Reckitt Benckiser

1. STUDY REPORT TITLE PAGE

EudraCT/IND Number:	2011-002341-35
Study Number:	GA1103
Protocol Title:	A randomised single dose two cohort study comparing the speed of raft formation assessed by gamma scintigraphy in healthy volunteers following administration of a single dose of Gaviscon® Strawberry Flavour Tablets (2 x 250 mg) or Gaviscon® Original Aniseed Relief (10 mL) versus matched placebos.
Study Phase:	II
Date First Subject Enrolled:	6 October 2011
Date Last Subject Completed:	16 December 2011
Report Date:	29 November 2012
Principal Investigator:	Dr S. Febbraro, Simbec Research Ltd, Merthyr Tydfil. CF48 4DR
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 RB company archive in Hull, UK

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Clinical Project Manager:		**Statistician:**	
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2. SYNOPSIS

<table>
<tr><td>Name of Sponsor/ Company:
Reckitt Benckiser Healthcare (UK) Limited</td><td rowspan="3">Individual Trial Table Referring to Part of the Dossier

Volume:

Page:</td><td rowspan="3">(For National Authority use only)</td></tr>
<tr><td>Name of Finished Product:
Gaviscon® Strawberry Flavour Tablets (2 x 250 mg), Gaviscon® Original Aniseed Relief (10 mL)</td></tr>
<tr><td>Name of Active Ingredient(s):
Sodium alginate, calcium carbonate, sodium hydrogen carbonate</td></tr>
<tr><td colspan="3">Title of Trial: A randomised single dose two cohort study comparing the speed of raft formation assessed by gamma scintigraphy in healthy volunteers following administration of a single dose of Gaviscon® Strawberry Flavour Tablets (2 x 250 mg) or Gaviscon® Original Aniseed Relief (10 mL) versus matched placebos.</td></tr>
<tr><td colspan="3">Investigator(s): Dr S. Febbraro</td></tr>
<tr><td colspan="3">Trial Site(s): Simbec Research Ltd, Merthyr Tydfil, UK</td></tr>
<tr><td colspan="3">Publication (reference): None</td></tr>
<tr><td colspan="2">Studied Period: 11 weeks
Date first subject enrolled: 06 October 2011
Date last subject completed: 16 December 2011</td><td>Phase of Development: II</td></tr>
<tr><td colspan="3">Objectives: The primary objective was to determine an appropriate methodology to assess speed of raft formation. In addition, the study compared the amount of time taken for a raft to form with 1) Gaviscon® Strawberry Flavoured Tablets versus placebo tablets and 2) Gaviscon® Original Aniseed Relief versus placebo liquid.</td></tr>
<tr><td colspan="3">Methodology: Subjects attended the clinic at Simbec on four occasions: a screening visit, two treatment visits (with an overnight stay before each dosing day) and a follow-up visit. At the screening visit, after consenting for screening procedures, subjects were assessed against the inclusion and exclusion criteria. An ECG was performed and vital signs and demographic data were recorded. After consenting for study procedures, subjects underwent a physical examination, provided a blood sample (for haematology, biochemistry and virology) and a urine sample (for urinalysis, ethanol and drugs of abuse (DOA) testing), and answered questions relating to their medical history.

On the evenings before the two dosing days, subjects provided a urine sample for ethanol and DOA and individually affirmed that they had complied with the restrictions of the study. Subjects stayed in the clinic overnight and fasted from 22:00 until the following morning when they received a standard meal radiolabelled with Technetium-99m (^{99m}Tc) (provided ethanol and DOA test results were negative). The investigational medicinal products (IMPs), radiolabelled with Indium-111 chloride (^{111}In) were administered 35 minutes after the start of the meal. Simultaneous anterior and posterior static images (60 seconds duration) of the stomach were acquired using a gamma camera immediately after the meal had finished and at 30 minutes after the start of the meal. Dynamic images of 30 seconds duration were taken for the first 5 minutes immediately after dosing. Dynamic images of 60 seconds duration were acquired from 5 to 15 minutes after dosing. Single images of 60 seconds duration were acquired at 20 minutes after dosing and then at 20-minute intervals up to 240 minutes. Subjects were individually questioned about symptoms and complaints at 120 and 240 minutes after dosing. Subjects remained under supervision until 4.5 hours after dosing, when they were discharged (if deemed appropriate by the Investigator). Study subjects returned to Simbec for the second treatment visit 3-7 days later.

At the follow-up visit, subjects underwent a physical examination (including vital signs and ECG) and provided a blood sample for haematology and biochemistry and a urine sample for urinalysis.</td></tr>
<tr><td colspan="3">Number of Subjects: Planned: 36 to be randomised, 30 to complete
Analysed: 36 (safety), 35 (efficacy)</td></tr>
</table>

Name of Sponsor/ Company: Reckitt Benckiser Healthcare (UK) Limited	**Individual Trial Table Referring to Part of the Dossier**	**(For National Authority use only)**
Name of Finished Product: Gaviscon® Strawberry Flavour Tablets (2 x 250 mg), Gaviscon® Original Aniseed Relief (10 mL)	**Volume:**	
Name of Active Ingredient(s): Sodium alginate, calcium carbonate, sodium hydrogen carbonate	**Page:**	

Test Product:

Gaviscon® Strawberry Flavour Tablets (chewable tablets), each tablet containing sodium alginate 250 mg, sodium hydrogen carbonate 133.5 mg, calcium carbonate 80 mg (PL 00063/0155).

Gaviscon® Original Aniseed Relief (oral suspension), containing 250 mg sodium alginate, 133.5 mg sodium bicarbonate and 80 mg calcium carbonate per 5ml (PL 00063/0126).

Duration of Treatment: Single dose of each treatment: 2 Gaviscon® Strawberry Flavour Tablets or 10 mL Gaviscon® Original Aniseed Relief

Reference Therapy:

Placebo tablets (chewable tablets) matched to Gaviscon® Strawberry Flavour Tablets

Placebo liquid (oral suspension) matched to Gaviscon® Original Aniseed Relief

Criteria for Evaluation:

Efficacy: The primary endpoint was the comparison of the distribution of Investigational Medicinal Product (IMP) in the stomach 5 minutes after dosing for Gaviscon® Strawberry Flavoured Tablets and Gaviscon® Original Aniseed Relief versus the corresponding placebo. The distribution of the IMP in the stomach after 5 minutes was defined as the area under the percentage retention of IMP curve for the upper stomach relative to the area under the percentage retention of IMP curve for the whole stomach at 5 minutes after dosing. The secondary endpoints were:

- IMP retention corrected for meal retention: the ratio of AUC(IMP) for the whole stomach relative to AUC(meal) for the whole stomach at selected time points.
- Distribution of IMP in the stomach: AUC(IMP) for the upper stomach relative to AUC(IMP) for the whole stomach at selected time points.
- Distribution of the meal in the stomach: AUC(meal) for the upper stomach relative to AUC(meal) for the whole stomach at selected time points.
- Time to half empty the IMP and meal for the whole stomach.
- The percentage of ^{111}In radioactivity (IMP) in the upper stomach over time for each test product.
- The percentage of ^{111}In radioactivity (IMP) in the lower stomach over time for each test product.
- The time taken to form 50%, 70%, 90% and 100% of the complete raft for each test product i.e. time taken to 50%, 70%, 90% and 100% of the maximum ^{111}In (IMP) counts in the upper stomach (for Gaviscon® Strawberry Flavoured Tablets and Gaviscon® Original Aniseed Liquid only).
- Percentage of raft present in the pre-defined region of interest over the 240-minute period.

Safety: Safety was assessed in terms of the overall proportion of subjects with adverse events AEs). AEs were recorded in the CRF after asking subjects whether they had experienced symptoms or complaints. Safety was also evaluated by comparing ECGs, vital signs and laboratory test results between the screening and follow-up visits.

Statistical Methods: The primary efficacy parameter, $AUC(IMP)_{0\text{-}5}$ (upper stomach) / $AUC(IMP)_{0\text{-}5}$ (whole stomach), was compared within each group between the test product and placebo using 2 separate analysis of variance (ANOVA) models of the log-transformed data with terms in the model for treatment sequence, subject within sequence, period and IMP. The mean differences in log-transformed AUC(IMP) for Gaviscon® Strawberry Flavour Tablets –

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placebo tablets and Gaviscon® Original Aniseed Relief - placebo liquid, and the 95% confidence interval, was computed using the adjusted (least squares) means and residual standard deviation and was de-transformed to give the least squares geometric mean gastric retention ratios of AUC(IMP) (Gaviscon® Strawberry Flavour Tablets / placebo tablets and Gaviscon® Original Aniseed Relief / placebo liquid) and the 95% confidence intervals.

The least squares geometric mean gastric retention ratios (Gaviscon® Strawberry Flavour Tablets / placebo tablets and Gaviscon® Original Aniseed Relief / placebo liquid) and their 95% confidence intervals was also computed using the same methods for the other secondary endpoints.

Gastric retention of the IMP i.e. AUC(IMP) was compared with gastric retention of the meal, AUC(meal), in both the whole stomach and the upper stomach and independently for each group and IMP, using ANOVA of the log-transformed data with terms in the model for period, subject within period and administration (IMP or meal). The geometric mean gastric retention ratios AUC(IMP) / AUC(meal) and their 95% confidence intervals were also computed.

Gastric distribution of the IMP, i.e. upper / whole ratio AUC(IMP) was compared with gastric distribution of the meal i.e. upper / whole ratio AUC(meal), for each group and each IMP, using ANOVA of the log-transformed data with terms in the model for period, subject within period and administration (IMP or meal). The geometric mean gastric distribution ratios (upper / whole ratio AUC(IMP)) / (Upper/Whole ratio AUC(meal)) and their 95% confidence intervals were also computed.

All hypothesis tests were performed using the 5% level of significance.

SUMMARY & CONCLUSIONS

EFFICACY RESULTS:

***Primary endpoint*:**

The ratio AUC(IMP) upper stomach / whole stomach, over the first 5 minutes, was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets ($p = 0.0054$). It was less for Gaviscon® Original Aniseed Relief than for placebo liquid, although the difference failed to reach statistical significance ($p = 0.1458$).

Exploratory analyses of the primary variable showed the ratio AUC(IMP) upper stomach / whole stomach was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets over 0-3 and 0-4 minutes ($p = 0.0319$ and 0.0138, respectively). However, the ratio AUC(IMP) upper stomach / whole stomach for Gaviscon® Original Aniseed Relief did not significantly exceed that of placebo liquid until 140 minutes ($p = 0.0482$).

Exploratory analyses of the IMP distribution at individual timepoints showed that the ratio IMP upper stomach / whole stomach was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets at 1, 3, 4 and 5 minutes ($p = 0.0312$, 0.0034, 0.0014 and 0.0001, respectively). However, the ratio IMP upper stomach / whole stomach for Gaviscon® Original Aniseed Relief did not significantly exceed that of placebo until 60 minutes after dosing ($p = 0.0130$).

These results suggest that using this method, the raft is shown to form more quickly with Gaviscon® Strawberry Flavour Tablets than with Gaviscon® Original Aniseed Relief.

Secondary endpoints:

IMP distribution (AUC(IMP) upper stomach / whole stomach) was significantly greater for Gaviscon® Strawberry Flavour Tablets compared with placebo over 0-240 minutes ($p < 0.0001$) and for Gaviscon® Original Aniseed Relief compared with placebo over 0 – 180 minutes ($p = 0.0459$).

The AUC(IMP) for the whole stomach over the first 5 minutes was significantly less for both Gaviscon® products than for the corresponding placebo ($p = 0.0005$ for Gaviscon® Strawberry

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Flavour Tablets and 0.0383 for Gaviscon® Original Aniseed Relief). When corrected for retention of the meal, this parameter was still significantly less for Gaviscon® Strawberry Flavour Tablets than for placebo tablets (p = 0.0004). It was also less for Gaviscon® Original Aniseed Relief than for placebo liquid, although the difference failed to achieve statistical significance (p = 0.0506). The relevance of the correction for retention of the meal, however, is questionable given the 'first 5 minutes' refers to time after dosing for the IMP but time after meal completion for the meal. Over the 240-minute period, however, both Gaviscon® products were retained to a greater extent in the whole stomach, when corrected for meal retention, than their corresponding placebos.

The mean time to half empty the Gaviscon® Strawberry Flavour Tablets from the whole stomach (169.12 minutes) was longer than that for the placebo tablets (56.55 minutes). The corresponding mean times for the Gaviscon® Original Aniseed Relief and placebo liquid were 108.72 and 78.41 minutes, respectively. The mean time to half empty the meal for both Gaviscon® products was similar to that for their corresponding placebos (105.69 and 104.41 minutes for Gaviscon® Strawberry Flavour Tablets and placebo tablets, respectively; 121.11 and 121.12 minutes for Gaviscon® Original Aniseed Relief and liquid placebo, respectively), confirming that the emptying of the meal was unaffected by whether the administered IMP was Gaviscon® or placebo. The mean time taken to half empty the IMP exceeded that to half empty the meal for Gaviscon® Strawberry Flavour Tablets, but was shorter than the time to half empty the meal for placebo tablets, Gaviscon® Original Aniseed Relief and placebo liquid.

The time taken to 50%, 70%, 90% and 100% of maximum 111In (IMP) counts in the upper stomach was shorter for Gaviscon® Original Aniseed Relief (0.01, 0.06, 1.97 and 11.22 minutes, respectively) than for Gaviscon® Strawberry Flavour Tablets (0.30, 0.93, 5.63 and 21.98 minutes, respectively). Although the protocol defined these times as the time taken to form the specified percentages of the complete raft, the IMP distribution results suggest that the raft is formed more slowly with the liquid than the tablet formulations, probably due to the liquid mixing with stomach contents. This is consistent with the fact that a greater proportion of liquid IMPs was observed in the lower stomach at earlier timepoints compared with tablet IMPs.

The AUC(meal) for the whole stomach, over the first 5 minutes, for each Gaviscon® product was not significantly different from that of the corresponding placebo (p = 0.7046 for Gaviscon® Strawberry Flavour Tablets and p = 0.5332 for Gaviscon® Original Aniseed Relief), confirming that the retention of the meal over this period was the same on both dosing days. The ratio AUC(meal) upper stomach / whole stomach over the first 5 minutes for both Gaviscon® products was also not significantly different from that of their corresponding placebos (p = 0.6448 for Gaviscon® Strawberry Flavour Tablets and p = 0.1594 for Gaviscon® Original Aniseed Relief), confirming that the distribution of the meal over this period was also the same on both dosing days.

Extra analyses conducted only for the tablet IMPs showed that Gaviscon® Strawberry Flavour Tablets was significantly superior to placebo tablets in terms of AUC(IMP) in the whole stomach; AUC(IMP) / AUC(meal) in the whole stomach and IMP distribution corrected for meal distribution i.e. (AUC(IMP) upper / whole) / (AUC(meal) upper / whole) over 0 - 240 minutes (p < 0.0001 for all). These results support the outcome of the Gaviscon® Strawberry Flavour Tablets versus placebo comparison for AUC(IMP) upper stomach / whole stomach, demonstrating the retention of the raft formed by Gaviscon® Strawberry Flavour Tablets over 240 minutes.

SAFETY RESULTS: There were no clinically significant safety issues identified during the study. Three mild AEs were reported, all of which were considered not related to study medication. There were no clinically significant changes in laboratory evaluations, vital signs or ECGs.

CONCLUSION: The model used in the pilot study was able to demonstrate early onset of raft formation for Gaviscon® Strawberry Flavour Tablets but not for Gaviscon® Original Aniseed Relief. It is therefore appropriate to use this model to compare Gaviscon® Strawberry Flavour

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<tr><td colspan="3">Tablets with placebo in a pivotal study, albeit with minor modifications to the methodology and analyses.</td></tr>
<tr><td colspan="3">Date of the report: 29 November 2012</td></tr>
</table>

3. TABLE OF CONTENTS

1. STUDY REPORT TITLE PAGE 1
2. SYNOPSIS 3
3. TABLE OF CONTENTS 8
3.1 List of Tables and Figures Contained in the Body of the Report 13
3.2 List of Appendices 14
4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS 16
5. ETHICS 17
5.1 Independent Ethics Committee (IEC) 17
5.2 Ethical Conduct of the Study 17
5.3 Subject Information and Consent 17
6. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE 17
7 INTRODUCTION 18
8. STUDY OBJECTIVES 19
9. INVESTIGATIONAL PLAN 19
9.1 Overall Study Design and Plan – Description 19
9.2 Discussion of Study Design, Including the Choice of Control Groups 19
9.3 Selection of Study Population 19
9.3.1 Inclusion Criteria 19
9.3.2 Exclusion Criteria 20
9.3.3 Removal of Subjects from Therapy or Assessment 21
9.4 Treatments 21
9.4.1 Identity of Investigational Products 21
9.4.2 Standard Test Meal 22
9.4.3 Method of Assigning Subjects to Treatment Groups 23
9.4.4 Selection of Doses in the Study 23
9.4.5 Selection of Timing of Dose for Each Subject 24
9.4.6 Blinding 24
9.4.7 Prior and Concomitant Therapy 25
9.4.8 Treatment Compliance 25
9.5 Efficacy and Safety Variables 25
9.5.1 Scintigraphic and Safety Measurements Assessed and Flowchart 26
9.5.1.1 Scintigraphic Variables 27

9.5.1.2 Safety Variables 29
9.5.2 Appropriateness of Measurements 31
9.5.3 Primary Efficacy Variables 32
9.5.4 Drug Concentration Measurements 32
9.6 Data Quality Assurance 32
9.7 Statistical Methods Planned in the Protocol and Determination of Sample Size 32
9.7.1 Statistical and Analytical Plans 32
9.7.2 Determination of Sample Size 35
9.8 Changes in the Conduct of the Study or Planned Analysis 35
9.8.1 Changes in the Conduct of the Study 35
9.8.2 Changes in the Planned Statistical Analysis of the Study 35
10. STUDY SUBJECTS 36
10.1 Disposition of Subjects 36
10.2 Protocol Deviations 37
11. EFFICACY EVALUATION 38
11.1 Data Sets Analysed 38
11.2 Demographic and Other Baseline Characteristics 38
11.2.1 Demographics 38
11.2.2 General History, Medical History, Physical Examination (Including Vital Signs) and Concomitant Medication 38
11.3 Measurements of Treatment Compliance 39
11.4 Scintigraphy Results 39
11.4.1 Analysis of Scintigraphy Data 39
11.4.1.1 Primary End-Point 39
11.4.1.2 Secondary endpoints 43
11.4.2 Analytical Issues 55
11.4.2.1 Adjustments for Covariates 55
11.4.2.2 Handling of Dropouts or Missing Data 56
11.4.2.3 Interim Analyses and Data Monitoring 56
11.4.2.4 Multi-site Studies 56
11.4.2.5 Multiple Comparison/Multiplicity 56
11.4.2.6 Use of an “Efficacy Subset” of Subjects 56

11.4.2.7 Active-Control Studies Intended to Show Equivalence 56
11.4.2.8 Examination of Subgroups 56
11.4.3 Tabulation of Individual Response Data 56
11.4.4 Drug Dose, Drug Concentration and Relationships to Response 56
11.4.5 Drug-Drug and Drug-Disease Interactions 56
11.4.6 By-subject Displays 56
11.4.7 Efficacy Conclusions 56
12 SAFETY EVALUATION 59
12.1 Extent of Exposure 59
12.2 Adverse Events (AEs) 59
12.2.1 Brief Summary of Events 59
12.2.2 Display of Adverse Events 59
12.2.3 Analysis of Adverse Events 59
12.3 Other Serious Adverse Events (SAEs) and other Significant Adverse Events 59
12.4 Clinical Laboratory Evaluation 60
12.4.1 Listing of Individual Laboratory Measurements by Subject and each Clinically Significant Abnormal Laboratory Value 60
12.4.2 Evaluation of Each Laboratory Parameter 60
12.5 Vital Signs, Physical Findings and other Observations Related to Safety 60
12.6 Safety Conclusions 60
13 DISCUSSION AND OVERALL CONCLUSIONS 60
13.1 Discussion 60
13.2 Conclusion 64
14. TABLES, FIGURES AND GRAPHS REFERRED TO BUT NOT INCLUDED IN THE TEXT 65
14.1 Demographic Data 65
Table 14.1.1 Subject Disposition : All Subjects Population 65
Table 14.1.2 Subject Withdrawals : All Subjects Population 66
Table 14.1.3 Protocol Deviations : All Subjects Population 67
Table 14.1.4 Subject Populations 68
Table 14.1.5 Subject Demographics: Safety Population 69
Table 14.1.6 Medical History – Safety Population 70
14.2 Efficacy Data 71

Table 14.2.1 Percentage Retention of 111In(IMP) for the Whole Stomach By Time and Treatment : ITT Population 71

Table 14.2.2 Percentage Retention of 111In(IMP) for the Upper Stomach By Time and Treatment : ITT Population 73

Table 14.2.3 Percentage Retention of 111In(IMP) for the Lower Stomach By Time and Treatment : ITT Population 75

Table 14.2.4 Percentage Retention of 99mTc(meal) for the Whole Stomach By Time and Treatment : ITT Population 77

Table 14.2.5 Percentage Retention of 99mTc(meal) for the Upper Stomach By Time and Treatment : ITT Population 79

Figure 14.2.1 Percentage Retention 81

Table 14.2.6 Analysis of ratio of Upper Stomach AUC(IMP)$_{0-5}$ to Whole Stomach AUC(IMP)$_{0-5}$ for Gaviscon Strawberry Flavour Tablets vs Placebo: ITT Population 85

Table 14.2.7 Analysis of ratio of Upper Stomach AUC(IMP)$_{0-5}$ to Whole Stomach AUC(IMP)$_{0-5}$ for Gaviscon Original Aniseed Relief vs Placebo: ITT Population 86

Table 14.2.8 Analysis of IMP Distribution (AUC Upper/AUC Whole) over each time point 87

Table 14.2.9 Analysis of IMP Distribution (Upper/Whole) over each time point 89

Table 14.2.10 AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes: ITT Population 91

Table 14.2.11 Analysis of AUC(IMP)$_{0-5}$ Relative to AUC(meal)$_{0-5}$ for the Whole Stomach for Gaviscon Strawberry Flavour Tablets: ITT Population 100

Table 14.2.12 Analysis of AUC(IMP)$_{0-5}$ Relative to AUC(meal)$_{0-5}$ for the Whole Stomach for Gaviscon Original Aniseed Relief: ITT Population 101

Table 14.2.13 AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minute: ITT Population 102

Table 14.2.14 Analysis of Ratio of Upper Stomach AUC(meal)$_{0-5}$ to Whole Stomach AUC(meal)$_{0-5}$ for Gaviscon Strawberry Flavour Tablets vs Placebo: ITT Population 111

Table 14.2.15 Analysis of Ratio of Upper Stomach AUC(meal)$_{0-5}$ to Whole Stomach AUC(meal)$_{0-5}$ for Gaviscon Original Aniseed Relief vs Placebo: ITT Population 112

Table 14.2.16 Time to Half Empty IMP and Meal for the Whole Stomach : ITT Population 113

Table 14.2.17 % Retention for the Whole Stomach and Upper Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes : ITT Population 114

Table 14.2.18 Time to Form 50%, 70%, 90% and 100% Complete Raft in the Upper Stomach : ITT Population 123

Table 14.2.19 Analysis of $AUC(IMP)_{0-5}$ for the Whole Stomach for Gaviscon Strawberry Flavour Tablets: ITT Population 124

Table 14.2.20 Analysis of $AUC(IMP)_{0-5}$ for the Whole Stomach for Gaviscon Original Aniseed Relief: ITT Population 125

Table 14.2.21 Analysis of $AUC(meal)_{0-5}$ for the Whole Stomach for Gaviscon Strawberry Flavour Tablets: ITT Population 126

Table 14.2.22 Analysis of $AUC(meal)_{0-5}$ for the Whole Stomach for Gaviscon Original Aniseed Relief: ITT Population 127

Table 14.2.23 Analysis of $AUC(IMP)_{0-5}$ vs $AUC(meal)_{0-5}$ for Gaviscon Strawberry Tablets : ITT Population 128

Table 14.2.24 Analysis of $AUC(IMP)_{0-5}$ vs $AUC(meal)_{0-5}$ for Gaviscon Original Aniseed Relief : ITT Population 129

Table 14.2.25 Analysis of ratio of Upper Stomach AUC_{0-5} to Whole Stomach AUC_{0-5} for Gaviscon Strawberry Flavour Tablet vs Meal : ITT Population 130

Table 14.2.26 Analysis of ratio of Upper Stomach AUC_{0-5} to Whole Stomach AUC_{0-5} for Gaviscon Original Aniseed Relief vs Meal : ITT Population 131

Table 14.2.27 AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes : ITT Population 132

Table 14.2.28 AUC(IMP) whole stomach; (AUC IMP / AUC Meal) whole stomach, and (AUC IMP upper / AUC IMP whole stomach) / (AUC meal upper stomach / AUC meal whole) 141

14.3 Safety Data 144

Table 14.3.1 Extent of Exposure to Study Medication: Safety Population 144

Table 14.3.2 Laboratory Data : Safety Population 145

Table 14.3.3 Vital Signs : Safety Population 146

Table 14.3.4 ECG Results : Safety Population 147

14.4 Displays of Adverse Events 148

14.4.1 Listings of Deaths, other Serious and Significant Adverse Events 148

14.4.2 Narratives of Deaths, other Serious and certain other Significant Adverse Events 148

14.4.3 Clinically Significant Abnormal Laboratory Value Listing (each subject) .. 148

15. REFERENCE LIST 149

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

Tables

Table 9.4.1 Effective dose associated with common diagnostic X-ray and nuclear medicine procedures 24

Table 9.5.1 Flowchart Procedures 26

Table 9.5.2 Scintigraphic image timing 27

Table 9.5.3 Rating Systems used to determine AE severity and relationship to study medication 31

Table 11.2.1 Demography – Safety Population 39

Table 11.4.3 Analysis of AUC(IMP) for the upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets: ITT population 42

Table 11.4.4 IMP distribution (upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets 43

Table 11.4.5 AUC(IMP) / AUC(meal) whole stomach for Gaviscon® Strawberry Flavour Tablets, Gaviscon® Original Aniseed Relief and their respective placebos: ITT population 44

Table 11.4.6 Analysis of $AUC(IMP)_{0-5}$ / $AUC(meal)_{0-5}$ for the whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets: ITT population 44

Table 11.4.7 Analysis of $AUC(IMP)_{0-5}$ / $AUC(meal)_{0-5}$ for the whole stomach for Gaviscon® Original Aniseed Relief and placebo liquid: ITT population 45

Table 11.4.8 AUC(IMP) upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets, Gaviscon® Original Aniseed Relief and their corresponding placebos: ITT population 46

Table 11.4.9 AUC(meal) upper stomach / whole stomach for Gaviscon® Strawberry Flavoured Tablets, Gaviscon® Original Aniseed Relief and their respective placebos: ITT population 48

Table 11.4.10 Analysis of $AUC(meal)_{0-5}$ for the upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets: ITT population 48

Table 11.4.11 Analysis of $AUC(meal)_{0-5}$ for the upper stomach / whole stomach for Gaviscon® Original Aniseed Relief and placebo liquid: ITT population 49

Table 11.4.12 Time to half empty the IMP and meal for the whole stomach for Gaviscon® Strawberry Flavour Tablets, Gaviscon® Original Aniseed Relief and their respective placebos: ITT population 49

Table 11.4.13 Time taken to form 50%, 70%, 90% and 100% of the maximum counts in the upper stomach for Gaviscon® Strawberry Flavour Tablets and Gaviscon® Original Aniseed Relief 53

Table 12.2.1 Adverse events in study GA1103 59

Table 12.1.1 Comparison of results of study GA1103 and GA0915 in terms of mean time to half empty IMP and meal 63

Figures

Figure 10.1.1 Disposition of Subjects 37

Figure 11.4.1 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Strawberry Flavour Tablets and placebo tablets over 5 minutes 41

Figure 11.4.2 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Original Aniseed Relief and placebo liquid over 5 minutes 41

Figure 11.4.3 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Strawberry Flavour Tablets and placebo tablets over 4 hours 47

Figure 11.4.4 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Original Aniseed Relief and placebo liquid over 4 hours 47

Figure 11.4.5 Percentage retention of Gaviscon® Strawberry Flavour Tablets and placebo tablets in the upper stomach 51

Figure 11.4.6 Percentage retention of Gaviscon® Original Aniseed Relief and liquid placebo in the upper stomach 52

3.2 List of Appendices

16 APPENDIX

16.1 STUDY INFORMATION

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 subjects receiving test drug(s) from specific batches, where more than one batch was used

16.1.7 Randomisation scheme and codes (subject 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 Radiolabelling Validation Report

16.1.12 Publications based on the study

16.1.13 Important publications referenced in the report – copies of papers

16.2 SUBJECT DATA LISTINGS

16.2.1 Discontinued subjects

16.2.2 Protocol Deviations

16.2.3 Subjects excluded from the efficacy analysis

16.2.4 Demographic data

16.2.5 Compliance and / or drug concentration data

16.2.6 Retention data

16.2.7 Adverse event listings

16.2.8 Listing of individual laboratory measurements by subject

16.3 CASE REPORT FORMS

16.3.1 CRFs for deaths, other serious adverse events and withdrawals for adverse events

16.3.2 Other CRFs submitted

16.4 INDIVIDUAL SUBJECT DATA LISTINGS (US ARCHIVAL LISTINGS)

4. LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Abbreviation in Full
ANOVA	Analysis of variance
AUC	Area under the percentage retention-time curve
AE	Adverse event
CRF	Case report form
CV	Curriculum vitae
ECG	Electrocardiogram
EU	European Union
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
HIV	Human immunodeficiency virus
ICH	International Conference on Harmonisation
IEC	Independent ethics committee
IMP	Investigational Medicinal Product
IMSU	Investigational Material Supplies Unit
^{111}In	Indium-111
ITT	Intent-to-treat
RB	Reckitt Benckiser Healthcare (UK) Ltd
ROI	Region of Interest
SAE	Serious adverse event
SD	Standard Deviation
^{99m}Tc	99m-Technetium
UK	United Kingdom (of Great Britain and Northern Ireland)

5. ETHICS

5.1 Independent Ethics Committee (IEC)

The name and full address of the single IEC consulted is provided in Appendix 16.1.3.

The study protocol, together with subject information and consent documents were reviewed and approved by South East Wales Local Research Ethics Committee (LREC) in a letter dated 07 July 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 Subject Information and Consent

Copies of a representative subject information sheet and a blank consent form (Version 1, dated 09 June 2011) are provided in Appendix 16.1.3.

At the screening visit, subjects were asked to provide written informed consent twice, firstly for screening procedures (questions relating to demographics and inclusion/ exclusion criteria, measurement of vital signs and conduct of an ECG) and then, after seeing the physician and discussing the purpose of the study, for further screening procedures (questions relating to medical history and medication, and provision of a blood and urine sample) and for participation in the randomised part of the study. Before being asked to sign, subjects were given the opportunity to read the subject information sheet and consent form, and to ask questions. The physician was required to sign the consent form to confirm that the subject had been provided with a copy of the consent forms and information sheets and that a full explanation of the study had been given. No protocol-related procedures were performed prior to the subject 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 vita (CV) of the Principal Investigator is also included in the Appendix.

The study was carried out at Simbec Research Limited under the guidance of the Principal Investigator, Dr S Febbraro. Some study-related activities were delegated to suitably qualified Simbec personnel. Data management and statistical analysis were conducted by the Statistical Analysis Group, all at Simbec Research Ltd.

The study drug supplies were packed and shipped to Simbec Research Ltd by the Investigational Material Supplies Unit (IMSU), Reckitt Benckiser Healthcare UK Ltd

(RB) Dansom Lane, Hull, HU8 7DS. The writing of the clinical study report was contracted to Clearcut Clinical Consulting Ltd. and monitoring was performed by Ann Ring, Clinical Research Consultant. RB was responsible for the expedited reporting of any serious adverse events to the relevant Regulatory Authorities.

7 INTRODUCTION

RB wished to determine the speed at which an alginate raft was formed by Gaviscon® Strawberry Flavour Tablets (chewable tablets) and Gaviscon® Original Aniseed Relief (liquid). This gamma scintigraphy pilot study was designed to define appropriate methodology and endpoints for the future assessment of speed of raft formation in a pivotal study.

Alginate raft formation and retention was assessed in this randomised, single-dose, open label, two cohort study. Previous studies performed by RB had successfully used gamma scintigraphy to demonstrate raft formation and retention for a range of alginate products, both liquid[1,2,3,4] and tablet[5,6,7,8,9,10].

Healthy volunteers were provided with a standard Technetium-99m (^{99m}Tc)-radiolabelled meal followed by Indium-111 (^{111}In)-radiolabelled test product. Each subject received one Gaviscon® product and its matching placebo in a randomised crossover manner. Single doses of 2 x 250 mg Gaviscon® Strawberry Flavour Tablets, 2 x 250 mg placebo tablets, 10 mL Gaviscon® Original Aniseed Relief and 10 mL placebo liquid were administered.

The potential risks to participating subjects were considered to be low. The adverse reactions that occur very rarely (<1/10,000) as a result of taking Gaviscon® products are allergic manifestations such as urticarial, bronchospasm, anaphylactic and anaphylactoid reactions as a result of subject sensitivity to the active ingredients (sodium alginate, sodium hydrogen carbonate, calcium carbonate) or the excipients (mannitol, macrogol 20,000, aspartame, magnesium stearate, xylitol, carmellose sodium, red iron oxide, strawberry cream flavour (PHS-048481) containing maltodextrin, modified starch 1450, vegetable oil and propylene glycol E1520, carbomer, methyl parahydroxybenzoate, propyl parahydroxybenzoate, saccharin sodium, fennel flavour, erythrosine, sodium hydroxide, water).

Healthy volunteers were not expected to derive any benefit from participation, although it was anticipated that this would help RB better understand the onset of action of the product. The risk/ benefit balance for the study was considered acceptable.

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.

8. STUDY OBJECTIVES

The primary objective was to define an appropriate methodology to assess speed of raft formation. In addition, the study compared the time taken to form a raft for 1) Gaviscon® Strawberry Flavoured Tablets versus a placebo tablets and 2) Gaviscon® Original Aniseed Relief versus a placebo liquid.

9. INVESTIGATIONAL PLAN

9.1 Overall Study Design and Plan – Description

The study protocol is included as Appendix 16.1.1. Unique pages from the case report form (CRF) are included as Appendix 16.1.2.

This was a randomised, single dose, open label, two cohort crossover study to compare the speed of raft formation assessed by gamma scintigraphy in healthy volunteers following administration of a single dose of Gaviscon® Strawberry Flavour Tablets (2 x 250 mg) or Gaviscon® Original Aniseed Relief (10 mL) versus matched placebos. There was a minimum 3-day and a maximum 7-day washout period between treatments.

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

A crossover design was appropriate given that a single dose of each treatment was required in order to determine the speed of raft formation. A two cohort design was appropriate given that the objective of the study was to compare the Gaviscon® formulations with their corresponding placebos and not to compare the two Gaviscon® formulations.

To minimise variability, procedures such as food and fluid intake, use of concomitant medications, posture and dosing were standardised throughout the study. The use of healthy volunteers was appropriate given the objective to determine raft formation as opposed to efficacy, and also served to avoid the variability that might be expected with patients.

As this was a pilot study, no formal statistical sample size justification was performed.

9.3 Selection of Study Population

Study personnel searched the Simbec volunteer database for potential subjects and contacted them to establish their interest before asking them to attend for screening.

9.3.1 Inclusion Criteria

Only subjects to whom all of the following conditions applied were included:

1) Age: ≥ 18 years, ≤ 45 years.
2) Sex: male.
3) Status: healthy volunteers with a body mass index of ≥ 20kg/m^2, ≤ 27kg/m^2.

4) Those who were willing to abstain from consuming alcohol from 48 hours prior to each dosing day.
5) Those who were willing to abstain from smoking tobacco whilst at the study centre
6) Those who were willing to consume both the standard radiolabelled meal, which contained scrambled eggs, and the radiolabelled study drug on each dosing day
7) Subjects who had given written informed consent

9.3.2 Exclusion Criteria

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

1) Those previously randomised into the study.
2) Those who had suffered a >6kg unexplained weight loss in the previous 6 months.
3) Those who had a history of gastro-oesophageal reflux or active gastrointestinal disease (particularly gastritis, gastroduodenal ulcer, gastrointestinal haemorrhage, mechanical obstruction or perforation) within the last year.
4) Those who showed evidence of clinically significant allergic, pulmonary, neurological, renal, hepatic, cardiovascular, psychiatric, metabolic, endocrine or haematological disease.
5) Those who were on a highly restricted salt diet.
6) Those with hypercalcaemia, nephrocalcinosis, recurrent calcium containing renal calculi, or phenylketonuria.
7) Those who had been hospitalised within the previous three months for major surgery or medical illness.
8) Those who had a clinically significant illness within the previous four weeks.
9) Those who had taken any prescription or non-prescription medication within the previous seven days, prior to the screening visit, which the Principal Investigator considers would have interfered with the study.
10) Those who had a history of drug hypersensitivity, which in the opinion of the Principal Investigator, might have interfered with the study.
11) Those who had a current or recent (within one year) history of alcohol abuse or abuse of any legal or illegal drugs, substances or solvents.
12) Those who consumed abnormal quantities of coffee or tea according to the Principal Investigator's judgement.
13) Those unable to communicate well with the Principal Investigator (i.e. language problem, poor mental development or impaired cerebral function) in the opinion of the Investigator.
14) Those with difficulty in swallowing or chewing (e.g. those who have loose teeth, dentures, fillings, etc).
15) Those who were known to be hypersensitive or allergic to any of the active substances (e.g. sodium alginate, sodium hydrogen carbonate, calcium carbonate) or any of the excipients.
16) Those previously randomised to the study.

17) Those who had participated in a clinical trial in the previous 12 weeks or had taken part in a total of four or more studies in the past 12 months.
18) Those who had participated in a study in which radioisotopes were administered or exposure to any radiation other than normal background radiation (e.g. X-rays, handling of radiolabelled materials) within the previous 12 months.
19) Those unable in the opinion of the Investigator to comply fully with the study requirements.

9.3.3 Removal of Subjects from Therapy or Assessment

The Investigator was able to withdraw a subject from the study at any time. Reasons for removing a subject from the study included, but were not limited to:

- Adverse events (AEs) that in the judgement of the Investigator may have caused severe or permanent harm (significant clinical deterioration is an adverse event)
- Violation of the study protocol
- In the Investigator's judgement, it was in the subject's best interest
- The subject declined further study participation

The primary reason for withdrawal was to be documented as one of the following: AEs; lost to follow-up; withdrawal of consent; protocol violation; death or other. The Investigator was to make reasonable attempts to contact any subjects who were lost to follow-up - a minimum of two documented telephone calls or a letter was considered reasonable.

If a subject was withdrawn prematurely from the study, the following assessments were to be carried out:

i) Vital signs
   - Blood pressure (after sitting for 5 minutes; mmHg)
   - Heart rate (DINAMAP compact vital signs monitor – Model TS or equivalent)
   - 12-lead ECG
   - Oral temperature (°C)

ii) Physical examination
iii) Laboratory Investigations
iv) Review of AEs
v) Review of concomitant medication

9.4 Treatments

9.4.1 Identity of Investigational Products

The following medications were supplied:

- Gaviscon® Strawberry Flavour Tablets (chewable tablets). Each tablet contained: 250 mg sodium alginate, 133.5 mg sodium bicarbonate and 80 mg calcium carbonate (PL 00063/0155).
- Gaviscon® Original Aniseed Relief (oral suspension). Five mL contained: 250 mg sodium alginate, 133.5 mg sodium hydrogen carbonate and 80 mg calcium carbonate (PL 00063/0126).
- Tablet Placebo (chewable tablets) matched to Gaviscon® Strawberry Flavour Tablets
- Liquid Placebo (oral suspension) matched to Gaviscon® Original Aniseed Relief

Both Gaviscon® products were manufactured to Good Manufacturing Practice (GMP) standards by Reckitt Benckiser Healthcare (UK) Ltd, Dansom Lane, Hull, HU8 7DS, UK. Placebo tablets and liquid were manufactured to GMP standards by Pharmaterials Ltd, Unit B, 5 Boulton Road, Reading, RG2 0NH, under the direction of Reading Scientific Services Ltd, Reading Science Centre, Whiteknights Campus, Pepper Lane, Reading, RG6 6LA, UK.

All drug supplies were packed and labelled to GMP standards by the Investigational Material Supplies Unit (IMSU), Reckitt Benckiser Healthcare (UK) Ltd, Dansom Lane, Hull, HU8 7DS, UK. As this was an open label trial, drug supplies were not blinded. They were shipped directly from the IMSU to Simbec Research Ltd.

Each IMP was radiolabelled with ^{111}In at Simbec Research Ltd. (by Cardiff Scintigraphics Ltd.) according to GMP. The total effective radiation dose was planned to be 0.82 mSV. Due to the short shelf-life of the final product, QP Certification was completed retrospectively.

An appropriate radiolabelling method was developed for each IMP. An *in vitro* procedure to confirm that the ^{111}In was effectively associated with the alginate raft formed by each Gaviscon® product for the duration of the assessment period (4 hours) was performed before the study to validate the methodology. A report describing the labelling methods and their validation was submitted to RB before the study. Each IMP was radiolabelled according to Good Manufacturing Practice GMP. ^{111}In was obtained from the Medical Physics Department at the University Hospital of Wales (UHW).

9.4.2 Standard Test Meal

On each of the two dosing days, subjects were required to consume a standard radiolabelled test meal comprising:

- 2 slices (60g) toasted white bread
- 200ml unsweetened orange juice
- 25g butter
- 30ml milk

- 2 eggs

The meal was served as scrambled eggs on toast with orange juice.

This meal had an approximate total calorific value of 2550 kJ (609 kcalories), containing approximately 34.1 g of protein, 46.0 g of fat and 51.4 g of carbohydrate. The approximate volume and weight of the meal were 430 mL and 435 g respectively.

^{99m}Tc as ^{99m}Tc MAA was obtained from the Medical Physics Department UHW. The eggs were labelled by the addition of a total of 1.5 MBq ^{99m}Tc MAA per egg before cooking. The eggs were then scrambled. Each subject received 3 MBq of ^{99m}Tc MAA with each test meal consumed.

The integrity of this method of labelling egg-containing meals has been established *in vitro*[11, 12]

The meal start and completion times were recorded in the CRF.

9.4.3 Method of Assigning Subjects to Treatment Groups

Drug supplies were randomised by RB IMSU according to a computer-produced randomisation schedule provided by the RB statistician and checked by a statistician not involved in the analysis of the study. When randomised to treatment, subjects were allocated a unique subject number in numerical sequence. Assignment of the treatment sequence according to the randomisation schedule ensured that the order of treatment allocation was balanced within each cohort.

RB IMSU held the master code for the randomisation schedule and supplied the Investigator with the randomisation code for each subject as an open list.

9.4.4 Selection of Doses in the Study

Each medication was given as a single dose on each dosing day. For Cohort 1, this consisted of either two 250 mg Gaviscon® Strawberry Flavour Tablets or two placebo tablets. For Cohort 2, this consisted of either 10 mL Gaviscon® Original Aniseed Relief or 10 mL liquid placebo (as defined in the randomisation schedule). On each dosing day, the medication was administered to the subject by the Investigator or delegated individual who instructed the subject how to take the medication. A new pack of Gaviscon® Strawberry Flavour Tablets and placebo tablets was used on each dosing day for radiolabelling. A new bottle of Gaviscon® Original Aniseed Relief and liquid placebo was used on each dosing day and the required amount of liquid decanted for radiolabelling. Individual doses of the radiolabelled IMP were assembled, according to the study randomisation schedule, into a dosing container, which was individually labelled in a manner compliant with Annex 13, Rev. 1 (Manufacture of Investigational Medicinal Products) of the EC guide to GMP. Subjects were dosed with tablet IMPs from a dosing container and with liquid IMPs from an oral dosing syringe while in close proximity to the gamma camera detectors. Subjects did not touch the study medication.

Radiation Dosimetry

The study medication and standard meal were radiolabelled as described in Sections 11.1.4 and 11.1.5 of the study protocol, respectively. The total effective radiation exposure was 0.82 millisieverts (mSv) per completed subject. In the UK the average annual dose of ionising radiation exposure from all sources (i.e. natural and man-made) is 2.7 mSv. For comparison, the effective dose associated with common diagnostic X-ray and nuclear medicine procedures is as follows:

Table 9.4.1 Effective dose associated with common diagnostic X-ray and nuclear medicine procedures

Radiographic Test	ED (mSv)	Equivalent Period of Natural Background Radiation
Barium enema	7.69	3.5 years
Barium meal	3.83	2.0 years
Thoracic spine x-ray	0.92	5.0 months
Skull x-ray	0.15	0.8 months
Chest x-ray	0.05	10.0 days
Nuclear Medicine Test		
Bone scan	2.15 - 3.83	1 to 1.7 years
Lung perfusion/Liver scan	0.92 - 1.22	5 to 7 months
Current Study		
Gastric Retention	0.82	Approximately 4.0 months

Source: National Radiological Protection Board[13]

9.4.5 Selection of Timing of Dose for Each Subject

Dosing occurred after an overnight stay in the unit and a fast of approximately 10 hours. Thirty-five minutes after starting the standard breakfast (radiolabelled with ^{99m}Tc) the subject received the study medication radiolabelled with ^{111}In. Dosing was staggered between subjects as required and a maximum of four subjects were dosed each day. The actual time of dosing, i.e. the time the subject started to take the allocated treatment, was recorded in the subject's CRF, which was signed by the person administering the dose. For subjects taking the tablet IMPs (Group 1) dosing occurred at T-1 minute to account for the time taken to chew the tablet. For subjects taking the liquid products (Group 2) dosing occurred at T0. After dosing, subjects remained under supervision until 4.5 hours after dosing, when they were discharged (if deemed appropriate by the Investigator).

9.4.6 Blinding

This study was open label. However, scintigraphic assessment of raft formation was unlikely to have been affected by knowledge of treatment.

9.4.7 Prior and Concomitant Therapy

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

The Investigator was to record any medications given for treatment of AEs on the concomitant medication page in the subject's CRF. Any medication taken by the subject during the course of the study was also to be recorded on this form. Any changes in concomitant therapy during the study were documented, including cessation of therapy, initiation of therapy and dose changes.

9.4.8 Treatment Compliance

Appropriately trained Simbec personnel watched each subject take the treatment and then conducted a mouth inspection. Any subject who did not take the medication as required was to be withdrawn from the study.

9.5 Efficacy and Safety Variables

No efficacy variables were assessed. Scintigraphic measurements are described in this section.

9.5.1 Scintigraphic and Safety Measurements Assessed and Flowchart

Table 9.5.1 Flowchart Procedures

Study Flowchart

Assessment	Screening visit	Treatment visit 1		Treatment visit 2		Follow-up visit
		Evening before dosing day 1 (up to 13 days after screening visit)	Dosing day 1 (up to 14 days after screening visit)	Evening before dosing day 2 (2–6 days after dosing day 1)	Dosing day 2 (3-7 days after dosing day 1)	(2-7 days after dosing day 2)
Demography	X					
Physical examination	X					X
Vital signs (including 12 lead ECG)	X					X
Medical history	X					
Ongoing conditions	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X
Blood samples for haematology, biochemistry and virology[1]	X					X
Urine sample for urinalysis	X					X
Urine sample for ethanol and drugs of abuse test	X	X[2]		X[2]		
Administer radiolabelled meal			X		X	
Gamma scintigraphy imaging			X		X	
Administer radiolabelled IMP			X		X	
Check for adverse events (AEs)		X	X	X	X	X

[1]Virology tested at screening only [2]Results confirmed the following morning

9.5.1.1 Scintigraphic Variables

Details of the acquisition and processing of gamma scintigraphy images of the radiolabelled alginate rafts and meals are provided in this section.

All images were taken while under supervision. The subjects remained seated throughout the imaging period. Simultaneous anterior and posterior images of the stomach were acquired by a dual head gamma camera as shown in Table 9.5.2 below.

Table 9.5.2 Scintigraphic image timing

Time relative to dosing (minutes)	Assessment
-45	Radioactive marker placement
-35	Standard radiolabelled meal started
-25 (approx)	Static image of 60 seconds duration acquired immediately after meal was finished
-5	Static image of 60 seconds duration acquired 30 minutes after meal was started
-1*	Radiolabelled IMP (tablet) administered with 10 mL unchilled still mineral water to sip
0*	Radiolabelled IMP (liquid) administered
0 to +5	Dynamic images of 30 seconds duration acquired immediately after dosing
+5 to +15	Dynamic images of 60 seconds duration acquired
+20	Static image of 60 seconds duration acquired
+40 and every 20 minutes thereafter up to +240 minutes	Static image of 60 seconds duration acquired

*Tablet IMP or Liquid IMP depending upon cohort.

Analysis of the scintigraphy images acquired was performed using commercially available nuclear medicine software (Odyssey V9.4B, Philips Medical Systems Limited) and image analysis software (Matlab (R2011b (7.13.0.564) The MathWorks Inc. US) including Image Processing Toolbox). Each image in each of the ^{99m}Tc and ^{111}In channels was analysed by creating three regions of interest (ROIs), one around the whole stomach, a second around the upper part of the stomach to assess the extent to which the IMP and food remained in this region, and a third to assess background activity.

The whole stomach region of interest were defined by summing images acquired for ^{99m}Tc (meal) over the first 45 - 60 minutes following administration of the test meal. The saturation setting was adjusted to approximately 5% and the stomach outline was manually drawn using the saturated pixels as a guide. Although the protocol stated that the saturation setting would be 10 – 20%, it was found that for a small number of images for some subjects, some of the In-111 counts were not contained within the stomach ROI. This was generally in cases where the In-111 was

concentrated at the very top of the stomach. By adjusting the saturation level to 5% prior to definition of the stomach ROI it was found that all In-111 counts were encompassed by the stomach ROI defined in this way.

The upper stomach was determined as follows: using the whole stomach ROI defined above, the longitudinal axis of the stomach was identified and a perpendicular line was drawn at the mid-point so as to divide the whole stomach into two regions. The upper part of the whole stomach ROI was re-traced back to the point of the intersection of the perpendicular line, which forms the lower margin of the ROI. This method has been reported in the literature[14]. This method is slightly different from that described in the protocol, which had been used for previous studies. In this pilot study, the definition of the upper stomach ROI had greater significance than earlier studies. Consequently the literature was reviewed to try to find a method which removed the subjectivity associated with identifying the midpoint of the lesser curvature of the stomach. The Americo publication provided such a method. The detected counts from the regions of interest around the stomach were corrected for background radiation and decay of the isotopes. The ^{99m}Tc counts were also corrected for ^{111}In scatterdown into the ^{99m}Tc channel. The activity in the stomach was calculated as the geometric mean of the anterior and posterior images to correct for the movement of the isotopes from the fundus to the antrum, since the fundus is closer to the posterior of the body[15].

Percentage retention of ^{99m}Tc (meal) and ^{111}In (IMP) at each time point for both regions of interest (the whole stomach and the upper part of the stomach) for each subject for each IMP was derived from the corrected count rates. Percentage retention of ^{99m}Tc(meal) in both the whole stomach and the upper stomach was based on the corrected ^{99m}Tc count in the whole stomach immediately after ingestion of the meal; percentage retention of ^{111}In(IMP) in both the whole and upper stomach was based on the maximum corrected ^{111}In count in the whole stomach after dosing with IMP.

Graphs of percentage retention over time for both ^{111}In(IMP) and ^{99m}Tc(meal) were drawn for each subject for both regions of interest for each IMP. Mean percentage retention (and its 95% confidence interval) was calculated at each time point for both regions of interest for each IMP (^{111}In) and ^{99m}Tc(meal) and summarised in tabular and graphical form.

Previous methods for the calculation of scatterdown could not be used in this study due to changes to the imaging schedule. Furthermore, for several previous studies scatterdown values had been calculated only for the Liquid Gaviscon phase due to difficulties arising from the slow transit of the Gaviscon Tablets. Therefore no scatter values could have been calculated for the cohort that received tablet IMP in the current study. The scatterdown value (62.32%) used in data processing was therefore derived from the previous study (GA0915). This was appropriate since GA0915 used similar inclusion/exclusion criteria e.g. BMI, age and gender.

Parameters derived from gamma scintigraphy counts were analysed as described in Section 9.7.1 (Statistical and Analytical Plans).

9.5.1.2 Safety Variables

All assessments were conducted by the Investigator or a delegated individual qualified by education and experience to perform the delegated tasks.

Medical History & Current Medical Status: A medical history was taken at the screening visit and the subject's current status as a healthy volunteer was confirmed by a physician. Smoking, alcohol and drugs of abuse history and use were collected at screening.

Demographics: Sex, date of birth, race (categorised as Caucasian, Asian, Afro-Caribbean, Other), height (m), weight (kg) and body mass index (kg/m^2) were collected at screening (baseline).

Concomitant Medication (and history at pre-study): At the screening visit, the medication and therapy history was recorded together with current medication and concomitant therapy taken during the previous 7 days. At the treatment visits and the follow-up visit, subjects were asked about any concomitant medication used since the previous visit.

Vital signs (inc 12-lead ECG): Blood pressure (five minutes sitting, mm Hg), 12 lead ECG, heart rate (beats/minute) and oral temperature (°C) were assessed at the screening and follow-up visits.

Physical Examination: A standard physical examination was conducted at the screening and follow-up visits. Clinically significant findings were documented in the CRF.

Haematology: The following were assessed from blood samples obtained at the screening and follow-up visits: Haemoglobin (g/dL), Red cells (10^{12}/L), Haemotocrit (ratio L/L), Mean cell volume (fl), Mean cell haemoglobin (pg), Mean cell haemoglobin concentration (g/L), White cells (10^9/L), Platelets (10^9/L), Differential white cell count (10^9/L), neutrophils, lymphocytes, monocytes, basophils and eosinophils.

Biochemistry: The following were assessed from blood samples obtained at the screening and follow-up visits: sodium (mmol/L), potassium (mmol/L), urea (mmol/L), creatinine (µmol/L), uric acid (mmol/L), glucose (mmol/L), calcium (mmol/L), inorganic phosphorus (mmol/L) total bilirubin (µmol/L), alkaline phosphatase (ALP, IU/L), alanine transaminase (ALT, IU/L), gamma glutamyl transferase (GGT, IU/L), α-hydroxybutyrate dehydrogenase (HBD, IU/L), creatine kinase (IU/L), total protein (g/L), albumin (g/L), cholesterol (mmol/L), triglycerides (mmol/L).

Urinalysis: The following tests were conducted using urine samples obtained at the screening and follow-up visits: dipstick test for pH, protein, glucose, ketones, bilirubin, blood and urobilinogen. If abnormal results were found, microscopy and culture were conducted.

Drugs of Abuse and Urine Alcohol: A urine sample was screened for drugs of abuse (opiates, amphetamine, cannabinoids, cocaine, barbiturates, benzodiazepines and methadone) and alcohol at screening and before dosing at each treatment visit.

Viral Serology: Testing for hepatitis B surface antigen, hepatitis C antibody, and HIV screening was conducted on a blood sample obtained at screening. Results were reported as positive or negative.

AEs: All AEs reported spontaneously by the subject or in response to questioning or observation by the Investigator were recorded in the subject's case report form. The Investigator or a designated deputy asked the subject: "Are you experiencing any symptoms or complaints?" at the screening visit and "Have you had any symptoms or complaints since you were last asked?" at each treatment visit before dosing and 2 and 4 hours after dosing. They were also asked this question when they attended the follow-up visit.

All AEs (including clinically significant laboratory abnormalities) were to be followed up whenever possible to resolution or until the Investigator believed there would be no further change, whichever was the earlier.

Each AE was recorded according to the criteria given below. "Relationship to study medication" was determined by the Investigator or by a medically qualified Co-investigator.

The rating systems used to determine the severity and relationship to study medication are given in Table 9.5.3.

Table 9.5.3 Rating Systems used to determine AE 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 used in the assessment of severity.
	Mild	The AE did not limit usual activities; the subject may experience slight discomfort.
	Moderate	The AE resulted in some limitation of usual activities; the subject may experience significant discomfort.
	Severe	The AE resulted in an inability to carry out usual activities; the subject may experience 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 is an anticipated response to the study medication; and that could not have been reasonably explained by the known characteristics of the subject's clinical state or concomitant therapy
	Possible	An AE that followed a reasonable temporal sequence from administration of the study medicines; that might have been an anticipated response to the study medication; but that could have been produced by the subject'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 subject's clinical state or concomitant therapy.
	None	An AE that was known beyond all reasonable doubt to be caused by the subject's state or concomitant therapy.

9.5.2 Appropriateness of Measurements

The methodology used in this study had previously been used to gain information about raft formation and gastric retention (Section 7). The main objective of this pilot study was to determine whether this methodology was appropriate for assessing speed of raft formation.

9.5.3 Primary Efficacy Variables

Efficacy was not assessed. The primary gamma scintigraphy variables are described in this section.

9.5.4 Drug Concentration Measurements

Drug concentrations were not measured.

9.6 Data Quality Assurance

This was a single-centre study and the same laboratory was used for all analyses. Laboratory results were subject to Quality Assurance procedures at Simbec Research Ltd.

The CRF was in a format familiar to Simbec staff, and a study initiation meeting was held to discuss the study-specific aspects of the trial. At this meeting study staff were trained on the RB AE and concomitant medication recording procedures. A pre-study briefing meeting was held by the Simbec Project Manager to train all study personnel on study-specific procedures.

100% of the CRFs were monitored on behalf of RB and 100% Source Data Verification was carried out on the following items:

- Subject Identity (date of birth, sex, initials, subject number)
- Smoking and alcohol status
- Healthy status of subject (clinically significant medical history and other disorders)

The following aspects of this study were subject to a GCP compliance audit, conducted by the GCP auditor at Simbec:

- Study database
- Study report
- Master CRF
- Scintigraphic data

Audit certificates are included in Appendix 16.1.8.

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

9.7.1 Statistical and Analytical Plans

Detailed documentation of statistical methods, as the final Statistical Analysis Plan, is presented in Appendix 16.1.9.

Efficacy data, including all parameters derived from the gamma scintigraphy count rates, were summarised for the ITT Population.

Percentage retention of ^{99m}Tc(meal) and ^{111}In(IMP) at each time point for all regions of interest (the whole stomach, the upper part of the stomach and the lower stomach (whole – upper)) for each subject for each IMP was derived from the corrected count rates. Percentage retention of ^{99m}Tc(meal) in the whole stomach and the upper/lower stomach was based on the corrected ^{99m}Tc count in the whole stomach immediately after ingestion of the meal; percentage retention of ^{111}In(IMP) in the whole and upper/lower stomach was based on the maximum corrected ^{111}In count in the whole stomach post-dosing with IMP.

Graphs of percentage retention over time for both ^{111}In(IMP) and ^{99m}Tc(meal) are presented for each subject for each region of interest for each IMP.

Mean percentage retention (and its 95% confidence interval) were calculated at each time point for each region of interest for each ^{111}In(IMP) and ^{99m}Tc(meal) and summarised in tabular and graphical form.

The areas under the percentage retention-time curves (AUCs) were calculated after 1, 2, 3, 4, 5, 10, 15, 60 and 240 minutes post dose/meal completion using the trapezoidal rule and defined for all regions of interest (upper/lower and whole stomach) as follows:

$AUC(IMP)_{0\text{-}t}$: Area under the ^{111}In(IMP) percentage retention-time curve between the time of swallowing and t minutes after swallowing the IMP.

$AUC(meal)_{0\text{-}t}$: Area under the ^{99m}Tc(meal) percentage retention-time curve between the time of meal completion and t minutes after meal completion.

Actual times of meal completion, dosing and gamma scintigraphy images were used to calculate AUCs. If the times of the gamma scintigraphy images were not exactly the scheduled number of minutes post dose/meal then linear interpolation between the two images either side was used to represent the percentage retention post dose/meal at that scheduled time. Linear interpolation was used to extrapolate AUC values from 0 – 5 minutes for the meal.

The AUC(IMP)s and AUC(meal)s were calculated for all regions of interest for each subject for each IMP and were summarised by IMP.

The time to half empty the IMP and meal (50% retention of ^{111}In(IMP) and ^{99m}Tc(meal)) was calculated for the whole stomach for each subject for each IMP and was summarised by IMP.

In addition, the time taken to form 50% of the complete raft (time taken to 50% maximum ^{111}In(IMP) counts in the upper stomach), 70% of the complete raft, 90% of the complete raft and 100% of the complete raft was calculated and summarised for Gaviscon® Strawberry Flavour Tablets and Gaviscon® Original Aniseed Relief.

The following derived parameters were also computed for each subject and for each IMP:

(i) IMP retention corrected for meal retention: the ratio of AUC(IMP) for the whole stomach relative to AUC(meal) for the whole stomach,

(ii) Distribution of IMP in the stomach: AUC(IMP) for the upper stomach relative to AUC(IMP) for the whole stomach, and

(iii) Distribution of the meal in the stomach: AUC(meal) for the upper stomach relative to AUC(meal) for the whole stomach.

IMP retention corrected for meal retention was summarised by IMP. Distribution of the IMP and the meal in the stomach was summarised independently for each IMP.

The primary efficacy parameter, $AUC(IMP)_{0-5}$ (upper stomach) / $AUC(IMP)_{0-5}$ (whole stomach), was compared within each group between the test product and placebo using two separate analysis of variance (ANOVA) models of the log-transformed data with terms in the model for treatment sequence, subject within sequence, period and IMP. The mean differences in log-transformed AUC(IMP) for Gaviscon® Strawberry Flavour Tablets – Placebo and Gaviscon® Original Aniseed Relief - Placebo and the 95% confidence interval were computed using the adjusted (least squares) means and residual standard deviation, and de-transformed to give the least squares geometric mean gastric retention ratios of AUC(IMP) (Gaviscon® Strawberry Flavour Tablets/Placebo and Gaviscon® Original Aniseed Relief/Placebo) and the 95% confidence intervals.

The least squares geometric mean gastric retention ratios (Gaviscon® Strawberry Flavour Tablets/Placebo and Gaviscon® Original Aniseed Relief/Placebo) and their 95% confidence intervals were also computed using the same methods for the other secondary endpoints.

Gastric retention of the IMP (AUC(IMP)) was compared with gastric retention of the meal (AUC(meal)) in both the whole stomach and the upper stomach and independently for each group and IMP, using ANOVA of the log-transformed data with terms in the model for period, subject within period and administration (IMP or meal). The geometric mean gastric retention ratios (AUC(IMP)/AUC(meal)) and their 95% confidence intervals were also computed.

Gastric distribution of the IMP (Upper/Whole ratio AUC(IMP)) was compared with gastric distribution of the meal (Upper/Whole ratio AUC(meal)) for each IMP, using ANOVA of the log-transformed data with terms in the model for period, subject within period and administration (IMP or meal). The geometric mean gastric distribution ratios (Upper/Whole ratio AUC(IMP))/(Upper/Whole ratio AUC(meal)) and their 95% confidence intervals was also computed.

All hypothesis tests were performed using the 5% level of significance.

9.7.2 Determination of Sample Size

As this was a pilot study, no formal statistical sample size justification was performed.

9.8 Changes in the Conduct of the Study or Planned Analysis

9.8.1 Changes in the Conduct of the Study

The protocol stated the imaging would be conducted 20 minutes after completion of the meal (i.e. 15 minutes before dosing). However, for logistical reasons this was changed to 30 minutes after completion of the meal (i.e. 5 minutes before dosing).

During study conduct, a protocol inconsistency regarding the timing of scintigraphic imaging was noted. Section 8.6 stated that the images would be taken every 20 minutes from the start of the meal to 4 hours. However, Section 10.3.3.1 stated that images would be taken every 20 minutes after dosing. The RB CPM confirmed that Section 10.3.3.1 was correct and this was documented in the Trial Master File.

9.8.2 Changes in the Planned Statistical Analysis of the Study

As this was a pilot study, it was appropriate that extra analyses not listed in the protocol were conducted.

The following comparisons were not listed as specific endpoints in the protocol but were analysed by Simbec:

- Comparison of each Gaviscon® product with its corresponding placebo in terms of $AUC(IMP)_{0-5}$ for the whole stomach.
- Comparison of each Gaviscon product with its corresponding placebo in terms of $AUC(meal)_{0-5}$ for the whole stomach.
- Comparison of AUC(IMP) versus AUC (meal) for both the upper and whole stomach over the first 5 minutes for both Gaviscon products.
- Comparison of $AUC(IMP)_{0-5}$ versus $AUC\ (meal)_{0-5}$ for the ratio of the upper to whole stomach for both Gaviscon® products.

Extra analyses not listed in the protocol conducted by RB included:

- Comparison of each Gaviscon® product with its corresponding placebo in terms of distribution of IMP i.e. AUC(IMP) upper stomach/ AUC(IMP) whole stomach at each scintigraphic imaging timepoint. The purpose of these extra analyses was to investigate raft formation at timepoints earlier than 5 minutes and also to compare the Gaviscon® products with their corresponding placebos in terms of this endpoint over 240 minutes.
- Comparison of each Gaviscon® product with its corresponding placebo in terms of distribution of IMP i.e. IMP upper stomach / whole stomach at each scintigraphic imaging timepoint. The purpose of this analysis was to look at the

sensitivity of this endpoint compared with AUC(IMP) upper stomach / whole stomach.

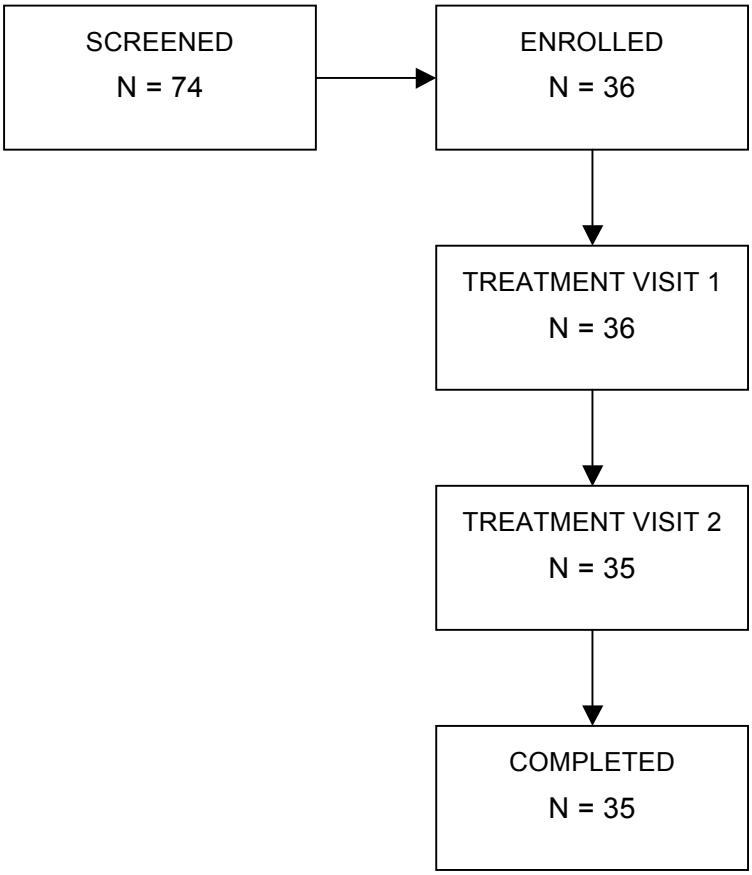
- Comparison of Gaviscon® Strawberry Flavour Tablets with placebo tablets in terms of AUC(IMP) in the whole stomach; AUC(IMP) / AUC(meal) in the whole stomach and IMP distribution corrected for meal distribution i.e. (AUC(IMP) upper / whole) / (AUC(meal) upper / whole) at each scintigraphic imaging timepoint. The purpose of these analyses was to compare the Gaviscon® Strawberry Flavour Tablets with placebo tablets in terms of these endpoints over 240 minutes.

10. STUDY SUBJECTS

10.1 Disposition of Subjects

Details of disposition and withdrawals for individual subjects are provided in Appendix 16.2.1, summarised in Tables 14.1.1 and 14.1.2 and presented schematically in Figure 10.1.1. Thirty-six subjects provided consent, were screened and received study medication during the first treatment visit. Of the 36 subjects who attended the second treatment visit, one subject did not receive the study medication because he tested positive for opiates. This subject was in the cohort receiving the liquid IMPs. Hence 18 subjects in the tablet cohort and 17 subjects in the liquid cohort completed both treatment visits. All 36 subjects attended the follow-up visit.

Figure 10.1.1 Disposition of Subjects



10.2 Protocol Deviations

A listing of individual subjects who deviated from the protocol is presented in Appendix 16.2.2. A summary of protocol deviations is presented in Table 14.1.3.

Dosing was performed late for 11 (30.6%) subjects (15 occurrences) and the follow-up visit was outside the visit window for two (5.6%) subjects. A gamma scintigraphy image was missed for three (18.3%) subjects. Only one subject (2.8%), who tested positive for opiates, was withdrawn due to a protocol violation.

The determined radioactivity at the intended time of dosing with batch 0348 of Gaviscon® Strawberry Flavour Tablets was incorrectly calculated because the incorrect date of dosing had been entered into the dose calibrator in error. This resulted in Subjects S013 and S014 receiving a greater level of radioactivity than that specified in the protocol. This increase was not considered significant and was deemed unlikely to affect the safety or wellbeing of the subjects or the scientific value of the study. Nevertheless, the Sponsor was informed. A file note was generated and reviewed by the ARSAC signatory. However, the committee was not informed because the level of the 'excess' dose was so small. Although it was not required by the ARSAC signatory, the subsequent dose of radioactivity was slightly reduced for the subjects in question so that the planned total study exposure was not exceeded.

11. EFFICACY EVALUATION

Efficacy was not determined. This section describes the evaluation of raft formation and retention.

11.1 Data Sets Analysed

Analyses of gastric retention data were performed on the data from all subjects who successfully completed both treatment visits (ITT population).

The strategy for the inclusion/exclusion of data was described in the SAP and was finalised after determination of subject evaluability, which took place before database lock. No subject who completed both treatment visits was excluded from the ITT population. The subject populations are given in Table 14.1.4.

11.2 Demographic and Other Baseline Characteristics

11.2.1 Demographics

The demographics of individual subjects are presented in Appendix 16.2.4. A summary of the demographics of the safety population is given in Table 14.1.5 and summarised in Table 11.2.1. All 36 subjects enrolled were male Caucasians.

11.2.2 General History, Medical History, Physical Examination (Including Vital Signs) and Concomitant Medication

Details of general history, medical history, physical examination findings, concomitant medications, vital signs and ECGs are provided for individual subjects in Appendix 16.2.4. Medical history is summarised in Table 14.1.6. There were no past medical histories that suggested the subjects were not suitable for inclusion as healthy volunteers. On physical examination, 12 subjects had dermatological abnormalities, one had an opthalmological abnormality and one had a gastrointestinal abnormality, but none was deemed clinically significant by the Investigator. Six subjects had abnormal findings on their ECGs but these were not deemed clinically significant. There was no clinically significant finding relating to pulse rate, blood pressure or oral temperature.

Table 11.2.1 Demography – Safety Population

Demographic Parameter		Cohort 1 (n = 18)	Cohort 2 (n = 18)
Age (years)	Mean	27.8	28.9
	SD	8.0	8.1
	Range	18 - 42	18 - 42
Height (cm)	Mean	1.8	1.8
	SD	0.1	0.1
	Range	1.67 - 1.86	1.63 - 1.84
Body Mass Index (kg/m^2)	Mean	24.28	24.54
	SD	1.77	1.29
	Range	20.7 - 26.5	21.7 - 26.9
Pre-study weight (kg)	Mean	74.85	76.61
	SD	6.58	6.64
	Range	64.0 - 86.8	63.4 - 91.1

Source: Table 14.1.5; SD: standard deviation

11.3 Measurements of Treatment Compliance

Simbec personnel (the physician or appropriately trained staff) observed each subject take the study medication and conducted a mouth inspection to ensure compliance with dosing. All subjects took the medication as required.

11.4 Scintigraphy Results

11.4.1 Analysis of Scintigraphy Data

Study visit dates are provided in Appendix 16.2.4 and gamma scintigraphy image acquisition times are provided in Appendix 16.2.6.

Percentage retention data of IMP and meal in the whole, upper and lower stomach for each subject at all timepoints are given in Appendix 16.2.6 and (with the exception of the meal in the lower stomach, for which data were not derived) are summarised in Tables 14.2.1 – 14.2.5. Percentage retention plots of IMP and meal (whole and upper stomach) are given for each subject in Appendix 16.2.6 and summarised in Figure 14.2.1.

In the following sections, the results are presented in the order of endpoints listed in the protocol. Extra analyses, not included in the protocol, are included where appropriate. Discussion of results is reserved for Section 13.1.

11.4.1.1 Primary End-Point

The primary endpoint was the distribution of IMP in the stomach 5 minutes after dosing for Gaviscon® Strawberry Flavour Tablets and Gaviscon® Original Aniseed

Relief versus the respective placebo. The distribution of the IMP in the stomach after 5 minutes was defined as the area under the percentage retention of IMP curve for the upper stomach relative to the area under the percentage retention of IMP curve for the whole stomach at the first 5 minutes i.e. $AUC(IMP)_{0-5}$ upper stomach / whole stomach.

Primary endpoint data are provided in Tables 14.2.6 and 14.2.7 and summarised in Tables 11.4.1 and 11.4.2.

Table 11.4.1 Analysis of $AUC(IMP)_{0-5}$ for the upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets: ITT population

	Gaviscon® Strawberry Flavour Tablets	Placebo Tablets
Geometric adjusted mean $AUC(IMP)_{0-5}$ upper stomach / whole stomach (CV)	0.79 (17.98)	0.65 (17.98)
Treatment ratio for Gaviscon® Strawberry Flavour Tablets / placebo tablets (95% confidence interval), p value	1.211 (1.068 - 1.374), 0.0054	

Source: Table 14.2.6; CV: geometric coefficient of variation

Table 11.4.2 Analysis of $AUC(IMP)_{0-5}$ for the upper stomach / whole stomach for Gaviscon® Original Aniseed Relief and placebo liquid: ITT population

	Gaviscon® Original Aniseed Relief	Placebo Liquid
Geometric adjusted mean $AUC(IMP)_{0-5}$ upper stomach / whole stomach (CV)	0.71 (17.30)	0.78 (17.30)
Treatment ratio for Gaviscon® Original Aniseed Relief / placebo liquid (95% confidence interval), p value	0.914 (0.806 - 1.036), 0.1458	

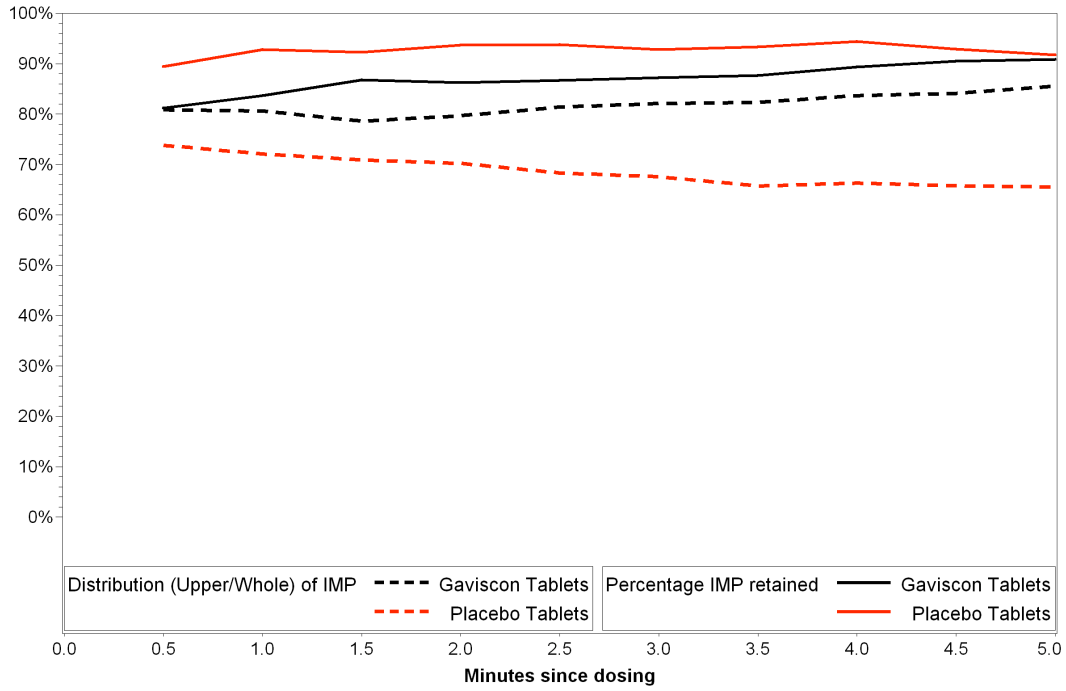
Source: Table 14.2.7; CV: geometric coefficient of variation

The ratio of the $AUC(IMP)_{0-5}$ upper stomach / whole stomach was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets ($p = 0.0054$), but was less for Gaviscon® Original Aniseed Relief than for placebo liquid, although the difference failed to achieve statistical significance ($p = 0.1458$).

Extra analyses of the primary variable

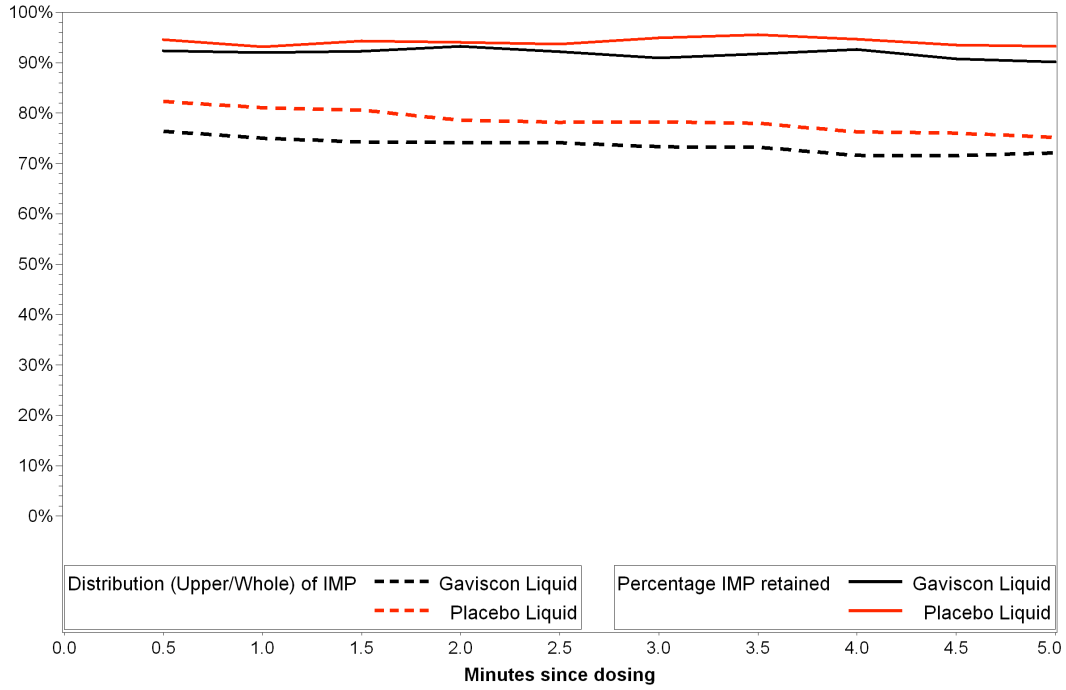
Extra analyses were carried out by RB to further explore the data. Figures 11.4.1 and 11.4.2 show the distribution (i.e. IMP upper stomach / whole stomach) and retention in the whole stomach over the first 5 minutes.

Figure 11.4.1 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Strawberry Flavour Tablets and placebo tablets over 5 minutes



Source: SAS datasets relating to Tables 14.2.1 and 14.2.2

Figure 11.4.2 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Original Aniseed Relief and placebo liquid over 5 minutes



Source: Source: SAS datasets relating to Tables 14.2.1 and 14.2.2

These figures show that retention was sufficiently high for the distribution data to be meaningful. The mean percentage IMP retained was higher for placebo tablets than for Gaviscon® Strawberry Flavour Tablets over the first 5 minutes. This is due to the slower transit of the active tablets, which were retained in the mouth for longer, increasing the time to peak counts in the stomach. However, the mean distribution profile was more favourable (i.e. a higher ratio of IMP upper stomach / whole stomach) for Gaviscon® Strawberry Flavour Tablets. There was little difference between Gaviscon® Original Aniseed Relief and placebo liquid in terms of either retention or distribution over the first five minutes.

Analysis of IMP distribution over selected time periods:

Analyses of IMP upper stomach / whole stomach for both Gaviscon® products versus their respective placebos, from dosing to all timepoints, are given in Table 14.2.8. Those analyses for 0-1, 0-2 and 0-3 minutes are summarised below for Gaviscon® Strawberry Flavour Tablets versus placebo tablets.

Table 11.4.3 Analysis of AUC(IMP) for the upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets: ITT population

	IMP Distribution (AUC upper stomach / AUC whole stomach)					
Minutes after dosing	Geometric LS Mean		Gaviscon® Strawberry Flavour Tablet / placebo tablet			
			Ratio	95% CI		P-value
	Gaviscon® Strawberry Flavour Tablet	Placebo tablet		Lower	Upper	
1	0.77	0.70	1.10	0.98	1.23	0.0882
2	0.76	0.69	1.11	0.99	1.25	0.0704
3	0.77	0.67	1.15	1.01	1.30	0.0319
4	0.78	0.66	1.18	1.04	1.34	0.0138

Source: Table 14.2.8; CI: Confidence Interval; LS: Least Squares

The AUC(IMP) upper stomach / whole stomach was greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets over 0-1, 0-2, 0-3 and 0-4 minutes, the treatment differences over 0-3 and 0-4 minutes achieving statistical significance.

The ratio AUC(IMP) upper stomach / whole stomach for Gaviscon® Original Aniseed Relief did not significantly exceed that of placebo liquid until 140 minutes ($p = 0.0482$).

Analysis of IMP distribution at individual timepoints:

Analyses of AUC(IMP) upper stomach / whole stomach for both Gaviscon® products versus their respective placebos at each timepoint are provided in Table 14.2.9. Those analyses at 1, 2, 3, 4 and 5 minutes are summarised in Table 11.4.4.

Table 11.4.4 IMP distribution (upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets

	IMP Distribution (upper stomach / whole stomach)					
Minutes since IMP	Geometric LS Mean		Gaviscon® Strawberry Flavour Tablet / Placebo tablet			
			Ratio	95% CI		P-Value
	Gaviscon® Strawberry Flavour Tablet	Placebo tablet		Lower	Upper	
1	0.77	0.68	1.13	1.01	1.26	0.0312
2	0.76	0.66	1.15	0.99	1.34	0.0679
3	0.80	0.63	1.26	1.09	1.45	0.0034
4	0.82	0.61	1.33	1.14	1.55	0.0014
5	0.84	0.62	1.35	1.19	1.53	0.0001

Source: Table 14.2.9; CI: Confidence Interval; LS: Least Squares

The IMP upper stomach / whole stomach was greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets at 1, 2, 3, 4 and 5 minutes, although the difference at 2 minutes did not achieve statistical significance.

The ratio IMP upper stomach / whole stomach for Gaviscon® Original Aniseed Relief did not significantly exceed that of placebo until 60 minutes after dosing (p = 0.0130) (Table 14.2.9).

11.4.1.2 Secondary endpoints

These are presented as described in the protocol.

IMP retention corrected for meal retention: the ratio of AUC(IMP) for the whole stomach relative to AUC(meal) for the whole stomach at selected time points.

The ratios AUC(IMP) / AUC(meal) for the whole stomach and upper stomach by treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes are provided in Table 14.2.10 and, for the whole stomach, are summarised in Table 11.4.5.

Table 11.4.5 AUC(IMP) / AUC(meal) whole stomach for Gaviscon® Strawberry Flavour Tablets, Gaviscon® Original Aniseed Relief and their respective placebos: ITT population

Timepoint (minutes)	Mean AUC(IMP) / AUC(meal) whole stomach			
	Gaviscon® Strawberry Flavour Tablets	Placebo Tablets	Gaviscon® Original Aniseed Relief	Placebo Liquid
1	0.81	0.90	0.91	0.93
2	0.84	0.91	0.92	0.94
3	0.85	0.92	0.92	0.94
4	0.86	0.93	0.92	0.94
5	0.87	0.93	0.92	0.94
10	0.90	0.93	0.91	0.94
14	0.92	0.92	0.91	0.93
60	1.00	0.79	0.87	0.82
240	1.38	0.65	0.95	0.68

Source: Table 14.2.10

Over 240 minutes, both Gaviscon® products were retained to a greater extent, relative to the meal, than their corresponding placebos.

A statistical comparison between each Gaviscon® product and its respective placebo in terms of AUC(IMP) / AUC(meal) for the whole stomach was conducted only over 0-5 minutes for both Gaviscon® products. These data are provided in Tables 14.2.11 and 14.2.12 and summarised in Tables 11.4.6 and 11.4.7.

Table 11.4.6 Analysis of $AUC(IMP)_{0-5}$ / $AUC(meal)_{0-5}$ for the whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets: ITT population

	Gaviscon® Strawberry Flavour Tablets	Placebo tablets
Geometric adjusted mean $AUC(IMP)_{0-5}$ / $AUC(meal)_{0-5}$ whole stomach (CV)	0.8678 (4.67)	0.9309 (4.67)
Treatment ratio for Gaviscon® Strawberry Flavour Tablets / placebo tablets (95% confidence interval), p value	0.932 (0.902 - 0.963), 0.0004	

Source: Table 14.2.11; CV: geometric coefficient of variation

Table 11.4.7 Analysis of $AUC(IMP)_{0-5}$ / $AUC(meal)_{0-5}$ for the whole stomach for Gaviscon® Original Aniseed Relief and placebo liquid: ITT population

	Gaviscon® Original Aniseed Relief	Placebo Liquid
Geometric adjusted mean $AUC(IMP)_{0-5}$/ $AUC(meal)_{0-5}$ whole stomach (CV)	0.9219 (3.28)	0.9442 (3.28)
Treatment ratio for Gaviscon® Original Aniseed Relief / placebo liquid (95% confidence interval), p value	0.976 (0.953 - 1.000), 0.0506	

Source: Table 14.2.12; CV: geometric coefficient of variation

When corrected for retention of the meal, the retention of IMP in the whole stomach over the first 5 minutes was significantly less for Gaviscon® Strawberry Flavour Tablets than for placebo tablets. The slow transit time of the active tablets from mouth to stomach compared with placebo tablets contributed to this difference, the 95% confidence intervals for the percent retention immediately after dosing being 74.5 – 81.7 for Gaviscon® Strawberry Flavour Tablets and 82.5 – 91.5 for placebo tablets (Table 14.2.1). When corrected for retention of the meal, the retention of IMP in the whole stomach over the first 5 minutes was also less for Gaviscon® Original Aniseed Relief than for placebo liquid, although the difference was not significant.

It should be noted that the times in tables 11.4.5, 11.4.6 and 11.4.7 relating to AUC(meal) refer to time after meal, whereas the times relating to AUC(IMP) refer to time after dosing. The IMP was not administered until approximately 25 minutes after the end of the meal. Hence data for the AUC(meal) for timepoints up to and including 15 minutes in Table 11.4.5 relate to before IMP was taken. In addition, although the first image of the meal (60 seconds duration) was taken immediately after meal completion, the next was not taken until 30 minutes after the start of the meal, so values for AUC(meal) in Table 11.4.5 at the early timepoints are extrapolated rather than actual values and do not necessarily reflect the AUC(meal) at those timepoints. The relevance of this data is therefore questionable. In addition, it is likely that less gastric emptying of the meal occurred over the extrapolated time points i.e. 0 – 5 minutes after meal completion, than occurred over the time the IMP emptying was actually measured i.e. 35 – 40 minutes after meal start (25 - 30 minutes after meal completion). Furthermore, meal retention at the time of the first image (immediately after meal completion) was 100% whereas for IMP, 100% was set at the time of maximum counts i.e. sometime after administration.

Distribution of IMP in the stomach: AUC(IMP) for the upper stomach relative to AUC(IMP) for the whole stomach at selected timepoints.

This relates to the primary variable, the analysis of which is presented in Section 11.4.1.1 for timepoints up to 5 minutes. The AUC(IMP) for the upper stomach / whole stomach by treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes is provided in Table 14.2.13 and summarised in Table 11.4.8.

Table 11.4.8 AUC(IMP) upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets, Gaviscon® Original Aniseed Relief and their corresponding placebos: ITT population

Timepoint (minutes)	AUC(IMP) upper stomach / whole stomach			
	Gaviscon® Strawberry Flavour Tablets	Placebo tablets	Gaviscon® Original Aniseed Relief	Placebo liquid
1	0.81	0.74	0.77	0.83
2	0.80	0.72	0.76	0.81
3	0.80	0.71	0.75	0.80
4	0.80	0.71	0.75	0.80
5	0.82	0.69	0.74	0.79
10	0.84	0.67	0.73	0.76
14	0.86	0.66	0.73	0.75
60	0.90	0.64	0.76	0.69
240	0.82	0.61	0.72	0.64

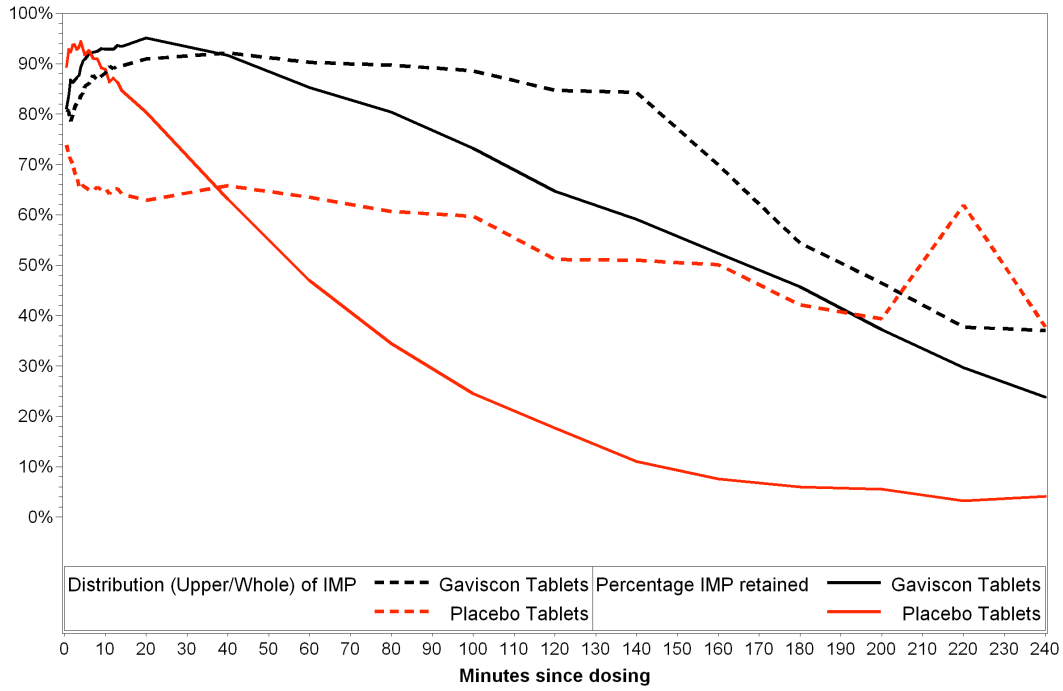
Source: Table 14.2.13

At each of the selected timepoints, the ratio AUC(IMP) upper stomach / whole stomach was greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets. Additional analyses by RB (Table 14.2.8) showed that this difference was significant at every timepoint from 3 minutes onwards, the p value for the comparison at 240 minutes being < 0.0001. Extra analyses by RB (Table 14.2.8) showed that the ratio AUC(IMP) upper stomach / whole stomach for Gaviscon® Original Aniseed Relief significantly exceeded that of placebo over 0-140 ($p = 0.0482$), 0-160 ($p = 0.0423$) and 0-180 ($p = 0.0459$) minutes.

These data are presented, together with retention data, in Figures 11.4.3 and 11.4.4. Retention data show that it took longer to achieve the maximum amount of Gaviscon® Strawberry Flavour Tablets in the stomach compared with placebo. For both liquid IMPs, the ratio IMP upper stomach / whole stomach decreased sharply initially, then increased for Gaviscon® Original Aniseed Relief but not for placebo, consistent with a delayed formation of the raft with Gaviscon® Original Aniseed Relief.

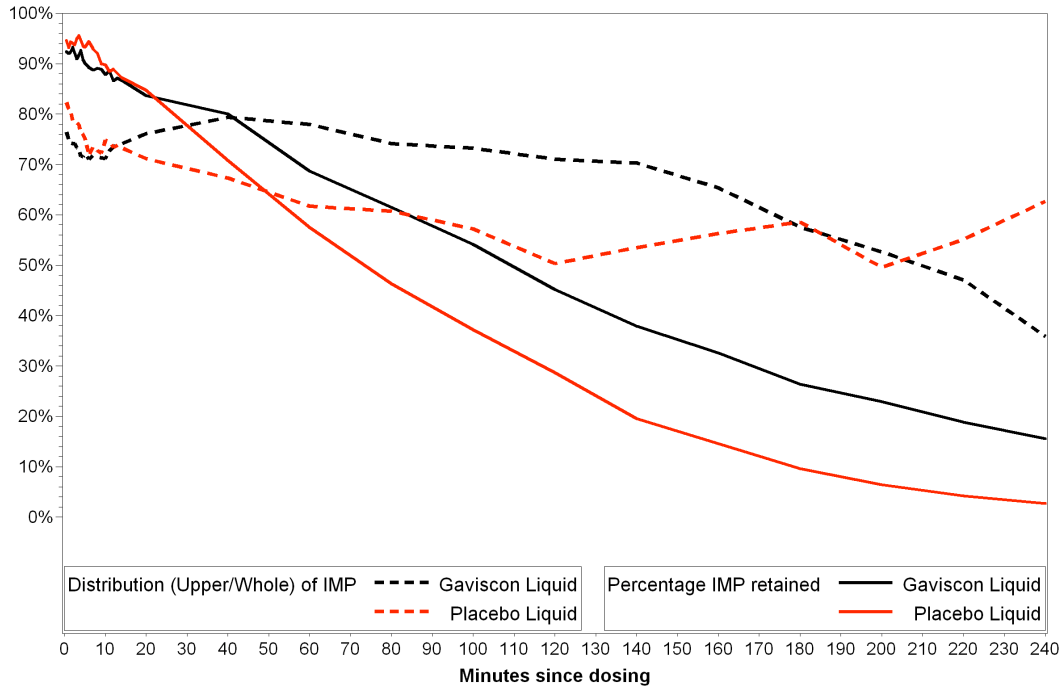
For some subjects, the upper retention was higher than the whole retention at later timepoints when very low counts were observed. This caused the spike at 220 minutes in Figure 11.4.3 with placebo tablets and suggests that the distribution data maybe less accurate at later timepoints.

Figure 11.4.3 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Strawberry Flavour Tablets and placebo tablets over 4 hours



Source: SAS datasets relating to Tables 14.2.1 and 14.2.2

Figure 11.4.4 Mean distribution (IMP upper stomach / whole stomach) and mean % retention of Gaviscon® Original Aniseed Relief and placebo liquid over 4 hours



Source: Source: SAS datasets relating to Tables 14.2.1 and 14.2.2

It should be noted that there are minor discrepancies between figures 11.4.3 / 11.4.4 and Tables 14.2.1 / 14.2.2. Simbec produced the tables while RB produced these figures, using raw data provided by Simbec. These discrepancies are due to minor differences in the method of interpolation of the values at each timepoint. There are no discrepancies in the data for the first 20 minutes, when all times were equal to the planned nominal times, and discrepancies were negligible up to 3 hours and more notable only during the last hour. These discrepancies do not affect the conclusions drawn from the results of this pilot study, the main purpose of which was to allow informed decisions to be made regarding the design of the subsequent pivotal study.

Distribution of the meal in the stomach: AUC(meal) for the upper stomach relative to AUC(meal) for the whole stomach at selected time points.

The AUC(meal) upper stomach / whole stomach by treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes is provided in Table 14.2.13 and summarised in Table 11.4.9.

Table 11.4.9 AUC(meal) upper stomach / whole stomach for Gaviscon® Strawberry Flavoured Tablets, Gaviscon® Original Aniseed Relief and their respective placebos: ITT population

Timepoint (minutes)	AUC(meal) upper stomach / whole stomach			
	Gaviscon® Strawberry Flavour Tablets	Placebo Tablets	Gaviscon® Original Aniseed Relief	Placebo Liquid
1	0.80	0.78	0.82	0.80
2	0.79	0.78	0.82	0.79
3	0.79	0.78	0.82	0.79
4	0.79	0.78	0.82	0.79
5	0.79	0.78	0.82	0.79
10	0.78	0.77	0.80	0.78
14	0.76	0.76	0.79	0.77
60	0.69	0.71	0.73	0.71
240	0.58	0.61	0.63	0.61

Source: Table 14.2.13

The AUC(meal) upper stomach / whole stomach decreased gradually over the assessment period for all four IMPs, with no marked difference between them

A statistical comparison between each Gaviscon® product and its respective placebo in terms of AUC(meal) upper stomach / whole stomach was conducted only over 0-5 minutes. These data are provided in Tables 14.2.14 14.2.15 and summarised in Tables 11.4.10 and 11.4.11.

Table 11.4.10 Analysis of $AUC(meal)_{0-5}$ for the upper stomach / whole stomach for Gaviscon® Strawberry Flavour Tablets and placebo tablets: ITT population

	Gaviscon® Strawberry Flavour Tablets	Placebo Tablets
Geometric adjusted mean AUC(meal)$_{0-5}$ upper stomach / whole stomach (CV)	0.78 (9.96)	0.77 (9.96)
Treatment ratio for Gaviscon Strawberry Flavour Tablets / Tablet Placebo (95% confidence interval), p value	1.016 (0.947 - 1.090), 0.6448	

Source: Table 14.2.14; CV: geometric coefficient of variation

Table 11.4.11 Analysis of AUC(meal)$_{0-5}$ for the upper stomach / whole stomach for Gaviscon® Original Aniseed Relief and placebo liquid: ITT population

	Gaviscon® Original Aniseed Relief	Liquid Placebo
Geometric adjusted mean AUC(meal)$_{0-5}$ upper stomach / whole stomach (CV)	0.81 (7.00)	0.78 (7.00)
Treatment ratio for Gaviscon® Original Aniseed Relief / placebo liquid (95% confidence interval), p value	1.036 (0.985 - 1.090), 0.1594	

Source: Table14.2.15; CV: geometric coefficient of variation

The ratio AUC(meal)$_{0-5}$ upper stomach / whole stomach for both Gaviscon® products was not significantly different from that of their respective placebos. This shows the distribution of the meal over that period was similar on both dosing days. However, these measurements relate to the period prior to the administration of the IMP. Hence, any differences could not be attributed to the effects of IMP. However, the fact that there was no marked difference between the distribution of the meal at the later timepoints suggests that, overall, the distribution of the meal was unaffected by whether the IMP was active or placebo.

Time to half empty the IMP and meal for the whole stomach

The mean time to half empty the IMP and meal for the whole stomach is provided for each subject in Appendix 16.2.6 and is summarised in Tables 14.2.16 and 11.4.12.

Table 11.4.12 Time to half empty the IMP and meal for the whole stomach for Gaviscon® Strawberry Flavour Tablets, Gaviscon® Original Aniseed Relief and their respective placebos: ITT population

		Time to half empty the IMP and meal for the whole stomach (minutes)			
		Gaviscon® Strawberry Flavour Tablets	Placebo tablets	Gaviscon® Original Aniseed Relief	Placebo liquid
IMP	Mean	169.12	56.55	108.72	78.41

	SD	58.007	20.215	57.050	47.094
	Range	42 - 239	9 - 87	15 - 239	20 - 157
Meal	Mean	105.69	104.41	121.11	121.12
	SD	15.974	18.437	25.819	28.450
	Range	67 - 132	68 - 134	77 - 167	79 - 166

Source: Table 14.2.16; SD: standard deviation

The mean time to half empty the IMP from the whole stomach was longer for both Gaviscon® products than that for their respective placebos, the difference from placebo being greater for Gaviscon® Strawberry Flavour Tablets than for Gaviscon® Original Aniseed Relief. The time to half empty the meal from the whole stomach for each Gaviscon® product was similar to that for the corresponding placebo, confirming that the emptying of the meal was unaffected by whether the administered IMP was Gaviscon® or placebo.

The percentage of ^{111}In radioactivity (IMP) in the upper stomach over time for each test product

Percentage retention of ^{111}In radioactivity (IMP) in the upper stomach by time and treatment is provided in Table 14.2.2 for all timepoints, in Table 14.2.17 for the selected timepoints and in Figures 11.4.5 and 11.4.6.

Figure 11.4.5 Percentage retention of Gaviscon® Strawberry Flavour Tablets and placebo tablets in the upper stomach

Figure 2 : Mean (95% C.I.) Percentage Retention 111In(IMP) for Upper Stomach by Treatment : ITT Population

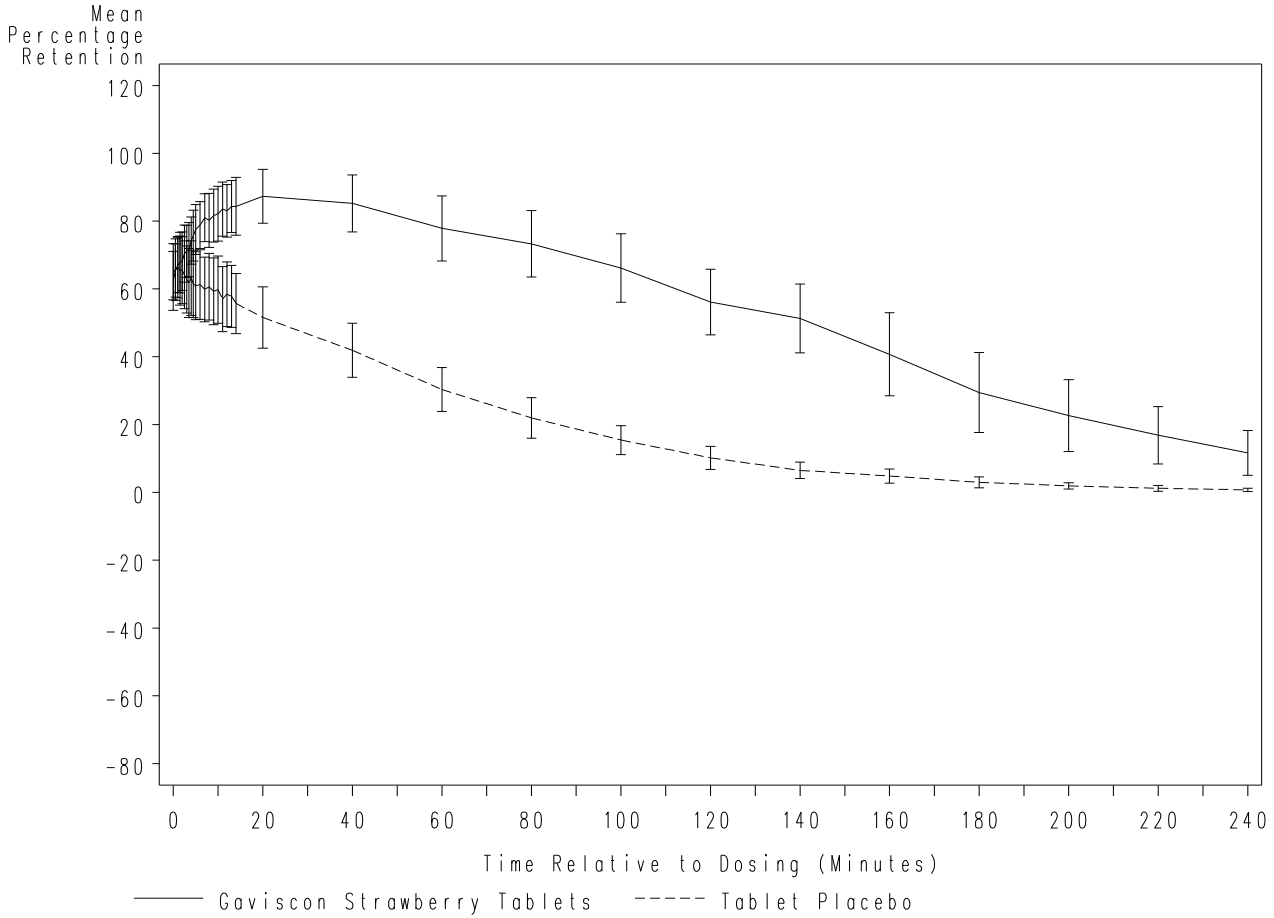
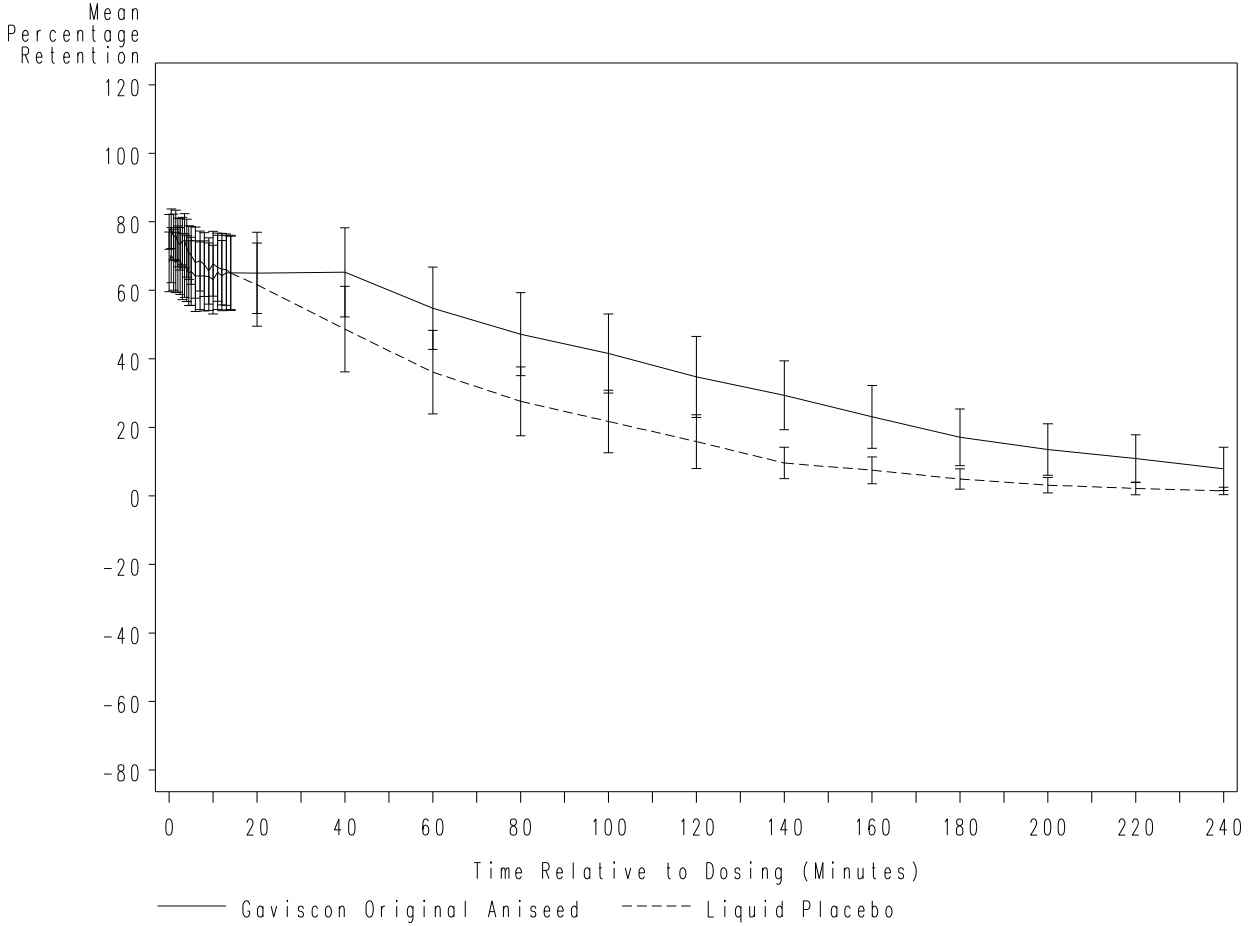


Figure 11.4.6 Percentage retention of Gaviscon® Original Aniseed Relief and liquid placebo in the upper stomach

Figure 6 : Mean (95% C.I.) Percentage Retention 111In(IMP) for Upper Stomach by Treatment : ITT Population



The mean maximum retention of Gaviscon® Strawberry Flavour Tablets in the upper stomach was not reached until 20 minutes after dosing, whereas that for placebo tablets was reached 0.5 minutes after dosing. Over the 240-minute period, the retention in the upper stomach was greater for Gaviscon® Strawberry Flavour Tablets than for placebo. There was less separation between the liquid IMPs, with retention of Gaviscon® Original Aniseed Relief being less than that of placebo for the first 13 minutes.

The percentage of ^{111}In radioactivity (IMP) in the lower stomach over time for each test product

Percentage retention of ^{111}In radioactivity (IMP) in the lower stomach by time and treatment is provided in Table 14.2.3. No figure is provided. A greater proportion of liquid IMPs was observed in the lower stomach at earlier timepoints compared with tablet IMPs.

The time taken to form 50%, 70%, 90% and 100% of the complete raft for each test product i.e. time taken to 50%, 70%, 90% and 100% of maximum ^{111}In (IMP) counts in the upper stomach (for Gaviscon® Strawberry Flavour Tablets and Gaviscon® Original Aniseed Relief only)

These data are presented for each subject in Appendix 16.2.6, and summarised in Tables 14.2.18 and 11.4.13.

Table 11.4.13 Time taken to form 50%, 70%, 90% and 100% of the maximum counts in the upper stomach for Gaviscon® Strawberry Flavour Tablets and Gaviscon® Original Aniseed Relief

Percentage of maximum counts in upper stomach		Time (minutes)	
		Gaviscon® Strawberry Flavoured Tablets	Gaviscon® Original Aniseed Relief
50	Mean	0.30	0.01
	SD	0.949	0.022
	Range	0.0 - 3.8	0.0 - 0.1
70	Mean	0.93	0.06
	SD	1.763	0.180
	Range	0.0 - 6.7	0.0 - 0.6
90	Mean	5.63	1.97
	SD	3.511	4.864
	Range	0.0 - 11.3	0.0 - 19.3
100	Mean	21.98	11.22
	SD	13.122	18.151
	Range	0.0 - 41.2	0.0 - 59.4

Source: Table 14.2.18; SD: standard deviation

The times taken to the selected percentages of the maximum ^{111}In (IMP) counts in the upper stomach was considerably shorter for Gaviscon® Original Aniseed Relief than for Gaviscon® Strawberry Flavour Tablets. However, given that the ratio

AUC(IMP) upper stomach / whole stomach for Gaviscon® Original Aniseed Relief (Figure 11.4.4) initially decreases before increasing to the maximum level (suggesting a delayed formation of the raft), the times relating to the percentages of counts in the upper stomach do not reflect time taken to form the specified percentages of the complete raft. This is discussed in Section 13.1.

Percentage of raft present in the pre-defined region of interest over the 4-hour period

These data have been presented in the above analyses.

Other comparisons not specified as endpoints in the protocol

The following Gaviscon® versus corresponding placebo comparisons over 0-5 minutes were provided.

Comparison of each Gaviscon® product with its corresponding placebo in terms of $AUC(IMP)_{0-5}$ for the whole stomach

$AUC(IMP)_{0-5}$ for the whole stomach is provided in Tables 14.2.19 and 14.20.

The $AUC(IMP)_{0-5}$ for the whole stomach was significantly less for both Gaviscon® products than for their respective placebos ($p = 0.0005$ for Gaviscon® Strawberry Flavour Tablets and $p = 0.0383$ for Gaviscon® Original Aniseed Relief). This reflects the delayed transit of the active products from the mouth to the stomach compared with the respective placebos.

Comparison of each Gaviscon® product with its corresponding placebo in terms of $AUC(meal)_{0-5}$ for the whole stomach

$AUC(meal)_{0-5}$ for the whole stomach is given in Tables 14.2.21 and 14.2.22.

The AUC(meal) for the whole stomach for each Gaviscon® product was not significantly different from that of its placebo ($p = 0.7046$ for Gaviscon® Strawberry Flavour Tablets and $p = 0.5332$ for Gaviscon Original Aniseed Relief). This suggests that retention of the meal over the first 5 minutes was the same on both dosing days (IMP had not been taken at this point). However, the relevance of this comparison is questionable for reasons previously described.

Comparison of $AUC(IMP)_{0-5}$ versus $AUC\ (meal)_{0-5}$ for the upper and whole stomach for both Gaviscon® products

$AUC(IMP)_{0-5}$ and $AUC(meal)_{0-5}$ for the whole and upper stomach are given in Tables 14.2.23 and 14.2.24.

In both the whole and upper stomach, the $AUC(IMP)_{0-5}$ for Gaviscon® Strawberry Flavour Tablets was less than the $AUC(meal)_{0-5}$, although the upper stomach comparison did not achieve statistical significance ($p < 0.0001$ for the whole stomach and $p = 0.0707$ for the upper stomach). The $AUC(IMP)_{0-5}$ for Gaviscon® Original Aniseed Relief was significantly less than the $AUC(meal)_{0-5}$ in both the whole and

upper stomach ($p < 0.0001$ for the whole stomach and $p = 0.0286$ for the upper stomach). Again, the relevance of these comparisons is questionable.

Comparison of $AUC(IMP)_{0-5}$ versus $AUC\ (meal)_{0-5}$ for the ratio of the upper to whole stomach for each Gaviscon® product

The ratio of the upper stomach AUC_{0-5} to that of the whole stomach AUC_{0-5} for IMP versus meal is given in Tables 14.2.25 and 14.2.26.

The distribution in the stomach of both Gaviscon® products was not significantly different from that of the meal over the first 5 minutes ($p = 0.9136$ for Gaviscon® Strawberry Flavour Tablets and $p = 0.1664$ for Gaviscon® Original Aniseed Relief).

The following analyses were carried out by RB for the Gaviscon® Strawberry Flavour Tablets versus placebo tablets only:

(1) AUC(IMP) in the whole stomach, (2) AUC(IMP) / AUC(meal) in the whole stomach and (3) IMP distribution corrected for meal distribution i.e. (AUC(IMP) upper / whole) / (AUC(meal) upper / whole)

These analyses are presented in Table 14.2.28. For each of these endpoints Gaviscon® Strawberry Flavour Tablets was superior to placebo tablets over 0-240 minutes ($p < 0.0001$ for all).

11.4.2 Analytical Issues

Detailed documentation of statistical methods, as the final Statistical Analysis Plan, is presented in Appendix 16.1.9.

For Subject 015 (phase 2), Subject 017 (phase 2) and Subject 031 (phases 1 and 2), the percentage retention of IMP in the upper stomach equaled or slightly exceeded that in the whole stomach. At each time point the same ROI was used to determine whole stomach and upper stomach retention. To define the ROIs for the stomach, the images were aligned (using the external marker as a reference) and summed and an outline of the whole stomach was manually drawn. The upper stomach ROI was manually traced around the whole stomach ROI. The lower margin of the upper stomach ROI was determined from the mid-point of the longitudinal axis[14]. These ROIs were then automatically re-applied to the individual aligned images. It is possible that, because the ROIs were manually drawn, the overlay of the upper stomach and whole stomach ROI was not perfect, which could have lead to occasions where the upper stomach counts could have very marginally exceeded the whole stomach counts (if the IMP was predominately distributed in the upper stomach).

11.4.2.1 Adjustments for Covariates

No adjustments were made for covariates.

11.4.2.2 Handling of Dropouts or Missing Data

One subject in the liquid cohort did not complete the second treatment visit, although he completed the follow-up visit. This subject was not included in the ITT analysis.

11.4.2.3 Interim Analyses and Data Monitoring

No interim analyses were performed and there was no data monitoring.

11.4.2.4 Multi-site Studies

This was a single centre study.

11.4.2.5 Multiple Comparison/Multiplicity

No adjustment for multiple comparisons was made.

11.4.2.6 Use of an "Efficacy Subset" of Subjects

No 'efficacy subsets' were analysed.

11.4.2.7 Active-Control Studies Intended to Show Equivalence

This study was not designed to test efficacy equivalence.

11.4.2.8 Examination of Subgroups

No sub-group was examined in this study.

11.4.3 Tabulation of Individual Response Data

In addition to tables giving group data for gamma scintigraphy variables, relevant individual subject data are presented in by-subject tabular listings in Appendix 16.2.6.

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.

11.4.5 Drug-Drug and Drug-Disease Interactions

This study did not investigate drug/drug or drug/disease interactions.

11.4.6 By-subject Displays

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

11.4.7 Efficacy Conclusions

Primary endpoint

- The ratio AUC(IMP) upper stomach / whole stomach, over the first 5 minutes, was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets (p = 0.0054). It was less for Gaviscon® Original Aniseed Relief than for placebo liquid, although the difference failed to reach statistical significance (p = 0.1458).

- Exploratory analyses of the primary variable showed the ratio AUC(IMP) upper stomach / whole stomach was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets over 0-3 and 0-4 minutes (p = 0.0319 and 0.0138, respectively). However, the ratio AUC(IMP) upper stomach / whole stomach for Gaviscon® Original Aniseed Relief did not significantly exceed that of placebo liquid until 140 minutes (p = 0.0482).

- Exploratory analyses of the IMP distribution at individual timepoints showed that the ratio IMP upper stomach / whole stomach was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo tablets at 1, 3, 4 and 5 minutes (p = 0.0312, 0.0034, 0.0014 and 0.0001, respectively). However, the ratio IMP upper stomach / whole stomach for Gaviscon® Original Aniseed Relief did not significantly exceed that of placebo until 60 minutes after dosing (p = 0.0130).

These results suggest that using this method, the raft is shown to form more quickly with Gaviscon® Strawberry Flavour Tablets than with Gaviscon® Original Aniseed Relief.

Secondary endpoints

- IMP distribution (AUC(IMP) upper stomach / whole stomach) was significantly greater for Gaviscon® Strawberry Flavour Tablets compared with placebo over 0-240 minutes (p < 0.0001) and for Gaviscon® Original Aniseed Relief compared with placebo over 0 – 180 minutes (p = 0.0459).

- The AUC(IMP) for the whole stomach over the first 5 minutes was significantly less for both Gaviscon® products than for the corresponding placebo (p = 0.0005 for Gaviscon® Strawberry Flavour Tablets and 0.0383 for Gaviscon® Original Aniseed Relief). When corrected for retention of the meal, this parameter was still significantly less for Gaviscon® Strawberry Flavour Tablets than for placebo tablets (p = 0.0004). It was also less for Gaviscon® Original Aniseed Relief than for placebo liquid, although the difference failed to achieve statistical significance (p = 0.0506). The relevance of the correction for retention of the meal, however, is questionable given the 'first 5 minutes' refers to time after dosing for the IMP but time after meal completion for the meal. Over the 240-minute period, however, both Gaviscon® products were retained to a greater extent in the whole stomach, when corrected for meal retention, than their corresponding placebos.

- The mean time to half empty the Gaviscon® Strawberry Flavour Tablets from the whole stomach (169.12 minutes) was longer than that for the placebo tablets (56.55 minutes). The corresponding mean times for the Gaviscon® Original

Aniseed Relief and placebo liquid were 108.72 and 78.41 minutes, respectively. The mean time to half empty the meal for both Gaviscon® products was similar to that for their corresponding placebos (105.69 and 104.41 minutes for Gaviscon® Strawberry Flavour Tablets and placebo tablets, respectively; 121.11 and 121.12 minutes for Gaviscon® Original Aniseed Relief and liquid placebo, respectively), confirming that the emptying of the meal was unaffected by whether the administered IMP was Gaviscon® or placebo. The mean time taken to half empty the IMP exceeded that to half empty the meal for Gaviscon® Strawberry Flavour Tablets, but was shorter than the time to half empty the meal for placebo tablets, Gaviscon® Original Aniseed Relief and placebo liquid.

- The time taken to 50%, 70%, 90% and 100% of maximum 111In (IMP) counts in the upper stomach was shorter for Gaviscon® Original Aniseed Relief (0.01, 0.06, 1.97 and 11.22 minutes, respectively) than for Gaviscon® Strawberry Flavour Tablets (0.30, 0.93, 5.63 and 21.98 minutes, respectively). Although the protocol defined these times as the time taken to form the specified percentages of the complete raft, the IMP distribution results suggest that the raft is formed more slowly with the liquid than the tablet formulations, probably due to the liquid mixing with stomach contents. This is consistent with the fact that a greater proportion of liquid IMPs was observed in the lower stomach at earlier timepoints compared with tablet IMPs.

- The AUC(meal) for the whole stomach, over the first 5 minutes, for each Gaviscon® product was not significantly different from that of the corresponding placebo ($p = 0.7046$ for Gaviscon® Strawberry Flavour Tablets and $p = 0.5332$ for Gaviscon® Original Aniseed Relief), confirming that the retention of the meal over this period was the same on both dosing days. The ratio AUC(meal) upper stomach / whole stomach over the first 5 minutes for both Gaviscon® products was also not significantly different from that of their corresponding placebos ($p = 0.6448$ for Gaviscon® Strawberry Flavour Tablets and $p = 0.1594$ for Gaviscon® Original Aniseed Relief), confirming that the distribution of the meal over this period was also the same on both dosing days.

- Extra analyses conducted only for the tablet IMPs showed that Gaviscon® Strawberry Flavour Tablets was significantly superior to placebo tablets in terms of AUC(IMP) in the whole stomach; AUC(IMP) / AUC(meal) in the whole stomach and IMP distribution corrected for meal distribution i.e. (AUC(IMP) upper / whole) / (AUC(meal) upper / whole) over 0 - 240 minutes ($p < 0.0001$ for all). These results support the outcome of the Gaviscon® Strawberry Flavour Tablets versus placebo comparison for AUC(IMP) upper stomach / whole stomach, demonstrating the retention of the raft formed by Gaviscon® Strawberry Flavour Tablets over 240 minutes.

12 SAFETY EVALUATION

All 36 subjects who received at least one dose of study medication are included in the safety analysis.

12.1 Extent of Exposure

The extent of exposure to study medication is summarised in Table 14.3.1. Eighteen subjects received a single dose of both tablet IMPs. Eighteen subjects received a single dose of liquid placebo and seventeen subjects received a single dose of Gaviscon® Original Aniseed Relief.

12.2 Adverse Events (AEs)

12.2.1 Brief Summary of Events

AEs per subject are listed in Appendix 16.2.7. Three subjects reported a total of three AEs (two headaches and one soft tissue injury). All were mild and none was related to study medication.

12.2.2 Display of Adverse Events

Table 12.2.1 Adverse events in study GA1103

System Organ Class	Preferred Term	Placebo	Gaviscon®
Nervous system disorders	Headache	2	0
Injury, poisoning and procedural complications	Soft tissue injury	1	0
Total		3	0

Source: Appendix 16.2.7

Subject 24 experienced a mild headache 5 days after receiving placebo liquid that resolved the following day.

Subject 31 experienced a mild soft tissue injury to the left arm 6 hours and 25 minutes after receiving placebo liquid that resolved 5 days later.

Subject 33 experienced a mild headache 5 days after receiving placebo liquid that resolved one hour later.

No event was deemed related to study medication.

12.2.3 Analysis of Adverse Events

Only three AEs occurred. Therefore no statistical analysis of AEs was conducted.

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

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

12.4 Clinical Laboratory Evaluation

Clinical laboratory evaluations were performed at screening and at the follow-up visit. There were no clinically significant abnormal laboratory values.

12.4.1 Listing of Individual Laboratory Measurements by Subject and each Clinically Significant Abnormal Laboratory Value

A listing of individual laboratory measurements by subject is given in Appendix 16.2.8.

12.4.2 Evaluation of Each Laboratory Parameter

The active moieties of the study medications have been licensed for use in man for many years and their safety profile is well established. In this study, a clinically significant laboratory abnormal value was defined as any value deemed to be clinically significant according to the investigator. Table 14.3.2 summarises the number and percentage of subjects with normal and abnormal laboratory assessments. No abnormal laboratory result was considered clinically significant by the investigator; nor was there any clinically significant shift in laboratory variables.

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

Vital sign and ECG data are presented for each subject in Appendix 16.2.4. Section 16, Listings 25 and 26, respectively. Mean vital signs data at screening and follow-up is presented in Table 14.3.3 and the number and percentage of subjects with normal and abnormal ECG results is presented in Table 14.3.4. All vital signs and ECG parameters were either within normal ranges or were not considered clinically significant by the investigating physician. No significant changes were noted during the follow-up visit.

12.6 Safety Conclusions

There were no clinically significant safety issues identified during the study. Three mild AEs were reported, all of which were considered not related to study medication. There were no clinically significant changes in laboratory evaluations, vital signs or ECGs.

13 DISCUSSION AND OVERALL CONCLUSIONS

13.1 Discussion

Discussion of primary endpoint data

Gaviscon® Strawberry Flavour Tablets versus placebo tablets

Although the percentage IMP present in the whole stomach was higher for placebo tablets than for Gaviscon® Strawberry Flavour Tablets over the first 5 minutes, the

distribution profile was significantly more favourable (i.e. a higher ratio of IMP upper stomach / whole stomach) for Gaviscon® Strawberry Flavour Tablets than placebo. This suggests that the process of raft formation by Gaviscon® Strawberry Flavour Tablets had begun within this period. Exploratory analyses of AUC(IMP) upper stomach / whole stomach at earlier timepoints suggested that the raft formation by Gaviscon® Strawberry Flavour Tablets may have begun earlier i.e. within the first 3 minutes.

Exploratory analyses of the distribution of IMP within the stomach at individual timepoints (as opposed to AUC up to those timepoints) showed that the ratio IMP upper stomach / whole stomach at 1, 3, 4 and 5 minutes was significantly greater for Gaviscon® Strawberry Flavour Tablets than for placebo. This suggests that at early timepoints, distribution of IMP at individual timepoints is a more sensitive endpoint than AUC. It also seems more intuitive, when determining onset of raft formation, that data prior to the timepoint in question should not be incorporated. It is recommended, therefore, that for the pivotal study the distribution of IMP at specified timepoints, rather than AUC, be used as the primary endpoint for assessment of speed of raft formation.

Gaviscon® Original Aniseed Relief versus placebo liquid

There was little difference between Gaviscon® Original Aniseed Relief and placebo liquid in terms of either retention or distribution over the first five minutes. The ratio of the AUC(IMP) for the upper stomach / whole stomach, over the first 5 minutes, was less for Gaviscon® Original Aniseed Relief than for placebo liquid, although the difference failed to reach statistical significance.

The ratio AUC(IMP) upper stomach / whole stomach for Gaviscon® Original Aniseed Relief did not significantly exceed that for placebo liquid until 140 minutes, and was significantly greater than that for placebo over 0-140, 0-160 and 0-180 minutes. Analysis of the distribution of IMP within the stomach at individual timepoints showed a significantly more favourable distribution for Gaviscon® Original Aniseed Relief profile compared with placebo at 60, 80, 100 and 140 minutes. Therefore, although the use of this endpoint detects a significant treatment difference in favour of Gaviscon® Original Aniseed Relief at earlier timepoints than the AUC method, the model was unable to demonstrate raft formation by Gaviscon® Original Aniseed Relief at timepoints relevant to onset of action claims.

Differences in speed of raft formation between Gaviscon® Strawberry Flavour Tablets and Gaviscon® Original Aniseed Relief

Although no statistical comparison of the two Gaviscon® formulations was conducted, it seems that the raft is formed more quickly, using this method, with Gaviscon® Strawberry Flavour Tablets than with Gaviscon® Original Aniseed Relief. Although a different cohort of subjects received tablet and liquid formulations, this is unlikely to contribute to the difference in speed of raft formation between the Gaviscon® formulations. It is more likely that this difference is due to the Gaviscon® Original Aniseed Relief mixing more readily with stomach contents, delaying the onset of raft

formation. This can be seen in Figure 11.4.4, which shows a reduction in the ratio of AUC (IMP) upper stomach / whole stomach for both Gaviscon® Original Aniseed Relief and placebo liquid over approximately the first 10 minutes, followed by an increase to the maximum value for the active product. The fact that a greater proportion of liquid IMPs was observed in the lower stomach at earlier timepoints compared with tablet IMPs is consistent with a greater mixing of liquid IMPs with stomach contents.

Discussion of secondary endpoint data

The $AUC(IMP)_{0-5}$ for the whole stomach was significantly less for both Gaviscon® products than for the corresponding placebos. In the case of Gaviscon® Strawberry Flavour Tablets, this is possibly due to their taking longer to reach the stomach than placebo, due to the alginates causing the IMP to stick to the teeth and oesophagus on route. The difference from placebo was less significant with Gaviscon® Original Aniseed Relief.

The time taken to form 50%, 70%, 90% and 100% of the complete raft for each test product is defined in the protocol (Sections 8.2 and 13.4.2) as time taken to 50%, 70%, 90% and 100% of maximum 111In (IMP) counts in the upper stomach. This conflicts with Section 13.4.3 of the protocol, which suggests that raft formation is to be considered in terms of distribution of IMP in the stomach. The times to 50%, 70%, 90% and 100% of maximum 111In (IMP) counts in the upper stomach were shorter for Gaviscon® Original Aniseed Relief than for Gaviscon® Strawberry Flavour Tablets. However, Figure 11.4.4 shows that although a high proportion of the Gaviscon® Original Aniseed Relief was present in the upper stomach almost immediately after dosing, this was also the case for placebo liquid. It is unlikely that this early high level of Gaviscon® Original Aniseed Relief in the upper stomach indicates the formation of a raft, but rather that, like liquid placebo, it enters the upper stomach and then mixes with stomach contents. Raft formation by Gaviscon® Original Aniseed Relief is therefore delayed. Although the Gaviscon® Strawberry Flavour Tablets take longer to reach the stomach, a separation from placebo is seen at earlier timepoints. These results suggest that time taken to form a percentage of the maximum 111In (IMP) counts in the upper stomach is not an appropriate endpoint for looking at the time taken to form a percentage of the raft, which should be related to the distribution within the stomach.

The time to half empty the IMP from the whole stomach was considerably longer for both Gaviscon® products than for the corresponding placebos, the difference from placebo being greater for Gaviscon® Strawberry Flavour Tablets. As expected, the time to half empty the meal from the whole stomach for both Gaviscon® products was similar to that for the corresponding placebos, confirming that the emptying of the meal was unaffected by whether the IMP was active or placebo. The meal was emptied in a shorter time when the administered IMP was a tablet than when it was a liquid, although different subject cohorts received tablet and liquid IMPs.

The relevance of the comparisons involving both AUC(IMP) and AUC(meal) at early timepoints is questionable because these analyses used time since dosing for the

IMP and time since completion of the meal (i.e. 25 minutes before dosing) for the meal. This is likely to have the greatest effect at the early timepoints. Therefore, it is recommended that for the pivotal study, the time since dosing be used for both IMP and meal in those endpoints designed to investigate speed of raft formation. For those endpoints designed to investigate gastric retention over the 240-minute period, it is appropriate to use time since dosing for the IMP and time since meal completion for the meal. In this pilot study, over the 240-minute period, both Gaviscon® products were retained to a greater extent in the whole stomach, when corrected for meal retention, than their corresponding placebos.

Extra Analyses of Gaviscon® Strawberry Flavour Tablets versus placebo over the 240-minute period:

It is planned that the pivotal study will also compare Gaviscon® Strawberry Flavour Tablets with placebo over 240 minutes to demonstrate duration of action. In the pilot study, superiority of Gaviscon® Strawberry Flavour Tablets over placebo tablets was demonstrated over 0 - 240 minutes for the endpoints AUC(IMP) upper stomach / whole stomach; AUC(IMP) in the whole stomach; AUC(IMP) / AUC(meal) in the whole stomach and IMP distribution corrected for meal distribution i.e. (AUC(IMP) upper stomach / whole stomach) / (AUC(meal) upper stomach / whole stomach).

Comparison with previous results:

The results of this pilot study (GA1103) were compared with those of GA0915, in which raft formation was investigated with a developmental formulation of Gaviscon® chewable tablets and Gaviscon® Peppermint Liquid Relief. The mean time taken to half empty the IMP and meal in each study is shown in Table 12.1.1.

Table 12.1.1 Comparison of results of study GA1103 and GA0915 in terms of mean time to half empty IMP and meal

	Mean time to half empty IMP and meal (range) (minutes)	
	GA1103	**GA0915**
Tablets[1]	169 (42 - 239)	195 (48 - 239)
Meal (on tablet dosing day)	106 (67 - 132)	101 (67 - 160)
Liquid[2]	109 (15 - 239)	136 (60 - 240)
Meal (on liquid dosing day)	121 (77 - 167)	95 (57 - 151)

[1]Gaviscon® Strawberry Flavour Tablets (GA1103), Gaviscon® chewable tablets (GA0915); [2]Gaviscon® Original Aniseed Relief (GA1103), Gaviscon® Peppermint Liquid Relief (GA0915)

Time to half empty IMP was shorter in GA1103 than in GA0915 for both IMPs, but the difference was greater for the liquid IMPs. In GA1103, several subjects in the cohort receiving liquid IMPs had considerably shorter times to half empty the IMP than had been observed previously.

The mean time to half empty the meal for the cohort of subjects receiving the liquid IMPs in GA1103 was longer than that for subjects in GA0915 and also longer than that for the cohort of subjects receiving tablet IMPs in GA1103. The slightly shorter time to empty IMP and the slightly longer time to empty the meal in GA1103 resulted in a greater than expected number of subjects for whom the AUC of the meal exceeded that of Gaviscon® Original Aniseed Relief.

The comparison of Gaviscon® Original Aniseed Relief with placebo liquid in terms of the primary endpoint could possibly have been affected by the unexpected faster emptying of IMP. However, the slower emptying of the meal in the cohort of subjects receiving liquid IMPs would not have affected the main conclusion drawn, since the primary endpoint of the pilot study did not involve the meal.

13.2 Conclusion

The model used in the pilot study was able to demonstrate early onset of raft formation for Gaviscon® Strawberry Flavour Tablets but not for Gaviscon® Original Aniseed Relief. It is therefore appropriate to use this model to compare Gaviscon® Strawberry Flavour Tablets with placebo in a pivotal study, albeit with minor modifications to the methodology and analyses.

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

14.1 Demographic Data

Table 14.1.1 Subject Disposition : All Subjects Population

	N (%)
Number of Volunteers Consented	36 (100.0%)
Number of Volunteers attending Dosing Day 1	36 (100.0%)
Number Receiving Meal	36 (100.0%)
Number Receiving Study Medication	36 (100.0%)
Number of Volunteers attending Dosing Day 2	36 (100.0%)
Number Receiving Meal	35 (97.2%)
Number Receiving Study Medication	35 (97.2%)
Number of Volunteers attending Post-Study Visit	36 (100.0%)

Output File: t01_disp; Produced: 01MAR2012 14:15; Final

Table 14.1.2 Subject Withdrawals : All Subjects Population

	N (%)
Number of Volunteers Entering Study	36 (100.0%)
Number of Volunteers Completing the Study	35 (97.2%)
Number of Volunteers Withdrawn	1 (2.8%)
Reasons for Withdrawal: Violation of Study Protocol	1 (2.8%)
Personal Reasons	0 (0.0%)
Adverse Event	0 (0.0%)
Lost to Follow-up	0 (0.0%)
Other	0 (0.0%)

Output File: t02_withd; Produced: 01MAR2012 15:14; Final

Table 14.1.3 Protocol Deviations : All Subjects Population

Description of Deviation	N (%)
Dosing performed late	11 (30.6%)
Post-Study Visit outside visit window	2 (5.6%)
Positive DOA result	1 (2.8%)
Missed gamma scintigraphy image	3 (8.3%)

Output File: t03_devi; Produced: 01MAR2012 15:41; Final

Table 14.1.4 Subject Populations

Populations	N (%)
Number of Volunteers in the Safety Population	36 (100.0%)
Number of Volunteers in the Intention to Treat Population	35 (97.2%)

Output File: t04_pops; Produced: 01MAR2012 15:50; Final

Table 14.1.5 Subject Demographics: Safety Population

Demographic Factor			Group 1	Group 2	Overall
Number of Volunteers			18	18	36
Consented	N (%)	Yes	18 (100.0%)	18 (100.0%)	36 (100.0%)
Race	N (%)	Caucasian	18 (100.0%)	18 (100.0%)	36 (100.0%)
Age (years)		N	18	18	36
		Mean	27.8	28.9	28.4
		S.D.	8.0	8.1	7.9
		Range	18 - 42	18 - 42	18 - 42
Height (m)		N	18	18	36
		Mean	1.8	1.8	1.8
		S.D.	0.1	0.1	0.1
		Range	1.67 - 1.86	1.63 - 1.84	1.63 - 1.86
Body Mass Index (kg/m^2)		N	18	18	36
		Mean	24.28	24.54	24.41
		S.D.	1.77	1.29	1.53
		Range	20.7 - 26.5	21.7 - 26.9	20.7 - 26.9
Pre-Study Weight (kg)		N	18	18	36
		Mean	74.85	76.61	75.73
		S.D.	6.58	6.64	6.58
		Range	64.0 - 86.8	63.4 - 91.1	63.4 - 91.1

Output File: t05_dmog; Produced: 01MAR2012 16:39; Final

Table 14.1.6 Medical History – Safety Population

Body System		Screening Visit N (%)
No. of Volunteers		36
Ears, Nose, & Throat	No Medical History Present	33 (91.7%)
	Medical History Present	3 (8.3%)
Opthalmological	No Medical History Present	33 (91.7%)
	Medical History Present	3 (8.3%)
Dermatological	No Medical History Present	33 (91.7%)
	Medical History Present	3 (8.3%)
Cardiovascular	No Medical History Present	36 (100.0%)
	Medical History Present	0 (0.0%)
Respiratory	No Medical History Present	33 (91.7%)
	Medical History Present	3 (8.3%)
Gastro-Intestinal	No Medical History Present	34 (94.4%)
	Medical History Present	2 (5.6%)
Genito-Urinary	No Medical History Present	34 (94.4%)
	Medical History Present	2 (5.6%)
Neurological	No Medical History Present	35 (97.2%)
	Medical History Present	1 (2.8%)
Psychiatric	No Medical History Present	33 (91.7%)
	Medical History Present	3 (8.3%)
Musculoskeletal	No Medical History Present	35 (97.2%)
	Medical History Present	1 (2.8%)
Endocrinological	No Medical History Present	36 (100.0%)
	Medical History Present	0 (0.0%)
Allergies	No Medical History Present	34 (94.4%)
	Medical History Present	2 (5.6%)

Output File: t07_medhist; Produced: 01MAR2012 16:53; Final

14.2 Efficacy Data

Table 14.2.1 Percentage Retention of 111In(IMP) for the Whole Stomach By Time and Treatment : ITT Population

	Percentage Retention									
	Gaviscon Strawberry Flavour Tablets					Tablet Placebo				
Relative Time	N	Mean	S.E.	95% C.I.	Not Recorded	N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	18					18				
IMMEDIATELY AFTER MEDICATION	18	78.1	1.71	74.5 - 81.7	0	18	87.0	2.13	82.5 - 91.5	0
0.5mins	18	81.2	1.01	79.1 - 83.4	0	18	89.5	1.22	86.9 - 92.1	0
1mins	18	83.7	1.69	80.1 - 87.2	0	18	92.8	1.12	90.5 - 95.2	0
1.5mins	18	86.8	1.28	84.1 - 89.5	0	18	92.3	1.03	90.1 - 94.5	0
2mins	18	86.2	1.42	83.2 - 89.2	0	18	93.7	1.23	91.1 - 96.3	0
2.5mins	18	86.7	1.31	83.9 - 89.5	0	18	93.8	0.92	91.9 - 95.7	0
3mins	18	87.2	1.38	84.3 - 90.1	0	18	92.8	1.03	90.6 - 95.0	0
3.5mins	18	87.7	1.91	83.7 - 91.7	0	18	93.4	0.91	91.5 - 95.3	0
4mins	18	89.4	1.44	86.4 - 92.4	0	18	94.4	1.19	91.9 - 96.9	0
4.5mins	18	90.5	1.77	86.8 - 94.3	0	18	92.9	1.04	90.7 - 95.1	0
5mins	18	90.9	1.25	88.2 - 93.5	0	18	91.7	1.66	88.2 - 95.2	0
6mins	18	91.9	0.97	89.9 - 94.0	0	18	92.7	2.01	88.4 - 96.9	0
7mins	18	92.3	0.86	90.5 - 94.1	0	18	91.0	2.04	86.7 - 95.4	0
8mins	18	92.4	1.12	90.1 - 94.8	0	18	91.0	2.28	86.2 - 95.8	0
9mins	18	93.0	0.92	91.1 - 95.0	0	18	89.2	2.91	83.1 - 95.3	0
10mins	18	92.9	1.09	90.6 - 95.2	0	18	88.9	3.19	82.2 - 95.7	0
11mins	18	92.9	1.25	90.2 - 95.5	0	18	86.3	3.09	79.8 - 92.9	0
12mins	18	92.9	1.15	90.5 - 95.3	0	18	87.1	3.53	79.7 - 94.6	0
13mins	18	93.6	1.22	91.0 - 96.2	0	18	86.4	3.39	79.2 - 93.5	0
14mins	18	93.5	1.51	90.3 - 96.6	0	18	84.7	3.55	77.2 - 92.2	0
20mins	18	95.4	1.69	91.9 - 99.0	0	18	80.3	4.03	71.8 - 88.8	0
40mins	18	91.7	3.11	85.1 - 98.2	0	18	62.8	4.27	53.8 - 71.8	0
1h	18	85.1	3.76	77.2 - 93.0	0	18	46.8	3.33	39.8 - 53.9	0
1h 20mins	18	80.4	4.19	71.5 - 89.2	0	18	34.5	3.13	27.9 - 41.2	0
1h 40mins	18	73.5	4.38	64.2 - 82.7	0	18	24.7	2.58	19.3 - 30.2	0
2h	18	64.8	4.31	55.7 - 73.9	0	18	17.8	2.17	13.2 - 22.4	0
2h 20mins	18	59.3	4.49	49.8 - 68.7	0	18	11.1	1.47	8.0 - 14.2	0
2h 40mins	17	52.9	4.98	42.3 - 63.4	1	17	7.8	1.20	5.2 - 10.3	1
3h	17	46.1	4.96	35.6 - 56.6	1	17	6.1	0.89	4.2 - 8.0	1
3h 20mins	17	38.3	5.04	27.6 - 48.9	1	17	4.6	0.69	3.2 - 6.1	1
3h 40mins	17	31.2	4.89	20.9 - 41.6	1	17	2.2	0.67	0.8 - 3.6	1
4h	17	24.8	4.42	15.5 - 34.2	1	17	1.9	0.58	0.6 - 3.1	1

Output File: t8_pcretain; Produced: 09MAR2012 12:04; Final

Percentage Retention

Relative Time	Gaviscon Original Aniseed Relief N	Mean	S.E.	95% C.I.	Not Recorded	Liquid Placebo N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	17					17				
IMMEDIATELY AFTER MEDICATION	17	86.9	1.76	83.1 - 90.6	0	17	89.9	0.90	88.0 - 91.8	0
0.5mins	17	92.4	1.05	90.1 - 94.6	0	17	94.6	1.10	92.3 - 97.0	0
1mins	17	92.0	0.93	90.0 - 94.0	0	17	93.2	1.37	90.3 - 96.1	0
1.5mins	17	92.3	1.14	89.9 - 94.7	0	17	94.3	0.98	92.3 - 96.4	0
2mins	17	93.2	1.11	90.9 - 95.6	0	17	94.1	1.07	91.8 - 96.4	0
2.5mins	17	92.2	1.14	89.8 - 94.6	0	17	93.7	1.04	91.6 - 95.9	0
3mins	17	91.0	1.60	87.6 - 94.4	0	17	95.0	0.85	93.2 - 96.8	0
3.5mins	17	91.7	1.51	88.5 - 94.9	0	17	95.5	1.01	93.4 - 97.7	0
4mins	17	92.6	1.46	89.5 - 95.7	0	17	94.7	0.98	92.6 - 96.7	0
4.5mins	17	90.8	1.61	87.4 - 94.2	0	17	93.5	1.02	91.3 - 95.6	0
5mins	17	90.1	2.06	85.8 - 94.5	0	17	93.3	0.73	91.7 - 94.8	0
6mins	17	89.3	2.35	84.3 - 94.3	0	17	94.4	0.72	92.9 - 96.0	0
7mins	17	88.8	2.28	83.9 - 93.6	0	17	92.9	0.79	91.2 - 94.6	0
8mins	17	89.1	2.92	82.9 - 95.3	0	17	92.1	1.88	88.1 - 96.1	0
9mins	17	88.9	3.06	82.4 - 95.4	0	17	89.9	2.23	85.2 - 94.7	0
10mins	17	87.9	2.99	81.6 - 94.2	0	17	89.8	2.20	85.1 - 94.4	0
11mins	17	88.5	3.13	81.9 - 95.2	0	17	88.4	2.81	82.5 - 94.4	0
12mins	17	86.6	3.21	79.8 - 93.4	0	17	88.9	3.00	82.6 - 95.3	0
13mins	17	87.1	3.35	80.0 - 94.3	0	17	88.1	3.05	81.6 - 94.6	0
14mins	17	86.7	3.69	78.9 - 94.5	0	17	87.2	3.44	79.9 - 94.5	0
20mins	17	83.5	4.07	74.9 - 92.2	0	16	84.7	4.69	74.7 - 94.7	1
40mins	16	80.1	4.81	69.8 - 90.3	1	16	70.8	6.85	56.2 - 85.4	1
1h	17	68.7	5.36	57.4 - 80.1	0	17	57.3	7.41	41.6 - 73.0	0
1h 20mins	17	61.6	5.31	50.4 - 72.9	0	17	46.4	7.00	31.5 - 61.2	0
1h 40mins	17	54.3	5.44	42.8 - 65.9	0	17	37.5	6.50	23.7 - 51.2	0
2h	17	45.4	5.30	34.2 - 56.7	0	17	28.8	5.92	16.3 - 41.4	0
2h 20mins	17	38.0	4.94	27.5 - 48.5	0	17	19.6	4.55	9.9 - 29.2	0
2h 40mins	17	32.8	4.36	23.5 - 42.0	0	17	14.6	3.65	6.9 - 22.4	0
3h	17	26.4	4.11	17.7 - 35.1	0	17	9.6	2.71	3.9 - 15.3	0
3h 20mins	17	23.0	3.67	15.2 - 30.8	0	17	6.5	2.04	2.1 - 10.8	0
3h 40mins	17	19.0	3.56	11.5 - 26.5	0	17	4.3	1.51	1.0 - 7.5	0
4h	17	15.7	3.45	8.4 - 23.1	0	17	2.8	1.01	0.6 - 4.9	0

Output File: t8_pcretain; Produced: 09MAR2012 12:04; Final

Table 14.2.2 Percentage Retention of 111In(IMP) for the Upper Stomach By Time and Treatment : ITT Population

	Percentage Retention									
	Gaviscon Strawberry Flavour Tablets					Tablet Placebo				
Relative Time	N	Mean	S.E.	95% C.I.	Not Recorded	N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	18					18				
IMMEDIATELY AFTER MEDICATION	18	62.4	4.13	53.7 - 71.1	0	18	65.1	3.92	56.8 - 73.3	0
0.5mins	18	65.4	3.73	57.6 - 73.3	0	18	65.7	4.31	56.6 - 74.8	0
1mins	18	67.0	3.83	59.0 - 75.1	0	18	66.4	4.31	57.4 - 75.5	0
1.5mins	18	67.8	4.23	58.9 - 76.7	0	18	65.4	4.83	55.3 - 75.6	0
2mins	18	68.2	4.10	59.6 - 76.9	0	18	65.5	4.67	55.7 - 75.4	0
2.5mins	18	70.4	3.99	62.0 - 78.9	0	18	64.2	4.75	54.2 - 74.2	0
3mins	18	71.1	3.63	63.5 - 78.8	0	18	62.8	4.68	52.9 - 72.7	0
3.5mins	18	71.6	3.78	63.6 - 79.6	0	18	61.8	4.81	51.6 - 71.9	0
4mins	18	74.3	3.29	67.3 - 81.2	0	18	63.2	5.21	52.2 - 74.2	0
4.5mins	18	75.7	3.55	68.2 - 83.2	0	18	61.5	4.71	51.6 - 71.5	0
5mins	18	77.6	3.48	70.2 - 84.9	0	18	60.9	4.75	50.9 - 71.0	0
6mins	18	78.9	3.28	71.9 - 85.8	0	18	61.3	4.87	51.0 - 71.6	0
7mins	18	81.0	3.35	74.0 - 88.1	0	18	59.9	4.52	50.4 - 69.4	0
8mins	18	80.2	3.78	72.3 - 88.2	0	18	60.6	4.65	50.8 - 70.5	0
9mins	18	81.6	3.70	73.8 - 89.4	0	18	59.3	4.67	49.4 - 69.2	0
10mins	18	82.2	3.82	74.1 - 90.2	0	18	59.8	4.69	49.9 - 69.7	0
11mins	18	83.6	3.78	75.6 - 91.5	0	18	57.0	4.55	47.4 - 66.6	0
12mins	18	83.1	3.69	75.3 - 90.8	0	18	58.5	4.51	48.9 - 68.0	0
13mins	18	84.3	3.64	76.6 - 92.0	0	18	57.8	4.34	48.7 - 67.0	0
14mins	18	84.4	4.04	75.8 - 92.9	0	18	55.7	4.21	46.8 - 64.6	0
20mins	18	87.4	3.77	79.4 - 95.3	0	18	51.6	4.28	42.5 - 60.6	0
40mins	18	85.2	3.98	76.8 - 93.6	0	18	41.9	3.77	33.9 - 49.9	0
1h	18	77.9	4.55	68.3 - 87.5	0	18	30.4	3.07	23.9 - 36.8	0
1h 20mins	18	73.3	4.64	63.5 - 83.1	0	18	22.0	2.83	16.0 - 27.9	0
1h 40mins	18	66.2	4.79	56.1 - 76.3	0	18	15.4	2.02	11.2 - 19.7	0
2h	18	56.1	4.60	46.4 - 65.9	0	18	10.2	1.61	6.8 - 13.6	0
2h 20mins	18	51.3	4.81	41.2 - 61.5	0	18	6.5	1.14	4.1 - 8.9	0
2h 40mins	17	40.7	5.78	28.5 - 53.0	1	17	4.8	0.99	2.7 - 6.9	1
3h	17	29.4	5.57	17.6 - 41.2	1	17	3.0	0.76	1.4 - 4.6	1
3h 20mins	17	22.6	4.99	12.1 - 33.2	1	17	1.9	0.43	1.0 - 2.8	1
3h 40mins	17	16.9	4.00	8.4 - 25.3	1	17	1.2	0.41	0.3 - 2.1	1
4h	17	11.7	3.11	5.1 - 18.3	1	17	0.7	0.23	0.2 - 1.2	1

Output File: t9_pcretain; Produced: 09MAR2012 12:04; Final

Percentage Retention

Relative Time	Gaviscon Original Aniseed Relief N	Mean	S.E.	95% C.I.	Not Recorded	Liquid Placebo N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	17					17				
IMMEDIATELY AFTER MEDICATION	17	68.3	4.09	59.6 - 77.0	0	17	77.1	2.40	72.0 - 82.2	0
0.5mins	17	70.3	3.79	62.2 - 78.3	0	17	78.0	2.71	72.2 - 83.7	0
1mins	17	68.9	4.20	60.0 - 77.8	0	17	75.6	3.15	68.9 - 82.3	0
1.5mins	17	68.1	4.16	59.3 - 76.9	0	17	76.0	3.47	68.7 - 83.4	0
2mins	17	69.1	4.55	59.5 - 78.8	0	17	74.0	3.36	66.8 - 81.1	0
2.5mins	17	68.5	4.60	58.8 - 78.3	0	17	73.4	3.54	65.9 - 81.0	0
3mins	17	66.9	4.56	57.3 - 76.6	0	17	74.4	3.27	67.4 - 81.3	0
3.5mins	17	67.2	4.37	58.0 - 76.5	0	17	74.5	3.72	66.6 - 82.4	0
4mins	17	66.3	4.52	56.8 - 75.9	0	17	72.3	3.99	63.9 - 80.8	0
4.5mins	17	65.0	4.47	55.6 - 74.5	0	17	71.0	3.69	63.2 - 78.9	0
5mins	17	65.6	4.70	55.6 - 75.5	0	17	70.2	3.98	61.8 - 78.6	0
6mins	17	64.1	4.89	53.8 - 74.5	0	17	68.1	4.89	57.7 - 78.5	0
7mins	17	64.2	4.66	54.3 - 74.1	0	17	68.5	4.14	59.8 - 77.3	0
8mins	17	64.2	4.82	54.0 - 74.4	0	17	67.5	4.39	58.2 - 76.8	0
9mins	17	64.0	4.66	54.1 - 73.9	0	17	65.6	4.57	55.9 - 75.3	0
10mins	17	63.1	4.73	53.1 - 73.2	0	17	67.8	4.47	58.3 - 77.2	0
11mins	17	65.3	5.12	54.4 - 76.1	0	17	66.7	4.70	56.8 - 76.7	0
12mins	17	64.3	4.84	54.0 - 74.6	0	17	66.2	4.93	55.7 - 76.6	0
13mins	17	65.1	5.12	54.3 - 76.0	0	17	66.0	4.92	55.6 - 76.5	0
14mins	17	65.1	5.19	54.1 - 76.1	0	17	65.1	5.06	54.3 - 75.8	0
20mins	17	65.1	5.60	53.2 - 77.0	0	16	61.6	5.69	49.5 - 73.8	1
40mins	16	65.3	6.11	52.2 - 78.3	1	16	48.7	5.87	36.2 - 61.2	1
1h	17	54.8	5.67	42.7 - 66.8	0	17	36.1	5.75	23.9 - 48.3	0
1h 20mins	17	47.2	5.71	35.1 - 59.3	0	17	27.6	4.75	17.5 - 37.7	0
1h 40mins	17	41.6	5.45	30.0 - 53.1	0	17	21.7	4.31	12.6 - 30.9	0
2h	17	34.7	5.57	22.9 - 46.6	0	17	15.8	3.71	8.0 - 23.7	0
2h 20mins	17	29.4	4.73	19.3 - 39.4	0	17	9.6	2.16	5.0 - 14.2	0
2h 40mins	17	23.1	4.32	13.9 - 32.2	0	17	7.5	1.85	3.6 - 11.4	0
3h	17	17.1	3.90	8.8 - 25.4	0	17	4.9	1.39	2.0 - 7.9	0
3h 20mins	17	13.5	3.56	6.0 - 21.1	0	17	3.1	1.07	0.9 - 5.4	0
3h 40mins	17	10.9	3.28	3.9 - 17.8	0	17	2.2	0.87	0.3 - 4.0	0
4h	17	7.9	2.97	1.6 - 14.2	0	17	1.4	0.51	0.4 - 2.5	0

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Table 14.2.3 Percentage Retention of 111In(IMP) for the Lower Stomach By Time and Treatment : ITT Population

Percentage Retention

	Gaviscon Strawberry Flavour Tablets					Tablet Placebo				
Relative Time	N	Mean	S.E.	95% C.I.	Not Recorded	N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	18					18				
IMMEDIATELY AFTER MEDICATION	18	15.7	3.94	7.4 - 24.0	0	18	22.0	4.61	12.2 - 31.7	0
0.5mins	18	15.8	3.94	7.5 - 24.1	0	18	23.8	4.68	13.9 - 33.7	0
1mins	18	16.6	4.14	7.9 - 25.4	0	18	26.4	4.84	16.2 - 36.6	0
1.5mins	18	19.0	4.64	9.2 - 28.8	0	18	26.8	4.75	16.8 - 36.8	0
2mins	18	18.0	4.56	8.4 - 27.7	0	18	28.1	4.87	17.9 - 38.4	0
2.5mins	18	16.3	4.03	7.8 - 24.8	0	18	29.6	4.60	19.9 - 39.3	0
3mins	18	16.1	4.15	7.4 - 24.9	0	18	30.0	4.51	20.5 - 39.5	0
3.5mins	18	16.1	4.11	7.4 - 24.7	0	18	31.6	4.32	22.5 - 40.7	0
4mins	18	15.1	3.88	6.9 - 23.3	0	18	31.2	4.57	21.6 - 40.9	0
4.5mins	18	14.8	3.85	6.7 - 22.9	0	18	31.4	4.21	22.5 - 40.3	0
5mins	18	13.3	3.59	5.7 - 20.9	0	18	30.8	3.70	23.0 - 38.6	0
6mins	18	13.1	3.60	5.5 - 20.7	0	18	31.4	3.46	24.1 - 38.7	0
7mins	18	11.3	3.12	4.7 - 17.8	0	18	31.1	3.23	24.3 - 38.0	0
8mins	18	12.2	3.57	4.7 - 19.7	0	18	30.3	3.35	23.3 - 37.4	0
9mins	18	11.4	3.29	4.4 - 18.3	0	18	29.9	2.91	23.8 - 36.1	0
10mins	18	10.7	3.23	3.9 - 17.5	0	18	29.2	2.46	24.0 - 34.3	0
11mins	18	9.3	2.94	3.1 - 15.5	0	18	29.3	2.30	24.5 - 34.2	0
12mins	18	9.8	2.96	3.6 - 16.1	0	18	28.7	2.06	24.3 - 33.0	0
13mins	18	9.3	2.89	3.2 - 15.4	0	18	28.5	1.86	24.6 - 32.4	0
14mins	18	9.1	2.92	2.9 - 15.3	0	18	29.0	2.07	24.6 - 33.3	0
20mins	18	8.1	2.39	3.0 - 13.1	0	18	28.7	1.94	24.6 - 32.8	0
40mins	18	6.4	1.44	3.4 - 9.5	0	18	20.9	1.99	16.7 - 25.1	0
1h	18	7.2	1.12	4.8 - 9.6	0	18	16.5	1.59	13.1 - 19.8	0
1h 20mins	18	7.1	0.80	5.4 - 8.7	0	18	12.6	1.15	10.2 - 15.0	0
1h 40mins	18	7.3	1.03	5.1 - 9.4	0	18	9.3	0.99	7.2 - 11.4	0
2h	18	8.7	0.91	6.8 - 10.6	0	18	7.6	0.70	6.1 - 9.1	0
2h 20mins	18	8.0	1.58	4.6 - 11.3	0	18	4.6	0.55	3.4 - 5.8	0
2h 40mins	17	12.2	2.62	6.6 - 17.7	1	17	2.9	0.37	2.2 - 3.7	1
3h	17	16.6	3.11	10.0 - 23.2	1	17	3.2	0.48	2.1 - 4.2	1
3h 20mins	17	15.6	2.91	9.4 - 21.8	1	17	2.7	0.38	1.9 - 3.5	1
3h 40mins	17	14.4	2.53	9.0 - 19.8	1	17	1.0	0.34	0.3 - 1.7	1
4h	17	13.2	2.45	8.0 - 18.4	1	17	1.1	0.42	0.3 - 2.0	1

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Percentage Retention

	Gaviscon Original Aniseed Relief					Liquid Placebo				
Relative Time	N	Mean	S.E.	95% C.I.	Not Recorded	N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	17					17				
IMMEDIATELY AFTER MEDICATION	17	18.5	4.09	9.9 - 27.2	0	17	12.8	2.19	8.2 - 17.5	0
0.5mins	17	22.1	4.12	13.4 - 30.8	0	17	16.6	2.31	11.7 - 21.5	0
1mins	17	23.1	4.30	14.0 - 32.2	0	17	17.6	2.80	11.6 - 23.5	0
1.5mins	17	24.2	4.67	14.3 - 34.1	0	17	18.3	3.33	11.2 - 25.4	0
2mins	17	24.1	4.53	14.5 - 33.7	0	17	20.1	3.28	13.2 - 27.1	0
2.5mins	17	23.7	4.27	14.6 - 32.7	0	17	20.3	3.18	13.6 - 27.0	0
3mins	17	24.0	4.13	15.3 - 32.8	0	17	20.6	3.15	13.9 - 27.3	0
3.5mins	17	24.5	4.23	15.6 - 33.5	0	17	21.0	3.63	13.3 - 28.7	0
4mins	17	26.3	4.39	17.0 - 35.6	0	17	22.3	3.77	14.3 - 30.3	0
4.5mins	17	25.8	4.35	16.6 - 35.0	0	17	22.5	3.72	14.6 - 30.3	0
5mins	17	24.6	3.87	16.4 - 32.8	0	17	23.1	3.80	15.0 - 31.1	0
6mins	17	25.1	3.89	16.9 - 33.4	0	17	26.4	4.61	16.6 - 36.2	0
7mins	17	24.5	3.86	16.4 - 32.7	0	17	24.3	3.77	16.4 - 32.3	0
8mins	17	24.9	3.83	16.8 - 33.0	0	17	24.6	3.54	17.1 - 32.1	0
9mins	17	24.9	3.64	17.2 - 32.6	0	17	24.3	3.49	16.9 - 31.7	0
10mins	17	24.8	3.63	17.1 - 32.5	0	17	22.0	3.41	14.8 - 29.3	0
11mins	17	23.3	3.64	15.5 - 31.0	0	17	21.7	3.26	14.8 - 28.6	0
12mins	17	22.3	3.60	14.7 - 29.9	0	17	22.7	3.28	15.8 - 29.7	0
13mins	17	22.0	3.71	14.2 - 29.9	0	17	22.0	3.14	15.4 - 28.7	0
14mins	17	21.6	3.47	14.2 - 28.9	0	17	22.1	2.97	15.9 - 28.5	0
20mins	17	18.5	3.28	11.5 - 25.4	0	16	23.0	3.46	15.7 - 30.4	1
40mins	16	14.8	2.86	8.7 - 20.9	1	16	22.1	3.15	15.4 - 28.8	1
1h	17	14.0	2.45	8.8 - 19.2	0	17	21.2	3.74	13.3 - 29.1	0
1h 20mins	17	14.4	2.71	8.7 - 20.1	0	17	18.8	3.78	10.7 - 26.8	0
1h 40mins	17	12.8	2.32	7.9 - 17.7	0	17	15.7	3.49	8.3 - 23.1	0
2h	17	10.7	2.31	5.8 - 15.6	0	17	13.0	2.95	6.7 - 19.3	0
2h 20mins	17	8.7	1.62	5.2 - 12.1	0	17	10.0	2.71	4.2 - 15.7	0
2h 40mins	17	9.7	2.28	4.9 - 14.5	0	17	7.2	2.04	2.8 - 11.5	0
3h	17	9.3	2.01	5.0 - 13.6	0	17	4.7	1.49	1.5 - 7.8	0
3h 20mins	17	9.5	2.07	5.1 - 13.9	0	17	3.3	1.12	1.0 - 5.7	0
3h 40mins	17	8.1	1.61	4.7 - 11.5	0	17	2.1	0.72	0.6 - 3.6	0
4h	17	7.9	1.59	4.5 - 11.2	0	17	1.3	0.54	0.2 - 2.5	0

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Table 14.2.4 Percentage Retention of 99mTc(meal) for the Whole Stomach By Time and Treatment : ITT Population

Percentage Retention

	Gaviscon Strawberry Flavour Tablets					Tablet Placebo				
Relative Time	N	Mean	S.E.	95% C.I.	Not Recorded	N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	18					18				
IMMEDIATELY AFTER COMPLETION OF THE MEAL	18	100.0	0.00		0	18	100.0	0.00		0
30mins AFTER START OF MEAL	18	93.9	1.18	91.4 - 96.4	0	18	93.6	1.60	90.2 - 96.9	0
IMMEDIATELY AFTER MEDICATION	18	94.7	1.74	91.0 - 98.3	0	18	92.5	1.17	90.1 - 95.0	0
0.5mins	18	95.4	1.69	91.8 - 98.9	0	18	93.8	1.20	91.3 - 96.3	0
1mins	18	94.8	1.63	91.3 - 98.2	0	18	91.8	1.22	89.3 - 94.4	0
1.5mins	18	93.8	1.78	90.0 - 97.5	0	18	92.5	1.35	89.6 - 95.3	0
2mins	18	94.3	1.74	90.6 - 98.0	0	18	92.4	1.41	89.4 - 95.4	0
2.5mins	18	93.3	1.52	90.1 - 96.5	0	18	92.4	1.31	89.7 - 95.2	0
3mins	18	93.6	1.62	90.2 - 97.0	0	18	92.2	1.53	88.9 - 95.4	0
3.5mins	18	92.0	1.62	88.6 - 95.5	0	18	92.2	1.37	89.3 - 95.1	0
4mins	18	91.9	1.42	88.9 - 94.9	0	18	90.9	1.73	87.3 - 94.6	0
4.5mins	18	92.5	1.89	88.5 - 96.5	0	18	91.5	1.54	88.3 - 94.8	0
5mins	18	91.9	1.84	88.0 - 95.8	0	18	90.6	1.46	87.6 - 93.7	0
6mins	18	91.5	1.90	87.5 - 95.5	0	18	90.1	1.46	87.0 - 93.2	0
7mins	18	90.9	2.03	86.7 - 95.2	0	18	89.6	1.44	86.6 - 92.6	0
8mins	18	89.6	2.06	85.3 - 94.0	0	18	88.3	1.64	84.9 - 91.8	0
9mins	18	90.0	2.14	85.5 - 94.5	0	18	89.0	1.41	86.0 - 92.0	0
10mins	18	89.3	1.94	85.2 - 93.4	0	18	88.0	1.51	84.8 - 91.2	0
11mins	18	88.2	1.94	84.1 - 92.3	0	18	87.8	1.71	84.2 - 91.4	0
12mins	18	88.2	2.14	83.7 - 92.7	0	18	87.0	1.63	83.5 - 90.4	0
13mins	18	87.3	2.16	82.8 - 91.9	0	18	86.6	1.47	83.5 - 89.7	0
14mins	18	87.6	2.15	83.1 - 92.1	0	18	86.1	1.45	83.1 - 89.2	0
20mins	18	83.9	1.95	79.8 - 88.0	0	18	82.4	1.49	79.3 - 85.5	0
40mins	18	71.1	1.97	66.9 - 75.2	0	18	70.1	1.91	66.0 - 74.1	0
1h	18	58.4	2.32	53.5 - 63.3	0	18	57.6	2.42	52.5 - 62.7	0
1h 20mins	18	47.2	2.31	42.3 - 52.1	0	18	44.6	2.78	38.7 - 50.5	0
1h 40mins	18	37.1	2.35	32.1 - 42.0	0	18	34.6	2.91	28.5 - 40.8	0
2h	18	28.0	2.04	23.7 - 32.3	0	18	25.0	2.45	19.8 - 30.1	0
2h 20mins	18	20.0	1.60	16.6 - 23.3	0	18	15.3	1.82	11.5 - 19.2	0
2h 40mins	17	15.0	1.14	12.5 - 17.4	1	17	11.7	1.40	8.7 - 14.6	1
3h	17	10.7	1.01	8.5 - 12.8	1	17	7.1	1.10	4.7 - 9.4	1
3h 20mins	17	7.9	0.90	6.0 - 9.8	1	17	4.7	0.71	3.2 - 6.3	1
3h 40mins	17	6.5	0.85	4.7 - 8.3	1	17	3.4	0.42	2.6 - 4.3	1
4h	17	6.0	0.64	4.7 - 7.4	1	17	3.1	0.39	2.3 - 4.0	1

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Percentage Retention

Relative Time	Gaviscon Original Aniseed Relief N	Mean	S.E.	95% C.I.	Not Recorded	Liquid Placebo N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	17					17				
IMMEDIATELY AFTER COMPLETION OF THE MEAL	17	100.0	0.00		0	17	100.0	0.00		0
30mins AFTER START OF MEAL	17	94.6	1.03	92.5 - 96.8	0	17	95.3	1.15	92.9 - 97.8	0
IMMEDIATELY AFTER MEDICATION	17	96.9	1.05	94.6 - 99.1	0	17	97.5	1.49	94.3 - 100.6	0
0.5mins	17	96.0	1.06	93.8 - 98.2	0	17	96.6	1.50	93.4 - 99.8	0
1mins	17	96.5	1.13	94.2 - 98.9	0	17	96.9	1.50	93.7 - 100.0	0
1.5mins	17	96.6	1.27	93.9 - 99.3	0	17	95.7	1.20	93.2 - 98.2	0
2mins	17	96.5	1.24	93.8 - 99.1	0	17	96.3	1.23	93.7 - 98.9	0
2.5mins	17	96.1	1.26	93.4 - 98.8	0	17	95.3	1.37	92.4 - 98.2	0
3mins	17	95.9	1.11	93.6 - 98.3	0	17	95.8	1.20	93.2 - 98.3	0
3.5mins	17	96.2	1.14	93.8 - 98.6	0	17	95.2	1.48	92.0 - 98.3	0
4mins	17	95.8	1.44	92.8 - 98.9	0	17	94.7	1.38	91.8 - 97.6	0
4.5mins	17	95.8	1.59	92.4 - 99.1	0	17	95.1	1.32	92.3 - 97.9	0
5mins	17	94.5	1.28	91.8 - 97.2	0	17	94.3	1.52	91.1 - 97.6	0
6mins	17	93.5	1.22	90.9 - 96.1	0	17	94.0	1.32	91.2 - 96.8	0
7mins	17	93.5	1.38	90.6 - 96.4	0	17	94.2	1.55	90.9 - 97.5	0
8mins	17	93.0	1.55	89.7 - 96.3	0	17	92.5	1.49	89.3 - 95.7	0
9mins	17	92.6	1.36	89.8 - 95.5	0	17	93.0	1.82	89.2 - 96.9	0
10mins	17	92.6	1.32	89.8 - 95.4	0	17	92.5	1.61	89.1 - 96.0	0
11mins	17	92.4	1.42	89.4 - 95.4	0	17	91.8	1.75	88.1 - 95.5	0
12mins	17	92.1	1.45	89.0 - 95.1	0	17	91.6	1.60	88.3 - 95.0	0
13mins	17	92.2	1.45	89.1 - 95.3	0	17	91.2	1.71	87.6 - 94.8	0
14mins	17	91.6	1.42	88.6 - 94.6	0	17	90.5	1.66	87.0 - 94.0	0
20mins	17	88.4	1.70	84.8 - 92.0	0	16	87.2	1.77	83.4 - 91.0	1
40mins	16	76.4	2.39	71.3 - 81.5	1	16	76.6	2.45	71.4 - 81.8	1
1h	17	65.2	3.03	58.8 - 71.6	0	17	65.3	3.18	58.6 - 72.0	0
1h 20mins	17	55.4	3.53	47.9 - 62.9	0	17	54.8	3.89	46.6 - 63.1	0
1h 40mins	17	46.2	3.65	38.5 - 54.0	0	17	45.2	4.33	36.0 - 54.4	0
2h	17	35.6	3.47	28.3 - 43.0	0	17	34.3	4.20	25.4 - 43.2	0
2h 20mins	17	25.9	3.00	19.5 - 32.3	0	17	25.0	3.61	17.3 - 32.6	0
2h 40mins	17	19.0	2.58	13.5 - 24.4	0	17	18.6	2.98	12.3 - 24.9	0
3h	17	15.2	2.16	10.6 - 19.8	0	17	13.6	2.29	8.8 - 18.5	0
3h 20mins	17	10.9	1.74	7.2 - 14.6	0	17	9.7	1.74	6.0 - 13.4	0
3h 40mins	17	8.6	1.54	5.3 - 11.8	0	17	6.5	1.24	3.8 - 9.1	0
4h	17	7.1	1.34	4.3 - 9.9	0	17	5.4	0.97	3.4 - 7.5	0

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Table 14.2.5 Percentage Retention of 99mTc(meal) for the Upper Stomach By Time and Treatment : ITT Population

	Percentage Retention									
	Gaviscon Strawberry Flavour Tablets					Tablet Placebo				
Relative Time	N	Mean	S.E.	95% C.I.	Not Recorded	N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	18					18				
IMMEDIATELY AFTER COMPLETION OF THE MEAL	18	79.8	1.99	75.6 - 84.0	0	18	78.6	2.68	73.0 - 84.3	0
30mins AFTER START OF MEAL	18	64.2	2.30	59.3 - 69.0	0	18	66.3	2.97	60.1 - 72.6	0
IMMEDIATELY AFTER MEDICATION	18	65.8	2.81	59.8 - 71.7	0	18	66.4	3.09	59.9 - 72.9	0
0.5mins	18	66.9	2.51	61.6 - 72.2	0	18	67.2	3.13	60.6 - 73.8	0
1mins	18	64.9	2.88	58.8 - 71.0	0	18	65.3	3.28	58.4 - 72.3	0
1.5mins	18	63.6	2.90	57.5 - 69.7	0	18	65.8	3.25	58.9 - 72.6	0
2mins	18	63.5	2.76	57.7 - 69.4	0	18	65.5	3.14	58.9 - 72.2	0
2.5mins	18	62.6	2.73	56.9 - 68.4	0	18	64.9	2.88	58.9 - 71.0	0
3mins	18	62.4	2.89	56.3 - 68.5	0	18	64.8	3.06	58.4 - 71.3	0
3.5mins	18	60.7	3.01	54.4 - 67.1	0	18	64.3	2.97	58.1 - 70.6	0
4mins	18	61.6	2.57	56.1 - 67.0	0	18	62.4	3.46	55.2 - 69.7	0
4.5mins	18	62.6	2.76	56.8 - 68.4	0	18	62.8	3.22	56.0 - 69.6	0
5mins	18	62.1	2.91	56.0 - 68.2	0	18	63.0	3.06	56.6 - 69.5	0
6mins	18	61.6	3.12	55.0 - 68.2	0	18	61.9	3.19	55.2 - 68.7	0
7mins	18	60.9	3.24	54.1 - 67.8	0	18	61.7	3.21	54.9 - 68.5	0
8mins	18	59.3	3.30	52.4 - 66.3	0	18	61.7	3.28	54.8 - 68.6	0
9mins	18	60.6	3.08	54.1 - 67.1	0	18	62.4	3.15	55.8 - 69.1	0
10mins	18	59.9	2.68	54.3 - 65.6	0	18	61.7	3.29	54.7 - 68.6	0
11mins	18	59.1	2.76	53.3 - 65.0	0	18	60.9	3.41	53.7 - 68.1	0
12mins	18	58.6	3.04	52.2 - 65.1	0	18	60.6	3.25	53.7 - 67.4	0
13mins	18	58.3	3.07	51.8 - 64.7	0	18	61.2	2.98	54.9 - 67.5	0
14mins	18	58.5	3.12	51.9 - 65.1	0	18	59.7	3.11	53.2 - 66.3	0
20mins	18	52.3	2.72	46.6 - 58.1	0	18	55.3	3.34	48.3 - 62.4	0
40mins	18	41.3	3.18	34.6 - 48.0	0	18	45.4	3.54	38.0 - 52.9	0
1h	18	30.7	2.93	24.5 - 36.9	0	18	34.1	3.39	27.0 - 41.3	0
1h 20mins	18	24.5	2.55	19.1 - 29.9	0	18	23.5	3.13	16.9 - 30.2	0
1h 40mins	18	17.3	2.38	12.3 - 22.3	0	18	17.5	2.68	11.9 - 23.2	0
2h	18	10.7	1.42	7.7 - 13.7	0	18	9.9	1.78	6.2 - 13.7	0
2h 20mins	18	6.6	0.88	4.7 - 8.5	0	18	4.2	0.96	2.2 - 6.2	0
2h 40mins	17	4.7	0.57	3.5 - 5.9	1	17	3.5	0.78	1.8 - 5.1	1
3h	17	3.5	0.58	2.2 - 4.7	1	17	1.8	0.53	0.7 - 2.9	1
3h 20mins	17	2.6	0.49	1.6 - 3.6	1	17	0.9	0.27	0.3 - 1.5	1
3h 40mins	17	2.3	0.41	1.4 - 3.1	1	17	0.9	0.23	0.4 - 1.4	1
4h	17	2.1	0.33	1.5 - 2.9	1	17	0.5	0.15	0.2 - 0.9	1

Output File: t12_pcretain; Produced: 09MAR2012 12:04; Final

Percentage Retention

Relative Time	Gaviscon Original Aniseed Relief N	Mean	S.E.	95% C.I.	Not Recorded	Liquid Placebo N	Mean	S.E.	95% C.I.	Not Recorded
No. of Volunteers	17					17				
IMMEDIATELY AFTER COMPLETION OF THE MEAL	17	82.7	2.46	77.5 - 87.9	0	17	79.8	1.93	75.7 - 83.9	0
30mins AFTER START OF MEAL	17	68.0	2.38	63.0 - 73.1	0	17	66.6	2.52	61.2 - 71.9	0
IMMEDIATELY AFTER MEDICATION	17	70.1	2.42	65.0 - 75.2	0	17	65.8	2.46	60.6 - 71.0	0
0.5mins	17	69.7	2.43	64.6 - 74.9	0	17	64.2	2.32	59.2 - 69.1	0
1mins	17	68.9	2.24	64.1 - 73.7	0	17	65.1	2.42	60.0 - 70.2	0
1.5mins	17	69.2	2.44	64.0 - 74.4	0	17	64.5	2.59	59.0 - 70.0	0
2mins	17	68.4	2.53	63.0 - 73.7	0	17	64.2	2.39	59.1 - 69.3	0
2.5mins	17	69.4	2.45	64.2 - 74.6	0	17	63.7	2.32	58.8 - 68.6	0
3mins	17	68.8	2.38	63.7 - 73.8	0	17	64.7	2.43	59.5 - 69.8	0
3.5mins	17	69.0	2.52	63.6 - 74.3	0	17	64.5	2.36	59.5 - 69.5	0
4mins	17	67.8	2.53	62.5 - 73.2	0	17	63.4	2.49	58.1 - 68.7	0
4.5mins	17	68.2	2.46	63.0 - 73.4	0	17	63.5	2.48	58.3 - 68.8	0
5mins	17	66.9	2.56	61.4 - 72.3	0	17	63.5	2.61	58.0 - 69.1	0
6mins	17	65.6	2.53	60.2 - 70.9	0	17	62.5	2.42	57.4 - 67.7	0
7mins	17	65.5	2.67	59.8 - 71.1	0	17	62.7	2.34	57.8 - 67.7	0
8mins	17	64.7	2.87	58.6 - 70.7	0	17	61.9	2.53	56.6 - 67.3	0
9mins	17	64.3	2.82	58.3 - 70.2	0	17	62.3	2.78	56.4 - 68.2	0
10mins	17	64.2	2.90	58.1 - 70.4	0	17	62.6	2.67	56.9 - 68.3	0
11mins	17	64.7	2.94	58.5 - 71.0	0	17	62.3	2.75	56.5 - 68.2	0
12mins	17	64.4	2.92	58.2 - 70.6	0	17	61.7	2.56	56.3 - 67.1	0
13mins	17	64.3	2.98	58.0 - 70.6	0	17	61.4	2.85	55.3 - 67.4	0
14mins	17	64.7	2.79	58.8 - 70.6	0	17	60.2	2.74	54.4 - 66.0	0
20mins	17	60.3	2.96	54.0 - 66.6	0	16	59.9	3.04	53.4 - 66.4	1
40mins	16	51.3	3.13	44.6 - 58.0	1	16	51.8	3.26	44.8 - 58.7	1
1h	17	40.4	3.28	33.5 - 47.4	0	17	41.1	3.71	33.2 - 49.0	0
1h 20mins	17	32.1	3.49	24.7 - 39.5	0	17	31.3	3.85	23.1 - 39.5	0
1h 40mins	17	24.8	3.15	18.1 - 31.5	0	17	23.6	3.49	16.2 - 31.0	0
2h	17	17.8	2.52	12.5 - 23.1	0	17	15.8	2.79	9.9 - 21.7	0
2h 20mins	17	10.4	1.63	6.9 - 13.8	0	17	8.3	1.50	5.1 - 11.5	0
2h 40mins	17	7.3	1.30	4.6 - 10.1	0	17	6.4	1.44	3.4 - 9.5	0
3h	17	5.8	1.12	3.4 - 8.2	0	17	4.0	0.82	2.3 - 5.7	0
3h 20mins	17	3.9	0.89	2.0 - 5.8	0	17	2.8	0.65	1.4 - 4.2	0
3h 40mins	17	2.9	0.81	1.1 - 4.6	0	17	1.6	0.42	0.7 - 2.5	0
4h	17	2.2	0.62	0.9 - 3.6	0	17	1.0	0.21	0.6 - 1.5	0

Output File: t12_pcretain; Produced: 09MAR2012 12:04; Final

Figure 14.2.1 Percentage Retention

Percentage Retention
Mean (95% C.I.)

Figure 1 : 111In(IMP) for Whole Stomach by Treatment : ITT Population

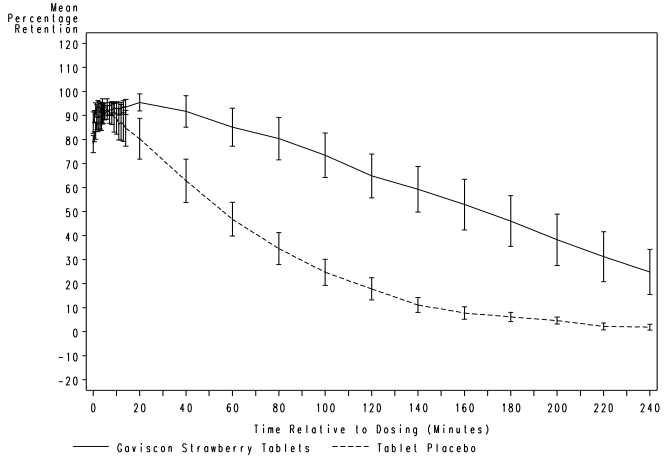


Figure 3 : 99mTc(Meal) for Whole Stomach by Treatment : ITT Population

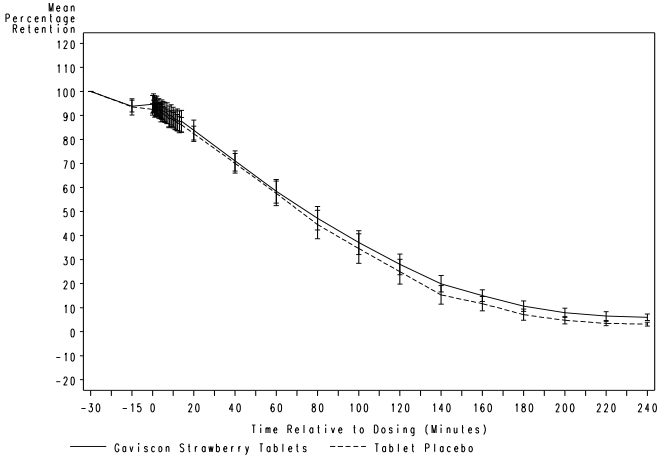


Figure 2 : 111In(IMP) for Upper Stomach by Treatment : ITT Population

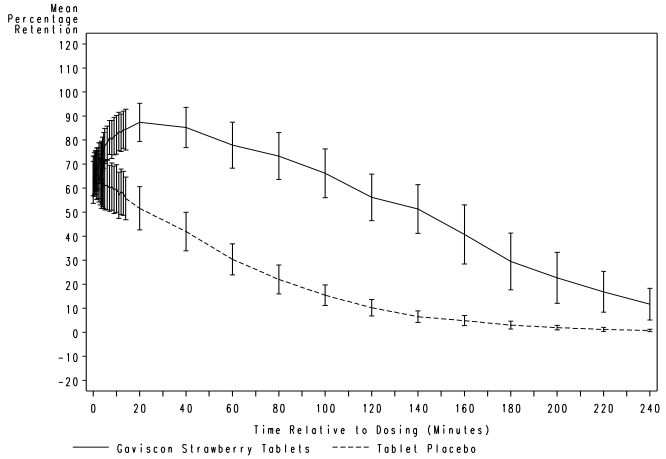
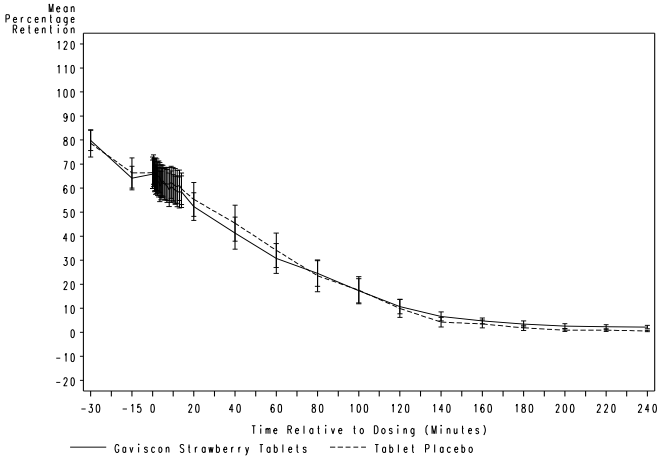


Figure 4 : 99mTc(Meal) for Upper Stomach by Treatment : ITT Population



Percentage Retention
Mean (95% C.I.)

Figure 5 : 111In(IMP) for Whole Stomach by Treatment : ITT Population

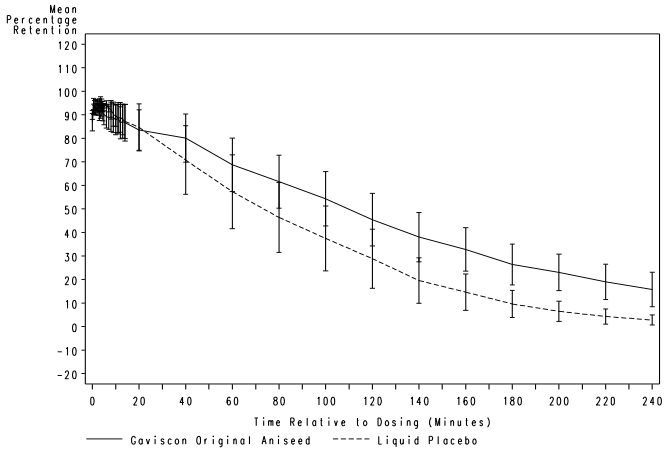


Figure 6 : 111In(IMP) for Upper Stomach by Treatment : ITT Population

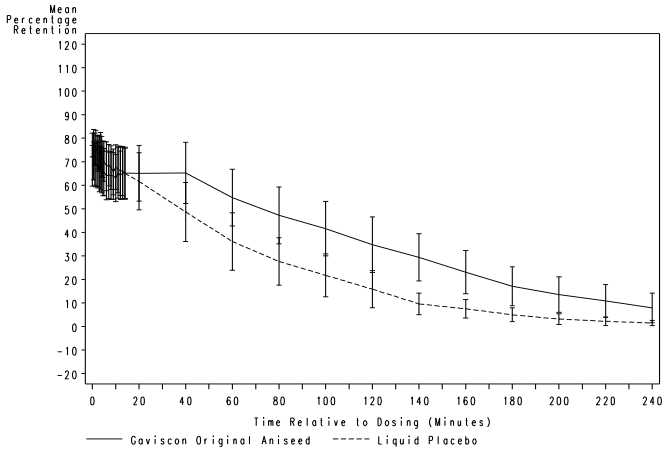


Figure 7 : 99mTc(Meal) for Whole Stomach by Treatment : ITT Population

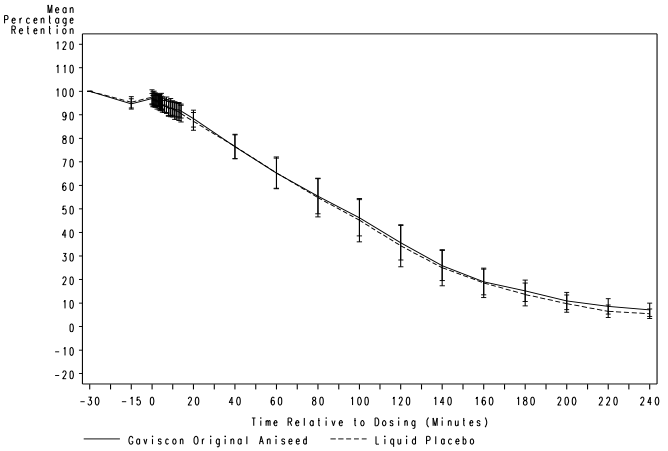
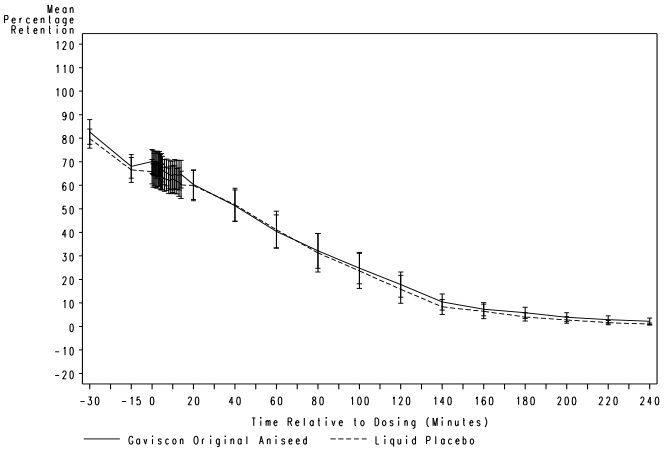


Figure 8 : 99mTc(Meal) for Upper Stomach by Treatment : ITT Population



Percentage Retention
Mean (95% C.I.)

Figure 9 : 111In(IMP) and 99mTc(Meal) for Whole Stomach (Gaviscon Strawberry Tablets only) : ITT Population

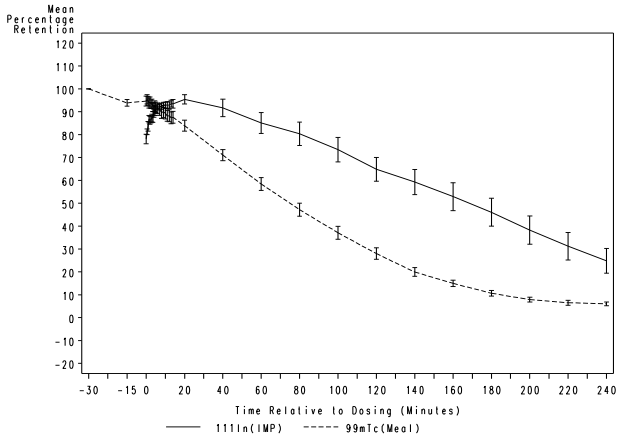


Figure 10 : 111In(IMP) and 99mTc(Meal) for Upper Stomach (Gaviscon Strawberry Tablets only) : ITT Population

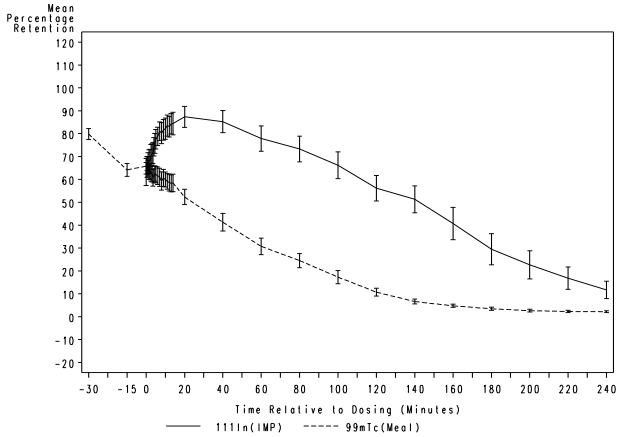


Figure 11 : 111In(IMP) and 99mTc(Meal) for Whole Stomach (Tablet Placebo only) : ITT Population

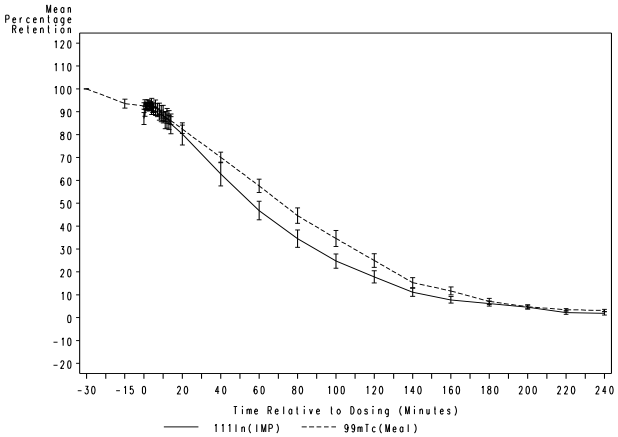
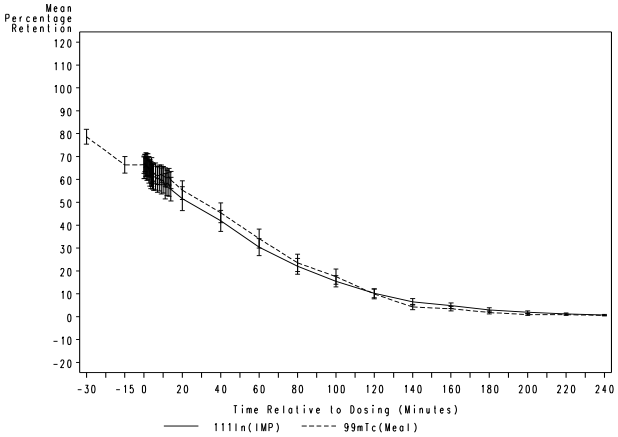


Figure 12 : 111In(IMP) and 99mTc(Meal) for Upper Stomach (Tablet Placebo only) : ITT Population



Percentage Retention
Mean (95% C.I.)

Figure 13 : 111In(IMP) and 99mTc(Meal) for Whole Stomach (Gaviscon Original Aniseed only) : ITT Population

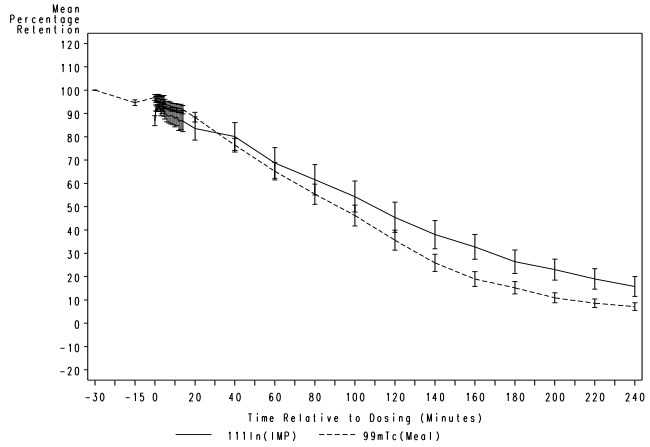


Figure 14 : 111In(IMP) and 99mTc(Meal) for Upper Stomach (Gaviscon Original Aniseed only) : ITT Population

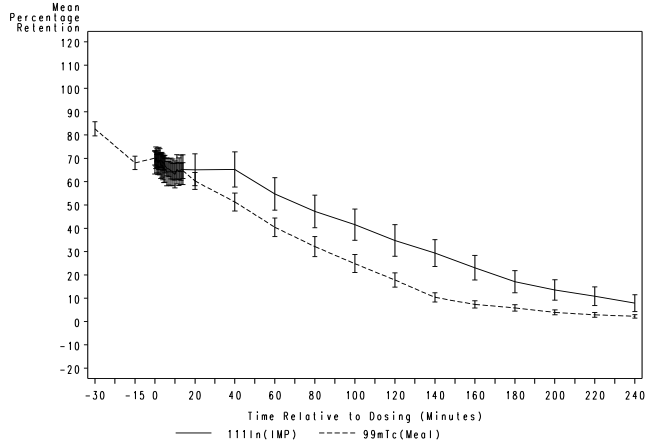


Figure 15 : 111In(IMP) and 99mTc(Meal) for Whole Stomach (Liquid Placebo only) : ITT Population

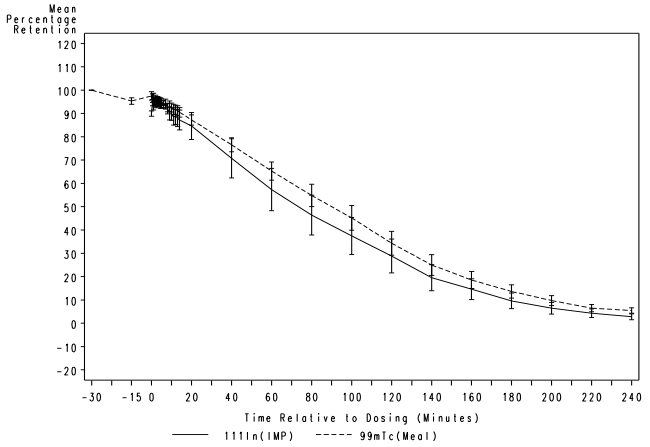


Figure 16 : 111In(IMP) and 99mTc(Meal) for Upper Stomach (Liquid Placebo only) : ITT Population

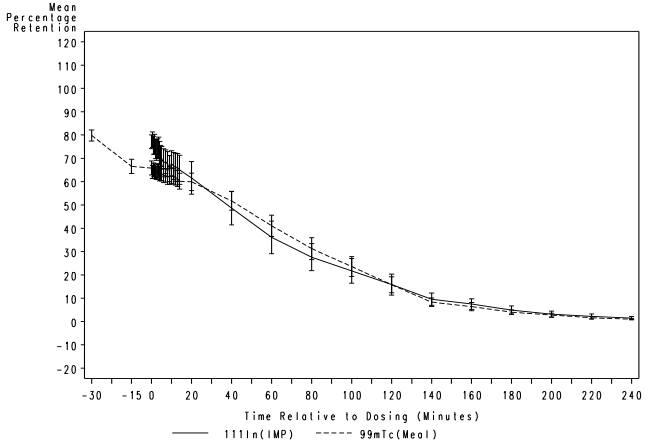


Table 14.2.6 Analysis of ratio of Upper Stomach AUC(IMP)$_{0-5}$ to Whole Stomach AUC(IMP)$_{0-5}$ for Gaviscon Strawberry Flavour Tablets vs Placebo: ITT Population

Analysis of ratio of Upper Stomach AUC(IMP)$_{0-5}$ to Whole Stomach AUC(IMP)$_{0-5}$ for Gaviscon Strawberry Flavour Tablets vs Placebo:
ITT Population

	Upper Stomach AUC$_{0-5}$ / Whole Stomach AUC$_{0-5}$		
	Gaviscon Strawberry Flavour Tablets		Tablet Placebo
Number of Volunteers	18		18
Summary Statistics			
N	18		18
Mean	0.82		0.69
SD	0.190		0.208
Range	0.34 - 1.00		0.23 - 0.92
Geometric Adjusted Mean (CV)	0.79 (17.98)		0.65 (17.98)
Comparison Gaviscon Tablets/Placebo			
Geometric Mean Ratio		1.211	
95% confidence interval		1.068 - 1.374	
p-value		0.0054	

Output File: t27_auc; Produced: 06JUN2012 10:45; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Period, Sequence, Subject within Sequence and Administration (i.e. Gaviscon Strawberry Flavour Tablets or Placebo)
CV : Geometric Coefficient of Variation

Table 14.2.7 Analysis of ratio of Upper Stomach AUC(IMP)$_{0-5}$ to Whole Stomach AUC(IMP)$_{0-5}$ for Gaviscon Original Aniseed Relief vs Placebo: ITT Population

Analysis of ratio of Upper Stomach AUC(IMP)$_{0-5}$ to Whole Stomach AUC(IMP)$_{0-5}$ for Gaviscon Original Aniseed Relief vs Placebo :
ITT Population

	Upper Stomach AUC$_{0-5}$ / Whole Stomach AUC$_{0-5}$		
	Gaviscon Original Aniseed Relief		Liquid Placebo
Number of Volunteers	17		17
Summary Statistics			
N	17		17
Mean	0.74		0.79
SD	0.188		0.137
Range	0.43 - 0.99		0.62 - 0.99
Geometric Adjusted Mean (CV)	0.71 (17.30)		0.78 (17.30)
Comparison Gaviscon Liquid/Placebo			
Geometric Mean Ratio		0.914	
95% confidence interval		0.806 - 1.036	
p-value		0.1458	

Output File: t28_auc; Produced: 06JUN2012 10:47; Final

Note: p-value from analysis of variance of log-transformed data adjusted
for Period, Sequence, Subject within Sequence and Administration (i.e. Gaviscon Original Aniseed Relief or Placebo)
CV : Geometric Coefficient of Variation

Table 14.2.8 Analysis of IMP Distribution (AUC Upper/AUC Whole) over each time point

	IMP Distribution (AUC Upper/ AUC Whole)					
	Gaviscon® Strawberry	Placebo Tablet	Gaviscon® Strawberry / Placebo Tablet			
Minutes since IMP	Geometric LS Mean	Geometric LS Mean	Ratio	95% CI		
				Lower	Upper	P-Value
0.5	0.77	0.71	1.08	0.97	1.20	0.1652
1	0.77	0.70	1.10	0.98	1.23	0.0882
1.5	0.77	0.69	1.11	0.99	1.24	0.0725
2	0.76	0.69	1.11	0.99	1.25	0.0704
2.5	0.77	0.68	1.13	1.00	1.27	0.0522
3	0.77	0.67	1.15	1.01	1.30	0.0319
3.5	0.77	0.67	1.16	1.03	1.32	0.0208
4	0.78	0.66	1.18	1.04	1.34	0.0138
4.5	0.78	0.66	1.20	1.05	1.36	0.0086
5	0.79	0.65	1.21	1.07	1.37	0.0054
6	0.80	0.65	1.24	1.09	1.40	0.0023
7	0.81	0.64	1.26	1.11	1.42	0.0011
8	0.82	0.64	1.27	1.13	1.44	0.0006
9	0.82	0.64	1.29	1.14	1.45	0.0004
10	0.83	0.64	1.29	1.15	1.45	0.0002
11	0.83	0.64	1.30	1.17	1.46	0.0001
12	0.83	0.64	1.31	1.18	1.47	<.0001
13	0.84	0.64	1.32	1.18	1.47	<.0001
14	0.84	0.63	1.33	1.19	1.48	<.0001
20	0.86	0.63	1.36	1.23	1.50	<.0001
40	0.88	0.63	1.40	1.30	1.52	<.0001
60	0.89	0.63	1.41	1.31	1.52	<.0001
80	0.89	0.63	1.42	1.32	1.53	<.0001
100	0.89	0.62	1.43	1.32	1.54	<.0001
120	0.89	0.62	1.43	1.32	1.55	<.0001
140	0.88	0.62	1.43	1.32	1.55	<.0001
160	0.87	0.61	1.42	1.32	1.54	<.0001
180	0.86	0.61	1.41	1.30	1.52	<.0001
200	0.84	0.61	1.39	1.28	1.50	<.0001
220	0.83	0.60	1.37	1.27	1.48	<.0001
240	0.81	0.60	1.36	1.25	1.47	<.0001

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Page 1 of 1

	IMP Distribution (AUC Upper/ AUC Whole)					
	Gaviscon® Original	Placebo Liquid	Gaviscon® Original / Placebo Liquid			
Minutes since IMP	Geometric LS Mean	Geometric LS Mean	Ratio	95% CI		
				Lower	Upper	P-Value
0.5	0.75	0.83	0.90	0.80	1.02	0.1067
1	0.74	0.82	0.91	0.80	1.02	0.1066
1.5	0.74	0.82	0.90	0.80	1.02	0.1042
2	0.73	0.81	0.90	0.80	1.03	0.1127
2.5	0.73	0.80	0.91	0.80	1.03	0.1280
3	0.72	0.80	0.91	0.80	1.03	0.1314
3.5	0.72	0.79	0.91	0.80	1.03	0.1283
4	0.72	0.79	0.91	0.80	1.03	0.1301
4.5	0.72	0.78	0.91	0.80	1.03	0.1361
5	0.71	0.78	0.91	0.81	1.04	0.1458
6	0.71	0.77	0.92	0.81	1.04	0.1690
7	0.71	0.76	0.93	0.82	1.04	0.1955
8	0.70	0.76	0.93	0.82	1.05	0.2271
9	0.70	0.75	0.93	0.83	1.06	0.2628
10	0.70	0.75	0.94	0.83	1.06	0.2842
11	0.70	0.75	0.94	0.83	1.07	0.3003
12	0.70	0.75	0.94	0.83	1.07	0.3313
13	0.70	0.74	0.94	0.83	1.08	0.3649
14	0.70	0.74	0.95	0.83	1.08	0.3956
20	0.71	0.73	0.97	0.85	1.11	0.6497
40	0.73	0.71	1.04	0.90	1.20	0.5685
60	0.74	0.68	1.08	0.94	1.24	0.2425
80	0.74	0.67	1.11	0.97	1.27	0.1180
100	0.74	0.66	1.13	0.99	1.29	0.0795
120	0.74	0.65	1.14	0.99	1.31	0.0611
140	0.73	0.64	1.15	1.00	1.32	0.0482
160	0.73	0.63	1.15	1.01	1.32	0.0423
180	0.73	0.63	1.15	1.00	1.32	0.0459
200	0.72	0.63	1.14	1.00	1.31	0.0564
220	0.71	0.63	1.13	0.99	1.30	0.0712
240	0.71	0.63	1.13	0.98	1.29	0.0884

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Page 1 of 1

Table 14.2.9 Analysis of IMP Distribution (Upper/Whole) over each time point

	IMP Distribution (Upper/Whole)					
	Gaviscon® Strawberry	Placebo Tablet	Gaviscon® Strawberry / Placebo Tablet			
Minutes since IMP	Geometric LS Mean	Geometric LS Mean	Ratio	95% CI		
				Lower	Upper	P-Value
0.5	0.78	0.70	1.11	0.98	1.25	0.0857
1	0.77	0.68	1.13	1.01	1.26	0.0312
1.5	0.75	0.67	1.13	0.97	1.30	0.1058
2	0.76	0.66	1.15	0.99	1.34	0.0679
2.5	0.78	0.64	1.23	1.06	1.43	0.0100
3	0.80	0.63	1.26	1.09	1.45	0.0034
3.5	0.80	0.62	1.29	1.10	1.52	0.0038
4	0.82	0.61	1.33	1.14	1.55	0.0014
4.5	0.82	0.62	1.33	1.16	1.52	0.0003
5	0.84	0.62	1.35	1.19	1.53	0.0001
6	0.84	0.61	1.38	1.21	1.57	0.0001
7	0.86	0.62	1.39	1.24	1.56	<.0001
8	0.85	0.62	1.36	1.21	1.54	<.0001
9	0.86	0.62	1.38	1.24	1.53	<.0001
10	0.86	0.63	1.38	1.24	1.54	<.0001
11	0.88	0.62	1.43	1.29	1.59	<.0001
12	0.88	0.63	1.38	1.25	1.53	<.0001
13	0.88	0.63	1.39	1.26	1.53	<.0001
14	0.88	0.62	1.41	1.28	1.55	<.0001
20	0.90	0.62	1.46	1.35	1.59	<.0001
40	0.92	0.64	1.43	1.28	1.60	<.0001
60	0.90	0.60	1.50	1.22	1.84	0.0007
80	0.89	0.58	1.55	1.31	1.84	<.0001
100	0.88	0.56	1.56	1.28	1.91	0.0002
120	0.84	0.45	1.88	1.39	2.54	0.0004
140	0.83	0.35	2.38	1.26	4.50	0.0107
160	0.64	0.42	1.53	1.10	2.14	0.0155
180	0.32	0.19	1.65	0.61	4.44	0.2983
200	0.27	0.33	0.81	0.40	1.67	0.5514
220	0.22	0.46	0.48	0.22	1.02	0.0568
240	0.30	0.44	0.69	0.41	1.17	0.1576

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Page 1 of 1

	IMP Distribution (Upper/Whole)					
	Gaviscon® Original	Placebo Liquid	Gaviscon® Original / Placebo Liquid			
Minutes since IMP	Geometric LS Mean	Geometric LS Mean	Ratio	95% CI		
				Lower	Upper	P-Value
0.5	0.74	0.82	0.91	0.80	1.02	0.1087
1	0.72	0.80	0.90	0.78	1.03	0.1209
1.5	0.71	0.80	0.90	0.78	1.03	0.1245
2	0.71	0.78	0.92	0.80	1.05	0.2051
2.5	0.71	0.77	0.92	0.81	1.06	0.2342
3	0.71	0.77	0.91	0.81	1.02	0.1098
3.5	0.71	0.77	0.92	0.82	1.03	0.1472
4	0.69	0.75	0.92	0.80	1.06	0.2111
4.5	0.69	0.75	0.92	0.80	1.06	0.2405
5	0.70	0.74	0.94	0.82	1.08	0.3924
6	0.68	0.69	0.99	0.86	1.15	0.9319
7	0.69	0.72	0.96	0.84	1.11	0.5778
8	0.69	0.71	0.97	0.83	1.14	0.6877
9	0.69	0.71	0.98	0.83	1.15	0.7826
10	0.69	0.73	0.94	0.80	1.11	0.4353
11	0.70	0.73	0.96	0.81	1.14	0.6432
12	0.71	0.72	0.99	0.84	1.17	0.9283
13	0.72	0.72	0.99	0.83	1.18	0.9071
14	0.72	0.72	1.00	0.86	1.17	0.9778
20	0.74	0.68	1.08	0.92	1.28	0.3266
40	0.77	0.66	1.16	0.99	1.35	0.0627
60	0.76	0.59	1.29	1.06	1.57	0.0130
80	0.71	0.58	1.23	1.01	1.49	0.0439
100	0.71	0.51	1.40	1.01	1.95	0.0464
120	0.62	0.37	1.69	0.99	2.89	0.0530
140	0.63	0.47	1.33	1.05	1.68	0.0227
160	0.40	0.49	0.82	0.32	2.09	0.6598
180	0.43	0.48	0.91	0.50	1.67	0.7470
200	0.32	0.42	0.75	0.35	1.63	0.4424
220	0.41	0.48	0.86	0.53	1.40	0.5420
240	0.25	0.48	0.53	0.24	1.16	0.1068

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Page 1 of 1

Table 14.2.10 AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes: ITT Population

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 1 minute: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	0.81	0.90	0.91	0.93
	SD	0.053	0.053	0.038	0.036
	Range	0.66 - 0.89	0.78 - 0.97	0.82 - 0.96	0.87 - 0.99
Upper Stomach	N	18	18	17	17
	Mean	0.82	0.85	0.87	0.98
	SD	0.212	0.232	0.265	0.164
	Range	0.25 - 1.19	0.25 - 1.22	0.47 - 1.38	0.79 - 1.25

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 2 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	0.84	0.91	0.92	0.94
	SD	0.053	0.040	0.028	0.032
	Range	0.69 - 0.91	0.81 - 0.97	0.87 - 0.97	0.86 - 0.98
Upper Stomach	N	18	18	17	17
	Mean	0.85	0.85	0.87	0.97
	SD	0.223	0.241	0.274	0.179
	Range	0.28 - 1.26	0.25 - 1.22	0.44 - 1.40	0.73 - 1.28

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 3 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	0.85	0.92	0.92	0.94
	SD	0.049	0.032	0.019	0.025
	Range	0.71 - 0.92	0.84 - 0.97	0.89 - 0.95	0.89 - 0.99
Upper Stomach	N	18	18	17	17
	Mean	0.87	0.85	0.87	0.97
	SD	0.228	0.245	0.283	0.186
	Range	0.30 - 1.30	0.24 - 1.20	0.42 - 1.42	0.71 - 1.28

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 4 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	0.86	0.93	0.92	0.94
	SD	0.049	0.026	0.024	0.022
	Range	0.73 - 0.92	0.87 - 0.97	0.87 - 0.96	0.90 - 0.98
Upper Stomach	N	18	18	17	17
	Mean	0.88	0.84	0.86	0.96
	SD	0.226	0.252	0.287	0.193
	Range	0.33 - 1.32	0.23 - 1.22	0.41 - 1.42	0.69 - 1.30

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 5 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	0.87	0.93	0.92	0.94
	SD	0.048	0.023	0.031	0.022
	Range	0.74 - 0.93	0.89 - 0.96	0.85 - 0.96	0.89 - 0.98
Upper Stomach	N	18	18	17	17
	Mean	0.91	0.84	0.86	0.96
	SD	0.222	0.255	0.293	0.200
	Range	0.36 - 1.33	0.23 - 1.21	0.41 - 1.43	0.67 - 1.31

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 10 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	0.90	0.93	0.91	0.94
	SD	0.038	0.053	0.065	0.028
	Range	0.81 - 0.96	0.76 - 0.99	0.74 - 0.97	0.88 - 0.97
Upper Stomach	N	18	18	17	17
	Mean	0.99	0.83	0.86	0.93
	SD	0.218	0.260	0.312	0.227
	Range	0.45 - 1.40	0.25 - 1.15	0.39 - 1.52	0.59 - 1.37

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 14 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	0.92	0.92	0.91	0.93
	SD	0.038	0.084	0.090	0.059
	Range	0.85 - 1.00	0.65 - 1.01	0.67 - 0.98	0.81 - 0.98
Upper Stomach	N	18	18	17	17
	Mean	1.06	0.82	0.87	0.93
	SD	0.228	0.259	0.329	0.252
	Range	0.50 - 1.42	0.26 - 1.14	0.39 - 1.60	0.56 - 1.43

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 60 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	1.00	0.79	0.87	0.82
	SD	0.127	0.164	0.182	0.213
	Range	0.66 - 1.21	0.34 - 1.00	0.46 - 1.12	0.49 - 1.06
Upper Stomach	N	18	18	17	17
	Mean	1.34	0.75	0.96	0.85
	SD	0.343	0.261	0.409	0.364
	Range	0.52 - 1.95	0.18 - 1.28	0.35 - 1.73	0.39 - 1.60

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

AUC(IMP) Relative to AUC(meal) for the Whole Stomach and Upper Stomach by Treatment after 240 minutes: ITT Population

		AUC(IMP) / AUC(meal)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
Whole Stomach	N	18	18	17	17
	Mean	1.38	0.66	0.95	0.68
	SD	0.343	0.179	0.346	0.275
	Range	0.52 - 2.00	0.25 - 1.06	0.42 - 1.56	0.28 - 1.15
Upper Stomach	N	18	18	17	17
	Mean	2.04	0.70	1.15	0.74
	SD	0.708	0.272	0.547	0.379
	Range	0.48 - 3.60	0.14 - 1.33	0.39 - 2.22	0.25 - 1.53

Output File: t21_auc; Produced: 06JUN2012 10:50; Final

Table 14.2.11 Analysis of $AUC(IMP)_{0-5}$ Relative to $AUC(meal)_{0-5}$ for the Whole Stomach for Gaviscon Strawberry Flavour Tablets: ITT Population

	Gaviscon Strawberry Flavour Tablets		Tablet Placebo
Number of Volunteers	18		18
Geometric Adjusted Mean Ratio (AUC(IMP) / AUC(meal)) (CV)	0.8678 (4.67)		0.9309 (4.67)
Treatment Ratio (Gaviscon Tablets/Placebo)			
Geometric Mean Ratio		0.932	
95% confidence interval		0.902 - 0.963	
p-value		0.0004	

Output File: t22_auc; Produced: 09MAR2012 14:28; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Treatment Sequence, Subject within Treatment Sequence, Period and Study Drug (i.e. Gaviscon Strawberry Flavour Tablets or Tablet Placebo).
CV : Geometric Coefficient of Variation

Table 14.2.12 Analysis of AUC(IMP)$_{0-5}$ Relative to AUC(meal)$_{0-5}$ for the Whole Stomach for Gaviscon Original Aniseed Relief: ITT Population

	Gaviscon Original Aniseed Relief		Liquid_Placebo
Number of Volunteers	17		17
Geometric Adjusted Mean Ratio (AUC(IMP) / AUC(meal)) (CV)	0.9219 (3.28)		0.9442 (3.28)
Treatment Ratio (Gaviscon Liquid/Placebo)			
Geometric Mean Ratio		0.976	
95% confidence interval		0.953 - 1.000	
p-value		0.0506	

Output File: t23_auc; Produced: 09MAR2012 14:29; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Treatment Sequence, Subject within Treatment Sequence, Period and Study Drug (i.e. Gaviscon Original Aniseed Relief or Liquid Placebo. CV : Geometric Coefficient of Variation

Table 14.2.13 AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minute: ITT Population

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 1 minute: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.81	0.74	0.77	0.83
	SD	0.204	0.209	0.181	0.103
	Range	0.26 - 1.00	0.25 - 0.96	0.47 - 1.01	0.67 - 0.99
Meal	N	18	18	17	17
	Mean	0.80	0.78	0.82	0.80
	SD	0.084	0.113	0.101	0.079
	Range	0.64 - 0.92	0.55 - 0.98	0.62 - 0.94	0.63 - 0.95

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 2 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.80	0.72	0.76	0.81
	SD	0.205	0.210	0.186	0.117
	Range	0.28 - 1.00	0.26 - 0.96	0.44 - 1.00	0.65 - 0.99
Meal	N	18	18	17	17
	Mean	0.79	0.78	0.82	0.79
	SD	0.083	0.112	0.100	0.078
	Range	0.64 - 0.91	0.55 - 0.98	0.62 - 0.94	0.64 - 0.95

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 3 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.80	0.71	0.75	0.80
	SD	0.202	0.209	0.188	0.123
	Range	0.30 - 1.00	0.24 - 0.94	0.42 - 1.00	0.63 - 0.99
Meal	N	18	18	17	17
	Mean	0.79	0.78	0.82	0.79
	SD	0.082	0.112	0.099	0.077
	Range	0.64 - 0.91	0.55 - 0.97	0.62 - 0.94	0.64 - 0.94

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 4 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.80	0.71	0.75	0.80
	SD	0.202	0.209	0.188	0.123
	Range	0.30 - 1.00	0.24 - 0.94	0.42 - 1.00	0.63 - 0.99
Meal	N	18	18	17	17
	Mean	0.79	0.78	0.82	0.79
	SD	0.082	0.112	0.099	0.077
	Range	0.64 - 0.91	0.55 - 0.97	0.62 - 0.94	0.64 - 0.94

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 5 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.82	0.69	0.74	0.79
	SD	0.190	0.208	0.188	0.137
	Range	0.34 - 1.00	0.23 - 0.92	0.43 - 0.99	0.62 - 0.99
Meal	N	18	18	17	17
	Mean	0.79	0.78	0.82	0.79
	SD	0.081	0.110	0.098	0.076
	Range	0.63 - 0.91	0.54 - 0.97	0.62 - 0.93	0.64 - 0.93

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 10 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.84	0.67	0.73	0.76
	SD	0.165	0.192	0.179	0.148
	Range	0.41 - 1.00	0.26 - 0.90	0.45 - 1.00	0.56 - 0.99
Meal	N	18	18	17	17
	Mean	0.78	0.77	0.80	0.78
	SD	0.078	0.108	0.096	0.073
	Range	0.63 - 0.90	0.53 - 0.96	0.62 - 0.91	0.65 - 0.92

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 14 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.86	0.66	0.73	0.75
	SD	0.154	0.177	0.174	0.148
	Range	0.44 - 1.00	0.28 - 0.87	0.46 - 0.99	0.54 - 0.99
Meal	N	18	18	17	17
	Mean	0.76	0.76	0.79	0.77
	SD	0.075	0.105	0.094	0.072
	Range	0.63 - 0.89	0.52 - 0.96	0.61 - 0.90	0.66 - 0.92

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 60 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.90	0.64	0.76	0.69
	SD	0.110	0.124	0.153	0.119
	Range	0.63 - 0.99	0.41 - 0.82	0.50 - 0.95	0.51 - 0.88
Meal	N	18	18	17	17
	Mean	0.69	0.71	0.73	0.71
	SD	0.077	0.112	0.092	0.084
	Range	0.58 - 0.84	0.48 - 0.92	0.55 - 0.86	0.51 - 0.91

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

AUC Upper Stomach Relative to AUC Whole Stomach by Treatment after 240 minutes: ITT Population

		Upper Stomach AUC / Whole Stomach AUC			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
No. of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	0.82	0.61	0.72	0.64
	SD	0.095	0.121	0.140	0.105
	Range	0.64 - 0.95	0.36 - 0.77	0.52 - 0.93	0.37 - 0.79
Meal	N	18	18	17	17
	Mean	0.58	0.61	0.63	0.61
	SD	0.094	0.116	0.095	0.093
	Range	0.42 - 0.73	0.32 - 0.79	0.45 - 0.78	0.41 - 0.84

Output File: t26_auc; Produced: 06JUN2012 10:53; Final

Table 14.2.14 Analysis of Ratio of Upper Stomach AUC(meal)$_{0-5}$ to Whole Stomach AUC(meal)$_{0-5}$ for Gaviscon Strawberry Flavour Tablets vs Placebo: ITT Population

	Upper Stomach AUC_{0-5} / Whole Stomach AUC_{0-5}		
	Gaviscon Strawberry Flavour Tablets		Tablet Placebo
Number of Volunteers	18		18
Summary Statistics			
N	18		18
Mean	0.79		0.78
SD	0.081		0.110
Range	0.63 - 0.91		0.54 - 0.97
Geometric Adjusted Mean (CV)	0.78 (9.96)		0.77 (9.96)
Comparison Gaviscon Tablets/Placebo			
Geometric Mean Ratio		1.016	
95% confidence interval		0.947 - 1.090	
p-value		0.6448	

Output File: t29_auc; Produced: 29FEB2012 14:54; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Period, Subject within Period and Administration (i.e. Gaviscon Strawberry Flavour Tablets or Placebo)
CV : Geometric Coefficient of Variation

Table 14.2.15 Analysis of Ratio of Upper Stomach AUC(meal)$_{0-5}$ to Whole Stomach AUC(meal)$_{0-5}$ for Gaviscon Original Aniseed Relief vs Placebo: ITT Population

	Upper Stomach AUC_{0-5} / Whole Stomach AUC_{0-5}		
	Gaviscon Original Aniseed Relief		Liquid Placebo
Number of Volunteers	17		17
Summary Statistics			
N	17		17
Mean	0.82		0.79
SD	0.098		0.076
Range	0.62 - 0.93		0.64 - 0.93
Geometric Adjusted Mean (CV)	0.81 (7.00)		0.78 (7.00)
Comparison Gaviscon Liquid/Placebo			
Geometric Mean Ratio		1.036	
95% confidence interval		0.985 - 1.090	
p-value		0.1594	

Output File: t30_auc; Produced: 09MAR2012 14:55; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Period, Subject within Period and Administration (i.e. Gaviscon Original Aniseed Relief or Placebo)
CV : Geometric Coefficient of Variation

Table 14.2.16 Time to Half Empty IMP and Meal for the Whole Stomach : ITT Population

		Time to Half Empty IMP (mins)			
		Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
Number of Volunteers		18	18	17	17
IMP	N	18	18	17	17
	Mean	169.12	56.55	108.72	78.41
	SD	58.007	20.215	57.050	47.094
	Range	42 - 239	9 - 87	15 - 239	20 - 157
Meal	N	18	18	17	17
	Mean	105.69	104.41	121.11	121.12
	SD	15.974	18.437	25.819	28.450
	Range	67 - 132	68 - 134	77 - 167	79 - 166

Output File: t17_halfempt; Produced: 09MAR2012 12:34; Final

Table 14.2.17 % Retention for the Whole Stomach and Upper Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes : ITT Population

% Retention for the Whole Stomach and Upper Stomach by Treatment after 1 minute : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	83.7	92.8	92.0	93.2
		SD	7.19	4.76	3.83	5.64
		Range	66.4 - 95.7	83.9 - 100.0	84.6 - 100.0	78.5 - 100.0
	Upper Stomach	N	18	18	17	17
		Mean	67.0	66.4	68.9	75.6
		SD	16.24	18.28	17.33	12.98
		Range	25.5 - 88.4	26.5 - 88.2	35.6 - 91.2	57.7 - 98.5
Meal	Whole Stomach	N	18	18	17	17
		Mean	94.8	91.8	96.5	96.9
		SD	6.93	5.18	4.65	6.18
		Range	79.5 - 106.8	79.5 - 100.2	87.1 - 106.0	87.0 - 109.8
	Upper Stomach	N	18	18	17	17
		Mean	64.9	65.3	68.9	65.1
		SD	12.23	13.93	9.25	9.97
		Range	37.5 - 81.6	32.9 - 87.1	51.1 - 85.4	42.3 - 85.0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 2 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	86.2	93.7	93.2	94.1
		SD	6.03	5.22	4.59	4.39
		Range	72.4 - 96.0	78.0 - 100.0	85.4 - 100.0	84.8 - 100.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	68.2	65.5	69.1	74.0
		SD	17.39	19.82	18.76	13.85
		Range	30.1 - 88.1	24.4 - 92.6	32.2 - 93.0	52.9 - 97.1
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	18	18	17	17
		Mean	94.3	92.4	96.5	96.3
		SD	7.39	5.96	5.12	5.07
		Range	77.6 - 110.4	84.5 - 106.3	86.2 - 103.3	85.2 - 104.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	63.5	65.5	68.4	64.2
		SD	11.71	13.34	10.42	9.87
		Range	39.0 - 79.9	39.1 - 88.9	47.2 - 85.4	43.4 - 86.9
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 3 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	87.2	92.8	91.0	95.0
		SD	5.85	4.38	6.59	3.50
		Range	74.1 - 98.5	83.0 - 100.0	79.1 - 100.0	88.4 - 100.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	71.1	62.8	66.9	74.4
		SD	15.42	19.86	18.81	13.50
		Range	36.7 - 92.5	16.7 - 85.8	32.6 - 89.8	52.9 - 95.8
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	18	18	17	17
		Mean	93.6	92.2	95.9	95.8
		SD	6.86	6.48	4.57	4.94
		Range	79.9 - 106.8	79.5 - 108.3	83.0 - 101.5	86.8 - 104.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	62.4	64.8	68.8	64.7
		SD	12.26	13.00	9.80	10.02
		Range	40.3 - 83.9	36.4 - 85.5	48.6 - 85.1	43.2 - 88.3
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 4 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	89.4	94.4	92.6	94.7
		SD	6.10	5.04	6.03	4.02
		Range	73.6 - 100.0	77.2 - 100.0	79.4 - 100.0	82.4 - 100.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	74.3	63.2	66.3	72.3
		SD	13.97	22.11	18.64	16.44
		Range	42.0 - 92.8	18.2 - 88.4	34.9 - 91.5	46.5 - 96.5
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	18	18	17	17
		Mean	91.9	90.9	95.8	94.7
		SD	6.04	7.34	5.93	5.69
		Range	79.9 - 103.2	72.9 - 107.2	82.0 - 102.7	85.0 - 104.5
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	61.6	62.4	67.8	63.4
		SD	10.91	14.66	10.43	10.28
		Range	45.3 - 85.2	26.6 - 86.4	46.8 - 85.3	41.3 - 86.0
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 5 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	90.9	91.7	90.1	93.3
		SD	5.31	7.04	8.49	3.00
		Range	78.3 - 100.0	70.1 - 100.0	65.4 - 100.0	85.9 - 96.7
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	77.6	60.9	65.6	70.2
		SD	14.77	20.16	19.39	16.42
		Range	40.5 - 95.0	21.2 - 86.3	32.6 - 93.6	45.9 - 94.2
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	18	18	17	17
		Mean	91.9	90.6	94.5	94.3
		SD	7.80	6.18	5.29	6.28
		Range	76.6 - 110.5	78.0 - 104.4	79.4 - 101.5	83.6 - 106.7
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	62.1	63.0	66.9	63.5
		SD	12.35	12.99	10.55	10.76
		Range	43.5 - 84.3	33.1 - 84.2	45.0 - 83.8	40.0 - 86.9
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 10 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	92.9	88.9	87.9	89.8
		SD	4.63	13.52	12.31	9.05
		Range	82.7 - 100.0	44.4 - 98.4	55.4 - 99.4	66.9 - 100.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	82.2	59.8	63.1	67.8
		SD	16.20	19.90	19.52	18.42
		Range	41.2 - 97.5	12.1 - 87.2	31.8 - 93.0	39.6 - 93.5
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	18	18	17	17
		Mean	89.3	88.0	92.6	92.5
		SD	8.24	6.39	5.46	6.64
		Range	72.0 - 108.5	75.5 - 98.1	79.1 - 100.3	79.3 - 102.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	59.9	61.7	64.2	62.6
		SD	11.36	13.97	11.96	11.02
		Range	40.9 - 81.3	30.1 - 82.6	42.8 - 82.9	39.8 - 84.1
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 14 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	93.5	84.7	86.7	87.2
		SD	6.41	15.06	15.21	14.20
		Range	73.5 - 100.0	37.9 - 98.2	51.4 - 99.7	56.4 - 100.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	84.4	55.7	65.1	65.1
		SD	17.13	17.87	21.40	20.87
		Range	41.0 - 100.2	14.7 - 79.0	31.7 - 97.4	33.6 - 94.8
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	18	18	17	17
		Mean	87.6	86.1	91.6	90.5
		SD	9.12	6.16	5.85	6.85
		Range	67.3 - 108.2	71.7 - 96.2	77.2 - 99.3	78.7 - 101.2
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	58.5	59.7	64.7	60.2
		SD	13.22	13.20	11.49	11.31
		Range	28.1 - 84.1	31.5 - 79.9	41.6 - 86.6	35.0 - 82.3
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 60 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	85.1	46.8	68.7	57.3
		SD	15.94	14.14	22.10	30.54
		Range	41.1 - 100.0	10.4 - 71.5	27.8 - 100.0	14.6 - 100.0
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	77.9	30.4	54.8	36.1
		SD	19.32	13.02	23.40	23.73
		Range	30.0 - 94.7	4.2 - 56.3	18.7 - 96.8	7.0 - 81.8
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	18	18	17	17
		Mean	58.4	57.6	65.2	65.3
		SD	9.84	10.25	12.49	13.12
		Range	32.3 - 71.8	31.7 - 73.5	41.3 - 86.0	41.5 - 84.4
		Not Recorded	0	0	0	0
	Upper Stomach	N	18	18	17	17
		Mean	30.7	34.1	40.4	41.1
		SD	12.42	14.36	13.54	15.30
		Range	7.7 - 53.1	1.6 - 54.8	16.0 - 67.4	11.2 - 65.7
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

% Retention for the Whole Stomach and Upper Stomach by Treatment after 240 minutes : ITT Population

			Percentage Retention (%)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		17	17	17	17
IMP	Whole Stomach	N	17	17	17	17
		Mean	24.8	1.9	15.7	2.8
		SD	18.24	2.40	14.22	4.17
		Range	0.2 - 53.4	0.0 - 8.0	0.0 - 56.4	0.0 - 15.3
		Not Recorded	0	0	0	0
	Upper Stomach	N	17	17	17	17
		Mean	11.7	0.7	7.9	1.4
		SD	12.83	0.97	12.23	2.11
		Range	0.2 - 44.9	0.0 - 3.7	0.0 - 50.5	0.0 - 6.7
		Not Recorded	0	0	0	0
Meal	Whole Stomach	N	17	17	17	17
		Mean	6.0	3.1	7.1	5.4
		SD	2.64	1.60	5.52	3.98
		Range	0.4 - 9.0	1.0 - 5.5	1.3 - 22.4	1.4 - 14.8
		Not Recorded	0	0	0	0
	Upper Stomach	N	17	17	17	17
		Mean	2.1	0.5	2.2	1.0
		SD	1.36	0.62	2.57	0.87
		Range	-0.1 - 4.8	-0.1 - 2.0	0.0 - 9.7	0.0 - 2.7
		Not Recorded	0	0	0	0

Output File: t13_pcretain; Produced: 06JUN2012 10:51; Final

Table 14.2.18 Time to Form 50%, 70%, 90% and 100% Complete Raft in the Upper Stomach : ITT Population

		Time to % Raft Formation (mins)	
		Gaviscon Strawberry Flavour Tablets	Gaviscon Original Aniseed Relief
Number of Volunteers		18	17
50% Raft Formation	N	18	17
	Mean	0.30	0.01
	SD	0.949	0.022
	Range	0.0 - 3.8	0.0 - 0.1
70% Raft Formation	N	18	17
	Mean	0.93	0.06
	SD	1.763	0.180
	Range	0.0 - 6.7	0.0 - 0.6
90% Raft Formation	N	18	17
	Mean	5.63	1.97
	SD	3.511	4.864
	Range	0.0 - 11.3	0.0 - 19.3
100% Raft Formation	N	18	17
	Mean	21.98	11.22
	SD	13.122	18.151
	Range	0.0 - 41.2	0.0 - 59.4

Output File: t18_raft; Produced: 09MAR2012 12:39; Final

Table 14.2.19 Analysis of $AUC(IMP)_{0-5}$ for the Whole Stomach for Gaviscon Strawberry Flavour Tablets: ITT Population

	Gaviscon Strawberry Flavour Tablets		Tablet Placebo
Number of Volunteers	18		18
Geometric Adjusted Mean AUC(IMP) (CV)	431.3 (4.79)		462.3 (4.79)
Treatment Ratio (Gaviscon Tablet/Placebo)			
Geometric Mean Ratio		0.933	
95% confidence interval		0.902 - 0.965	
p-value		0.0005	

Output File: t15_auc; Produced: 09MAR2012 14:04; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Treatment Sequence, Subject within Treatment Sequence, Period and Study IMP (i.e. Gaviscon Strawberry Flavour Tablets or Tablet Placebo).
CV : Geometric Coefficient of Variation

Table 14.2.20 Analysis of AUC(IMP)$_{0-5}$ for the Whole Stomach for Gaviscon Original Aniseed Relief: ITT Population

	Gaviscon Original Aniseed Relief		Liquid Placebo
Number of Volunteers	17		17
Geometric Adjusted Mean AUC(IMP) (CV)	458.3 (3.18)		469.8 (3.18)
Treatment Ratio (Gaviscon Liquid/Placebo)			
Geometric Mean Ratio		0.976	
95% confidence interval		0.953 - 0.998	
p-value		0.0383	

Output File: t16_auc; Produced: 09MAR2012 14:05; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Treatment Sequence, Subject within Treatment Sequence, Period and Study Drug (i.e. Gaviscon Original Aniseed Relief or Liquid Placebo).
CV : Geometric Coefficient of Variation

Table 14.2.21 Analysis of AUC(meal)$_{0-5}$ for the Whole Stomach for Gaviscon Strawberry Flavour Tablets: ITT Population

	Gaviscon Strawberry Flavour Tablets		Tablet Placebo
Number of Volunteers	18		18
Geometric Adjusted Mean AUC(IMP) (CV)	497.0 (0.53)		496.6 (0.53)
Treatment Ratio (Gaviscon Tablet/Placebo)			
Geometric Mean Ratio		1.001	
95% confidence interval		0.997 - 1.004	
p-value		0.7046	

Output File: t15_auc; Produced: 09MAR2012 14:06; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Treatment Sequence, Subject within Treatment Sequence, Period and Study Drug (i.e. Gaviscon Strawberry Flavour Tablets or Tablet Placebo).
CV : Geometric Coefficient of Variation

Table 14.2.22 Analysis of AUC(meal)$_{0\text{-}5}$ for the Whole Stomach for Gaviscon Original Aniseed Relief: ITT Population

	Gaviscon Original Aniseed Relief		Liquid Placebo
Number of Volunteers	17		17
Geometric Adjusted Mean AUC(IMP) (CV)	497.1 (0.40)		497.6 (0.40)
Treatment Ratio (Gaviscon Liquid/Placebo)			
Geometric Mean Ratio		0.999	
95% confidence interval		0.996 - 1.002	
p-value		0.5332	

Output File: t16_auc; Produced: 09MAR2012 14:08; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Treatment Sequence, Subject within Treatment Sequence, Period and Study Drug (i.e. Gaviscon Original Aniseed Relief or Liquid Placebo).
CV : Geometric Coefficient of Variation

Table 14.2.23 Analysis of AUC(IMP)$_{0-5}$ vs AUC(meal)$_{0-5}$ for Gaviscon Strawberry Tablets : ITT Population

		AUC$_{0-5}$ (%.min)		
		Gaviscon Strawberry Tablets		Meal
Number of Volunteers		18		18
Whole Stomach	Summary Statistics			
	N	18		18
	Mean	432.0		497.0
	SD	24.42		2.84
	Range	369.2 - 466.4		491.0 - 502.4
	Geometric Adjusted Mean (CV)	431.3 (4.04)		497.0 (4.04)
	Comparison : Gaviscon Tablets/Meal			
	Geometric Mean Ratio		0.868	
	95% confidence interval		0.843 - 0.893	
	p-value		<0.0001	
Upper Stomach	Summary Statistics			
	N	18		18
	Mean	350.8		391.1
	SD	77.49		40.50
	Range	153.1 - 446.0		318.9 - 452.8
	Geometric Adjusted Mean (CV)	340.3 (21.01)		389.0 (21.01)
	Comparison : Gaviscon Tablets/Meal			
	Geometric Mean Ratio		0.875	
	95% confidence interval		0.756 - 1.013	
	p-value		0.0707	

Output File: t24_auc; Produced: 09MAR2012 14:40; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Period, Subject within Period, and Administration (i.e. 111In(IMP) or 99mTc(meal))

CV : Geometric Coefficient of Variation

Table 14.2.24 Analysis of AUC(IMP) $_{0-5}$ vs AUC(meal) $_{0-5}$ for Gaviscon Original Aniseed Relief : ITT Population

		AUC_{0-5} (%.min)		
		Gaviscon Original Aniseed Relief		Meal
Number of Volunteers		17		17
Whole Stomach	Summary Statistics			
	N	17		17
	Mean	458.4		497.1
	SD	14.89		2.21
	Range	423.2 - 474.5		493.0 - 500.5
	Geometric Adjusted Mean (CV)	458.2 (2.41)		497.2 (2.41)
	Comparison : Gaviscon Liquid/Meal			
	Geometric Mean Ratio		0.922	
	95% confidence interval		0.906 - 0.938	
	p-value		<0.0001	
Upper Stomach	Summary Statistics			
	N	17		17
	Mean	338.7		405.5
	SD	86.16		48.93
	Range	187.1 - 445.9		309.9 - 460.4
	Geometric Adjusted Mean (CV)	327.4 (25.37)		402.3 (25.37)
	Comparison : Gaviscon Liquid/Meal			
	Geometric Mean Ratio		0.814	
	95% confidence interval		0.679 - 0.976	
	p-value		0.0286	

Output File: t25_auc; Produced: 09MAR2012 14:42; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Period, Subject within Period, and Administration (i.e. 111In(IMP) or 99mTc(meal))

CV : Geometric Coefficient of Variation

Table 14.2.25 Analysis of ratio of Upper Stomach AUC_{0-5} to Whole Stomach AUC_{0-5} for Gaviscon Strawberry Flavour Tablet vs Meal : ITT Population

	Upper Stomach AUC_{0-5} / Whole Stomach AUC_{0-5}		
	Gaviscon Strawberry Flavour Tablet		Meal
Number of Volunteers	18		18
Summary Statistics			
N	18		18
Mean	0.82		0.79
SD	0.190		0.080
Range	0.34 - 1.00		0.63 - 0.91
Geometric Adjusted Mean (CV)	0.79 (22.70)		0.78 (22.70)
Comparison Gaviscon Liquid/Meal			
Geometric Mean Ratio		1.008	
95% confidence interval		0.861 - 1.180	
p-value		0.9136	

Output File: t31_auc; Produced: 09MAR2012 14:59; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Period, Subject within Period and Administration (i.e. Gaviscon Strawberry Flavour Tablet or Meal)
CV : Geometric Coefficient of Variation

Table 14.2.26 Analysis of ratio of Upper Stomach AUC_{0-5} to Whole Stomach AUC_{0-5} for Gaviscon Original Aniseed Relief vs Meal : ITT Population

	Upper Stomach AUC_{0-5} / Whole Stomach AUC_{0-5}		
	Gaviscon Original Aniseed Relief		Meal
Number of Volunteers	17		17
Summary Statistics			
N	17		17
Mean	0.74		0.82
SD	0.188		0.098
Range	0.43 - 0.99		0.62 - 0.93
Geometric Adjusted Mean (CV)	0.71 (25.42)		0.81 (25.42)
Comparison Gaviscon Liquid/Meal			
Geometric Mean Ratio		0.883	
95% confidence interval		0.736 - 1.059	
p-value		0.1664	

Output File: t32_auc; Produced: 23MAR2012 15:03; Final

Note: p-value from analysis of variance of log-transformed data adjusted for Period, Subject within Period and Administration (i.e. Gaviscon Original Aniseed Relief or Meal)
CV : Geometric Coefficient of Variation

Table 14.2.27 AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 1, 2, 3, 4, 5, 10, 14, 60 and 240 minutes : ITT Population

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 1 minute : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	81.0	89.7	90.9	93.1
		SD	5.34	5.25	3.82	3.64
		Range	66.2 - 89.1	78.1 - 97.0	82.1 - 96.3	86.8 - 98.8
	Upper Stomach	N	18	18	17	17
		Mean	65.1	65.7	69.5	77.2
		SD	16.09	17.60	15.55	10.89
		Range	22.3 - 81.3	22.9 - 87.4	43.6 - 90.0	60.9 - 96.2
Meal	Whole Stomach	N	18	18	17	17
		Mean	99.9	99.9	99.9	99.9
		SD	0.11	0.14	0.09	0.10
		Range	99.6 - 100.1	99.6 - 100.1	99.7 - 100.0	99.7 - 100.0
	Upper Stomach	N	18	18	17	17
		Mean	79.5	78.3	82.4	79.5
		SD	8.37	11.31	10.07	7.85
		Range	63.9 - 91.5	55.0 - 97.8	62.3 - 94.4	63.3 - 94.9

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 2 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	166.9	182.5	183.4	187.1
		SD	10.70	7.78	5.57	6.41
		Range	138.0 - 181.4	161.7 - 192.9	174.8 - 192.7	173.0 - 196.5
	Upper Stomach	N	18	18	17	17
		Mean	132.8	131.4	138.0	152.6
		SD	32.80	36.74	32.20	23.58
		Range	48.8 - 167.8	47.0 - 175.2	83.0 - 183.6	117.1 - 193.3
Meal	Whole Stomach	N	18	18	17	17
		Mean	199.5	199.5	199.5	199.6
		SD	0.45	0.55	0.35	0.41
		Range	198.6 - 200.4	198.5 - 200.5	198.9 - 200.1	198.9 - 200.1
	Upper Stomach	N	18	18	17	17
		Mean	158.3	156.2	164.1	158.5
		SD	16.59	22.49	19.99	15.51
		Range	127.7 - 182.5	109.2 - 195.3	124.4 - 187.6	126.9 - 188.7

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 3 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	253.6	276.0	275.5	281.2
		SD	14.95	9.39	5.52	7.65
		Range	213.5 - 276.3	252.5 - 289.8	266.0 - 283.2	266.8 - 295.4
	Upper Stomach	N	18	18	17	17
		Mean	202.8	195.6	206.3	226.4
		SD	48.98	56.06	50.08	36.60
		Range	78.5 - 258.6	65.5 - 264.6	116.6 - 271.5	173.6 - 287.4
Meal	Whole Stomach	N	18	18	17	17
		Mean	298.9	298.8	299.0	299.1
		SD	1.02	1.23	0.80	0.91
		Range	296.8 - 300.9	296.6 - 301.2	297.5 - 300.2	297.5 - 300.3
	Upper Stomach	N	18	18	17	17
		Mean	236.5	233.5	245.2	237.0
		SD	24.68	33.56	29.77	23.02
		Range	191.4 - 273.1	162.5 - 292.6	186.4 - 279.7	190.8 - 281.5

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 4 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	341.6	369.5	367.3	376.4
		SD	19.84	10.01	9.33	8.81
		Range	291.3 - 369.4	346.9 - 383.0	346.8 - 379.7	360.7 - 391.7
	Upper Stomach	N	18	18	17	17
		Mean	275.0	258.0	273.2	300.3
		SD	63.71	76.18	67.85	50.85
		Range	114.9 - 350.2	85.6 - 349.1	152.0 - 361.1	237.2 - 382.8
Meal	Whole Stomach	N	18	18	17	17
		Mean	398.1	397.9	398.2	398.4
		SD	1.82	2.19	1.41	1.62
		Range	394.3 - 401.6	394.0 - 402.2	395.5 - 400.3	395.6 - 400.5
	Upper Stomach	N	18	18	17	17
		Mean	314.1	310.3	325.7	314.8
		SD	32.64	44.52	39.42	30.38
		Range	255.2 - 363.1	214.9 - 389.6	248.2 - 370.6	254.9 - 373.2

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 5 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	432.0	462.5	458.4	470.1
		SD	24.42	11.06	14.89	10.86
		Range	369.2 - 466.4	440.6 - 477.9	423.2 - 474.5	443.9 - 487.5
	Upper Stomach	N	18	18	17	17
		Mean	350.8	319.8	338.7	371.5
		SD	77.49	96.21	86.16	66.01
		Range	153.1 - 446.0	104.0 - 429.3	187.1 - 445.9	284.7 - 474.4
Meal	Whole Stomach	N	18	18	17	17
		Mean	497.0	496.7	497.1	497.5
		SD	2.84	3.42	2.21	2.53
		Range	491.0 - 502.4	490.7 - 503.4	493.0 - 500.5	493.1 - 500.8
	Upper Stomach	N	18	18	17	17
		Mean	391.0	386.7	405.5	392.1
		SD	40.50	55.38	48.93	37.60
		Range	318.9 - 452.8	266.5 - 486.4	309.9 - 460.4	319.4 - 463.9

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 10 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	893.5	916.7	903.5	931.0
		SD	37.47	52.16	63.58	28.15
		Range	796.2 - 948.6	737.3 - 958.8	734.5 - 959.1	878.2 - 971.5
	Upper Stomach	N	18	18	17	17
		Mean	752.4	621.3	659.6	710.2
		SD	142.28	192.38	180.69	150.20
		Range	375.1 - 926.0	220.4 - 855.8	347.4 - 916.5	492.4 - 948.0
Meal	Whole Stomach	N	18	18	17	17
		Mean	988.0	986.6	988.5	990.0
		SD	11.35	13.70	8.84	10.13
		Range	964.1 - 1009.8	962.8 - 1013.6	971.9 - 1002.2	972.4 - 1003.0
	Upper Stomach	N	18	18	17	17
		Mean	765.9	760.6	795.4	770.4
		SD	78.50	108.65	94.88	72.53
		Range	636.8 - 896.4	511.7 - 966.4	601.3 - 891.8	645.8 - 916.7

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 14 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	1359.5	1347.6	1339.4	1371.8
		SD	50.59	121.68	130.20	86.54
		Range	1245.3 - 1431.9	943.1 - 1444.4	999.0 - 1439.6	1185.4 - 1456.0
	Upper Stomach	N	18	18	17	17
		Mean	1171.2	907.8	983.5	1040.2
		SD	213.11	283.02	281.62	245.96
		Range	599.0 - 1415.0	309.9 - 1255.8	510.0 - 1395.4	683.6 - 1419.3
Meal	Whole Stomach	N	18	18	17	17
		Mean	1473.0	1469.9	1474.1	1477.5
		SD	25.54	30.82	19.89	22.80
		Range	1419.2 - 1522.0	1416.2 - 1530.6	1436.9 - 1504.9	1437.8 - 1506.8
	Upper Stomach	N	18	18	17	17
		Mean	1124.7	1121.8	1169.6	1134.7
		SD	115.56	161.22	138.88	107.33
		Range	935.0 - 1330.9	735.4 - 1440.1	871.6 - 1315.0	950.7 - 1369.2

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 60 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	5471.4	4293.3	4845.8	4594.5
		SD	523.54	856.12	987.70	1164.26
		Range	3854.4 - 5774.5	1805.3 - 5314.0	2600.2 - 5774.0	2740.8 - 5876.7
	Upper Stomach	N	18	18	17	17
		Mean	4961.3	2837.9	3767.5	3266.4
		SD	943.55	942.44	1320.11	1219.76
		Range	2575.1 - 5623.2	762.5 - 4371.7	1471.5 - 5506.2	1569.3 - 4978.7
Meal	Whole Stomach	N	18	18	17	17
		Mean	5489.1	5425.1	5598.2	5597.2
		SD	342.40	265.16	236.37	262.08
		Range	4735.1 - 6093.1	4910.1 - 5821.0	5020.1 - 5913.7	5076.8 - 5988.0
	Upper Stomach	N	18	18	17	17
		Mean	3787.5	3880.8	4082.2	3963.7
		SD	514.63	685.62	572.12	511.11
		Range	2864.3 - 4942.6	2359.6 - 5210.0	2766.5 - 5008.5	2629.8 - 5094.8

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

AUC(IMP) for the Whole Stomach and Upper Stomach by Treatment after 240 minutes : ITT Population

			AUC (%.min)			
			Gaviscon Strawberry Flavour Tablets	Tablet Placebo	Gaviscon Original Aniseed Relief	Liquid Placebo
	Number of Volunteers		18	18	17	17
IMP	Whole Stomach	N	18	18	17	17
		Mean	15409.0	6999.1	11675.0	8522.1
		SD	3679.61	1831.36	4112.76	4024.28
		Range	6828.3 - 19204.7	2599.0 - 9490.9	4549.2 - 19960.9	3128.5 - 15410.9
	Upper Stomach	N	18	18	17	17
		Mean	12909.1	4460.2	8722.5	5481.4
		SD	4047.63	1723.30	4219.12	2906.47
		Range	4572.7 - 18194.8	966.3 - 7306.5	2552.7 - 18538.2	1716.5 - 11128.9
Meal	Whole Stomach	N	18	18	17	17
		Mean	11344.4	10773.7	12464.8	12345.2
		SD	1441.26	1537.20	2160.02	2390.02
		Range	7548.3 - 13030.3	7518.6 - 13277.2	8897.6 - 16661.4	8649.1 - 15987.2
	Upper Stomach	N	18	18	17	17
		Mean	6607.1	6684.9	7860.9	7598.3
		SD	1456.66	1877.03	1896.34	1900.03
		Range	3690.2 - 9552.1	3229.0 - 10142.4	4015.5 - 11250.1	3522.6 - 10092.4

Output File: t14_auc; Produced: 07JUN2012 08:55; Final

Table 14.2.28 AUC(IMP) whole stomach; (AUC IMP / AUC Meal) whole stomach, and (AUC IMP upper / AUC IMP whole stomach) / (AUC meal upper stomach / AUC meal whole)

Analysis of IMP Retention in Whole Stomach up to each time point

	AUC IMP Whole Stomach					
	Gaviscon® Strawberry	Placebo Tablet	Gaviscon® Strawberry / Placebo Tablet			
Minutes since IMP	Geometric LS Mean	Geometric LS Mean	Ratio	95% CI		
				Lower	Upper	P-Value
0.5	39.74	44.01	0.90	0.87	0.94	<.0001
1	80.87	89.56	0.90	0.87	0.93	<.0001
1.5	123.39	135.83	0.91	0.88	0.94	<.0001
2	166.57	182.31	0.91	0.88	0.94	<.0001
2.5	209.75	229.18	0.92	0.89	0.95	<.0001
3	253.19	275.84	0.92	0.89	0.95	<.0001
3.5	296.86	322.39	0.92	0.89	0.95	<.0001
4	341.06	369.34	0.92	0.89	0.95	0.0001
4.5	385.99	416.18	0.93	0.90	0.96	<.0001
5	431.28	462.33	0.93	0.90	0.96	<.0001
6	522.60	554.42	0.94	0.91	0.97	0.0004
7	614.69	646.10	0.95	0.92	0.98	0.0024
8	707.02	736.87	0.96	0.93	0.99	0.0122
9	799.74	826.60	0.97	0.94	1.00	0.0526
10	892.69	915.12	0.98	0.94	1.01	0.1722
11	985.53	1002.10	0.98	0.94	1.02	0.3936
12	1078.37	1088.04	0.99	0.95	1.03	0.6601
13	1171.58	1173.85	1.00	0.96	1.04	0.9269
14	1265.08	1258.36	1.01	0.96	1.05	0.8078
20	1829.85	1741.53	1.05	0.99	1.11	0.0774
40	3691.02	3127.62	1.18	1.09	1.27	0.0003
60	5439.44	4177.81	1.30	1.20	1.41	<.0001
80	7066.99	4945.73	1.43	1.31	1.56	<.0001
100	8564.42	5493.08	1.56	1.43	1.70	<.0001
120	9897.69	5879.54	1.68	1.54	1.85	<.0001
140	11083.55	6145.93	1.80	1.65	1.98	<.0001
160	12138.58	6319.08	1.92	1.75	2.11	<.0001
180	13051.80	6447.02	2.02	1.85	2.22	<.0001
200	13808.73	6561.18	2.10	1.92	2.31	<.0001
220	14402.33	6645.81	2.17	1.97	2.39	<.0001
240	14869.57	6716.80	2.21	2.00	2.45	<.0001

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Page 1 of 1

Analysis of IMP Retention corrected for the meal in the Whole Stomach up to each time point

	Whole Stomach (AUC IMP/ AUC Meal)					
	Gaviscon® Strawberry	Placebo Tablet	Gaviscon® Strawberry / Placebo Tablet			
Minutes since IMP	Geometric LS Mean	Geometric LS Mean	Ratio	95% CI		
				Lower	Upper	P-Value
0.5	0.82	0.91	0.90	0.87	0.94	<.0001
1	0.83	0.93	0.90	0.87	0.93	<.0001
1.5	0.85	0.94	0.91	0.88	0.94	<.0001
2	0.86	0.94	0.91	0.88	0.94	<.0001
2.5	0.87	0.95	0.91	0.88	0.94	<.0001
3	0.87	0.95	0.92	0.89	0.95	<.0001
3.5	0.88	0.95	0.92	0.89	0.95	<.0001
4	0.88	0.95	0.92	0.89	0.95	<.0001
4.5	0.89	0.96	0.93	0.90	0.96	0.0001
5	0.89	0.96	0.93	0.90	0.96	0.0003
6	0.90	0.96	0.94	0.91	0.97	0.0012
7	0.91	0.95	0.95	0.92	0.98	0.0038
8	0.91	0.95	0.96	0.93	0.99	0.0127
9	0.92	0.95	0.97	0.93	1.00	0.0407
10	0.92	0.95	0.97	0.94	1.01	0.1156
11	0.92	0.94	0.98	0.95	1.02	0.2803
12	0.93	0.94	0.99	0.95	1.03	0.5427
13	0.93	0.93	1.00	0.96	1.04	0.8371
14	0.93	0.93	1.00	0.96	1.04	0.8561
20	0.94	0.90	1.05	1.00	1.10	0.0604
40	0.97	0.83	1.17	1.10	1.25	0.0001
60	1.00	0.78	1.29	1.20	1.39	<.0001
80	1.03	0.73	1.42	1.31	1.52	<.0001
100	1.07	0.69	1.54	1.43	1.66	<.0001
120	1.11	0.67	1.66	1.54	1.79	<.0001
140	1.15	0.65	1.77	1.64	1.90	<.0001
160	1.19	0.64	1.87	1.74	2.01	<.0001
180	1.23	0.63	1.96	1.82	2.11	<.0001
200	1.27	0.63	2.02	1.88	2.18	<.0001
220	1.30	0.63	2.07	1.92	2.24	<.0001
240	1.32	0.63	2.11	1.94	2.29	<.0001

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Page 1 of 1

Analysis of IMP distribution corrected for the meal distribution up to each time point

	(AUC IMP Upper / AUC IMP Whole) / (AUC Meal Upper / AUC Meal Whole)					
	Gaviscon® Strawberry	Placebo Tablet	Gaviscon® Strawberry / Placebo Tablet			
Minutes since IMP	Geometric LS Mean	Geometric LS Mean	Ratio	95% CI		
				Lower	Upper	P-Value
0.5	1.04	0.96	1.08	0.94	1.24	0.2407
1	1.04	0.95	1.10	0.96	1.26	0.1543
1.5	1.04	0.94	1.11	0.97	1.27	0.1336
2	1.04	0.93	1.12	0.96	1.29	0.1291
2.5	1.04	0.92	1.13	0.97	1.31	0.1030
3	1.04	0.91	1.15	0.99	1.34	0.0707
3.5	1.05	0.90	1.17	1.00	1.36	0.0499
4	1.05	0.89	1.18	1.01	1.38	0.0348
4.5	1.06	0.88	1.20	1.03	1.40	0.0233
5	1.07	0.88	1.21	1.04	1.41	0.0156
6	1.08	0.87	1.24	1.07	1.44	0.0074
7	1.09	0.87	1.26	1.09	1.46	0.0038
8	1.10	0.86	1.28	1.11	1.47	0.0022
9	1.11	0.86	1.29	1.12	1.48	0.0014
10	1.12	0.86	1.30	1.13	1.49	0.0009
11	1.12	0.86	1.31	1.15	1.49	0.0005
12	1.13	0.86	1.32	1.16	1.50	0.0004
13	1.14	0.86	1.32	1.16	1.50	0.0003
14	1.14	0.86	1.33	1.17	1.51	0.0002
20	1.16	0.85	1.36	1.22	1.53	<.0001
40	1.24	0.87	1.42	1.31	1.55	<.0001
60	1.30	0.89	1.45	1.34	1.56	<.0001
80	1.34	0.91	1.47	1.37	1.58	<.0001
100	1.39	0.93	1.49	1.38	1.60	<.0001
120	1.42	0.95	1.49	1.39	1.60	<.0001
140	1.44	0.97	1.49	1.39	1.60	<.0001
160	1.46	0.98	1.48	1.39	1.59	<.0001
180	1.45	0.99	1.46	1.37	1.56	<.0001
200	1.44	1.00	1.45	1.36	1.54	<.0001
220	1.43	1.00	1.43	1.35	1.52	<.0001
240	1.42	1.01	1.41	1.33	1.50	<.0001

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Page 1 of 1

14.3 Safety Data

Table 14.3.1 Extent of Exposure to Study Medication: Safety Population

			Phase 1 N (%)	Phase 2 N (%)
Number of Volunteers			36	36
Standard Radiolabelled Meal	Consumed		36 (100.0%)	35 (97.2%)
	Not Consumed		0 (0.0%)	1 (2.8%)
Study Medication	Administered	Gaviscon Strawberry Flavour Tablets	9 (25.0%)	9 (25.0%)
		Tablet Placebo	9 (25.0%)	9 (25.0%)
		Gaviscon Original Aniseed Relief	9 (25.0%)	8 (22.2%)
		Liquid Placebo	9 (25.0%)	9 (25.0%)
	Not Administered	Gaviscon Strawberry Flavour Tablets	0 (0.0%)	0 (0.0%)
		Tablet Placebo	0 (0.0%)	0 (0.0%)
		Gaviscon Original Aniseed Relief	0 (0.0%)	1 (2.8%)
		Liquid Placebo	0 (0.0%)	0 (0.0%)

Output File: t33_extexp; Produced: 02MAR2012 11:46; Final

Table 14.3.2 Laboratory Data : Safety Population

		Screening Visit N (%)	Post-study Visit N (%)
No. of Volunteers		36	36
Bio./Haem./Urin.	Normal	8 (22.2%)	2 (5.6%)
	Abnormal (Not Clinically Significant)	28 (77.8%)	34 (94.4%)
	Abnormal (Clinically Significant)	0 (0.0%)	0 (0.0%)

Output File: t34_haemass; Produced: 02MAR2012 11:13; Final

Note: Only results recorded at scheduled visits included in this summary.

Table 14.3.3 Vital Signs : Safety Population

Vital Sign		Screening Visit	Post-study Visit	Change from Screening to Post-study
No. of Volunteers	N	36	36	36
Systolic Blood Pressure (mmHg)	N	36	36	36
	Mean	125.9	127.2	1.4
	S.D.	7.8	8.6	9.1
	Range	106 - 140	113 - 142	-17 - 18
Diastolic Blood Pressure (mmHg)	N	36	36	36
	Mean	72.0	72.4	0.4
	S.D.	8.0	7.4	6.3
	Range	57 - 87	60 - 87	-12 - 12
Pulse Rate (bpm)	N	36	36	36
	Mean	59.6	63.1	3.5
	S.D.	9.7	11.1	7.6
	Range	42 - 87	36 - 86	-15 - 16
Oral Temperature (°C)	N	36	36	36
	Mean	36.33	36.34	0.02
	S.D.	0.32	0.30	0.32
	Range	35.9 - 37.2	35.9 - 37.0	-0.6 - 0.6

Output File: t35_vital; Produced: 02MAR2012 11:29; Final

Table 14.3.4 ECG Results : Safety Population

		Screening Visit N (%)	Post-study Visit N (%)
No. of Volunteers		36	36
ECG Results	Normal	34 (94.4%)	31 (86.1%)
	Abnormal (Not Clinically Significant)	2 (5.6%)	5 (13.9%)
	Abnormal (Clinically Significant)	0 (0.0%)	0 (0.0%)

Output File: t36_ecg; Produced: 02MAR2012 11:32; Final

14.4 Displays of Adverse Events

No additional displays of adverse events are provided.

14.4.1 Listings of Deaths, other Serious and Significant Adverse Events

Not applicable.

14.4.2 Narratives of Deaths, other Serious and certain other Significant Adverse Events

Not applicable.

14.4.3 Clinically Significant Abnormal Laboratory Value Listing (each subject)

No clinically significant abnormal laboratory values were found.

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