The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

GSK Medicine: Nicotine		
Study Number: S2540345		
Title: An evaluation of the 4mg nicotine mint lozenge for the relief of cognitive impairment associated with nicotine withdrawal.		
Rationale: To compare the effect of the 4 mg nicotine mint lozenge to placebo on ability to concentrate, as measured by the Rapid Visual Information Processing (RVIP) task		
Phase: IV		
Study Period: 6th January 2006 to 20th April 2006		
Study Design: This was a randomised, multiple dose, single centre, double blind, placebo controlled, two period crossover study conducted in adult smokers. Subjects attended a screening visit and two treatment periods that were separated by at least 48 hours. At each treatment visit, subjects were sequestered at the study site and prohibited from smoking for 18 hours prior to treatment. Approximately 90 minutes prior to the first dose, subjects were administered the cognitive tests. Subjects were then dosed with one of the study treatments at time 0 and then every 2 hours thereafter, for a total of four doses. Thirty (30) minutes after each dosing subjects were administered the cognitive tests.		
Centre: 1, UK		
Indication: Smoking Cessation		
Treatments: **Test product:** A single dose of a 4 mg nicotine mint lozenge was given every 2 hours for 6 hours, for a total of four doses. **Reference product:** A single dose of a placebo lozenge was given every 2 hours for 6 hours, for a total of four doses.		
Objectives: **Primary objective:** To compare the effect of the 4 mg nicotine mint lozenge to placebo on ability to concentrate, as measured by the Rapid Visual Information Processing (RVIP) task. **Secondary objective:** To compare the effect of the 4 mg nicotine mint lozenge to placebo on psychomotor function, short-term memory, selective attention and alertness, sensorimotor performance and safety by the incidence and intensity of adverse events.		
Primary Endpoint: Rapid Visual Information Processing (RVIP) scores **Secondary Endpoints:** Cognitive tests: CTT (Continuous Tracking Task), STM (Short Term Memory), **Stroop** and CRT (Choice Reaction Time) tasks and adverse events		
Statistical Methods: The primary analysis was performed on the scores from the RVIP task, specifically the mean valid response time and number of valid responses. Averages were calculated over the first dose, first two doses, first three doses, and all four doses. A mixed model analysis of covariance (ANCOVA) was performed on each average, with treatment and period as fixed effects, baseline as the covariate, and subject as a random effect. Adjusted treatment means were calculated. Secondary analysis was performed on the other cognitive tests: CTT, STM, Stroop and CRT tasks, using the same statistical methods as in the primary analysis.		
Study Population- Overall		

Treatment Sequence	Nicotine-Placebo	Placebo-Nicotine
Number of Subjects screened:	50	
Randomised, n (%)	12 (100.0)	12 (100.0)
Completed, n (%)	10 (83.3)	10 (83.3)
Subjects not completing the study, n (%)	2 (16.7)	2 (16.7)
Due to adverse event (AEs)	0	1 (8.3)
Due to withdrawal of consent	2 (16.7)	1 (8.3)
Demographics (All Randomized Subjects)		
Sex, n (%)		

Males	3 (25.0)	6 (50.0)
Females	9 (75.0)	6 (50.0)
Race, n (%)		
Caucasian	11 (91.7)	11 (91.7)
Asian	0	1 (8.3)
Other	1 (8.3)	0
Mean Age, years (Standard Deviation [SD])	27.8 (7.90)	29.8 (8.02)
Primary Efficacy Results		
Table 1: Rapid Visual Information Processing (RVIP)		
Number of Valid Responses		
1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	58.8 (22.51)	53.0 (21.90)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0900	
First 2 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	58.5 (21.59)	50.7 (20.20)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0107	
First 3 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	59.4 (20.94)	50.5 (19.53)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0046	
All 4 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	60.3 (20.70)	50.8 (20.08)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0026	
Mean Valid Reaction Time (ms)		
1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	470.5 (65.28)	489.9 (58.72)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0113	
First 2 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	468.9 (57.37)	495.9 (65.74)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0003	
First 3 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	463.8 (56.76)	492.1 (66.69)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0002	
All 4 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	461.1 (56.83)	490.8 (66.97)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0003	
[1] Treatment effect P-value from mixed-model ANCOVA		
Secondary Efficacy Results		

Table 2 Continuous Tracking Task (CTT)		
Overall Mean Reaction Time (ms)		
1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	685.6 (92.64)	749.4 (112.16)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	<.0001	
First 2 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	692.3 (90.34)	755.5 (104.24)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0002	
First 3 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	694.1 (89.39)	752.7 (97.05)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0008	
All 4 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	700.4 (93.03)	750.5 (92.22)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0104	
Overall Mean Tracking Error		
1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	9.0 (2.30)	11.3 (4.06)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0021	
First 2 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	9.0 (2.20)	11.8 (4.26)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0013	
First 3 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	9.0 (2.40)	11.8 (4.47)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0019	
All 4 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	8.9 (2.40)	11.9 (4.71)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0014	
[1]Treatment effect P-value from mixed-model ANCOVA		
Table 3: Sternberg Short-term Memory Scanning (STM)		
Overall Mean for Valid Responses		
1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	673.9 (141.63)	783.6 (140.65)
Treatment comparison (Nicotine versus Placebo)		
P-Value [1]	0.0003	
First 2 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	690.5 (138.95)	776.6 (133.22)
Treatment comparison (Nicotine versus		

Placebo)		
p-Value [1]	0.0024	
First 3 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	690.6 (137.63)	782.0 (139.13)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0006	
All 4 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	679.5 (132.33)	770.4 (137.66)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0002	
Table 4: Stroop Task		
Number of Valid Responses		
1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	293.8 (6.04)	285.9 (14.40)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0088	
First 2 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	291.6 (8.78)	285.5 (11.17)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0372	
First 3 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	291.3 (8.11)	284.7 (11.79)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0311	
All 4 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	291.8 (7.27)	284.9 (10.22)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0107	
Mean Valid Reaction Time (ms)		
1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	543.6 (59.27)	559.3 (54.28)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0398	
First 2 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	537.8 (50.13)	557.8 (53.31)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0119	
First 3 Doses	Nicotine	Placebo
N	22	22
Mean (SD)	533.3 (49.53)	555.9 (57.14)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0052	

All 4 Doses		
N	22	22
Mean (SD)	527.6 (47.44)	550.7 (58.67)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0033	

[1]Treatment effect P-value from mixed-model ANCOVA

Table 5: Choice Reaction Time (CRT)

Recognition Reaction Time (ms)

1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	358.5 (65.34)	386.4 (65.64)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.2659	
First 2 Doses	**Nicotine**	**Placebo**
N	22	22
Mean (SD)	358.6 (63.02)	390.7 (69.07)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0937	
First 3 Doses	**Nicotine**	**Placebo**
N	22	22
Mean (SD)	358.3 (63.05)	386.6 (67.76)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.1829	
All 4 Doses	**Nicotine**	**Placebo**
N	22	22
Mean (SD)	357.6 (61.91)	386.8 (71.00)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.1450	

Motor Reaction Time (ms)

1st dose	Nicotine	Placebo
N	22	22
Mean (SD)	248.4 (37.88)	258.6 (44.63)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.0657	
First 2 Doses	**Nicotine**	**Placebo**
N	22	22
Mean (SD)	250.1 (45.35)	254.6 (44.03)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.3115	
First 3 Doses	**Nicotine**	**Placebo**
N	22	22
Mean (SD)	249.3 (41.87)	254.0 (43.85)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.2532	
All 4 Doses	**Nicotine**	**Placebo**
N	22	22
Mean (SD)	247.1 (41.09)	254.6 (44.17)
Treatment comparison (Nicotine versus Placebo)		
p-Value [1]	0.1291	
Total Reaction Time (ms)		

1st dose	Nicotine	Placebo	
N	22	22	
Mean (SD)	607.0 (79.81)	645.0 (90.12)	
Treatment comparison (Nicotine versus Placebo)			
p-Value [1]	0.0341		
First 2 Doses	Nicotine	Placebo	
N	22	22	
Mean (SD)	608.7 (85.80)	645.3 (93.71)	
Treatment comparison (Nicotine versus Placebo)			
p-Value [1]	0.0981		
First 3 Doses	Nicotine	Placebo	
N	22	22	
Mean (SD)	607.6 (84.99)	640.6 (92.70)	
Treatment comparison (Nicotine versus Placebo)			
p-Value [1]	0.1312		
All 4 Doses	Nicotine	Placebo	
N	22	22	
Mean (SD)	604.7 (84.66)	641.4 (94.02)	
Treatment comparison (Nicotine versus Placebo)			
P-Value [1]	0.0212		
Table 6: Adverse Events (AE's)			
	Subjects with AEs with Nicotine		
	Yes	No	Didn't Use
Subjects with AEs with Placebo			
Yes	5 (29.4%)	1 (5.9%)	2 (11.8%)
No	8 (47.1%)	0	0
Didn't Use	1 (5.9%)	0	0
Serious Adverse Events (SAEs) - On-Therapy			
No serious adverse events were reported			