for treatment group and centre and a covariates for baseline throat soreness and baseline swollen throat.

The change from pre-dose to one hour post-dose in the functional impairment scale (each component and overall total score) will be analysed by ANCOVA with factors for treatment group and centre and with covariates for the baseline throat soreness and the relevant baseline functional impairment score (Table 14.2.65).

For the consumer questionnaire, questions on non-numeric ordinal scales will be analysed using a proportional odds model[3] using PROC LOGISTIC in SAS with factors for treatment group and centre and a covariate for baseline throat soreness severity. Questions on numeric

ordinal scales will be analysed using the same ANCOVA model as the primary efficacy endpoint, except for the following two questions, viz: “How much do you feel like your best overall?” and “How happy are you, in relation to your throat?” both asked one and two hours post-dosing. These will be analysed by ANCOVA with factors for treatment group and centre and with covariates for the baseline throat soreness and the relevant baseline score for the specific question (Tables 14.2.66 to 14.2.79).

Data from the URTI questionnaire at two hours will be tabulated, but not formally analysed (Table 14.2.80).

Mean profiles from baseline to two hours will be presented by treatment group for change from baseline in the following: throat soreness, difficulty in swallowing and swollen throat. Mean profiles by treatment group will also be presented for sore throat relief and throat numbness (Figures 14.2.1 to 14.2.5).

4.5 Exploratory Analysis

Analyses of the primary efficacy endpoint will be performed by key baseline characteristics. For each subgroup, the main effect and treatment-by-subgroup interaction terms will be added to the standard model used in the primary endpoint analysis. Key variables of interest will be centre (Table 14.2.81), baseline throat soreness severity (≤median, >median; Table 14.2.82), baseline difficulty in swallowing (≤median, >median; Table 14.2.83), baseline swollen throat (≤median, >median; Table 14.2.84), age at study entry (≤median, >median; Table 14.2.85), gender (Table 14.2.86) and total score from tonsillo-pharyngitis assessment at baseline (≤median, >median; Table 14.2.87). Any interactions that seem noteworthy will have their nature described. These models will be used to estimate treatment comparisons within the subgroups that correspond with the sub-grouping factor. For the investigation of baseline throat soreness severity subgroup effect, the model fitted will be analysis of variance (ANOVA) rather than ANCOVA as baseline throat soreness severity will be considered a two-level factor rather than as a continuous covariate.

4.6 Safety analysis

All randomised patients who take the dose of study medication will be included in the analysis of safety.

Extent of exposure

Extent of exposure will be described by whether the patient took the trial medication (Table 14.3.1).

Adverse events

All treatment emergent adverse events will be listed and tabulated by treatment, severity, relationship to therapy and primary system organ class according to the latest version of MedDRA available at the time of database lock. In counting the number of events reported, a continuous event, i.e. reported more than once and which did not cease, will be counted only once; non-continuous adverse events reported several times by the same patient will be

counted as multiple events. Events present immediately prior to the dose of study medication that do not worsen in severity, will not be included. Events with start dates during follow-up (i.e. more than 24 hours after dosing) will not be considered treatment emergent and will be listed separately.

Differences between treatment groups in the proportion of patients reporting treatment emergent adverse events will be compared via chi-square tests (Tables 14.3.2 to 14.3.5).

Narratives of deaths, serious and other significant adverse events will be provided in the relevant section of the study report.

A complete listing of all adverse events will be provided in Appendix 16.2 to the study report.

Withdrawals

The number of patients who withdraw from the study will be presented. The timings and reasons for withdrawal will be summarised by treatment (Table 14.1.1).

Concomitant medications

Concomitant medications commencing during the study will be coded using the ATC level 2 categories from the WHO dictionary (Table 14.3.6).

4.7 Key Data Items

A second statistician within WCT will check all the analyses relating to the primary efficacy endpoint and the following variables:

- AUC from baseline to 2 hours for change from baseline of severity of throat soreness and difficulty in swallowing
- AUC from baseline to 2 hours for throat numbness and sore throat relief.

The checking procedure will involve writing independent SAS programs and comparing the output produced with the results in the relevant tables.

WCT analysis programs used to create programs and listings are a combination of fully validated SAS macros and SAS derived datasets. All macros are validated using one or more appropriate datasets with independently established results, All SAS programs used to create tables and listings are stored electronically. Each program used to create a table or listing is configured to produce a corresponding SAS log file. This log file is stored in an appropriately named subdirectory, and is replaced each time the program is run, such that only the most recent copy is retained.

4.8 Change to Planned Protocol Analysis

None.

5. REFERENCES

(1) TH0705, Clinical Study report, Reckitt Benckiser, Healthcare, Data on File.

(2) SAS Institute Inc. The SAS System, Version 9.2. Cary, NC, SAS Institute Inc. 2004.

(3) McCullagh P. “Regression models for ordinal data (with discussion)”. Journal of the Royal Statistical Society, Series B, 1980, 42(2), 109-142.

6. TABLES TO BE INCLUDED IN THE CLINICAL STUDY REPORT

Table number	Table Title
14.1 Demographics Data	
14.1.1	Details of withdrawal – Safety set
14.1.2	Demographics – Full analysis set
14.1.3	Primary diagnosis – Full analysis set
14.1.4	Throat descriptor questionnaire – Full analysis set
14.1.5	Relevant previous medical history – Full analysis set
14.1.6	Relevant ongoing medical history – Full analysis set
14.1.7	Screening assessments – Full analysis set
14.1.8	URTI Questionnaire at screening (symptoms over the past 24 hours) – Full analysis set
14.1.9	URTI Questionnaire at pre-dose – Full analysis set
14.1.10	Baseline efficacy assessments – Full analysis set
14.1.11	Concomitant medication ongoing at randomisation – Full analysis set
14.2 Efficacy Data	
14.2.1.1	Primary efficacy endpoint - Change from baseline in throat soreness at 120 minutes post dose - Full analysis set
14.2.1.2	Primary efficacy endpoint - Change from baseline in throat soreness at 120 minutes post dose – Per-protocol set
14.2.2.1	AUC from baseline to two hours post dose for the change from baseline in throat soreness - Full analysis set
14.2.2.2	AUC from baseline to two hours post dose for the change from baseline in throat soreness – Per-protocol set
14.2.3	Change from baseline in throat soreness at 1 minute post dose - Full analysis set
14.2.4	Change from baseline in throat soreness at 5 minutes post dose - Full analysis set
14.2.5	Change from baseline in throat soreness at 10 minutes post dose - Full analysis set
14.2.6	Change from baseline in throat soreness at 15 minutes post dose - Full analysis set
14.2.7	Change from baseline in throat soreness at 30 minutes post dose - Full analysis set
14.2.8	Change from baseline in throat soreness at 45 minutes post dose - Full analysis set
14.2.9	Change from baseline in throat soreness at 60 minutes post dose - Full analysis set
14.2.10	Change from baseline in throat soreness at 75 minutes post dose - Full analysis set
14.2.11	Change from baseline in throat soreness at 90 minutes post dose - Full analysis set
14.2.12	Change from baseline in throat soreness at 105 minutes post dose - Full analysis set
14.2.13.1	AUC from baseline to two hours post-dose for sore throat relief (TOTPAR) - Full analysis set
14.2.13.2	AUC from baseline to two hours post-dose for sore throat relief (TOTPAR) – Per-protocol set

Table number	Table Title
14.2.14	Sore throat relief at 1 minute post dose - Full analysis set
14.2.15	Sore throat relief at 5 minutes post dose - Full analysis set
14.2.16	Sore throat relief at 10 minutes post dose - Full analysis set
14.2.17	Sore throat relief at 15 minutes post dose - Full analysis set
14.2.18	Sore throat relief at 30 minutes post dose - Full analysis set
14.2.19	Sore throat relief at 45 minutes post dose - Full analysis set
14.2.20	Sore throat relief at 60 minutes post dose - Full analysis set
14.2.21	Sore throat relief at 75 minutes post dose - Full analysis set
14.2.22	Sore throat relief at 90 minutes post dose - Full analysis set
14.2.23	Sore throat relief at 105 minutes post dose - Full analysis set
14.2.24	Sore throat relief at 120 minutes post dose - Full analysis set
14.2.25	Onset of analgesia - Time to first reporting of moderate pain relief - Full analysis set
14.2.26.1	AUC from baseline to two hours post dose for the change from baseline in difficulty in swallowing - Full analysis set
14.2.26.2	AUC from baseline to two hours post dose for the change from baseline in difficulty in swallowing – Per-protocol set
14.2.27	Change from baseline in difficulty in swallowing at 1 minute post dose - Full analysis set
14.2.28	Change from baseline in difficulty in swallowing at 5 minutes post dose - Full analysis set
14.2.29	Change from baseline in difficulty in swallowing at 10 minutes post dose - Full analysis set
14.2.30	Change from baseline in difficulty in swallowing at 15 minutes post dose - Full analysis set
14.2.31	Change from baseline in difficulty in swallowing at 30 minutes post dose - Full analysis set
14.2.32	Change from baseline in difficulty in swallowing at 45 minutes post dose - Full analysis set
14.2.33	Change from baseline in difficulty in swallowing at 60 minutes post dose - Full analysis set
14.2.34	Change from baseline in difficulty in swallowing at 75 minutes post dose - Full analysis set
14.2.35	Change from baseline in difficulty in swallowing at 90 minutes post dose - Full analysis set
14.2.36	Change from baseline in difficulty in swallowing at 105 minutes post dose - Full analysis set
14.2.37	Change from baseline in difficulty in swallowing at 120 minutes post dose - Full analysis set
14.2.38	AUC from baseline to two hours post dose for the change from baseline in swollen throat - Full analysis set
14.2.39	Change from baseline in swollen throat at 1 minute post dose - Full analysis set
14.2.40	Change from baseline in swollen throat at 5 minutes post dose - Full analysis set
14.2.41	Change from baseline in swollen throat at 10 minutes post dose - Full analysis set
14.2.42	Change from baseline in swollen throat at 15 minutes post dose - Full analysis set
14.2.43	Change from baseline in swollen throat at 30 minutes post dose - Full analysis set

Table number	Table Title
14.2.44	Change from baseline in swollen throat at 45 minutes post dose - Full analysis set
14.2.45	Change from baseline in swollen throat at 60 minutes post dose - Full analysis set
14.2.46	Change from baseline in swollen throat at 75 minutes post dose - Full analysis set
14.2.47	Change from baseline in swollen throat at 90 minutes post dose - Full analysis set
14.2.48	Change from baseline in swollen throat at 105 minutes post dose - Full analysis set
14.2.49	Change from baseline in swollen throat at 120 minutes post dose - Full analysis set
14.2.50.1	AUC from baseline to two hours post-dose for throat numbness - Full analysis set
14.2.50.2	AUC from baseline to two hours post-dose for throat numbness – Per-protocol set
14.2.51	Change from baseline in throat numbness at 1 minute post dose - Full analysis set
14.2.52	Change from baseline in throat numbness at 5 minutes post dose - Full analysis set
14.2.53	Change from baseline in throat numbness at 10 minutes post dose - Full analysis set
14.2.54	Change from baseline in throat numbness at 15 minutes post dose - Full analysis set
14.2.55	Change from baseline in throat numbness at 30 minutes post dose - Full analysis set
14.2.56	Change from baseline in throat numbness at 45 minutes post dose - Full analysis set
14.2.57	Change from baseline in throat numbness at 60 minutes post dose - Full analysis set
14.2.58	Change from baseline in throat numbness at 75 minutes post dose - Full analysis set
14.2.59	Change from baseline in throat numbness at 90 minutes post dose - Full analysis set
14.2.60	Change from baseline in throat numbness at 105 minutes post dose - Full analysis set
14.2.61	Change from baseline in throat numbness at 120 minutes post dose - Full analysis set
14.2.62	Patient's Global Evaluation of the Study Medication as a Treatment of Sore Throat (GLOBAL) at two hours - Full analysis set
14.2.63	Practitioner's Clinical Assessment of the Study Medication as a Treatment of Sore Throat (CLIN) at two hours - Full analysis set
14.2.64	Overall treatment rating at two hours - Full analysis set
14.2.65	Consumer questionnaire: Change from baseline in the individual and total scores from Functional Impairment Scale at one hours post-dose - Full analysis set
14.2.66	Consumer questionnaire: How quickly did you feel any numbing sensation at one minute post-dose - Full analysis set
14.2.67	Consumer questionnaire: How much do you think the lozenge soothed your throat at five minutes post-dose - Full analysis set
14.2.68	Consumer questionnaire: How deep down within the throat was any

Table number	Table Title
	numbing felt at 20 minutes post-dose - Full analysis set
14.2.69	Consumer questionnaire: Intensity of any numbing sensation at 20 minutes post-dose - Full analysis set
14.2.70	Consumer questionnaire: Strength of any numbing sensation at 20 minutes post-dose - Full analysis set
14.2.71	Consumer questionnaire: Change from baseline in how much the patient felt like their best overall at one and two hours post-dose - Full analysis set
14.2.72	Consumer questionnaire: Change from baseline in degree of happiness in relation to their throat at one and two hours post-dose - Full analysis set
14.2.73	Consumer questionnaire: Thinking about this lozenge, how much do you agree or disagree with the phrase “I feel less distracted than before I took the lozenge” at two hours post-dose - Full analysis set
14.2.74	Consumer questionnaire: Thinking about this lozenge, how much do you agree or disagree with the phrase “I feel better than before I took the lozenge” at two hours post-dose - Full analysis set
14.2.75	Consumer questionnaire: Thinking about this lozenge, how much do you agree or disagree with the phrase “The lozenge took my mind off the pain” at two hours post-dose - Full analysis set
14.2.76	Consumer questionnaire: Thinking about this lozenge, how much do you agree or disagree with the phrase “I feel happier than before I took the lozenge” at two hours post-dose - Full analysis set
14.2.77	Consumer questionnaire: Thinking about this lozenge, how much do you agree or disagree with the phrase “The lozenge targeted my throat pain” at two hours post-dose - Full analysis set
14.2.78	Consumer questionnaire: Thinking about this lozenge, how much do you agree or disagree with the phrase “The experience of this lozenge is soothing” at two hours post-dose - Full analysis set
14.2.79	Consumer questionnaire: How deep down within the throat was the relief felt at two hours post-dose - Full analysis set
14.2.80	URTI questionnaire at two hours - Full analysis set
14.2.81	Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by centre - Full analysis set
14.2.82	Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by baseline throat soreness severity - Full analysis set
14.2.83	Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by baseline difficulty in swallowing - Full analysis set
14.2.84	Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by baseline swollen throat - Full analysis set
14.2.85	Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by age at study entry - Full analysis set
14.2.86	Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by gender - Full analysis set
14.2.87	Primary efficacy endpoint – Change from baseline in throat soreness at 120 minutes post dose by total score from tonsillo-pharyngitis assessment at baseline - Full analysis set

14.3 Safety Data

Table number	Table Title
14.3.1	Extent of exposure to study medication - Safety set
14.3.2	Summary of treatment emergent adverse event reporting – Safety set
14.3.3	MedDRA Summary of treatment emergent adverse events by primary system organ class – Safety set
14.3.4	MedDRA Summary of treatment emergent adverse events by primary system organ class and preferred term – Safety set
14.3.5	MedDRA Summary of treatment emergent adverse events by primary system organ class, preferred term, severity and relationship to study medication – Safety set
14.3.6	Concomitant medication commencing during the study – Safety set

7. FIGURES TO BE INCLUDED IN THE CLINICAL STUDY REPORT

Figure number	Figure Title
14.2.1	Mean treatment profiles for change from baseline in throat soreness - Full analysis set
14.2.2	Mean treatment profiles for sore throat relief - Full analysis set
14.2.3	Mean treatment profiles for change from baseline in difficulty swallowing - Full analysis set
14.2.4	Mean treatment profiles for change from baseline in swollen throat - Full analysis set
14.2.5	Mean treatment profiles for throat numbness - Full analysis set

Approval for implementation of Statistical Analysis Plan

Title:	**A multi centre, randomised, double blind, single dose parallel group, placebo controlled study to investigate the efficacy of Strepsils Plus and Strepsils Extra in the treatment of sore throat due to upper respiratory tract infection.**
Reference:	**TH1017/SAP**
Version:	**1.0**
Date effective:	**27-APR-11**
Author:	**Michael Goulder: Senior Statistician**
Author's signature:	Michael A Goulder **Date:** 03-MAY-11

The above Statistical Analysis Plan has been reviewed and approved by the Sponsor:

Name of Approver:	**Emma Field**
Position:	**Clinical Project Manager, Reckitt Benckiser**
Signature for	_____ Date: 03/May/2011
Name of Approver:	**Gary Smith**
Position:	**Senior Statistician, Reckitt Benckiser**
Signature for	_____ Date: 03/May/2011

6. TABLES TO BE INCLUDED IN THE CLINICAL STUDY REPORT

Table number	Table Title
14.1 Demographics Data	
14.1.1	Details of withdrawal – Safety set
14.1.2	Demographics – Full analysis set
14.1.3	Primary diagnosis – Full analysis set
14.1.4	Throat descriptor questionnaire – Full analysis set
14.1.5	Relevant previous medical history – Full analysis set
14.1.6	Relevant ongoing medical history – Full analysis set
14.1.7	Screening assessments – Full analysis set
14.1.8	URTI Questionnaire at screening (symptoms over the past 24 hours) – Full analysis set
14.1.9	URTI Questionnaire at pre-dose – Full analysis set
14.1.10	Baseline efficacy assessments – Full analysis set
14.1.11	Concomitant medication ongoing at randomisation – Full analysis set
14.2 Efficacy Data	
14.2.1.1	Primary efficacy endpoint - Change from baseline in throat soreness at 120 minutes post dose - Full analysis set
14.2.1.2	Primary efficacy endpoint - Change from baseline in throat soreness at 120 minutes post dose – Per-protocol set
14.2.2.1	AUC from baseline to two hours post dose for the change from baseline in throat soreness - Full analysis set
14.2.2.2	AUC from baseline to two hours post dose for the change from baseline in throat soreness – Per-protocol set
14.2.3	Change from baseline in throat soreness at 1 minute post dose - Full analysis set
14.2.4	Change from baseline in throat soreness at 5 minutes post dose - Full analysis set
14.2.5	Change from baseline in throat soreness at 10 minutes post dose - Full analysis set
14.2.6	Change from baseline in throat soreness at 15 minutes post dose - Full analysis set
14.2.7	Change from baseline in throat soreness at 30 minutes post dose - Full analysis set
14.2.8	Change from baseline in throat soreness at 45 minutes post dose - Full analysis set
14.2.9	Change from baseline in throat soreness at 60 minutes post dose - Full analysis set
14.2.10	Change from baseline in throat soreness at 75 minutes post dose - Full analysis set
14.2.11	Change from baseline in throat soreness at 90 minutes post dose - Full analysis set

14.2.12	Change from baseline in throat soreness at 105 minutes post dose - Full analysis set
14.2.13.1	AUC from baseline to two hours post-dose for sore throat relief (TOTPAR) - Full analysis set
14.2.13.2	AUC from baseline to two hours post-dose for sore throat relief (TOTPAR) – Per-protocol set

APPENDIX 16.1.10 DOCUMENTATION OF INTER-LABORATORY STANDARDISATION METHODS AND QUALITY ASSURANCE PROCEDURES IF USED.

This appendix is not relevant for this study as there were no laboratory assessments.

APPENDIX 16.1.11 PUBLICATIONS BASED ON THE STUDY

This appendix is not relevant for this study as there have been no publications based on its results.

APPENDIX 16.1.12 IMPORTANT PUBLICATIONS REFERENCED IN THE REPORT

No publications referred to in the report are appended.

APPENDIX 16.2

PATIENT DATA LISTINGS

Listing number	Listing Title
16.2.1	**Discontinued patients**
	No patients withdrew from the study
16.2.2	**Protocol deviations**
16.2.2.1	Patient data listing of patients excluded from the per-protocol set – Full analysis set
16.2.3	**Patients excluded from the efficacy analysis**
16.2.3.1	Patient data listing of inclusion in analysis populations
16.2.4	**Demographic data**
16.2.4.1	Patient data listing of demographic data – Full analysis set
16.2.4.2	Patient data listing of medical history data – Full analysis set
16.2.4.3	Patient data listing of concomitant medications stopped prior to randomisation – Full analysis set
16.2.4.4	Patient data listing of concomitant medications ongoing at randomisation – Full analysis set
16.2.4.5	Patient data listing of concomitant medications starting post-randomisation – Full analysis set
16.2.4.6	Patient data listing of baseline efficacy assessments – Full analysis set
16.2.5	**Compliance and/or drug concentration data**
16.2.5.1	Patient data listing of exposure – Full analysis set
16.2.6	**Individual efficacy response data**
16.2.6.1	Patient data listing of AUC (0-2 hours) data – Full analysis set
16.2.6.2	Patient data listing of difficulty in swallowing, swollen throat and throat numbness data – Full analysis set
16.2.7	**Adverse event listings (each patient)**
16.2.7.1	Patient data listing of treatment emergent adverse events - Part 1 - Safety set

16.2.7.2 Patient data listing of treatment emergent adverse events - Part 2 - Safety set

16.2.8 Listing of individual laboratory measurements by patient

1.1 NONE

16.2.9 Other data listings

1.2 NONE

APPENDIX 16.2.1 DISCONTINUED PATIENTS

This appendix is not appropriate for this study because no patients were discontinued.

APPENDIX 16.2.2 PROTOCOL DEVIATIONS

Listing 16.2.2.1
Patient data listing of patients excluded from the per-protocol set
Full analysis set

Centre number	Patient number	Treatment group	Throat soreness <6 at baseline	Difficulty in swallowing <=50 mm at baseline	Swollen throat <=33 mm at baseline	No symptoms on URTI questionnaire at baseline	Inadmissible timing of assessments
1	048	Strepsils Plus				Yes	
2	017	Strepsils Plus			Yes		
3	249	Strepsils Plus			Yes		
5	175	Strepsils Plus			Yes		
7	106	Strepsils Plus		Yes			
1	049	Strepsils Extra				Yes	
2	005	Strepsils Extra					Yes
3	238	Strepsils Extra	Yes	Yes			
3	248	Strepsils Extra			Yes		
3	250	Strepsils Extra	Yes	Yes	Yes		
8	203	Strepsils Extra				Yes	
1	046	Placebo				Yes	
1	050	Placebo	Yes			Yes	
3	252	Placebo	Yes	Yes			
5	178	Placebo		Yes			
8	202	Placebo		Yes			

”.

APPENDIX 16.2.3 PATIENTS EXCLUDED FROM THE EFFICACY ANALYSIS

Listing 16.2.3.1
Patient data listing of inclusion in analysis populations

Centre number	Patient number	Treatment group	Full analysis set	Per-protocol set	Safety set
1	034	Strepsils Plus	Yes	Yes	Yes
1	038	Strepsils Plus	Yes	Yes	Yes
1	041	Strepsils Plus	Yes	Yes	Yes
1	044	Strepsils Plus	Yes	Yes	Yes
1	048	Strepsils Plus	Yes	No	Yes
1	051	Strepsils Plus	Yes	Yes	Yes
1	052	Strepsils Plus	Yes	Yes	Yes
1	057	Strepsils Plus	Yes	Yes	Yes
1	059	Strepsils Plus	Yes	Yes	Yes
1	061	Strepsils Plus	Yes	Yes	Yes
2	002	Strepsils Plus	Yes	Yes	Yes
2	006	Strepsils Plus	Yes	Yes	Yes
2	007	Strepsils Plus	Yes	Yes	Yes
2	012	Strepsils Plus	Yes	Yes	Yes
2	016	Strepsils Plus	Yes	Yes	Yes
2	017	Strepsils Plus	Yes	No	Yes
2	019	Strepsils Plus	Yes	Yes	Yes
2	022	Strepsils Plus	Yes	Yes	Yes
2	025	Strepsils Plus	Yes	Yes	Yes
2	029	Strepsils Plus	Yes	Yes	Yes
2	032	Strepsils Plus	Yes	Yes	Yes
3	232	Strepsils Plus	Yes	Yes	Yes
3	235	Strepsils Plus	Yes	Yes	Yes
3	239	Strepsils Plus	Yes	Yes	Yes
3	243	Strepsils Plus	Yes	Yes	Yes
3	245	Strepsils Plus	Yes	Yes	Yes
3	249	Strepsils Plus	Yes	No	Yes
3	251	Strepsils Plus	Yes	Yes	Yes
3	254	Strepsils Plus	Yes	Yes	Yes
4	133	Strepsils Plus	Yes	Yes	Yes
4	138	Strepsils Plus	Yes	Yes	Yes
4	140	Strepsils Plus	Yes	Yes	Yes

Centre number	Patient number	Treatment group	Full analysis set	Per-protocol set	Safety set
4	142	Strepsils Plus	Yes	Yes	Yes
4	147	Strepsils Plus	Yes	Yes	Yes
4	148	Strepsils Plus	Yes	Yes	Yes
4	151	Strepsils Plus	Yes	Yes	Yes
4	154	Strepsils Plus	Yes	Yes	Yes
4	156	Strepsils Plus	Yes	Yes	Yes
4	161	Strepsils Plus	Yes	Yes	Yes
5	167	Strepsils Plus	Yes	Yes	Yes
5	171	Strepsils Plus	Yes	Yes	Yes
5	172	Strepsils Plus	Yes	Yes	Yes
5	175	Strepsils Plus	Yes	No	Yes
5	180	Strepsils Plus	Yes	Yes	Yes
5	181	Strepsils Plus	Yes	Yes	Yes
6	070	Strepsils Plus	Yes	Yes	Yes
6	074	Strepsils Plus	Yes	Yes	Yes
6	077	Strepsils Plus	Yes	Yes	Yes
6	079	Strepsils Plus	Yes	Yes	Yes
7	102	Strepsils Plus	Yes	Yes	Yes
7	106	Strepsils Plus	Yes	No	Yes
7	108	Strepsils Plus	Yes	Yes	Yes
7	109	Strepsils Plus	Yes	Yes	Yes
7	110	Strepsils Plus	Yes	Yes	Yes
7	115	Strepsils Plus	Yes	Yes	Yes
7	117	Strepsils Plus	Yes	Yes	Yes
7	123	Strepsils Plus	Yes	Yes	Yes
7	125	Strepsils Plus	Yes	Yes	Yes
7	127	Strepsils Plus	Yes	Yes	Yes
7	128	Strepsils Plus	Yes	Yes	Yes
8	200	Strepsils Plus	Yes	Yes	Yes
8	205	Strepsils Plus	Yes	Yes	Yes
8	206	Strepsils Plus	Yes	Yes	Yes
8	209	Strepsils Plus	Yes	Yes	Yes
1	036	Strepsils Extra	Yes	Yes	Yes
1	039	Strepsils Extra	Yes	Yes	Yes
1	042	Strepsils Extra	Yes	Yes	Yes
1	043	Strepsils Extra	Yes	Yes	Yes
1	047	Strepsils Extra	Yes	Yes	Yes
1	049	Strepsils Extra	Yes	No	Yes

Centre number	Patient number	Treatment group	Full analysis set	Per-protocol set	Safety set
1	053	Strepsils Extra	Yes	Yes	Yes
1	055	Strepsils Extra	Yes	Yes	Yes
1	058	Strepsils Extra	Yes	Yes	Yes
1	062	Strepsils Extra	Yes	Yes	Yes
2	004	Strepsils Extra	Yes	Yes	Yes
2	005	Strepsils Extra	Yes	No	Yes
2	008	Strepsils Extra	Yes	Yes	Yes
2	010	Strepsils Extra	Yes	Yes	Yes
2	013	Strepsils Extra	Yes	Yes	Yes
2	018	Strepsils Extra	Yes	Yes	Yes
2	020	Strepsils Extra	Yes	Yes	Yes
2	026	Strepsils Extra	Yes	Yes	Yes
2	027	Strepsils Extra	Yes	Yes	Yes
2	030	Strepsils Extra	Yes	Yes	Yes
2	033	Strepsils Extra	Yes	Yes	Yes
3	233	Strepsils Extra	Yes	Yes	Yes
3	236	Strepsils Extra	Yes	Yes	Yes
3	238	Strepsils Extra	Yes	No	Yes
3	244	Strepsils Extra	Yes	Yes	Yes
3	246	Strepsils Extra	Yes	Yes	Yes
3	248	Strepsils Extra	Yes	No	Yes
3	250	Strepsils Extra	Yes	No	Yes
3	253	Strepsils Extra	Yes	Yes	Yes
4	134	Strepsils Extra	Yes	Yes	Yes
4	137	Strepsils Extra	Yes	Yes	Yes
4	141	Strepsils Extra	Yes	Yes	Yes
4	144	Strepsils Extra	Yes	Yes	Yes
4	145	Strepsils Extra	Yes	Yes	Yes
4	152	Strepsils Extra	Yes	Yes	Yes
4	153	Strepsils Extra	Yes	Yes	Yes
4	158	Strepsils Extra	Yes	Yes	Yes
4	159	Strepsils Extra	Yes	Yes	Yes
4	162	Strepsils Extra	Yes	Yes	Yes
5	169	Strepsils Extra	Yes	Yes	Yes
5	170	Strepsils Extra	Yes	Yes	Yes
5	173	Strepsils Extra	Yes	Yes	Yes
5	177	Strepsils Extra	Yes	Yes	Yes
5	179	Strepsils Extra	Yes	Yes	Yes

Centre number	Patient number	Treatment group	Full analysis set	Per-protocol set	Safety set
6	067	Strepsils Extra	Yes	Yes	Yes
6	071	Strepsils Extra	Yes	Yes	Yes
6	075	Strepsils Extra	Yes	Yes	Yes
6	076	Strepsils Extra	Yes	Yes	Yes
7	101	Strepsils Extra	Yes	Yes	Yes
7	105	Strepsils Extra	Yes	Yes	Yes
7	107	Strepsils Extra	Yes	Yes	Yes
7	111	Strepsils Extra	Yes	Yes	Yes
7	113	Strepsils Extra	Yes	Yes	Yes
7	119	Strepsils Extra	Yes	Yes	Yes
7	120	Strepsils Extra	Yes	Yes	Yes
7	122	Strepsils Extra	Yes	Yes	Yes
7	124	Strepsils Extra	Yes	Yes	Yes
7	129	Strepsils Extra	Yes	Yes	Yes
7	130	Strepsils Extra	Yes	Yes	Yes
8	199	Strepsils Extra	Yes	Yes	Yes
8	203	Strepsils Extra	Yes	No	Yes
8	204	Strepsils Extra	Yes	Yes	Yes
8	208	Strepsils Extra	Yes	Yes	Yes
8	211	Strepsils Extra	Yes	Yes	Yes
1	035	Placebo	Yes	Yes	Yes
1	037	Placebo	Yes	Yes	Yes
1	040	Placebo	Yes	Yes	Yes
1	045	Placebo	Yes	Yes	Yes
1	046	Placebo	Yes	No	Yes
1	050	Placebo	Yes	No	Yes
1	054	Placebo	Yes	Yes	Yes
1	056	Placebo	Yes	Yes	Yes
1	060	Placebo	Yes	Yes	Yes
2	001	Placebo	Yes	Yes	Yes
2	003	Placebo	Yes	Yes	Yes
2	009	Placebo	Yes	Yes	Yes
2	011	Placebo	Yes	Yes	Yes
2	014	Placebo	Yes	Yes	Yes
2	015	Placebo	Yes	Yes	Yes
2	021	Placebo	Yes	Yes	Yes
2	023	Placebo	Yes	Yes	Yes
2	024	Placebo	Yes	Yes	Yes

Centre number	Patient number	Treatment group	Full analysis set	Per-protocol set	Safety set
2	028	Placebo	Yes	Yes	Yes
2	031	Placebo	Yes	Yes	Yes
3	234	Placebo	Yes	Yes	Yes
3	237	Placebo	Yes	Yes	Yes
3	240	Placebo	Yes	Yes	Yes
3	241	Placebo	Yes	Yes	Yes
3	242	Placebo	Yes	Yes	Yes
3	247	Placebo	Yes	Yes	Yes
3	252	Placebo	Yes	No	Yes
3	255	Placebo	Yes	Yes	Yes
4	135	Placebo	Yes	Yes	Yes
4	136	Placebo	Yes	Yes	Yes
4	139	Placebo	Yes	Yes	Yes
4	143	Placebo	Yes	Yes	Yes
4	146	Placebo	Yes	Yes	Yes
4	149	Placebo	Yes	Yes	Yes
4	150	Placebo	Yes	Yes	Yes
4	155	Placebo	Yes	Yes	Yes
4	157	Placebo	Yes	Yes	Yes
4	160	Placebo	Yes	Yes	Yes
5	166	Placebo	Yes	Yes	Yes
5	168	Placebo	Yes	Yes	Yes
5	174	Placebo	Yes	Yes	Yes
5	176	Placebo	Yes	Yes	Yes
5	178	Placebo	Yes	No	Yes
6	069	Placebo	Yes	Yes	Yes
6	072	Placebo	Yes	Yes	Yes
6	073	Placebo	Yes	Yes	Yes
6	078	Placebo	Yes	Yes	Yes
6	080	Placebo	Yes	Yes	Yes
7	100	Placebo	Yes	Yes	Yes
7	103	Placebo	Yes	Yes	Yes
7	104	Placebo	Yes	Yes	Yes
7	112	Placebo	Yes	Yes	Yes
7	114	Placebo	Yes	Yes	Yes
7	116	Placebo	Yes	Yes	Yes
7	118	Placebo	Yes	Yes	Yes
7	121	Placebo	Yes	Yes	Yes

Centre number	Patient number	Treatment group	Full analysis set	Per-protocol set	Safety set
7	126	Placebo	Yes	Yes	Yes
7	131	Placebo	Yes	Yes	Yes
8	201	Placebo	Yes	Yes	Yes
8	202	Placebo	Yes	No	Yes
8	207	Placebo	Yes	Yes	Yes
8	210	Placebo	Yes	Yes	Yes

TH1017

(Data Set Identification)

LISTING OF NON EVALUABLE PATIENTS

Centre Number/Investigator Name: 01. Dr Paul Conn

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Plus	048	Male	48	No symptoms on URTI questionnaire at baseline	Protocol Deviation

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Extra	049	Male	51	No symptoms on URTI questionnaire at baseline	Protocol Deviation

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Placebo	046	Male	28	No symptoms on URTI questionnaire at baseline	Protocol Deviation
Placebo	050	Male	41	2: Throat soreness <6 at baseline, No symptoms on URTI questionnaire at baseline	Protocol Deviations

Centre Number/Investigator Name: 02. Dr Damien McNally

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Plus	017	Female	23	Swollen throat <=33mm at baseline	Protocol Deviation

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Extra	005	Male	27	Inadmissible timing of assessments	Protocol Deviation

Centre Number/Investigator Name: 03. Dr Malcolm McCaughey

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Plus	249	Female	40	Swollen throat <=33mm at baseline	Protocol Deviation

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Extra	238	Female	36	2: Throat soreness <6 at baseline, Difficulty <=50mm at baseline	Protocol Deviations
Strepsils Extra	248	Female	56	Swollen throat <=33mm at baseline	Protocol Deviation
Strepsils Extra	250	Male	18	3: Throat soreness <6 at baseline, Difficulty <=50mm at baseline, Swollen throat <=33mm at baseline	Protocol Deviations

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Placebo	252	Female	41	2: Throat soreness <6 at baseline, Difficulty <=50mm at baseline,	Protocol Deviations

Centre Number/Investigator Name: 05. Dr Nigel Hart

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Plus	175	Female	55	Swollen throat <=33mm at baseline	Protocol Deviation

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Placebo	178	Female	22	Difficulty <=50mm at baseline,	Protocol Deviation

Centre Number/Investigator Name: 07. Dr Gerry McKeague

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Plus	106	Female	18	Difficulty <=50mm at baseline,	Protocol Deviation

Centre Number/Investigator Name: 08. Dr Sean Haigney

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Strepsils Extra	203	Male	51	No symptoms on URTI questionnaire at baseline	Protocol Deviation

Treatment	Patient No	Sex	Age	Observation Excluded	Reason
Placebo	202	Male	20	Difficulty <=50mm at baseline,	Protocol Deviation

APPENDIX 16.2.4 DEMOGRAPHIC DATA

Listing 16.2.4.1
Patient data listing of demographic data
Full Analysis set

Centre number	Patient number	Treatment group	Age (years)	Gender	Race	Drank alcohol	Number of units of alcohol drank per week	Smoking status	Number of cigarettes per day	Duration of sore throat (days)	Duration of upper respiratory tract infection (days)
1	034	Strepsils Plus	24	Female	Caucasian	Yes	6	Current	20	1	1
1	038	Strepsils Plus	58	Female	Caucasian	No		Never		1	1
1	041	Strepsils Plus	18	Female	Caucasian	Yes	7	Never		2	2
1	044	Strepsils Plus	27	Male	Caucasian	Yes	20	Former	15	2	2
1	048	Strepsils Plus	48	Male	Caucasian	No		Current	20	2	2
1	051	Strepsils Plus	63	Male	Caucasian	Yes	6	Current	10	3	3
1	052	Strepsils Plus	57	Female	Caucasian	No		Never		2	2
1	057	Strepsils Plus	45	Female	Caucasian	No		Current	15	3	3
1	059	Strepsils Plus	51	Male	Caucasian	No		Current	4	0	1
1	061	Strepsils Plus	23	Female	Caucasian	Yes	6	Never		1	1
2	002	Strepsils Plus	30	Female	Caucasian	No		Former	60	1	1
2	006	Strepsils Plus	21	Male	Caucasian	No		Current	2	3	3
2	007	Strepsils Plus	32	Male	Caucasian	No		Current	5	3	3
2	012	Strepsils Plus	52	Male	Caucasian	No		Current	20	3	3
2	016	Strepsils Plus	18	Male	Caucasian	Yes	5	Never		3	3
2	017	Strepsils Plus	23	Female	Caucasian	Yes	10	Former	3	3	3
2	019	Strepsils Plus	18	Female	Caucasian	Yes	5	Never		3	3
2	022	Strepsils Plus	30	Female	Caucasian	Yes	5	Current	5	1	1
2	025	Strepsils Plus	21	Female	Caucasian	Yes	10	Current	10	1	1
2	029	Strepsils Plus	24	Female	Caucasian	Yes	4	Never		1	1
2	032	Strepsils Plus	37	Male	Caucasian	Yes	10	Current	20	2	2
3	232	Strepsils Plus	27	Male	Caucasian	Yes	9	Former	1	2	2
3	235	Strepsils Plus	29	Female	Caucasian	No		Never		3	3
3	239	Strepsils Plus	33	Female	Caucasian	Yes	2	Never		3	3
3	243	Strepsils Plus	28	Male	Caucasian	Yes	21	Current	4	3	3
3	245	Strepsils Plus	22	Female	Caucasian	Yes	5	Current	4	3	3
3	249	Strepsils Plus	40	Female	Caucasian	Yes	4	Current	40	2	2
3	251	Strepsils Plus	22	Male	Caucasian	Yes	24	Current	15	2	2
3	254	Strepsils Plus	19	Male	Caucasian	Yes	12	Current	10	2	2

Centre number	Patient number	Treatment group	Age (years)	Gender	Race	Drank alcohol	Number of units of alcohol drank per week	Smoking status	Number of cigarettes per day	Duration of sore throat (days)	Duration of upper respiratory tract infection (days)
4	133	Strepsils Plus	21	Female	Caucasian	No		Never		4	3
4	138	Strepsils Plus	20	Female	Caucasian	No		Never		1	1
4	140	Strepsils Plus	27	Female	Caucasian	Yes	2	Former	2	1	1
4	142	Strepsils Plus	63	Female	Caucasian	No		Never		2	2
4	147	Strepsils Plus	45	Female	Caucasian	Yes	1	Never		3	3
4	148	Strepsils Plus	28	Female	Caucasian	Yes	6	Never		1	1
4	151	Strepsils Plus	73	Female	Caucasian	No		Former	5	1	1
4	154	Strepsils Plus	25	Female	Caucasian	No		Never		1	1
4	156	Strepsils Plus	18	Male	Caucasian	Yes	5	Former	1	2	2
4	161	Strepsils Plus	57	Female	Caucasian	No		Former	25	2	2
5	167	Strepsils Plus	19	Female	Caucasian	Yes	1	Never		3	2
5	171	Strepsils Plus	58	Female	Caucasian	Yes	1	Never		2	2
5	172	Strepsils Plus	25	Female	Caucasian	Yes	2	Never		2	2
5	175	Strepsils Plus	55	Female	Caucasian	Yes	2	Never		1	1
5	180	Strepsils Plus	18	Female	Caucasian	No		Never		2	2
5	181	Strepsils Plus	64	Female	Caucasian	No		Former	2	3	3
6	070	Strepsils Plus	64	Female	Caucasian	Yes	1	Never		3	3
6	074	Strepsils Plus	24	Male	Caucasian	Yes	10	Current	10	3	2
6	077	Strepsils Plus	61	Female	Caucasian	Yes	1	Never		2	2
6	079	Strepsils Plus	24	Female	Caucasian	Yes	2	Never		1	1
7	102	Strepsils Plus	23	Male	Caucasian	Yes	10	Never		2	2
7	106	Strepsils Plus	18	Female	Caucasian	Yes	6	Never		3	3
7	108	Strepsils Plus	18	Male	Caucasian	Yes	15	Current	1	2	2
7	109	Strepsils Plus	19	Male	Caucasian	Yes	12	Current	1	4	4
7	110	Strepsils Plus	18	Female	Caucasian	No		Never		4	4
7	115	Strepsils Plus	22	Male	Caucasian	Yes	10	Never		3	3
7	117	Strepsils Plus	21	Female	Caucasian	Yes	9	Never		3	3
7	123	Strepsils Plus	19	Female	Caucasian	Yes	7	Never		1	1
7	125	Strepsils Plus	25	Female	Caucasian	Yes	8	Never		2	2
7	127	Strepsils Plus	21	Male	Caucasian	Yes	4	Never		2	2
7	128	Strepsils Plus	19	Male	Caucasian	Yes	1	Never		3	3
8	200	Strepsils Plus	23	Female	Caucasian	No		Never		2	2
8	205	Strepsils Plus	18	Female	Caucasian	Yes	4	Never		3	3
8	206	Strepsils Plus	31	Female	Caucasian	Yes	1	Never		2	2
8	209	Strepsils Plus	47	Female	Caucasian	Yes	1	Never		2	2
1	036	Strepsils Extra	59	Female	Caucasian	Yes	8	Current	4	2	2

Centre number	Patient number	Treatment group	Age (years)	Gender	Race	Drank alcohol	Number of units of alcohol drank per week	Smoking status	Number of cigarettes per day	Duration of sore throat (days)	Duration of upper respiratory tract infection (days)
1	039	Strepsils Extra	39	Female	Caucasian	Yes	8	Never		2	2
1	042	Strepsils Extra	18	Female	Caucasian	Yes	14	Current	10	1	1
1	043	Strepsils Extra	24	Female	Caucasian	Yes	2	Never		2	2
1	047	Strepsils Extra	51	Female	Caucasian	No		Former	30	3	3
1	049	Strepsils Extra	51	Male	Caucasian	No		Current	10	1	1
1	053	Strepsils Extra	29	Female	Caucasian	Yes	2	Never		1	1
1	055	Strepsils Extra	30	Female	Caucasian	No		Current	5	2	2
1	058	Strepsils Extra	27	Female	Caucasian	No		Current	8	2	2
1	062	Strepsils Extra	31	Female	Caucasian	Yes	2	Never		3	3
2	004	Strepsils Extra	49	Female	Caucasian	Yes	1	Never		1	1
2	005	Strepsils Extra	27	Male	Caucasian	No		Never		3	3
2	008	Strepsils Extra	19	Female	Caucasian	Yes	10	Never		2	2
2	010	Strepsils Extra	40	Male	Caucasian	Yes	4	Current	10	3	3
2	013	Strepsils Extra	30	Male	Caucasian	Yes	20	Current	10	3	3
2	018	Strepsils Extra	18	Female	Caucasian	Yes	4	Never		2	2
2	020	Strepsils Extra	23	Male	Caucasian	Yes	4	Never		2	2
2	026	Strepsils Extra	18	Female	Caucasian	Yes	6	Never		2	2
2	027	Strepsils Extra	29	Female	Caucasian	No		Never		1	1
2	030	Strepsils Extra	25	Female	Caucasian	No		Former	20	1	1
2	033	Strepsils Extra	18	Female	Caucasian	Yes	10	Never		3	3
3	233	Strepsils Extra	21	Male	Caucasian	Yes	12	Never		1	1
3	236	Strepsils Extra	19	Female	Caucasian	Yes	14	Never		1	1
3	238	Strepsils Extra	36	Female	Caucasian	Yes	12	Current	20	2	2
3	244	Strepsils Extra	27	Male	Caucasian	Yes	21	Current	15	3	3
3	246	Strepsils Extra	26	Male	Caucasian	Yes	21	Current	12	4	4
3	248	Strepsils Extra	56	Female	Caucasian	No		Never		3	3
3	250	Strepsils Extra	18	Male	Caucasian	Yes	24	Current	15	2	2
3	253	Strepsils Extra	19	Male	Caucasian	Yes	24	Current	2	2	2
4	134	Strepsils Extra	51	Female	Caucasian	Yes	5	Former	20	3	3
4	137	Strepsils Extra	46	Female	Caucasian	Yes	5	Former	30	2	2
4	141	Strepsils Extra	22	Female	Caucasian	Yes	4	Never		2	2
4	144	Strepsils Extra	46	Female	Caucasian	Yes	12	Current	20	1	1
4	145	Strepsils Extra	43	Male	Caucasian	Yes	1	Never		2	2
4	152	Strepsils Extra	25	Female	Caucasian	Yes	1	Never		0	0
4	153	Strepsils Extra	68	Female	Caucasian	No		Never		2	2
4	158	Strepsils Extra	42	Female	Caucasian	No		Never		0	0

Centre number	Patient number	Treatment group	Age (years)	Gender	Race	Drank alcohol	Number of units of alcohol drank per week	Smoking status	Number of cigarettes per day	Duration of sore throat (days)	Duration of upper respiratory tract infection (days)
4	159	Strepsils Extra	32	Female	Caucasian	No		Never		2	2
4	162	Strepsils Extra	25	Female	Caucasian	Yes	1	Never		2	2
5	169	Strepsils Extra	18	Female	Caucasian	Yes	5	Never		1	1
5	170	Strepsils Extra	26	Female	Caucasian	Yes	4	Current	2	3	3
5	173	Strepsils Extra	49	Female	Caucasian	No		Never		2	2
5	177	Strepsils Extra	26	Male	Caucasian	No		Current	10	1	1
5	179	Strepsils Extra	32	Male	Caucasian	Yes	15	Current	30	3	3
6	067	Strepsils Extra	18	Female	Caucasian	No		Never		1	3
6	071	Strepsils Extra	37	Female	Caucasian	Yes	6	Current	6	4	4
6	075	Strepsils Extra	41	Male	Caucasian	Yes	12	Current	12	3	3
6	076	Strepsils Extra	22	Female	Caucasian	Yes	9	Current	6	3	3
7	101	Strepsils Extra	20	Female	Caucasian	Yes	6	Former	1	2	2
7	105	Strepsils Extra	20	Female	Caucasian	Yes	2	Never		2	2
7	107	Strepsils Extra	25	Female	Asian	Yes	3	Never		1	1
7	111	Strepsils Extra	22	Female	Caucasian	Yes	2	Never		1	1
7	113	Strepsils Extra	22	Male	Caucasian	Yes	20	Never		3	3
7	119	Strepsils Extra	19	Female	Caucasian	Yes	12	Never		3	3
7	120	Strepsils Extra	20	Male	Caucasian	No		Former	1	3	3
7	122	Strepsils Extra	27	Female	Caucasian	No		Never		2	2
7	124	Strepsils Extra	18	Male	Caucasian	Yes	2	Never		2	2
7	129	Strepsils Extra	41	Male	Caucasian	Yes	2	Never		2	2
7	130	Strepsils Extra	19	Female	Caucasian	Yes	12	Never		3	3
8	199	Strepsils Extra	20	Male	Caucasian	Yes	12	Current	10	1	1
8	203	Strepsils Extra	51	Male	Caucasian	Yes	10	Current	20	0	0
8	204	Strepsils Extra	20	Male	Caucasian	Yes	20	Never		2	2
8	208	Strepsils Extra	32	Female	Caucasian	No		Former	1	2	2
8	211	Strepsils Extra	56	Female	Caucasian	No		Former	20	1	1
1	035	Placebo	27	Female	Caucasian	Yes	15	Current	2	3	3
1	037	Placebo	22	Female	Caucasian	Yes	2	Current	10	1	1
1	040	Placebo	45	Male	Caucasian	Yes	4	Never		1	1
1	045	Placebo	23	Male	Caucasian	Yes	4	Current	20	2	2
1	046	Placebo	28	Male	Caucasian	Yes	24	Current	5	3	3
1	050	Placebo	41	Male	Caucasian	Yes	12	Never		2	2
1	054	Placebo	42	Female	Caucasian	Yes	2	Former	10	3	3
1	056	Placebo	40	Male	Caucasian	Yes	4	Never		3	3
1	060	Placebo	24	Male	Caucasian	Yes	20	Current	8	0	0

Centre number	Patient number	Treatment group	Age (years)	Gender	Race	Drank alcohol	Number of units of alcohol drank per week	Smoking status	Number of cigarettes per day	Duration of sore throat (days)	Duration of upper respiratory tract infection (days)
2	001	Placebo	51	Female	Caucasian	No		Former	3	2	3
2	003	Placebo	25	Male	Caucasian	Yes	12	Former	7	2	2
2	009	Placebo	20	Female	Caucasian	Yes	10	Never		3	3
2	011	Placebo	46	Male	Caucasian	Yes	1	Current	30	3	0
2	014	Placebo	19	Female	Caucasian	No		Current	15	2	2
2	015	Placebo	18	Male	Caucasian	Yes	6	Never		2	2
2	021	Placebo	36	Male	Asian	No		Never		3	3
2	023	Placebo	25	Female	Caucasian	No		Never		3	3
2	024	Placebo	23	Female	Caucasian	Yes	15	Current	4	2	2
2	028	Placebo	28	Male	Caucasian	Yes	12	Current	5	0	0
2	031	Placebo	34	Female	Caucasian	Yes	6	Never		3	3
3	234	Placebo	22	Female	Caucasian	Yes	2	Current	1	3	3
3	237	Placebo	58	Male	Caucasian	No		Never		2	2
3	240	Placebo	38	Female	Caucasian	No		Current	12	3	3
3	241	Placebo	18	Male	Caucasian	Yes	1	Current	10	3	3
3	242	Placebo	23	Male	Caucasian	Yes	20	Current	40	3	3
3	247	Placebo	19	Male	Caucasian	Yes	24	Never		2	2
3	252	Placebo	41	Female	Caucasian	Yes	4	Current	10	2	2
3	255	Placebo	44	Female	Caucasian	Yes	1	Never		2	2
4	135	Placebo	51	Male	Caucasian	Yes	14	Never		3	3
4	136	Placebo	42	Female	Caucasian	Yes	9	Never		2	2
4	139	Placebo	50	Male	Caucasian	No		Never		2	2
4	143	Placebo	35	Male	Caucasian	Yes	10	Current	10	1	1
4	146	Placebo	33	Male	Caucasian	No		Never		4	4
4	149	Placebo	19	Male	Caucasian	Yes	4	Never		2	2
4	150	Placebo	30	Male	Caucasian	No		Current	10	1	1
4	155	Placebo	40	Male	Caucasian	Yes	12	Former	10	1	1
4	157	Placebo	43	Female	Caucasian	No		Never		2	2
4	160	Placebo	32	Male	Caucasian	No		Former	10	2	2
5	166	Placebo	35	Female	Caucasian	Yes	6	Never		3	3
5	168	Placebo	22	Male	Caucasian	Yes	10	Former	10	1	1
5	174	Placebo	47	Female	Caucasian	No		Never		1	1
5	176	Placebo	50	Male	Asian	No		Never		1	1
5	178	Placebo	22	Female	Caucasian	No		Current	20	3	3
6	069	Placebo	45	Male	Caucasian	No		Never		3	3
6	072	Placebo	18	Female	Caucasian	Yes	1	Never		1	1

Centre number	Patient number	Treatment group	Age (years)	Gender	Race	Drank alcohol	Number of units of alcohol drank per week	Smoking status	Number of cigarettes per day	Duration of sore throat (days)	Duration of upper respiratory tract infection (days)
6	073	Placebo	37	Male	Caucasian	Yes	15	Never		2	2
6	078	Placebo	66	Male	Caucasian	Yes	6	Never		2	2
6	080	Placebo	31	Male	Caucasian	Yes	10	Never		3	3
7	100	Placebo	23	Female	Caucasian	Yes	10	Never		1	1
7	103	Placebo	23	Female	Caucasian	Yes	4	Never		3	3
7	104	Placebo	31	Male	Caucasian	Yes	4	Never		3	3
7	112	Placebo	18	Female	Caucasian	Yes	4	Never		3	3
7	114	Placebo	20	Female	Caucasian	Yes	18	Never		2	2
7	116	Placebo	22	Male	Caucasian	Yes	4	Former	1	2	2
7	118	Placebo	19	Female	Caucasian	Yes	10	Never		2	2
7	121	Placebo	21	Male	Caucasian	Yes	12	Never		3	3
7	126	Placebo	19	Male	Caucasian	Yes	10	Never		3	3
7	131	Placebo	19	Female	Afro-Caribbean	Yes	10	Never		2	2
8	201	Placebo	33	Male	Caucasian	Yes	4	Current	10	3	3
8	202	Placebo	20	Male	Caucasian	Yes	16	Current	10	3	3
8	207	Placebo	31	Male	Caucasian	No		Current	5	2	2
8	210	Placebo	28	Female	Caucasian	Yes	2	Never		1	1

Listing 16.2.4.2
Patient data listing of medical history data
Full Analysis set

Centre number	Patient number	Treatment group	Medical history details	Medical history category	Ongoing at randomisation
1	034	Strepsils Plus	MIGRAINE	Neurological	Yes
1	044	Strepsils Plus	INSOMNIA	Other	Yes
1	044	Strepsils Plus	SLEEP DISTURBANCES	Psychiatric	Yes
1	048	Strepsils Plus	TYPE 2 DIABETES	Endocrine/metabolic	Yes
1	048	Strepsils Plus	HYPERTENSION	Cardiovascular	Yes
1	048	Strepsils Plus	DYSPEPSIA	Gastrointestinal	Yes
1	048	Strepsils Plus	ROTATOR CUFF SYNDROME	Musculoskeletal	Yes
1	048	Strepsils Plus	IMPOTENCE	Endocrine/metabolic	Yes
1	057	Strepsils Plus	MIGRAINE	Neurological	No
1	057	Strepsils Plus	CHESTY COUGH	Respiratory	Yes
1	059	Strepsils Plus	RHEUMATOID ARTHRITIS	Musculoskeletal	Yes
1	059	Strepsils Plus	SEBORRHOEIC ECZEMA	Dermatological	Yes
1	059	Strepsils Plus	MEMORY LOSS	Other	Yes
1	061	Strepsils Plus	PSORIASIS	Dermatological	Yes
2	002	Strepsils Plus	CONSTIPATION	Gastrointestinal	Yes
2	002	Strepsils Plus	DEPRESSIVE DISORDER	Psychiatric	Yes
2	002	Strepsils Plus	INSOMNIA	Psychiatric	Yes
2	002	Strepsils Plus	ASTHMA	Respiratory	Yes
2	002	Strepsils Plus	BACK PAIN	Musculoskeletal	Yes
2	007	Strepsils Plus	DEPRESSION	Psychiatric	Yes
2	007	Strepsils Plus	PSORIASIS	Dermatological	Yes
2	012	Strepsils Plus	TYPE 2 DIABETES	Endocrine/metabolic	Yes
2	012	Strepsils Plus	DEPRESSION	Psychiatric	Yes
2	012	Strepsils Plus	HYPOTHYROIDISM	Endocrine/metabolic	Yes
2	012	Strepsils Plus	LEFT KIDNEY REMOVED	Urogenital	No
2	016	Strepsils Plus	TYPE 1 DIABETES	Endocrine/metabolic	Yes
2	032	Strepsils Plus	POST-TRAUMATIC STRESS DISORDER	Psychiatric	Yes
2	032	Strepsils Plus	ANXIETY	Psychiatric	Yes
2	032	Strepsils Plus	ALCOHOL DEPENDANCE SYNDROME	Psychiatric	Yes
3	235	Strepsils Plus	PSORIASIS	Dermatological	Yes
3	235	Strepsils Plus	DEPRESSION	Psychiatric	Yes
3	239	Strepsils Plus	PARAMYTONIA CONGENITA	Musculoskeletal	Yes
3	243	Strepsils Plus	SLIPPED DISC	Musculoskeletal	Yes
3	243	Strepsils Plus	INSOMNIA	Psychiatric	Yes

Centre number	Patient number	Treatment group	Medical history details	Medical history category	Ongoing at randomisation
3	249	Strepsils Plus	OBESITY	Gastrointestinal	Yes
3	249	Strepsils Plus	DEPRESSION	Psychiatric	Yes
3	249	Strepsils Plus	INSOMNIA	Psychiatric	Yes
3	251	Strepsils Plus	ACNE	Dermatological	Yes
4	140	Strepsils Plus	CONJUNCTIVITIS	Eyes	Yes
4	142	Strepsils Plus	ESSENTIAL HYPERTENSION	Cardiovascular	Yes
4	142	Strepsils Plus	HYPOTHYROIDISM	Endocrine/metabolic	Yes
4	142	Strepsils Plus	SLEEP DISTURBANCE	Other	Yes
4	142	Strepsils Plus	ACHING MUSCLES	Musculoskeletal	Yes
4	147	Strepsils Plus	LUPUS ERYTHEMATOSUS	Autoimmune	Yes
4	147	Strepsils Plus	RHEUMATOID ARTHRITIS	Musculoskeletal	Yes
4	154	Strepsils Plus	STYE	Eyes	Yes
4	161	Strepsils Plus	OSTEOARTHRITIS	Musculoskeletal	Yes
4	161	Strepsils Plus	PURE HYPERCHOLESTEROLAEMIA	Cardiovascular	Yes
4	161	Strepsils Plus	ASTHMA	Respiratory	Yes
4	161	Strepsils Plus	FEMALE STERILISATION	Surgery	No
4	161	Strepsils Plus	DEPRESSION	Psychiatric	Yes
4	161	Strepsils Plus	DYSPEPSIA	Gastrointestinal	Yes
5	167	Strepsils Plus	HEAVY PERIODS	Other	Yes
5	171	Strepsils Plus	DEPRESSIVE DISORDER	Psychiatric	Yes
5	171	Strepsils Plus	OESOPHAGITIS	Gastrointestinal	Yes
5	171	Strepsils Plus	BACK PAIN	Musculoskeletal	Yes
5	171	Strepsils Plus	FIBROMYALGIA	Musculoskeletal	Yes
5	171	Strepsils Plus	IRRITABLE BOWEL SYNDROME	Gastrointestinal	Yes
5	171	Strepsils Plus	MIGRAINE HEADACHES	Neurological	Yes
5	171	Strepsils Plus	TONSILECTOMY	Surgery	No
5	171	Strepsils Plus	LAPAROSCOPIC BILATERAL FEMALE STERILISATION	Surgery	No
5	171	Strepsils Plus	URINARY INCONTINENCE	Urogenital	Yes
5	171	Strepsils Plus	MOUTH ULCERS	Other	Yes
5	172	Strepsils Plus	CHRONIC CONSTIPATION	Gastrointestinal	Yes
5	172	Strepsils Plus	ANXIETY STAKES	Psychiatric	Yes
5	172	Strepsils Plus	DEPRESSIVE DISORDER	Psychiatric	Yes
5	172	Strepsils Plus	HEARTBURN	Gastrointestinal	Yes
5	175	Strepsils Plus	DIABETES MELLITUS TYPE II	Endocrine/metabolic	Yes
5	175	Strepsils Plus	HEARTBURN	Gastrointestinal	Yes
5	181	Strepsils Plus	ESSENTIAL HYPERTENSION	Cardiovascular	Yes
5	181	Strepsils Plus	DIABETES MELLITUS TYPE II	Endocrine/metabolic	Yes
5	181	Strepsils Plus	OSTEOARTHRITIS	Musculoskeletal	Yes
5	181	Strepsils Plus	HIATUS HERNIA	Gastrointestinal	Yes

Centre number	Patient number	Treatment group	Medical history details	Medical history category	Ongoing at randomisation
5	181	Strepsils Plus	FOOT PAIN	Musculoskeletal	Yes
5	181	Strepsils Plus	HAYFEVER	Allergies/Drug sensitivity	Yes
6	070	Strepsils Plus	ELEVATED CHOLESTEROL	Cardiovascular	Yes
6	070	Strepsils Plus	INDIGESTION	Gastrointestinal	Yes
6	070	Strepsils Plus	MENOPAUSE	Urogenital	Yes
6	074	Strepsils Plus	ECZEMA	Dermatological	Yes
6	077	Strepsils Plus	HYSTERECTOMY	Surgery	No
6	077	Strepsils Plus	BI-POLAR	Psychiatric	Yes
6	079	Strepsils Plus	TONSILLECTOMY	Surgery	No
6	079	Strepsils Plus	ASTHMA	Respiratory	No
6	079	Strepsils Plus	HAY FEVER	Allergies/Drug sensitivity	Yes
7	109	Strepsils Plus	NAIL FUNGAL INFECTION (TOE)	Dermatological	Yes
8	206	Strepsils Plus	ASTHMA	Respiratory	Yes
8	206	Strepsils Plus	GALLSTONES	Gastrointestinal	Yes
8	209	Strepsils Plus	HYPOTHYROIDISM	Endocrine/metabolic	Yes
1	036	Strepsils Extra	COPD	Respiratory	Yes
1	036	Strepsils Extra	HYPOTHYROIDISM	Endocrine/metabolic	Yes
1	036	Strepsils Extra	HYSTERECTOMY	Surgery	No
1	036	Strepsils Extra	DEPRESSION	Psychiatric	Yes
1	036	Strepsils Extra	RESTLESS LEGS	Musculoskeletal	Yes
1	036	Strepsils Extra	KERATOSIS	Dermatological	Yes
1	036	Strepsils Extra	HEARTBURN	Gastrointestinal	Yes
1	036	Strepsils Extra	ADHESIVE CAPSULITIS	Musculoskeletal	Yes
1	047	Strepsils Extra	OSTEOARTHRITIS	Musculoskeletal	Yes
1	047	Strepsils Extra	DYSPEPSIA	Gastrointestinal	Yes
1	047	Strepsils Extra	HEADACHE	Other	Yes
1	047	Strepsils Extra	TOTAL ABDOMINAL HYSTERECTOMY	Surgery	No
1	049	Strepsils Extra	MILD COPD	Respiratory	Yes
1	049	Strepsils Extra	PSORIASIS	Dermatological	Yes
1	055	Strepsils Extra	ECZEMA	Dermatological	Yes
1	058	Strepsils Extra	MODERATE DEPRESSION	Psychiatric	Yes
1	062	Strepsils Extra	ASTHMA	Respiratory	Yes
2	004	Strepsils Extra	ASTHMA	Respiratory	Yes
2	005	Strepsils Extra	DEPRESSION	Psychiatric	Yes
2	005	Strepsils Extra	FRACTURED VERTEBRAE	Musculoskeletal	Yes
2	010	Strepsils Extra	ASTHMA	Respiratory	Yes
2	010	Strepsils Extra	FUNGAL NAIL INFECTION	Dermatological	Yes
2	010	Strepsils Extra	ARTHRALGIA	Musculoskeletal	Yes
2	010	Strepsils Extra	GASTRO-OESOPHAGEAL REFLUX	Gastrointestinal	Yes

Centre number	Patient number	Treatment group	Medical history details	Medical history category	Ongoing at randomisation
2	013	Strepsils Extra	DEPRESSION	Psychiatric	Yes
2	030	Strepsils Extra	ASTHMA	Respiratory	Yes
3	238	Strepsils Extra	HYPOTHYROIDISM	Endocrine/metabolic	Yes
3	238	Strepsils Extra	LOW MOOD	Psychiatric	Yes
3	238	Strepsils Extra	DEPRESSION	Psychiatric	Yes
3	238	Strepsils Extra	OBESITY	Other	Yes
3	238	Strepsils Extra	INSOMNIA	Neurological	Yes
3	244	Strepsils Extra	INSOMNIA	Neurological	Yes
3	244	Strepsils Extra	ANXIETY	Psychiatric	Yes
3	248	Strepsils Extra	DEPRESSION	Psychiatric	Yes
3	248	Strepsils Extra	OSTEOARTHRITIS	Musculoskeletal	Yes
3	250	Strepsils Extra	ADHD	Psychiatric	Yes
3	250	Strepsils Extra	ACNE	Dermatological	Yes
4	134	Strepsils Extra	MENOPAUSE	Endocrine/metabolic	Yes
4	153	Strepsils Extra	IMPAIRED GLUCOSE TOLERANCE	Endocrine/metabolic	Yes
4	153	Strepsils Extra	ESSENTIAL HYPERTENSION	Cardiovascular	Yes
4	153	Strepsils Extra	HYPOTHYROIDISM	Endocrine/metabolic	Yes
4	153	Strepsils Extra	ASTHMA	Respiratory	Yes
4	153	Strepsils Extra	DRY EYES	Eyes	Yes
4	158	Strepsils Extra	STERILISATION	Surgery	No
4	159	Strepsils Extra	MIGRAINE HEADACHE	Neurological	Yes
4	159	Strepsils Extra	RHEUMATOID ARTHRITIS	Musculoskeletal	Yes
4	159	Strepsils Extra	DEPRESSION	Psychiatric	Yes
5	173	Strepsils Extra	TONSILECTOMY	Surgery	No
5	173	Strepsils Extra	SYNOVITIS AND TENOSYNOVITIS RIGHT SHOULDER	Musculoskeletal	Yes
5	173	Strepsils Extra	CERVICALGIA	Musculoskeletal	Yes
5	173	Strepsils Extra	HEADACHES	Other	Yes
5	177	Strepsils Extra	ALCOHOL DEPENDENCE SYNDROME	Psychiatric	No
5	179	Strepsils Extra	MIGRAINE HEADACHE	Other	Yes
5	179	Strepsils Extra	HEARTBURN	Gastrointestinal	Yes
5	179	Strepsils Extra	LOW BACK PAIN	Musculoskeletal	Yes
6	067	Strepsils Extra	PHYSIOLOGICAL IRON DEFICIENCY	Other	Yes
6	075	Strepsils Extra	SURGERY - TONSILLECTOMY	Surgery	No
7	105	Strepsils Extra	CROHN'S DISEASE	Gastrointestinal	Yes
7	105	Strepsils Extra	MILD ASTHMA CONTROLLED	Respiratory	Yes
7	120	Strepsils Extra	DEPRESSION	Psychiatric	Yes
7	129	Strepsils Extra	HYPERTENSION	Cardiovascular	Yes
8	199	Strepsils Extra	DEPRESSION	Psychiatric	Yes
8	199	Strepsils Extra	INSOMNIA	Psychiatric	Yes

Centre number	Patient number	Treatment group	Medical history details	Medical history category	Ongoing at randomisation
8	203	Strepsils Extra	TYPE 2 DIABETES MELLITUS	Endocrine/metabolic	Yes
8	203	Strepsils Extra	SENSORINEURAL HEARING LOSS	Ears	Yes
8	203	Strepsils Extra	APPENDICETOMY	Gastrointestinal	No
8	203	Strepsils Extra	TONSILLECTOMY	Nose/throat	No
8	204	Strepsils Extra	KNEE PAIN	Musculoskeletal	Yes
8	211	Strepsils Extra	HYPERLIPIDAEMIA	Cardiovascular	Yes
8	211	Strepsils Extra	OEDEMA	Other	Yes
8	211	Strepsils Extra	FOOT PAIN	Musculoskeletal	Yes
1	037	Placebo	INSERTION OF MIRENA COIL	Other	Yes
1	040	Placebo	DIABETES	Endocrine/metabolic	Yes
1	040	Placebo	HYPERTENSION	Cardiovascular	Yes
1	054	Placebo	BACK PAIN	Musculoskeletal	Yes
1	054	Placebo	DEPRESSION	Psychiatric	Yes
1	054	Placebo	CONGENITAL CEREBRAL PALSY	Neurological	Yes
1	054	Placebo	ECZEMA	Dermatological	Yes
1	054	Placebo	VITAMIN B DEFIENCY	Other	Yes
1	054	Placebo	OSTEOARTHRITIS	Musculoskeletal	Yes
2	001	Placebo	TYPE 2 DIABETES MELLITUS	Endocrine/metabolic	Yes
2	001	Placebo	ASTHMA	Respiratory	Yes
2	001	Placebo	DEPRESSIVE DISORDER	Psychiatric	Yes
2	001	Placebo	VAGINAL THRUSH	Urogenital	No
2	001	Placebo	LOW BACK PAIN	Musculoskeletal	Yes
2	001	Placebo	STERILISATION	Surgery	No
2	011	Placebo	DEPRESSION	Psychiatric	Yes
2	011	Placebo	SCIATICA	Musculoskeletal	Yes
2	011	Placebo	ESSENTIAL HYPERTENSION	Cardiovascular	Yes
2	011	Placebo	ASTHMA	Respiratory	Yes
2	021	Placebo	DRY SKIN	Dermatological	Yes
2	028	Placebo	DERMATITIS	Dermatological	Yes
2	028	Placebo	RASH ON NECK	Dermatological	Yes
2	031	Placebo	DEPRESSION	Psychiatric	Yes
2	031	Placebo	ESSENTIAL HYPERTENSION	Cardiovascular	Yes
3	234	Placebo	PSORIATIC ARTHROPATHY	Musculoskeletal	Yes
3	234	Placebo	ARTHRITIS	Musculoskeletal	Yes
3	237	Placebo	GUILLAN BARRE SYNDROME	Neurological	No
3	237	Placebo	ARTHRITIS	Musculoskeletal	Yes
3	237	Placebo	COLECTOMY	Gastrointestinal	Yes
3	240	Placebo	ECZEMA	Dermatological	Yes
3	242	Placebo	INSOMNIA	Psychiatric	Yes

Centre number	Patient number	Treatment group	Medical history details	Medical history category	Ongoing at randomisation
3	242	Placebo	ATTENTION DEFICIT DISORDER	Psychiatric	Yes
3	247	Placebo	ADHD	Psychiatric	Yes
3	255	Placebo	SURGICAL STERILIZATION	Urogenital	No
4	136	Placebo	PALPATATIONS	Cardiovascular	Yes
4	136	Placebo	PURE HYPERLIPIDAEMIA	Cardiovascular	Yes
4	139	Placebo	HYPOTHYROIDISM	Endocrine/metabolic	Yes
4	143	Placebo	TONSILLECTOMY	Nose/throat	No
4	143	Placebo	RING WORM	Dermatological	Yes
4	146	Placebo	HEADACHE	Musculoskeletal	Yes
4	150	Placebo	TONSILLECTOMY	Surgery	No
4	157	Placebo	FEMALE STERILISATION	Surgery	No
4	157	Placebo	DEPRESSION	Psychiatric	Yes
4	157	Placebo	DRY SKIN	Dermatological	Yes
4	157	Placebo	ASTHMA	Respiratory	Yes
4	157	Placebo	URGENCY OF MICTURITION	Urogenital	Yes
4	160	Placebo	DEPRESSION	Psychiatric	Yes
5	166	Placebo	LOW BACK PAIN	Musculoskeletal	Yes
5	166	Placebo	MENORRHAGIA	Other	Yes
5	166	Placebo	LAPROSCOPY, HYSTEROSCOPY AND STERILISATION	Surgery	No
5	168	Placebo	MYRINGOTOMY AND INSERTION GROMMETS LEFT EAR	Ears	No
5	174	Placebo	DYSPEPSIA	Gastrointestinal	Yes
5	176	Placebo	GASTRO OESOPHAGEUS REFLUX DISEASE	Gastrointestinal	Yes
5	178	Placebo	MENORRHAGIA	Other	Yes
6	069	Placebo	HEPATIC STEATOSIS	Gastrointestinal	Yes
6	069	Placebo	STRESS RELATED PROBLEMS	Psychiatric	Yes
6	078	Placebo	HIGH CHOLESTEROL	Cardiovascular	Yes
6	080	Placebo	TONSILLECTOMY	Surgery	No
7	100	Placebo	MILD ASTHMA CONTROLLED	Respiratory	Yes
7	100	Placebo	DEPRESSION	Psychiatric	Yes
7	100	Placebo	KIWI FRUIT ALLERGY	Allergies/Drug sensitivity	Yes
7	104	Placebo	ULCERATIVE COLITIS	Gastrointestinal	Yes
7	112	Placebo	MILD ASTHMA	Respiratory	Yes
8	201	Placebo	SEIZURE	Neurological	Yes
8	202	Placebo	NASAL SEPTAL INJURY FOLLOWING TRAUME	Nose/throat	Yes
8	207	Placebo	ASTHMA	Respiratory	Yes
8	207	Placebo	INSOMNIA	Other	Yes
8	207	Placebo	DYSPEPSIA	Gastrointestinal	Yes
8	210	Placebo	LOW BACK PAIN	Musculoskeletal	Yes

Listing 16.2.4.3
Patient data listing of concomitant medications stopped prior to randomisation set -
Full Analysis set

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
1	034	Strepsils Plus	Paracetamol	ANALGESICS	Migraine	-9	-8	1
1	038	Strepsils Plus	Paracetamol	ANALGESICS	Knee osteoarthritis	-2666	-1	2665
1	038	Strepsils Plus	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Knee osteoarthritis	-2666	-1	2665
1	038	Strepsils Plus	Co Dydramol	ANALGESICS	Knee osteoarthritis	-1124	-1	1123
1	048	Strepsils Plus	Aspirin	ANTITHROMBOTIC AGENTS	Type 2 diabetes	-343	-1	342
1	048	Strepsils Plus	Paracetamol	ANALGESICS	Rotator cuff syndrome	-2485	-1	2484
1	059	Strepsils Plus	Co-Codamol	ANALGESICS	Rheumatoid arthritis	-1781	-1	1780
2	002	Strepsils Plus	Kapake	ANALGESICS	Back pain	-1618	-1	1617
2	012	Strepsils Plus	Aspirin	ANTITHROMBOTIC AGENTS	Type 2 diabetes	-770	-1	769
3	232	Strepsils Plus	Lockets	COUGH AND COLD PREPARATIONS	Sore throat	-2	-1	1
3	239	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	-1	-1	0
3	243	Strepsils Plus	Tramadol	ANALGESICS	Slipped disc	-3345	-1	3344
4	133	Strepsils Plus	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Sore throat	0	0	0
4	140	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	-1	-1	0
4	147	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	-3	0	3

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
4	151	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	0	0	0
4	154	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	-1	-1	0
4	161	Strepsils Plus	Tramadol hydrochloride	ANALGESICS	Oesteoarthritis	-565	-1	564
5	171	Strepsils Plus	Co-codamol	ANALGESICS	Fibromyalgia	-1831	-1	1830
5	181	Strepsils Plus	Tramadol	ANALGESICS	Osteoarthritis	-1426	-1	1425
7	106	Strepsils Plus	Paracetamol	ANALGESICS	Analgesia sore throat	0	0	0
7	110	Strepsils Plus	Paracetamol	ANALGESICS	Analgesia sore throat	-2	-1	1
7	110	Strepsils Plus	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Analgesia sore throat	-2	-1	1
7	117	Strepsils Plus	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Sore throat	-1	-1	0
7	123	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	-1	-1	0
8	200	Strepsils Plus	Otrovine nasal spray	NASAL PREPARATIONS	URTI	-1	0	1
8	206	Strepsils Plus	Strepsil	THROAT PREPARATIONS	Sore throat	-2	-2	0
1	036	Strepsils Extra	Paracetamol	ANALGESICS	Capsulities of shoulder	-951	-1	950
1	036	Strepsils Extra	Co codamol	ANALGESICS	Capsulitis of shoulder	-739	-1	738
1	047	Strepsils Extra	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Osteoarthritis	-1	-1	0
1	047	Strepsils Extra	Diclofenac gel	OTHER DERMATOLOGICAL PREPARATIONS	Osteoarthritis	-539	-1	538
1	047	Strepsils Extra	CO-Codamol	ANALGESICS	Osteoarthritis	-4324	-1	4323
2	005	Strepsils Extra	Diclofenac	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Fractured vertibrae	-46	-2	44

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
2	005	Strepsils Extra	Co-codamol	ANALGESICS	Fractured vertibrae	-46	-2	44
2	005	Strepsils Extra	Diazepam	PSYCHOLEPTICS	Fractured vertibrae	-46	-2	44
3	233	Strepsils Extra	Nurofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Sore throat	0	0	0
3	248	Strepsils Extra	Celecoxib	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Osteoarthritis	-180	-2	178
4	145	Strepsils Extra	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Sore throat	-1	-1	0
4	158	Strepsils Extra	Co codamol 8/500	ANALGESICS	Sore throat	0	0	0
4	162	Strepsils Extra	Co-codamol 8/500	ANALGESICS	Sore throat	-1	-1	0
7	101	Strepsils Extra	Oraldene mouthwash	STOMATOLOGICAL PREPARATIONS	Sore throat	0	0	0
7	111	Strepsils Extra	Lemsip	ANALGESICS	Analgesia - Sore throat	-1	-1	0
7	113	Strepsils Extra	Paracetamol	ANALGESICS	Sore throat	-2	-2	0
7	120	Strepsils Extra	Paracetamol	ANALGESICS	Sore throat	0	0	0
8	199	Strepsils Extra	Mirtazepine	PSYCHOANALEPTICS	Insomnia	-5	-5	0
8	204	Strepsils Extra	Diclofenac sodium	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Knee pain	-55	-1	54
8	204	Strepsils Extra	Paracetamol	ANALGESICS	URTI	-3	-3	0
8	208	Strepsils Extra	Paracetamol	ANALGESICS	Headache	-8	-8	0
8	208	Strepsils Extra	Lemsip	ANALGESICS	URTI	-2	-2	0
1	040	Placebo	Aspirin	ANTITHROMBOTIC AGENTS	Diabetes	-2779	-1	2778
1	054	Placebo	Co-codamol	ANALGESICS	Back pain	-3912	-1	3911

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
1	054	Placebo	Diclofenac sodium	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Back pain	-3807	-1	3806
1	054	Placebo	Diclofenac gel	OTHER DERMATOLOGICAL PREPARATIONS	Osteoarthritis	-2510	-1	2509
2	001	Placebo	Tramadol mr	ANALGESICS	Low back pain	-110	-1	109
2	001	Placebo	Clotrimazole cream + pessary	GYNECOLOGICAL ANTIINFECTIVES AND ANTISEPTICS	Vaginal thrush	-27	-7	20
2	001	Placebo	Paracetamol	ANALGESICS	Low back pain	-1085	-1	1084
2	011	Placebo	Tramadol hydrochloride	ANALGESICS	Sciatica	-783	-2	781
3	234	Placebo	Codeine Phosphate	COUGH AND COLD PREPARATIONS	Cough	-3	-1	2
3	240	Placebo	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Sore throat	-1	-1	0
3	241	Placebo	Paracetamol	ANALGESICS	Sore throat	0	0	0
3	255	Placebo	Paracetamol	ANALGESICS	Sore throat	-1	-1	0
4	143	Placebo	Paracetamol	ANALGESICS	Sore throat	0	0	0
4	146	Placebo	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Headache	-3	0	3
5	166	Placebo	Co-codamol	ANALGESICS	Low back pain	-358	-1	357
5	166	Placebo	Mefenamic acid	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Menorrhagia	-43	-1	42
6	078	Placebo	Paracetamol	ANALGESICS	Sore throat	-2	-1	1
6	078	Placebo	Atorvastatin	LIPID MODIFYING AGENTS	High cholesterol	-235	-10	225
7	100	Placebo	Paracetamol	ANALGESICS	Sore throat analgesia	0	0	0
7	100	Placebo	Citalopram	PSYCHOANALEPTICS	Depression	-28	0	28

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
7	103	Placebo	Paracetamol	ANALGESICS	Sore throat analgesia	-4	0	4
7	103	Placebo	Microgynon	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-31	-4	27
7	112	Placebo	Paracetamol	ANALGESICS	Sore throat	0	0	0
7	121	Placebo	Paracetamol	ANALGESICS	Sore throat	-1	-1	0
8	210	Placebo	Paracetamol	ANALGESICS	Sore throat	-1	-1	0

Listing 16.2.4.4
Patient data listing of concomitant medications ongoing at randomisation-
Full Analysis set

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
1	034	Strepsils Plus	Logynon	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraceptive	-2712		
1	038	Strepsils Plus	Paroxetine	PSYCHOANALEPTICS	Depression	-110		
1	044	Strepsils Plus	Hydroxyzine hydrochloride	PSYCHOLEPTICS	Insomnia	-237		
1	044	Strepsils Plus	Risperidone	PSYCHOLEPTICS	Sleep disturbances	-175		
1	048	Strepsils Plus	Simvastatin	LIPID MODIFYING AGENTS	Type 2 diabetes	-343		
1	048	Strepsils Plus	Peptac liquid	DRUGS FOR ACID RELATED DISORDERS	Dyspepsia	-3795		
1	048	Strepsils Plus	Sildenafil	UROLOGICALS	Impotence	-328		
1	057	Strepsils Plus	Salbutamol inhaler	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Chesty cough	-2064		
1	059	Strepsils Plus	Prednisolone	CORTICOSTEROIDS FOR SYSTEMIC USE	Rheumatoid arthritis	-2926		
1	059	Strepsils Plus	Adcal D3	MINERAL SUPPLEMENTS	Rheumatoid arthritis	-2578		
1	059	Strepsils Plus	Alendronic acid	DRUGS FOR TREATMENT OF BONE DISEASES	Rheumatoid arthritis	-2619		
1	059	Strepsils Plus	Modrasone cream	CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	Seborrhoeic eczema	-2157		
1	059	Strepsils Plus	Etodalac m/r	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Rheumatoid arthritis	-2164		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
1	059	Strepsils Plus	Folic acid	ALL OTHER THERAPEUTIC PRODUCTS	Rheumatoid arthritis	-3111		
1	059	Strepsils Plus	Omeprazole	DRUGS FOR ACID RELATED DISORDERS	Rheumatoid arthritis	-2360		
1	059	Strepsils Plus	Methotrexate	ANTINEOPLASTIC AGENTS	Rheumatoid arthritis	-3111		
1	061	Strepsils Plus	Exorex lotion	ANTIPSORIATICS	Psoriasis	-797		
1	061	Strepsils Plus	Polytar emollient	ANTIPSORIATICS	Psoriasis	-83		
1	061	Strepsils Plus	Calcipotriol	ANTIPSORIATICS	Psoriasis	-31		
2	002	Strepsils Plus	Sodium picosolfate	LAXATIVES	Constipation	-62		
2	002	Strepsils Plus	Manevac	UNSPECIFIED HERBAL AND TRADITIONAL MEDICINE	Constipation	-26		
2	002	Strepsils Plus	Venlafaxine	PSYCHOANALEPTICS	Depressive disorder	-112		
2	002	Strepsils Plus	Venlafaxine	PSYCHOANALEPTICS	Depressive disorder	-1042		
2	002	Strepsils Plus	Zolpidem	PSYCHOLEPTICS	Insomnia	-1987		
2	002	Strepsils Plus	Desogestrel	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraceptive pill	-1117		
2	002	Strepsils Plus	Salbutamol	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1254		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
2	002	Strepsils Plus	Seretide	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1121		
2	002	Strepsils Plus	Diazepam	PSYCHOLEPTICS	Depressive disorder	-1285		
2	007	Strepsils Plus	Capasal shampoo	ANTIPSORIATICS	Psoriasis	-2098		
2	007	Strepsils Plus	Diprobase cream	EMOLLIENTS AND PROTECTIVES	Psoriasis	-2795		
2	007	Strepsils Plus	Calcipotriol cream	ANTIPSORIATICS	Psoriasis	-1126		
2	007	Strepsils Plus	Dermol	ANTISEPTICS AND DISINFECTANTS	Psoriasis	-562		
2	007	Strepsils Plus	Sertraline hydrochloride	PSYCHOANALEPTICS	Depression	-562		
2	007	Strepsils Plus	Diazepam	PSYCHOLEPTICS	Depression	-2875		
2	007	Strepsils Plus	Temazepam	PSYCHOLEPTICS	Depression	-2900		
2	012	Strepsils Plus	Fluoxetine	PSYCHOANALEPTICS	Depression	-4058		
2	012	Strepsils Plus	Temazepam	PSYCHOLEPTICS	Depression	-4058		
2	012	Strepsils Plus	Thyroxine	THYROID THERAPY	Hypothyroidism	-4058		
2	012	Strepsils Plus	Simvastatin	LIPID MODIFYING AGENTS	Type 2 diabetes	-770		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
2	012	Strepsils Plus	Insulin	DRUGS USED IN DIABETES	Type 2 diabetes	-770		
2	016	Strepsils Plus	Insulin	DRUGS USED IN DIABETES	Type 1 diabetes			
2	016	Strepsils Plus	Novorapid insulin	DRUGS USED IN DIABETES	Type 1 diabetes			
2	025	Strepsils Plus	MICROGYNON	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	CONTRACEPTION	-792		
2	032	Strepsils Plus	Chlorpromazine	PSYCHOLEPTICS	Anxiety	-3425		
2	032	Strepsils Plus	Olanzapine	PSYCHOLEPTICS	Anxiety	-27		
2	032	Strepsils Plus	Sertraline hydrochloride	PSYCHOANALEPTICS	Anxiety	-1454		
2	032	Strepsils Plus	Diazepam	PSYCHOLEPTICS	Anxiety	-3169		
2	032	Strepsils Plus	Temazepam	PSYCHOLEPTICS	Anxiety	-3425		
2	032	Strepsils Plus	Diazepam	PSYCHOLEPTICS	Anxiety	-3716		
3	235	Strepsils Plus	Duloxetine	PSYCHOANALEPTICS	Depression	-87		
3	235	Strepsils Plus	Duac once daily	ANTI-ACNE PREPARATIONS	Psoriasis	-833		
3	243	Strepsils Plus	Stilnoct	PSYCHOLEPTICS	Insomnia	-4806		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
3	243	Strepsils Plus	Diazepam	PSYCHOLEPTICS	Slipped disc	-3345		
3	245	Strepsils Plus	Cerazette	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraceptive pill	-75		
3	249	Strepsils Plus	Orlistat	ANTIOBESITY PREPARATIONS, EXCL. DIET PRODUCTS	Obesity	-824		
3	249	Strepsils Plus	Escitalopram	PSYCHOANALEPTICS	Depression	-341		
3	249	Strepsils Plus	Temazepam	PSYCHOLEPTICS	Insomnia	-222		
3	249	Strepsils Plus	Diazepam	PSYCHOLEPTICS	Depression	-540		
3	251	Strepsils Plus	Roaccutane	ANTI-ACNE PREPARATIONS	Acne	-218		
4	138	Strepsils Plus	Microgynon 30	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-106		
4	140	Strepsils Plus	Pregnacare	VITAMINS	Iron supplement	-291		
4	142	Strepsils Plus	Irbesartan	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	Essential hypertension	-1051		
4	142	Strepsils Plus	Hydrochlorothiazide	DIURETICS	Essential hypertension	-1051		
4	142	Strepsils Plus	Nebivolol	BETA BLOCKING AGENTS	Essential hypertension	-2858		
4	142	Strepsils Plus	Levothyroxine	THYROID THERAPY	Hypothyroidism	-2300		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
4	142	Strepsils Plus	Zolpidem	PSYCHOLEPTICS	Sleep disturbances	-157		
4	147	Strepsils Plus	Hydroxychloroquine	ANTIPROTOZOALS	Lupus erythematosus	-1030		
4	147	Strepsils Plus	Omeprazole	DRUGS FOR ACID RELATED DISORDERS	Rheumatoid arthritis	-2037		
4	161	Strepsils Plus	Esomeprazole	DRUGS FOR ACID RELATED DISORDERS	Cholecystetomy post / counter act Tramadol	-68		
4	161	Strepsils Plus	Atorvastatin	LIPID MODIFYING AGENTS	Pure hypercholesterolaemia	-593		
4	161	Strepsils Plus	Citalopram hidrobromide	PSYCHOANALEPTICS	Depression	-417		
4	161	Strepsils Plus	Peptac liquid	DRUGS FOR ACID RELATED DISORDERS	Dyspepsia	-420		
4	161	Strepsils Plus	Qvar easi breathe	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-55		
4	161	Strepsils Plus	Salamol easi breathe	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-55		
5	171	Strepsils Plus	Diazepam	PSYCHOLEPTICS	Depressive disorder	-3263		
5	171	Strepsils Plus	Lansoprazole	DRUGS FOR ACID RELATED DISORDERS	Oesophagitis	-21		
5	171	Strepsils Plus	Solifenacin	UROLOGICALS	Urinary incontinence	-966		
5	171	Strepsils Plus	Duloxetine	PSYCHOANALEPTICS	Depressive disorder	-619		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
5	171	Strepsils Plus	Alverine citrate	DRUGS FOR FUNCTIONAL GASTROINTESTINAL DISORDERS	Irritable bowel syndrome	-1374		
5	171	Strepsils Plus	Hexetine mouthwash	STOMATOLOGICAL PREPARATIONS	Mouth ulcers	-2766		
5	172	Strepsils Plus	Femodene tablets	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-1505		
5	172	Strepsils Plus	Escitalopram	PSYCHOANALEPTICS	Depressive disorder	-1400		
5	172	Strepsils Plus	Movicol	LAXATIVES	Chronic constipation	-194		
5	172	Strepsils Plus	Lansoprazole	DRUGS FOR ACID RELATED DISORDERS	Heartburn	-420		
5	175	Strepsils Plus	Metformin	DRUGS USED IN DIABETES	Type II diabetes mellitus	-2626		
5	181	Strepsils Plus	Metformin	DRUGS USED IN DIABETES	Diabetes mellitus type II	-406		
5	181	Strepsils Plus	Simvastatin	LIPID MODIFYING AGENTS	Prophylaxis - cardiovascular risk	-406		
5	181	Strepsils Plus	Bendroflumethiazide	DIURETICS	Essential hypertension	-1426		
5	181	Strepsils Plus	Esomeprazole	DRUGS FOR ACID RELATED DISORDERS	Hiatus hernia	-1269		
5	181	Strepsils Plus	Perindopril	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	Essential hypertension	-406		
5	181	Strepsils Plus	Cetirizine	ANTIHISTAMINES FOR SYSTEMIC USE	Hayfever	-1426		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
6	070	Strepsils Plus	Simvastatin	LIPID MODIFYING AGENTS	Cholesterol lowering	-1878		
6	070	Strepsils Plus	Lansoprazole	DRUGS FOR ACID RELATED DISORDERS	Indigestion	-1148		
6	077	Strepsils Plus	Cipralex	PSYCHOANALEPTICS	Bipolar	-1543		
6	077	Strepsils Plus	Risperdal	PSYCHOLEPTICS	Bipolar	-1543		
6	077	Strepsils Plus	Premarin (HRT)	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Post hysterectomy	-3369		
6	079	Strepsils Plus	Cetirizine	ANTIHISTAMINES FOR SYSTEMIC USE	Hay fever	-4648		
6	079	Strepsils Plus	Yasmin	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-791		
7	106	Strepsils Plus	Yasmin	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-13		
7	117	Strepsils Plus	Microgynon 30	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-16		
7	125	Strepsils Plus	Yasmin	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-9		
8	200	Strepsils Plus	Cerazette	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-101		
8	205	Strepsils Plus	Cerazette	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Oral contraception	-151		
8	209	Strepsils Plus	Levothyroxine	THYROID THERAPY	Hypothyroidism	-1177		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
1	036	Strepsils Extra	Ranitidine	DRUGS FOR ACID RELATED DISORDERS	Heartburn	-2749		
1	036	Strepsils Extra	Levothyroxine	THYROID THERAPY	Hypothyroidism	-1143		
1	036	Strepsils Extra	E45 cream	EMOLLIENTS AND PROTECTIVES	Keratosis	-1289		
1	036	Strepsils Extra	Terbutaline Inhaler	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	COPD	-797		
1	036	Strepsils Extra	Topal	DRUGS FOR ACID RELATED DISORDERS	Heartburn	-796		
1	036	Strepsils Extra	Promethazine	PSYCHOLEPTICS	Depression	-861		
1	036	Strepsils Extra	Estraderm patch	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Hysterectomy	-469		
1	036	Strepsils Extra	Symbicort inhaler	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	COPD	-225		
1	036	Strepsils Extra	Quinine sulphate	OTHER DRUGS FOR DISORDERS OF THE MUSCULO-SKELETAL SYSTEM	Restless legs syndrome	-257		
1	036	Strepsils Extra	Dosulepin	PSYCHOANALEPTICS	Depression	-1554		
1	042	Strepsils Extra	Cerazette	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraceptive	-1056		
1	047	Strepsils Extra	Omeprazole	DRUGS FOR ACID RELATED DISORDERS	Dyspepsia	-575		
1	047	Strepsils Extra	Propanolol	BETA BLOCKING AGENTS	Migraine Headache	-610		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
1	049	Strepsils Extra	Terbutaline inhaler	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	COPD	-2157		
1	049	Strepsils Extra	Emulsifying ointment	EMOLLIENTS AND PROTECTIVES	Psoriasis	-915		
1	049	Strepsils Extra	Bethametasone	CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	Psoriasis	-1036		
1	049	Strepsils Extra	Symbicort	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	COPD	-2332		
1	053	Strepsils Extra	Logynon	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-4193		
1	055	Strepsils Extra	Diprosone	CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	Eczema	-12		
1	055	Strepsils Extra	Modrasone	CORTICOSTEROIDS, DERMATOLOGICAL PREPARATIONS	Eczema	-12		
1	058	Strepsils Extra	Citalopram	PSYCHOANALEPTICS	Depression	-134		
1	062	Strepsils Extra	Salbutamol	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1904		
2	004	Strepsils Extra	Seretide	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-860		
2	004	Strepsils Extra	Salbutamol	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-3417		
2	010	Strepsils Extra	Salbutamol	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1347		
2	010	Strepsils Extra	Budesonide + Formoterol	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1067		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
2	010	Strepsils Extra	Montelukast	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1008		
2	010	Strepsils Extra	Lansoprazole	DRUGS FOR ACID RELATED DISORDERS	Gastro-oesophageal reflux	-2302		
2	010	Strepsils Extra	Terbinafine cream	ANTIFUNGALS FOR DERMATOLOGICAL USE	Fungal nail infection	-1434		
2	010	Strepsils Extra	Tramadol	ANALGESICS	Arthralgia	-2470		
2	013	Strepsils Extra	Zolpidem	PSYCHOLEPTICS	Depression	-1837		
2	013	Strepsils Extra	Flexofenadine	ANTIHISTAMINES FOR SYSTEMIC USE	Depression	-1469		
2	013	Strepsils Extra	Risperidone	PSYCHOLEPTICS	Depression	-1913		
2	013	Strepsils Extra	Diazepam	PSYCHOLEPTICS	Depression	-556		
3	238	Strepsils Extra	Orlistat	ANTIOBESITY PREPARATIONS, EXCL. DIET PRODUCTS	Obesity	-352		
3	238	Strepsils Extra	Levothyroxine	THYROID THERAPY	Hypothyroidism	-28		
3	244	Strepsils Extra	Zoplicone	PSYCHOLEPTICS	Insomnia	-392		
3	244	Strepsils Extra	Diazepam	PSYCHOLEPTICS	Anxiety	-392		
3	248	Strepsils Extra	Amitriptyline	PSYCHOANALEPTICS	Depression	-1216		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
3	248	Strepsils Extra	Adcal	MINERAL SUPPLEMENTS	Calcium supplement	-33		
3	250	Strepsils Extra	Atomexetine	PSYCHOANALEPTICS	ADHD	-104		
4	134	Strepsils Extra	Premique Low Dose 1/m	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Menopause	-654		
4	134	Strepsils Extra	Adcal D3	MINERAL SUPPLEMENTS	Menopause	-2235		
4	141	Strepsils Extra	Ethinylestradiol	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-816		
4	141	Strepsils Extra	Drospirenone	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-816		
4	144	Strepsils Extra	Paracetamol	ANALGESICS	Sore throat	-2		
4	153	Strepsils Extra	Tears naturale	OPHTHALMOLOGICALS	Dry eyes	-347		
4	153	Strepsils Extra	Levothyroxine	THYROID THERAPY	Hypothyroidism	-2237		
4	153	Strepsils Extra	Valsartan	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	Essential hypertension	-1972		
4	153	Strepsils Extra	Amlodipine	CALCIUM CHANNEL BLOCKERS	Essential hypertension	-1912		
4	153	Strepsils Extra	Atenol	BETA BLOCKING AGENTS	Essential hypertension	-4705		
4	153	Strepsils Extra	Fluticasone nasal spray	NASAL PREPARATIONS	Asthma	-1064		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
4	153	Strepsils Extra	Inegy	LIPID MODIFYING AGENTS	Impaired glucose tolerance	-1929		
4	153	Strepsils Extra	Clenil modulite	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-384		
4	158	Strepsils Extra	Conjugated oestrogens	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Post sterilisation	-130		
4	159	Strepsils Extra	Methotrexate	ANTINEOPLASTIC AGENTS	Arthritis	-142		
4	159	Strepsils Extra	Cyclizine	ANTIHISTAMINES FOR SYSTEMIC USE	Nausea from methotrexate	-2294		
4	159	Strepsils Extra	Citalopram hydrobromide	PSYCHOANALEPTICS	Depression	-1042		
5	177	Strepsils Extra	Thiamine	VITAMINS	Prophylaxis/Alcohol dependence	-3		
5	177	Strepsils Extra	Disulfiram	OTHER NERVOUS SYSTEM DRUGS	Alcohol dependence	-3		
5	179	Strepsils Extra	Omeprazole	DRUGS FOR ACID RELATED DISORDERS	Heartburn	-413		
6	067	Strepsils Extra	Ferrous fumarate	ANTIANEMIC PREPARATIONS	Physiological iron deficicency	-984		
6	076	Strepsils Extra	Dianette	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Oral contraception			
7	101	Strepsils Extra	Marvelon	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-15		
7	105	Strepsils Extra	Mesalazine	ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	Crohn's disease	-330		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
7	107	Strepsils Extra	Ovranette	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-14		
7	120	Strepsils Extra	Citalopram	PSYCHOANALEPTICS	Depression	-101		
7	129	Strepsils Extra	Amias	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	Hypertension	-1179		
8	211	Strepsils Extra	Simvastatin	LIPID MODIFYING AGENTS	Hyperlipidaemia	-83		
8	211	Strepsils Extra	Bendrofluazide	DIURETICS	Oedema	-448		
8	211	Strepsils Extra	Paracetamol	ANALGESICS	Foot pain	-1179		
1	035	Placebo	Logynon	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraceptive	-2959		
1	040	Placebo	Metformin	DRUGS USED IN DIABETES	Diabetes	-2779		
1	040	Placebo	Simvastatin	LIPID MODIFYING AGENTS	Diabetes	-2779		
1	040	Placebo	Lisinopril	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	Hypertension	-711		
1	040	Placebo	Levemer insulin	DRUGS USED IN DIABETES	Diabetes	-2779		
1	040	Placebo	Novorapid	DRUGS USED IN DIABETES	Diabetes	-2779		
1	040	Placebo	Amilodipine	CALCIUM CHANNEL BLOCKERS	Hypertension	-677		
1	054	Placebo	Fluoxetine	PSYCHOANALEPTICS	Depression	-238		
1	054	Placebo	Hydroxocobalamin	ANTIANEMIC PREPARATIONS	Vitamin b12 deficency	-1375		
1	054	Placebo	Double base gel	ALL OTHER NON-THERAPEUTIC PRODUCTS	Eczema	-2551		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
2	001	Placebo	Diazepam	PSYCHOLEPTICS	Depressive disorder	-4254		
2	001	Placebo	Ibuprofen gel	TOPICAL PRODUCTS FOR JOINT AND MUSCULAR PAIN	Low back pain	-22		
2	001	Placebo	Salbutamol	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1178		
2	001	Placebo	Seretide	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1021		
2	001	Placebo	Duloxetine	PSYCHOANALEPTICS	Depressive disorder	-827		
2	001	Placebo	Quetiapine	PSYCHOLEPTICS	Depressive disorder	-827		
2	001	Placebo	Metformin	DRUGS USED IN DIABETES	Type 2 diabetes	-461		
2	001	Placebo	Simvastatin	LIPID MODIFYING AGENTS	Type 2 diabetes	-461		
2	011	Placebo	Fluoxetine hydrochloride	PSYCHOANALEPTICS	Depression	-1969		
2	011	Placebo	Amitriptyline hydrochloride	PSYCHOANALEPTICS	Sciatica	-7		
2	011	Placebo	Ramipril	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	Essential hypertension	-1388		
2	011	Placebo	Ramipril	AGENTS ACTING ON THE RENIN-ANGIOTENSIN SYSTEM	Essential hypertension	-783		
2	014	Placebo	Hormonal implant	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception			
2	021	Placebo	EURAX CREAM	ANTIPRURITICS, INCL. ANTIHISTAMINES, ANESTHETICS, ETC.	DRY SKIN	-28		
2	021	Placebo	CETIRIZINE	ANTIHISTAMINES FOR SYSTEMIC USE	DRY SKIN	-28		
2	023	Placebo	Yasmin	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	CONTRACEPTION	-1170		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
2	028	Placebo	Dermal 200	ANTISEPTICS AND DISINFECTANTS	Dermatitis	-56		
2	028	Placebo	Unguentum m cream	EMOLLIENTS AND PROTECTIVES	Dermatitis	-56		
2	028	Placebo	Flexitol Heel Balm	EMOLLIENTS AND PROTECTIVES	Dermatitis	-56		
2	028	Placebo	Dermal Cream	ANTISEPTICS AND DISINFECTANTS	Dermatitis	-93		
2	031	Placebo	Fluoxetine	PSYCHOANALEPTICS	Depression	-50		
2	031	Placebo	Propanolol	BETA BLOCKING AGENTS	Essential hypertension	-22		
2	031	Placebo	Ethinylestradiol and desogestrel	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-858		
3	234	Placebo	Depo Medrone	CORTICOSTEROIDS FOR SYSTEMIC USE	Psoriatic arthropathy	-178		
3	242	Placebo	Zopiclone	PSYCHOLEPTICS	Insomnia	-750		
3	242	Placebo	Chlorpromazine	PSYCHOLEPTICS	Attention deficit disorder	-1324		
4	136	Placebo	Verapamil	CALCIUM CHANNEL BLOCKERS	Palpitations	-2110		
4	136	Placebo	Atorvastatin	LIPID MODIFYING AGENTS	Hyperlipidaemia	-522		
4	139	Placebo	Levothyroxine	THYROID THERAPY	Hypothyroidism	-2545		
4	143	Placebo	Lamasil cream 1%	ANTIFUNGALS FOR DERMATOLOGICAL USE	Ring worm	-8		
4	143	Placebo	Sporanox	ANTIMYCOTICS FOR SYSTEMIC USE	Ring worm	-8		
4	157	Placebo	Diprobath emollient	EMOLLIENTS AND PROTECTIVES	Dry skin	-26		
4	157	Placebo	Oxybutynin hydrochloride	UROLOGICALS	Urgency of micturition	-22		
4	157	Placebo	Salbutamol inhaler	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-1894		
4	157	Placebo	Qvar easi breathe	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma	-985		

entre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Study day medication commenced	Study day medication stopped	Duration of use (days)
4	160	Placebo	Paroxetine hydrochloride	PSYCHOANALEPTICS	Depression	-34		
5	176	Placebo	Lansoprazole	DRUGS FOR ACID RELATED DISORDERS	Gastro oesophageal reflux disease	-1895		
6	069	Placebo	Sertraline	PSYCHOANALEPTICS	Stress related problem	-1240		
6	069	Placebo	Vitamin E liquid	VITAMINS	Hepatic steatosis	-751		
6	072	Placebo	Microgynon 30	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-264		
6	078	Placebo	Simvastatin	LIPID MODIFYING AGENTS	High cholesterol	-1		
7	100	Placebo	Implanon	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-279		
7	104	Placebo	Azathioprine	IMMUNOSUPPRESSANTS	Ulcerative colitis	-1016		
7	104	Placebo	Pentasa	ANTIDIARRHEALS, INTESTINAL ANTIINFLAMMATORY/ANTIINFECTIVE AGENTS	Ulcerative colitis	-1016		
7	112	Placebo	Cerazette	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-14		
8	207	Placebo	Zopiclone	PSYCHOLEPTICS	Insomnia	-4092		
8	207	Placebo	Lansoprazole	DRUGS FOR ACID RELATED DISORDERS	Dyspepsia	-1900		
8	207	Placebo	Symbicort	DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES	Asthma			
8	210	Placebo	Depo Provera	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM	Contraception	-3370		

Listing 16.2.4.5
Patient data listing of concomitant medications starting post randomisation-
Full Analysis set

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Time commenced in relation to study medication dose (hours)	Time stopped in relation to study medication dose (hours)	Duration of use (hours)	Ongoing
3	232	Strepsils Plus	Strepsil	THROAT PREPARATIONS	Sore throat	5.67	25.67	20.00	
3	239	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	4.00			Yes
3	243	Strepsils Plus	Tramadol	ANALGESICS	Slipped disc	2.50			Yes
4	133	Strepsils Plus	Penicillin V	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	4.15			Yes
4	140	Strepsils Plus	Fucidic acid 1%	OPHTHALMOLOGICALS	Conjunctivitis	9.83			Yes
4	140	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	9.83	30.83	21.00	
4	142	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	9.38	55.38	46.00	
4	147	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	4.47			Yes

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Time commenced in relation to study medication dose (hours)	Time stopped in relation to study medication dose (hours)	Duration of use (hours)	Ongoing
4	147	Strepsils Plus	Amoxicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	4.47			Yes
5	171	Strepsils Plus	Doxycycline	ANTIBACTERIALS FOR SYSTEMIC USE	Upper respiratory tract infection				
5	181	Strepsils Plus	Tramadol	ANALGESICS	Osteoarthritis	4.75			Yes
6	077	Strepsils Plus	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Sore throat	3.35	20.35	17.00	
7	106	Strepsils Plus	Penicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Tonsillitis	2.83			Yes
7	108	Strepsils Plus	Penicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	2.83			Yes
7	108	Strepsils Plus	Paracetamol	ANALGESICS	Analgesia sore throat	2.83			Yes
7	109	Strepsils Plus	Clarythromycin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	23.33			Yes
7	109	Strepsils Plus	Terbinafine	ANTIFUNGALS FOR DERMATOLOGICAL USE	Nail fungal infection	23.33			Yes
7	110	Strepsils Plus	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Analgesia sore throat	9.17	9.17	0.00	
7	110	Strepsils Plus	Penicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	21.83			Yes
7	110	Strepsils Plus	Co-codamol	ANALGESICS	Analgesia sore throat	22.67	22.67	0.00	
7	123	Strepsils Plus	Paracetamol	ANALGESICS	Sore throat	7.50	7.50	0.00	
7	127	Strepsils Plus	Penicillen V	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	2.75			Yes
7	127	Strepsils Plus	Diclofenac	STOMATOLOGICAL PREPARATIONS	Sore throat	20.25			Yes
7	128	Strepsils Plus	Penicillin V	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	3.25			Yes

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2		Indication	Time commenced in relation to study medication dose (hours)	Time stopped in relation to study medication dose (hours)	Duration of use (hours)	Ongoing
7	128	Strepsils Plus	Ibuprofen	ANTIINFLAMMATORY ANTIRHEUMATIC PRODUCTS	AND	Sore throat	3.25			Yes
8	200	Strepsils Plus	Otrovine	NASAL PREPARATIONS		URTI	3.40			Yes
8	200	Strepsils Plus	Strepsil	THROAT PREPARATIONS		URTI	3.52			Yes
8	200	Strepsils Plus	Panadol	ANALGESICS		Headache	11.02	11.02	0.00	
8	200	Strepsils Plus	Nurofen	ANTIINFLAMMATORY ANTIRHEUMATIC PRODUCTS	AND	Headache	15.38			Yes
8	200	Strepsils Plus	Glycerine cough mixture	COUGH AND COLD PREPARATIONS		URTI	20.60			Yes
1	036	Strepsils Extra	Pencillin	ANTIBACTERIALS FOR SYSTEMIC USE		Sore throat	23.00			Yes
1	047	Strepsils Extra	Penicillin V	ANTIBACTERIALS FOR SYSTEMIC USE		Sore throat	25.00			Yes
3	248	Strepsils Extra	Strepsils	THROAT PREPARATIONS		Sore throat	10.25			Yes
4	144	Strepsils Extra	Penicillin V	ANTIBACTERIALS FOR SYSTEMIC USE		Sore throat	7.75			Yes
4	145	Strepsils Extra	Ibuprofen	ANTIINFLAMMATORY ANTIRHEUMATIC PRODUCTS	AND	Sore throat	4.87	4.87	0.00	
4	158	Strepsils Extra	Co codamol 8/500	ANALGESICS		Sore throat	4.40			Yes
4	158	Strepsils Extra	Amoxicillin	ANTIBACTERIALS FOR SYSTEMIC USE		Sore throat	4.40			Yes

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Time commenced in relation to study medication dose (hours)	Time stopped in relation to study medication dose (hours)	Duration of use (hours)	Ongoing
6	071	Strepsils Extra	Amoxicillin	ANTIBACTERIALS FOR SYSTEMIC USE	URTI	6.78			Yes
7	111	Strepsils Extra	Paracetamol	ANALGESICS	Fever	2.17			Yes
7	111	Strepsils Extra	Penicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	2.67			Yes
7	120	Strepsils Extra	Paracetamol	ANALGESICS	Sore throat	3.50			Yes
7	120	Strepsils Extra	Eryhtromycin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	7.00			Yes
7	122	Strepsils Extra	Multivitamin	VITAMINS	Sore throat	7.50	7.50	0.00	
8	208	Strepsils Extra	Paracetamol	ANALGESICS	URTI	4.35			Yes
8	208	Strepsils Extra	Sinex nasal spray	NASAL PREPARATIONS	Nasal congestion	9.60			Yes
3	241	Placebo	Phenoxymethylpenicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	2.25			Yes
3	241	Placebo	Paracetamol	ANALGESICS	Sore throat	4.25			Yes
3	255	Placebo	Paracetamol	ANALGESICS	Sore throat	9.75			Yes
4	135	Placebo	Amoxicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Throat infection	9.75			Yes
4	136	Placebo	Co amoxiclav	ANTIBACTERIALS FOR SYSTEMIC USE	Throat infection	20.15			Yes
4	139	Placebo	Lemsip	ANALGESICS	For sore throat	4.50	4.50	0.00	

Centre number	Patient number	Treatment group	Drug	WHO ATC level 2	Indication	Time commenced in relation to study medication dose (hours)	Time stopped in relation to study medication dose (hours)	Duration of use (hours)	Ongoing
4	146	Placebo	Diclofenac	STOMATOLOGICAL PREPARATIONS	Sore throat	2.37			Yes
4	146	Placebo	Penicillin V	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	4.37			Yes
4	149	Placebo	Pencillin V	ANTIBACTERIALS FOR SYSTEMIC USE	Throat infection	22.02			Yes
4	150	Placebo	Amoxicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat	5.80			Yes
6	069	Placebo	Co-codamol	ANALGESICS	Pr earache R ear	11.18			Yes
6	069	Placebo	Difflam spray 0.15%	STOMATOLOGICAL PREPARATIONS	Sore throat	12.18			Yes
6	072	Placebo	Phenoxymethylpenicillin	ANTIBACTERIALS FOR SYSTEMIC USE	URTI	15.50			Yes
6	078	Placebo	Paracetamol	ANALGESICS	Sore throat	3.28	17.28	14.00	
6	078	Placebo	Codeine	COUGH AND COLD PREPARATIONS	Sore throat	3.28	17.28	14.00	
6	078	Placebo	Difflam spray	STOMATOLOGICAL PREPARATIONS	Sore throat	3.28	17.28	14.00	
7	100	Placebo	Paracetamol	ANALGESICS	Sore throat analgesia	2.83	18.83	16.00	
7	103	Placebo	Paracetamol	ANALGESICS	Analgesia sore throat	2.25			Yes
7	103	Placebo	Penicillin	ANTIBACTERIALS FOR SYSTEMIC USE	Sore throat tonsillitis	2.25			Yes
7	112	Placebo	Difflam throat spray	STOMATOLOGICAL PREPARATIONS	Sore throat	4.00	4.00	0.00	
7	114	Placebo	Ibuprofen	ANTIINFLAMMATORY AND ANTIRHEUMATIC PRODUCTS	Sore throat	23.83			Yes
7	121	Placebo	Paracetamol	ANALGESICS	Sore throat	8.00	8.00	0.00	
7	131	Placebo	Lemsip Paracetamol	ANALGESICS	Sore throat	2.67			Yes
8	202	Placebo	Soothers	ALL OTHER THERAPEUTIC PRODUCTS	Sore throat	6.45			Yes

Listing 16.2.4.6

Patient data listing of baseline efficacy assessments- Full analysis set

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
1	034	Strepsils Plus	4	6	0	0	10	7	68	46
1	038	Strepsils Plus	6	7	5	4	22	6	65	66
1	041	Strepsils Plus	5	5	5	3	18	9	87	85
1	044	Strepsils Plus	6	6	0	0	12	6	71	68
1	048	Strepsils Plus	5	5	0	0	10	10	89	54
1	051	Strepsils Plus	5	5	1	1	12	6	75	73
1	052	Strepsils Plus	5	10	5	5	25	10	92	95
1	057	Strepsils Plus	7	7	5	5	24	7	75	73
1	059	Strepsils Plus	7	10	4	0	21	6	73	75
1	061	Strepsils Plus	7	7	7	7	28	7	78	77
2	002	Strepsils Plus	9	10	10	10	39	10	97	98
2	006	Strepsils Plus	8	9	8	8	33	8	81	71
2	007	Strepsils Plus	8	8	2	8	26	8	78	75
2	012	Strepsils Plus	5	7	7	7	26	7	75	77
2	016	Strepsils Plus	8	8	7	7	30	8	92	90
2	017	Strepsils Plus	5	7	5	5	22	7	64	20
2	019	Strepsils Plus	6	7	6	6	25	7	75	68
2	022	Strepsils Plus	6	6	5	5	22	7	69	72
2	025	Strepsils Plus	6	6	8	8	28	6	75	76

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
2	029	Strepsils Plus	7	7	6	0	20	7	88	91
2	032	Strepsils Plus	7	8	5	5	25	8	79	74
3	232	Strepsils Plus	9	9	5	5	28	6	70	74
3	235	Strepsils Plus	5	7	4	4	20	6	79	52
3	239	Strepsils Plus	9	6	1	0	16	6	57	52
3	243	Strepsils Plus	0	5	0	4	9	6	55	53
3	245	Strepsils Plus	5	7	8	0	20	7	75	53
3	249	Strepsils Plus	6	7	5	0	18	7	69	
3	251	Strepsils Plus	5	5	5	5	20	6	55	57
3	254	Strepsils Plus	6	8	5	0	19	6	68	57
4	133	Strepsils Plus	6	6	4	3	19	7	62	49
4	138	Strepsils Plus	8	8	7	6	29	8	91	93
4	140	Strepsils Plus	7	8	6	6	27	8	80	75
4	142	Strepsils Plus	0	4	0	0	4	6	60	52
4	147	Strepsils Plus	5	6	3	0	14	6	63	64
4	148	Strepsils Plus	7	7	6	6	26	7	73	71
4	151	Strepsils Plus	3	6	5	5	19	6	63	42
4	154	Strepsils Plus	0	0	0	0	0	7	78	45
4	156	Strepsils Plus	7	7	6	6	26	7	75	75
4	161	Strepsils Plus	8	8	7	7	30	8	81	84
5	167	Strepsils Plus	3	5	1	0	9	7	66	53

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
5	171	Strepsils Plus	6	6	0	0	12	6	59	58
5	172	Strepsils Plus	6	7	6	6	25	7	60	66
5	175	Strepsils Plus	10	9	6	0	25	9	85	31
5	180	Strepsils Plus	6	7	0	0	13	8	74	48
5	181	Strepsils Plus	6	6	0	0	12	7	65	69
6	070	Strepsils Plus	7	6	7	5	25	7	66	40
6	074	Strepsils Plus	7	6	6	5	24	8	77	70
6	077	Strepsils Plus	4	6	6	1	17	8	62	50
6	079	Strepsils Plus	7	7	8	7	29	8	71	72
7	102	Strepsils Plus	2	6	2	2	12	7	67	56
7	106	Strepsils Plus	8	8	6	3	25	6	45	36
7	108	Strepsils Plus	9	9	1	1	20	10	95	72
7	109	Strepsils Plus	3	7	4	1	15	6	61	49
7	110	Strepsils Plus	5	8	6	6	25	6	64	84
7	115	Strepsils Plus	7	7	7	5	26	7	68	68
7	117	Strepsils Plus	8	8	7	6	29	8	79	83
7	123	Strepsils Plus	4	7	5	4	20	6	75	91
7	125	Strepsils Plus	6	7	8	6	27	7	73	69
7	127	Strepsils Plus	2	8	3	0	13	8	76	59
7	128	Strepsils Plus	3	7	2	0	12	7	68	61
8	200	Strepsils Plus	8	7	0	0	15	7	66	79

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
8	205	Strepsils Plus	6	8	5	0	19	7	62	78
8	206	Strepsils Plus	7	8	0	0	15	9	82	82
8	209	Strepsils Plus	1	7	4	1	13	8	73	69
1	036	Strepsils Extra	7	7	7	7	28	7	72	72
1	039	Strepsils Extra	2	8	0	0	10	8	82	79
1	042	Strepsils Extra	8	8	4	3	23	8	89	88
1	043	Strepsils Extra	9	9	2	2	22	9	87	85
1	047	Strepsils Extra	0	10	5	0	15	8	82	77
1	049	Strepsils Extra	6	6	0	0	12	6	65	64
1	053	Strepsils Extra	7	6	8	8	29	6	58	70
1	055	Strepsils Extra	8	8	8	8	32	8	86	88
1	058	Strepsils Extra	5	10	5	0	20	7	76	75
1	062	Strepsils Extra	6	7	3	3	19	6	74	72
2	004	Strepsils Extra	9	9	9	8	35	8	91	91
2	005	Strepsils Extra	5	8	0	0	13	7	57	42
2	008	Strepsils Extra	8	9	7	5	29	9	88	77
2	010	Strepsils Extra	5	8	4	0	17	7	65	52
2	013	Strepsils Extra	10	10	10	1	31	10	99	99
2	018	Strepsils Extra	7	7	4	3	21	8	76	55
2	020	Strepsils Extra	6	6	6	6	24	6	73	72
2	026	Strepsils Extra	5	8	0	0	13	7	86	95

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
2	027	Strepsils Extra	7	7	5	5	24	7	73	72
2	030	Strepsils Extra	6	9	5	2	22	8	91	81
2	033	Strepsils Extra	9	7	6	0	22	7	80	88
3	233	Strepsils Extra	5	7	0	0	12	6	67	69
3	236	Strepsils Extra	4	6	3	2	15	6	69	60
3	238	Strepsils Extra	0	6	6	2	14	4	49	53
3	244	Strepsils Extra	4	7	5	9	25	6	68	70
3	246	Strepsils Extra	5	6	4	6	20	7	65	60
3	248	Strepsils Extra	5	5	3	4	17	6	64	1
3	250	Strepsils Extra	4	4	10	0	18	5	47	17
3	253	Strepsils Extra	4	8	8	0	20	6	56	58
4	134	Strepsils Extra	7	7	7	6	27	7	74	75
4	137	Strepsils Extra	7	7	6	6	26	7	87	75
4	141	Strepsils Extra	3	6	1	0	10	7	66	54
4	144	Strepsils Extra	7	7	7	7	28	7	73	70
4	145	Strepsils Extra	1	4	0	0	5	7	75	67
4	152	Strepsils Extra	4	8	0	0	12	7	67	42
4	153	Strepsils Extra	8	8	6	6	28	10	88	87
4	158	Strepsils Extra	9	9	8	5	31	9	93	94
4	159	Strepsils Extra	8	8	8	6	30	8	86	85
4	162	Strepsils Extra	8	8	8	8	32	8	83	63

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
5	169	Strepsils Extra	6	7	0	0	13	6	69	88
5	170	Strepsils Extra	4	5	0	0	9	7	52	39
5	173	Strepsils Extra	8	9	8	8	33	7	70	71
5	177	Strepsils Extra	7	6	3	0	16	8	75	77
5	179	Strepsils Extra	8	7	6	6	27	10	99	69
6	067	Strepsils Extra	6	6	6	4	22	8	70	59
6	071	Strepsils Extra	9	10	10	5	34	10	96	96
6	075	Strepsils Extra	6	7	4	0	17	7	75	77
6	076	Strepsils Extra	6	8	8	6	28	7	67	65
7	101	Strepsils Extra	3	6	7	5	21	7	73	67
7	105	Strepsils Extra	5	7	4	0	16	7	63	70
7	107	Strepsils Extra	6	6	5	2	19	7	63	52
7	111	Strepsils Extra	8	9	5	4	26	8	82	69
7	113	Strepsils Extra	5	7	6	6	24	7	74	74
7	119	Strepsils Extra	3	5	2	2	12	6	62	53
7	120	Strepsils Extra	7	8	8	6	29	7	82	90
7	122	Strepsils Extra	7	6	6	0	19	6	70	69
7	124	Strepsils Extra	5	7	8	4	24	7	67	76
7	129	Strepsils Extra	6	7	5	3	21	7	74	77
7	130	Strepsils Extra	1	6	6	0	13	6	55	35
8	199	Strepsils Extra	7	9	0	0	16	10	82	82

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
8	203	Strepsils Extra	8	7	6	7	28	8	55	56
8	204	Strepsils Extra	2	7	3	0	12	7	60	55
8	208	Strepsils Extra	8	8	6	3	25	8	75	62
8	211	Strepsils Extra	4	7	7	3	21	7	73	52
1	035	Placebo	4	5	4	4	17	7	67	54
1	037	Placebo	1	6	0	0	7	7	71	54
1	040	Placebo	7	8	1	1	17	9	91	89
1	045	Placebo	5	5	1	1	12	7	69	63
1	046	Placebo	7	7	7	0	21	7	68	65
1	050	Placebo	0	8	1	1	10	5	74	68
1	054	Placebo	5	10	5	2	22	7	75	73
1	056	Placebo	9	9	1	1	20	7	77	75
1	060	Placebo	4	10	3	3	20	6	71	72
2	001	Placebo	4	8	7	7	26	8	96	94
2	003	Placebo	6	7	6	6	25	7	100	100
2	009	Placebo	6	8	5	0	19	8	84	77
2	011	Placebo	7	8	5	5	25	8	93	95
2	014	Placebo	6	8	6	2	22	7	68	50
2	015	Placebo	4	8	5	0	17	7	74	55
2	021	Placebo	10	6	4	5	25	7	73	73
2	023	Placebo	7	7	6	6	26	7	72	69

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
2	024	Placebo	5	8	4	4	21	7	77	85
2	028	Placebo	7	8	7	5	27	7	70	71
2	031	Placebo	6	7	6	5	24	8	58	62
3	234	Placebo	7	7	4	0	18	7	81	69
3	237	Placebo	2	7	0	0	9	7	68	64
3	240	Placebo	1	6	6	2	15	6	62	67
3	241	Placebo	0	6	8	8	22	7	61	74
3	242	Placebo	3	5	7	0	15	7	61	96
3	247	Placebo	5	7	3	0	15	7	66	66
3	252	Placebo	2	8	0	0	10	5	49	50
3	255	Placebo	6	6	0	0	12	7	69	48
4	135	Placebo	7	8	7	6	28	8	74	77
4	136	Placebo	8	8	7	7	30	8	86	90
4	139	Placebo	7	8	7	6	28	7	80	62
4	143	Placebo	5	6	5	6	22	6	69	56
4	146	Placebo	7	9	7	4	27	9	75	52
4	149	Placebo	7	9	7	7	30	9	84	84
4	150	Placebo	0	4	0	0	4	8	61	51
4	155	Placebo	7	7	8	8	30	8	83	81
4	157	Placebo	7	9	6	6	28	9	86	83
4	160	Placebo	7	8	7	7	29	8	82	80

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
5	166	Placebo	0	6	0	0	6	6	52	38
5	168	Placebo	2	5	1	0	8	7	74	64
5	174	Placebo	6	6	0	0	12	6	55	42
5	176	Placebo	8	8	4	4	24	8	75	67
5	178	Placebo	5	6	0	0	11	6	49	37
6	069	Placebo	9	9	7	7	32	9	95	92
6	072	Placebo	6	7	3	2	19	7	56	77
6	073	Placebo	7	6	6	4	23	6	59	61
6	078	Placebo	8	8	4	4	24	7	67	70
6	080	Placebo	5	7	6	0	18	6	64	54
7	100	Placebo	6	7	5	0	18	9	77	66
7	103	Placebo	6	8	6	3	23	9	85	66
7	104	Placebo	7	8	7	7	29	8	65	68
7	112	Placebo	6	8	7	4	25	7	74	71
7	114	Placebo	8	7	4	3	22	6	56	56
7	116	Placebo	5	5	7	2	19	6	61	51
7	118	Placebo	4	6	3	3	16	6	73	58
7	121	Placebo	6	6	4	4	20	7	56	46
7	126	Placebo	5	7	7	6	25	7	73	78
7	131	Placebo	6	7	8	6	27	6	64	68
8	201	Placebo	5	7	6	0	18	6	57	54

Centre number	Patient number	Treatment group	Functional Impairment Scale: Talking	Functional Impairment Scale: Swallowing	Functional Impairment Scale: Concentrating	Functional Impairment Scale: Reading	Functional Impairment Scale: Total score	Throat soreness	Difficulty swallowing	Swollen throat
8	202	Placebo	4	6	5	3	18	6	49	48
8	207	Placebo	8	7	6	6	27	8	66	74
8	210	Placebo	6	8	5	3	22	7	60	35

APPENDIX 16.2.5 COMPLIANCE AND/OR DRUG CONCENTRATION DATA

Patient compliance and drug concentration data were not measured in this study".

Listing 16.2.5.1
Patient data listing of exposure-
Full analysis set

Centre number	Patient number	Treatment group	Date of administration	Time of administration
1	034	Strepsils Plus	03-02-2011	14:00
1	038	Strepsils Plus	21-02-2011	10:15
1	041	Strepsils Plus	21-02-2011	15:30

Centre number	Patient number	Treatment group	Date of administration	Time of administration
1	044	Strepsils Plus	23-02-2011	15:30
1	048	Strepsils Plus	02-03-2011	14:00
1	051	Strepsils Plus	08-03-2011	14:00
1	052	Strepsils Plus	10-03-2011	9:00
1	057	Strepsils Plus	14-03-2011	16:00
1	059	Strepsils Plus	25-03-2011	11:01
1	061	Strepsils Plus	28-03-2011	15:30
2	002	Strepsils Plus	08-02-2011	12:10
2	006	Strepsils Plus	09-02-2011	10:28
2	007	Strepsils Plus	09-02-2011	10:55
2	012	Strepsils Plus	10-02-2011	10:30
2	016	Strepsils Plus	11-02-2011	9:15
2	017	Strepsils Plus	11-02-2011	11:35
2	019	Strepsils Plus	11-02-2011	13:04
2	022	Strepsils Plus	24-02-2011	12:45
2	025	Strepsils Plus	04-03-2011	13:38
2	029	Strepsils Plus	14-03-2011	9:30
2	032	Strepsils Plus	23-03-2011	11:40
3	232	Strepsils Plus	02-02-2011	12:20
3	235	Strepsils Plus	07-02-2011	10:45
3	239	Strepsils Plus	15-02-2011	15:00
3	243	Strepsils Plus	28-02-2011	17:00

Centre number	Patient number	Treatment group	Date of administration	Time of administration
3	245	Strepsils Plus	28-02-2011	17:00
3	249	Strepsils Plus	02-03-2011	11:45
3	251	Strepsils Plus	02-03-2011	11:45
3	254	Strepsils Plus	03-03-2011	13:00
4	133	Strepsils Plus	09-02-2011	18:01
4	138	Strepsils Plus	15-02-2011	11:00
4	140	Strepsils Plus	16-02-2011	11:10
4	142	Strepsils Plus	18-02-2011	12:37
4	147	Strepsils Plus	22-02-2011	17:32
4	148	Strepsils Plus	24-02-2011	10:59
4	151	Strepsils Plus	04-03-2011	13:04
4	154	Strepsils Plus	09-03-2011	15:08
4	156	Strepsils Plus	14-03-2011	16:30
4	161	Strepsils Plus	29-03-2011	17:00
5	167	Strepsils Plus	16-02-2011	15:09
5	171	Strepsils Plus	25-02-2011	15:30
5	172	Strepsils Plus	09-03-2011	14:45
5	175	Strepsils Plus	11-03-2011	10:45
5	180	Strepsils Plus	23-03-2011	14:55
5	181	Strepsils Plus	23-03-2011	15:15
6	070	Strepsils Plus	22-02-2011	19:17
6	074	Strepsils Plus	04-03-2011	15:03

Centre number	Patient number	Treatment group	Date of administration	Time of administration
6	077	Strepsils Plus	24-03-2011	14:39
6	079	Strepsils Plus	28-03-2011	14:43
7	102	Strepsils Plus	09-02-2011	16:00
7	106	Strepsils Plus	15-02-2011	15:10
7	108	Strepsils Plus	16-02-2011	15:10
7	109	Strepsils Plus	17-02-2011	15:10
7	110	Strepsils Plus	18-02-2011	12:50
7	115	Strepsils Plus	25-02-2011	15:20
7	117	Strepsils Plus	02-03-2011	14:20
7	123	Strepsils Plus	08-03-2011	14:30
7	125	Strepsils Plus	10-03-2011	15:20
7	127	Strepsils Plus	16-03-2011	15:15
7	128	Strepsils Plus	16-03-2011	15:15
8	200	Strepsils Plus	10-02-2011	15:44
8	205	Strepsils Plus	01-03-2011	13:39
8	206	Strepsils Plus	04-03-2011	12:49
8	209	Strepsils Plus	23-03-2011	14:29
1	036	Strepsils Extra	09-02-2011	15:00
1	039	Strepsils Extra	21-02-2011	14:30
1	042	Strepsils Extra	21-02-2011	15:45
1	043	Strepsils Extra	21-02-2011	16:00
1	047	Strepsils Extra	01-03-2011	14:00

Centre number	Patient number	Treatment group	Date of administration	Time of administration
1	049	Strepsils Extra	02-03-2011	15:15
1	053	Strepsils Extra	10-03-2011	11:00
1	055	Strepsils Extra	14-03-2011	11:30
1	058	Strepsils Extra	15-03-2011	14:00
1	062	Strepsils Extra	29-03-2011	16:00
2	004	Strepsils Extra	08-02-2011	15:30
2	005	Strepsils Extra	09-02-2011	9:44
2	008	Strepsils Extra	09-02-2011	13:45
2	010	Strepsils Extra	10-02-2011	10:08
2	013	Strepsils Extra	10-02-2011	14:40
2	018	Strepsils Extra	11-02-2011	13:05
2	020	Strepsils Extra	11-02-2011	14:38
2	026	Strepsils Extra	09-03-2011	13:38
2	027	Strepsils Extra	10-03-2011	15:45
2	030	Strepsils Extra	16-03-2011	11:20
2	033	Strepsils Extra	24-03-2011	12:45
3	233	Strepsils Extra	03-02-2011	15:30
3	236	Strepsils Extra	08-02-2011	14:15
3	238	Strepsils Extra	09-02-2011	12:09
3	244	Strepsils Extra	28-02-2011	17:00
3	246	Strepsils Extra	28-02-2011	17:00
3	248	Strepsils Extra	02-03-2011	11:45

Centre number	Patient number	Treatment group	Date of administration	Time of administration
3	250	Strepsils Extra	02-03-2011	11:45
3	253	Strepsils Extra	03-03-2011	13:00
4	134	Strepsils Extra	11-02-2011	11:30
4	137	Strepsils Extra	14-02-2011	13:01
4	141	Strepsils Extra	18-02-2011	10:51
4	144	Strepsils Extra	21-02-2011	10:15
4	145	Strepsils Extra	21-02-2011	17:38
4	152	Strepsils Extra	07-03-2011	17:24
4	153	Strepsils Extra	08-03-2011	16:15
4	158	Strepsils Extra	21-03-2011	12:36
4	159	Strepsils Extra	23-03-2011	10:33
4	162	Strepsils Extra	30-03-2011	12:00
5	169	Strepsils Extra	23-02-2011	15:05
5	170	Strepsils Extra	23-02-2011	16:10
5	173	Strepsils Extra	09-03-2011	15:30
5	177	Strepsils Extra	11-03-2011	15:40
5	179	Strepsils Extra	23-03-2011	14:45
6	067	Strepsils Extra	10-02-2011	14:24
6	071	Strepsils Extra	24-02-2011	11:13
6	075	Strepsils Extra	24-03-2011	10:09
6	076	Strepsils Extra	24-03-2011	10:39
7	101	Strepsils Extra	08-02-2011	15:30

Centre number	Patient number	Treatment group	Date of administration	Time of administration
7	105	Strepsils Extra	15-02-2011	15:00
7	107	Strepsils Extra	16-02-2011	15:10
7	111	Strepsils Extra	18-02-2011	12:50
7	113	Strepsils Extra	24-02-2011	14:10
7	119	Strepsils Extra	03-03-2011	14:10
7	120	Strepsils Extra	04-03-2011	15:00
7	122	Strepsils Extra	08-03-2011	14:30
7	124	Strepsils Extra	09-03-2011	15:15
7	129	Strepsils Extra	25-03-2011	15:00
7	130	Strepsils Extra	30-03-2011	14:20
8	199	Strepsils Extra	09-02-2011	14:45
8	203	Strepsils Extra	24-02-2011	14:20
8	204	Strepsils Extra	25-02-2011	14:30
8	208	Strepsils Extra	23-03-2011	13:24
8	211	Strepsils Extra	25-03-2011	14:09
1	035	Placebo	07-02-2011	10:00
1	037	Placebo	10-02-2011	14:30
1	040	Placebo	21-02-2011	15:00
1	045	Placebo	25-02-2011	10:00
1	046	Placebo	28-02-2011	11:00
1	050	Placebo	04-03-2011	9:30
1	054	Placebo	14-03-2011	10:30

Centre number	Patient number	Treatment group	Date of administration	Time of administration
1	056	Placebo	14-03-2011	14:00
1	060	Placebo	28-03-2011	14:00
2	001	Placebo	08-02-2011	11:50
2	003	Placebo	08-02-2011	14:43
2	009	Placebo	09-02-2011	13:45
2	011	Placebo	10-02-2011	10:15
2	014	Placebo	10-02-2011	15:20
2	015	Placebo	11-02-2011	9:03
2	021	Placebo	23-02-2011	15:45
2	023	Placebo	01-03-2011	14:45
2	024	Placebo	04-03-2011	12:57
2	028	Placebo	10-03-2011	16:00
2	031	Placebo	22-03-2011	9:50
3	234	Placebo	03-02-2011	15:30
3	237	Placebo	08-02-2011	15:15
3	240	Placebo	16-02-2011	12:15
3	241	Placebo	21-02-2011	15:45
3	242	Placebo	24-02-2011	12:30
3	247	Placebo	02-03-2011	11:45
3	252	Placebo	03-03-2011	13:00
3	255	Placebo	15-03-2011	12:15
4	135	Placebo	11-02-2011	12:15

Centre number	Patient number	Treatment group	Date of administration	Time of administration
4	136	Placebo	11-02-2011	13:21
4	139	Placebo	15-02-2011	18:00
4	143	Placebo	18-02-2011	17:30
4	146	Placebo	22-02-2011	16:38
4	149	Placebo	25-02-2011	10:59
4	150	Placebo	02-03-2011	16:12
4	155	Placebo	14-03-2011	12:30
4	157	Placebo	15-03-2011	16:30
4	160	Placebo	29-03-2011	10:22
5	166	Placebo	16-02-2011	14:36
5	168	Placebo	23-02-2011	14:25
5	174	Placebo	11-03-2011	10:15
5	176	Placebo	11-03-2011	11:30
5	178	Placebo	23-03-2011	14:30
6	069	Placebo	22-02-2011	18:49
6	072	Placebo	01-03-2011	17:30
6	073	Placebo	01-03-2011	17:58
6	078	Placebo	24-03-2011	15:13
6	080	Placebo	31-03-2011	10:03
7	100	Placebo	04-02-2011	14:10
7	103	Placebo	10-02-2011	15:00
7	104	Placebo	11-02-2011	15:05

Centre number	Patient number	Treatment group	Date of administration	Time of administration
7	112	Placebo	23-02-2011	16:00
7	114	Placebo	24-02-2011	14:10
7	116	Placebo	01-03-2011	15:00
7	118	Placebo	02-03-2011	14:20
7	121	Placebo	04-03-2011	15:00
7	126	Placebo	10-03-2011	15:20
7	131	Placebo	30-03-2011	14:20
8	201	Placebo	16-02-2011	14:18
8	202	Placebo	22-02-2011	13:33
8	207	Placebo	16-03-2011	13:04
8	210	Placebo	25-03-2011	13:31

APPENDIX 16.2.6 INDIVIDUAL EFFICACY RESPONSE DATA

Listing 16.2.6.1
Patient data listing of AUC (0 to 2 hours) data
Full analysis set

Throat soreness measured on an 11-point scale where 0 = Not sore, 10 = Very sore
Sore throat relief measured on a 7-point scale where 0 = No relief, 1 = Slight relief, 2 = Mild relief, 3 = Moderate relief, 4 = Considerable relief, 5 = Almost considerable relief, 6 = Complete relief
Difficulty in swallowing measured on a 100mm VAS scale where 0mm = Not difficult, 100mm = Very difficult
Swollen throat measured on a 100mm VAS scale where 0mm = Not Swollen, 100mm = Very Swollen
Throat numbness measured on a 5-point scale where 1= None, 2 = Mild, 3 = Moderate, 4 = Considerable, 5 = Complete

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
1	034	Strepsils Plus	-2.08	1.12	-23.8	-12.2	2.04
1	038	Strepsils Plus	1.55	1.00	10.5	8.8	3.30
1	041	Strepsils Plus	-2.41	2.73	-25.3	-27.9	2.79
1	044	Strepsils Plus	-1.85	3.25	-19.8	-16.7	2.69
1	048	Strepsils Plus	-9.44	5.49	-83.3	-49.8	4.62
1	051	Strepsils Plus	-2.35	2.20	-17.0	-20.2	2.64
1	052	Strepsils Plus	0.00	0.00	3.6	0.3	1.00
1	057	Strepsils Plus	-6.85	5.93	-71.0	-66.4	4.96
1	059	Strepsils Plus	-3.23	2.61	-47.6	-49.8	2.35

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
1	061	Strepsils Plus	0.94	1.30	4.3	5.2	1.62
2	002	Strepsils Plus	-1.02	1.15	-2.7	-3.7	2.02
2	006	Strepsils Plus	0.13	3.95	7.4	16.1	3.99
2	007	Strepsils Plus	0.00	0.69	-0.6	5.1	3.81
2	012	Strepsils Plus	-1.00	3.30	1.8	-3.1	3.30
2	016	Strepsils Plus	-2.00	2.50	-17.6	-16.6	3.12
2	017	Strepsils Plus	-0.98	0.91	-9.2	-11.9	1.20
2	019	Strepsils Plus	-1.52	1.25	-16.6	-8.3	1.95
2	022	Strepsils Plus	-3.00	2.06	-17.3	-23.5	1.49
2	025	Strepsils Plus	-3.30	2.44	-59.8	-59.8	1.69
2	029	Strepsils Plus	-0.90	0.94	-10.9	-14.1	1.81
2	032	Strepsils Plus	0.00	0.90	1.2	-4.4	1.69
3	232	Strepsils Plus	-2.00	2.80	-28.8	-35.2	2.93
3	235	Strepsils Plus	-1.39	3.01	-25.4	-18.1	2.97
3	239	Strepsils Plus	-1.00	0.00	-15.2	-20.9	1.29
3	243	Strepsils Plus	-0.13	1.97	-1.1	6.7	2.30
3	245	Strepsils Plus	0.00	0.00	-4.3	-4.4	1.00
3	249	Strepsils Plus	-3.57	3.42	-40.9		3.30
3	251	Strepsils Plus	0.00	2.26	-16.9	1.0	2.89

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
3	254	Strepsils Plus	-0.60	2.01	-22.8	1.9	1.59
4	133	Strepsils Plus	-2.89	2.08	-20.5	-10.4	1.98
4	138	Strepsils Plus	-4.14	3.95	-51.7	-55.8	3.80
4	140	Strepsils Plus	-2.24	1.55	-16.9	-11.4	2.24
4	142	Strepsils Plus	0.10	2.20	-31.6	-25.1	1.62
4	147	Strepsils Plus	-2.16	1.06	-20.1	-18.2	1.45
4	148	Strepsils Plus	-2.33	2.64	-30.2	-30.2	2.55
4	151	Strepsils Plus	-2.77	1.33	-47.6	-27.2	1.00
4	154	Strepsils Plus	-2.49	1.16	-49.0	-10.2	2.00
4	156	Strepsils Plus	-3.47	2.53	-32.2	-35.6	2.43
4	161	Strepsils Plus	0.00	0.00	9.2	5.1	1.00
5	167	Strepsils Plus	-3.24	0.74	-21.6	14.4	1.19
5	171	Strepsils Plus	-0.08	0.08	1.8	4.8	1.08
5	172	Strepsils Plus	-0.81	0.29	-3.1	-9.6	1.18
5	175	Strepsils Plus	-2.58	2.70	7.4	-16.7	1.00
5	180	Strepsils Plus	-3.44	2.63	-31.0	-14.2	2.97
5	181	Strepsils Plus	-2.86	1.43	-38.5	-40.2	1.08
6	070	Strepsils Plus	-0.99	1.25	-12.8	8.8	1.26
6	074	Strepsils Plus	-3.07	2.78	-27.3	-19.7	2.65

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
6	077	Strepsils Plus	-0.29	0.70	-0.3	1.5	1.31
6	079	Strepsils Plus	-1.37	2.84	-4.7	-5.3	2.85
7	102	Strepsils Plus	-2.13	0.78	-21.9	-12.2	1.18
7	106	Strepsils Plus	-0.35	1.30	-15.1	-13.1	1.80
7	108	Strepsils Plus	-1.00	0.00	-15.5	5.6	1.00
7	109	Strepsils Plus	-2.49	2.24	-14.0	-8.6	1.49
7	110	Strepsils Plus	-1.99	1.91	-17.8	-23.3	1.41
7	115	Strepsils Plus	-2.35	2.37	-32.4	-34.6	1.60
7	117	Strepsils Plus	-4.14	3.01	-38.5	-45.0	2.78
7	123	Strepsils Plus	-0.23	0.56	0.6	-1.3	1.13
7	125	Strepsils Plus	-0.91	1.32	-10.2	-0.8	1.83
7	127	Strepsils Plus	-0.34	0.30	-4.2	7.6	1.16
7	128	Strepsils Plus	0.24	0.18	1.5	9.1	1.18
8	200	Strepsils Plus	-5.93	4.80	-56.9	-57.9	3.55
8	205	Strepsils Plus	-2.35	2.37	-11.9	-4.1	2.98
8	206	Strepsils Plus	-0.08	0.08	2.1	1.5	1.08
8	209	Strepsils Plus	-2.05	2.86	-17.4	-13.6	3.01
1	036	Strepsils Extra	0.37	4.98	-62.2	-62.5	3.97
1	039	Strepsils Extra	-6.27	5.25	-65.6	-62.6	4.54

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
1	042	Strepsils Extra	-2.54	1.31	-39.7	-44.9	1.68
1	043	Strepsils Extra	-4.87	3.25	-49.8	-53.5	3.66
1	047	Strepsils Extra	-0.83	0.95	-7.4	-0.2	1.50
1	049	Strepsils Extra	-1.63	3.96	-24.4	-27.7	2.28
1	053	Strepsils Extra	-1.67	2.04	-29.3	-42.7	2.04
1	055	Strepsils Extra	-3.53	1.10	-71.4	-76.4	1.74
1	058	Strepsils Extra	-5.68	4.68	-65.1	-63.7	3.91
1	062	Strepsils Extra	-4.09	4.11	-63.8	-60.8	4.15
2	004	Strepsils Extra	-3.71	2.60	-50.7	-49.0	2.93
2	005	Strepsils Extra	-2.83	3.05	-16.3	-4.4	3.10
2	008	Strepsils Extra	-5.00	2.97	-59.6	-45.7	3.20
2	010	Strepsils Extra	-0.41	0.98	1.8	5.3	1.19
2	013	Strepsils Extra	-4.35	2.26	-41.9	-43.5	3.22
2	018	Strepsils Extra	-2.89	2.15	-34.8	-29.0	1.74
2	020	Strepsils Extra	-1.37	1.16	-15.5	-12.4	1.43
2	026	Strepsils Extra	0.00	0.00	1.8	0.6	1.08
2	027	Strepsils Extra	-1.56	0.96	-28.4	-34.3	2.23
2	030	Strepsils Extra	-1.68	1.81	-21.7	-10.9	2.68
2	033	Strepsils Extra	-2.13	3.58	-21.2	-29.7	3.62

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
3	233	Strepsils Extra	0.50	0.50	2.1	1.7	1.50
3	236	Strepsils Extra	-2.49	3.76	-47.5	-42.7	3.95
3	238	Strepsils Extra	-3.53	5.77	-45.3	-49.0	4.58
3	244	Strepsils Extra	-1.68	2.03	-28.8	-8.3	2.18
3	246	Strepsils Extra	-2.23	2.25	-36.0	-24.1	2.69
3	248	Strepsils Extra	0.00	0.00	4.7	-1.0	1.00
3	250	Strepsils Extra	0.07	3.14	-4.7	28.5	3.50
3	253	Strepsils Extra	-2.59	1.41	-23.6	-27.3	2.00
4	134	Strepsils Extra	-0.98	0.98	-10.8	-13.8	1.54
4	137	Strepsils Extra	-2.85	1.79	-35.0	-25.4	1.98
4	141	Strepsils Extra	-2.83	2.26	-18.0	-2.0	2.70
4	144	Strepsils Extra	0.00	0.00	2.2	4.6	1.00
4	145	Strepsils Extra	-0.26	1.97	-8.9	1.3	1.18
4	152	Strepsils Extra	-3.37	2.81	-32.4	-9.5	2.87
4	153	Strepsils Extra	-6.55	3.62	-63.2	-62.7	1.39
4	158	Strepsils Extra	-4.54	3.48	-50.9	-53.2	3.41
4	159	Strepsils Extra	0.00	0.13	-5.0	-4.9	1.04
4	162	Strepsils Extra	0.00	1.41	-11.9	1.5	1.04
5	169	Strepsils Extra	1.08	1.36	3.5	-21.0	1.58

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
5	170	Strepsils Extra	-1.70	0.89	4.1	6.5	1.26
5	173	Strepsils Extra	-2.56	3.66	-26.0	-24.1	3.08
5	177	Strepsils Extra	-5.67	3.07	-56.3	-59.3	1.06
5	179	Strepsils Extra	-3.80	0.74	-39.7	-8.8	1.45
6	067	Strepsils Extra	-1.60	1.76	-20.4	-8.6	2.28
6	071	Strepsils Extra	-3.04	2.70	-10.9	-6.7	2.66
6	075	Strepsils Extra	-6.64	5.72	-68.9	-24.4	1.10
6	076	Strepsils Extra	-1.15	1.27	-7.8	-8.4	1.44
7	101	Strepsils Extra	-4.42	4.18	-49.1	-44.5	3.81
7	105	Strepsils Extra	-1.10	2.09	3.7	-3.1	2.66
7	107	Strepsils Extra	-0.61	1.70	-5.5	6.1	1.70
7	111	Strepsils Extra	0.42	0.68	-0.4	4.8	1.43
7	113	Strepsils Extra	-2.66	2.74	-22.8	-31.2	1.85
7	119	Strepsils Extra	-4.05	3.18	-29.2	-28.3	3.37
7	120	Strepsils Extra	-0.64	1.23	-8.8	-17.4	1.93
7	122	Strepsils Extra	-0.37	0.47	-13.2	-12.5	1.33
7	124	Strepsils Extra	-3.23	3.80	-36.9	-3.9	3.16
7	129	Strepsils Extra	-2.91	2.66	-30.1	-29.0	1.97
7	130	Strepsils Extra	-1.73	2.06	-16.4	-13.1	2.12

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
8	199	Strepsils Extra	-3.07	1.88	-13.1	-10.1	1.70
8	203	Strepsils Extra	-6.12	2.55	-53.9	-55.2	2.47
8	204	Strepsils Extra	-0.94	1.09	-7.6	2.9	1.49
8	208	Strepsils Extra	-1.41	1.12	-18.3	-9.0	1.80
8	211	Strepsils Extra	-4.33	2.70	-45.7	-28.7	2.87
1	035	Placebo	0.07	0.29	-2.3	8.8	1.25
1	037	Placebo	0.00	0.00	0.0	9.2	1.12
1	040	Placebo	-7.31	0.00	-10.4	-11.5	1.00
1	045	Placebo	-0.02	0.00	8.1	13.6	1.00
1	046	Placebo	-0.94	0.94	-6.2	-2.5	1.94
1	050	Placebo	0.00	0.00	-5.1	3.9	1.00
1	054	Placebo	0.00	0.00	-2.5	-0.3	3.00
1	056	Placebo	0.00	0.00	4.1	4.4	1.00
1	060	Placebo	-0.94	0.00	-6.9	-7.6	1.00
2	001	Placebo	0.13	2.96	2.7	-9.0	2.99
2	003	Placebo	0.00	0.00	-0.0	0.0	1.00
2	009	Placebo	-2.66	2.85	-7.3	-5.2	1.93
2	011	Placebo	-2.06	1.88	-23.9	-26.8	2.99
2	014	Placebo	0.00	0.00	-3.4	-0.8	2.99

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
2	015	Placebo	0.56	1.00	8.2	-47.9	1.00
2	021	Placebo	0.36	0.23	-5.8	6.3	1.18
2	023	Placebo	-0.98	2.18	-5.1	-3.3	2.84
2	024	Placebo	1.00	0.00	6.3	-4.8	1.00
2	028	Placebo	0.00	0.00	3.1	1.5	1.00
2	031	Placebo	-2.35	0.29	-2.6	3.9	1.29
3	234	Placebo	-0.81	0.00	-13.8	-1.2	1.00
3	237	Placebo	-3.70	1.14	-40.4	-38.6	2.22
3	240	Placebo	0.00	0.00	-14.3	-21.7	1.00
3	241	Placebo	-0.41	0.45	-14.3	-8.1	1.43
3	242	Placebo	-4.07	1.83	-23.1	-30.4	2.00
3	247	Placebo	-0.62	0.00	2.2	-1.9	1.00
3	252	Placebo	-1.63	1.79	-26.6	-26.8	1.98
3	255	Placebo	-1.00	0.00	-13.2	8.1	2.95
4	135	Placebo	-0.42	0.00	-4.1	-11.5	1.00
4	136	Placebo	0.73	0.00	5.1	0.6	1.00
4	139	Placebo	-1.43	1.04	-17.0	-7.9	1.81
4	143	Placebo	-2.02	0.76	-32.0	-13.6	1.00
4	146	Placebo	-7.73	0.38	-6.3	6.2	1.38

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
4	149	Placebo	-1.91	0.94	-11.6	-10.6	1.94
4	150	Placebo	0.00	0.13	-8.9	1.3	1.00
4	155	Placebo	-0.94	0.43	-22.2	-22.1	2.95
4	157	Placebo	-2.36	1.99	-7.8	-2.2	2.30
4	160	Placebo	0.00	0.00	4.5	6.8	1.00
5	166	Placebo	-0.89	0.89	-12.0	-5.8	1.00
5	168	Placebo	-1.06	1.14	-9.0	-0.5	1.82
5	174	Placebo	-0.69	0.81	-12.9	-9.1	1.81
5	176	Placebo	0.00	0.00	1.9	8.7	1.06
5	178	Placebo	-1.91	1.79	-13.5	8.7	1.63
6	069	Placebo	0.00	0.00	-5.7	-2.1	1.00
6	072	Placebo	-2.97	1.54	-18.4	-32.9	2.80
6	073	Placebo	-1.25	1.28	-15.3	-17.2	1.93
6	078	Placebo	-1.00	1.00	3.8	1.7	1.00
6	080	Placebo	0.43	0.21	1.2	-3.0	1.00
7	100	Placebo	-0.50	0.00	4.3	9.6	1.00
7	103	Placebo	-0.04	0.00	-1.3	1.7	1.00
7	104	Placebo	-1.00	0.02	2.7	1.9	1.02
7	112	Placebo	-2.33	1.33	-12.8	-26.5	1.66

Centre number	Patient number	Treatment group	AUC for change from baseline in throat soreness	AUC from baseline for sore throat relief	AUC for change from baseline in difficulty swallowing	AUC for change from baseline in swollen throat	AUC from baseline for throat numbness
7	114	Placebo	-0.66	2.59	-6.3	23.9	2.10
7	116	Placebo	0.13	0.00	2.2	11.0	1.00
7	118	Placebo	0.00	2.33	-10.5	4.0	2.99
7	121	Placebo	-3.20	2.26	-29.7	-16.1	2.47
7	126	Placebo	-1.72	1.51	-15.8	-19.3	1.87
7	131	Placebo	0.02	0.10	6.3	3.3	1.10
8	201	Placebo	-0.39	2.37	-6.8	-4.5	1.91
8	202	Placebo	-0.97	0.97	-9.6	-9.0	1.97
8	207	Placebo	-3.55	3.78	-48.3	-51.1	3.64
8	210	Placebo	-0.81	1.00	0.6	0.0	1.58

Listing 16.2.6.2
Patient data listing of difficulty in swallowing, swollen throat and throat numbness data-Full analysis set

See Separate Attachment

APPENDIX 16.2.7 ADVERSE EVENT LISTINGS (EACH PATIENT)

Listing 16.2.7.1

Patient data listing of treatment emergent adverse events - Part 1

Safety set

A treatment emergent adverse event is any event commencing within 24 hours of the dose of study medication

Centre number	Patient number	Treatment group	Age (yr)	Gender	Race	Adverse event as recorded on CRF	Serious adverse event	Start time (h) in relation to dose of study medication	Stop time (h) in relation to dose of study medication	Duration of AE (h)
8	200	Strepsils Plus	23	Female	Caucasian	Headache	No	10.27	15.27	5.00
7	111	Strepsils Extra	22	Female	Caucasian	Fever/pyrexia	No	1.63	2.67	1.03
7	111	Strepsils Extra	22	Female	Caucasian	Nausea	No	9.17	72.35	63.18
6	069	Placebo	45	Male	Caucasian	Earache R ear	No	11.18		
6	073	Placebo	37	Male	Caucasian	Heartburn	No	8.53	16.53	8.00
7	116	Placebo	22	Male	Caucasian	Headache	No	0.75	0.83	0.08
8	207	Placebo	31	Male	Caucasian	Feeling tired (lethargy)	No	23.93	25.93	2.00

APPENDIX 16.2.8 LISTING OF OTHER OBSERVATIONS RELATING TO SAFETY

This appendix is not relevant.

APPENDIX 16.3 CASE REPORT FORMS

This appendix is not relevant because no patients died, experienced serious adverse events or withdrew due to adverse events in this study.

APPENDIX 16.2.4 INDIVIDUAL PATIENT DATA LISTINGS (US ARCHIVAL LISTINGS)

The information required for this Appendix is not applicable for this study. It will be provided as a report addendum if required by a regulatory authority.