A Phase Three, Multicenter, Randomized, Double-Blind, Placebo Controlled Study to Evaluate the Efficacy of the Travelers' Diarrhea Vaccine System

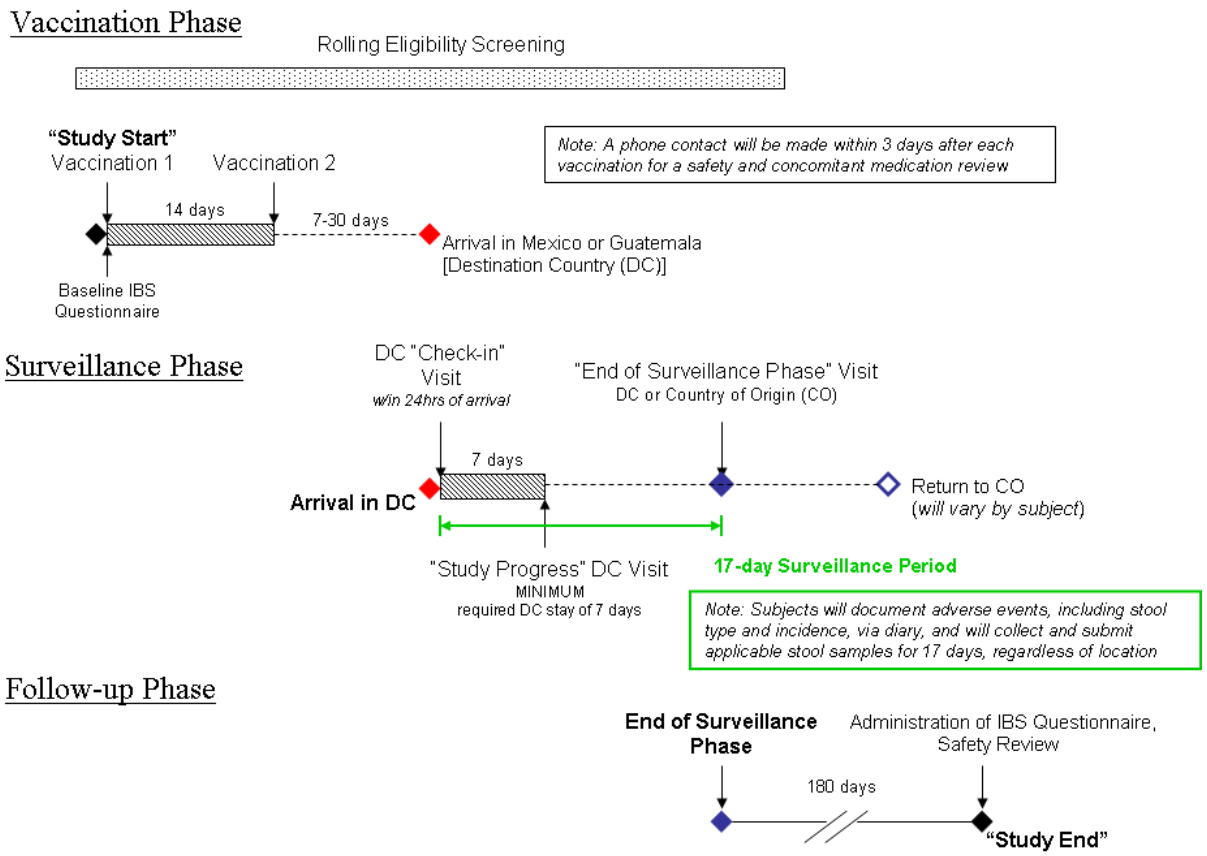
Protocol Number: ELT301
EudraCT number: 2008-008726-75
ClinicalTrials.gov id: NCT00993681

Sponsor: Intercell USA, Inc.
20 Firstfield Road
Gaithersburg, Maryland 20878

Name of Investigational Product: Heat-Labile Enterotoxin of *Escherichia coli*

Overall Study Design and Plan

Study ELT301 was a multicenter, randomized, double-blinded, placebo-controlled study designed to evaluate the efficacy of the TD Vaccine System in travelers to Latin America. This pivotal field efficacy study was designed to enroll up to 2,400 eligible male and female subjects (18 to 64 years). This study was conducted across multiple clinical sites in travelers beginning their study participation in the United Kingdom and Germany, herein referred to as the Country of Origin (CO), before traveling to Mexico or Guatemala [Destination Country (DC)] for surveillance. Two transcutaneous immunizations (skin preparation with the skin preparation system (SPS):Buffer and LT or placebo patch application) were performed 14 days apart, on alternating deltoids by a clinician in the CO. Subjects received 37.5µg LT or placebo patches according to randomized (1:1) group assignment. Patches were to be worn for six hours prior to removal by the subject.



Efficacy assessments were based on subject diary-reported diarrheal events and analysis of stool samples submitted during the Surveillance Phase for detection of ETEC and other co-pathogens. The primary endpoint of the study was incidence of cases with VPO reported during the Surveillance Phase; a VPO is a case of moderate/severe diarrhea in which LT, LT and ST or ST toxins (ETEC) are detected by either PCR or DNA hybridization (and no co-pathogen is detected) from diarrheal stool samples that are collected during the first diarrheal episode.

Main objective of the trial:
The primary objective of the study was to evaluate the efficacy of the Travelers' Diarrhea (TD) Vaccine System to prevent moderate to severe enterotoxigenic E. coli (ETEC) disease in travelers to Mexico and Guatemala.

Analysis Populations of Randomized Subjects

Analysis Populations	Group 1 (37.5□g LT) N=1016 n (%)	Group 2 (Placebo) N=1020 n (%)	Overall N=2036 n (%)
Intent-to-Treat (ITT) [1]	1016 (100)	1020 (100)	2036 (100)
Safety [2]	1014 (>99)	1018 (>99)	2032 (>99)
Modified ITT (mITT) [3]	921 (91)	912 (89)	1833 (90)
Per Protocol (PPP) [4]	821 (81)	823 (81)	1644 (81)
Reasons for Exclusion from PPP [5]			
Did not receive two vaccinations	50 (5)	45 (4)	95 (5)
Did not complete the DC Check-in Visit	55 (5)	65 (6)	120 (6)
Received less than five hours exposure at either vaccination	21 (2)	34 (3)	55 (3)
Used antibiotics or antibacterials in DC [6]	31 (3)	20 (2)	51 (3)
Used antipropulsives in DC [6]	8 (<1)	5 (<1)	13 (<1)
Less than 11 days between vaccinations	2 (<1)	2 (<1)	4 (<1)
Arrived in DC less than seven days after Vaccination 2	2 (<1)	2 (<1)	4 (<1)
Vaccination error	2 (<1)	2 (<1)	4 (<1)
Used bismuth products in DC [6]	2 (<1)	1 (<1)	3 (<1)

Note: Percentages are based on the number of randomized subjects.
[1] All consented, randomized subjects.
[2] All subjects who received at least one vaccination (active or placebo) as randomized.
[3] All consented, randomized subjects who entered the DC within the study period.
[4] All subjects who were consented, randomized, received both study vaccinations as randomized, arrived in the DC, successfully attended the DC Check-in and Study Progress Visits, and completed the Surveillance Phase Diary information for each day up through the date of completion of the Study Progress Visit.
[5] With the exception of the category "Did not receive two vaccinations", only those subjects that received two vaccinations were counted. A subject may have been counted more than once. Subjects were counted for each PPP exclusion criterion met. Subject 2030165 and Subject 2070024 were excluded from the PPP by the ECAC prior to the Blinded Safety Review. Subsequent to the review, data for these subjects was changed such that they no longer met the PPP exclusion criteria. However, they continue to be excluded from the PPP for the reasons stated during the Blinded Safety Review.
[6] Use of antibiotics/antibacterials/antipropulsives in DC - For subjects who had a diarrheal episode, use was disallowed prior to the fourth stool sample. For subjects who did not have an episode, use was disallowed during DC visit.
DC=Destination Country; N=Number of randomized subjects per group; n=Number of subjects in the category indicated per group.

Demographic Characteristics

	Safety Population [1]			mITT Population [2]			PPP [3]		
	Group 1 (37.5□g LT) N=1014	Group 2 (Placebo) N=1018	Overall N=2032	Group 1 (37.5□g LT) N=921	Group 2 (Placebo) N=912	Overall N=1833	Group 1 (37.5□g LT) N=821	Group 2 (Placebo) N=823	Overall N=1644
Age (years) [4]									
Mean (SD)	28.6 (8.76)	28.5 (8.87)	28.6 (8.81)	28.5 (8.71)	28.5 (8.94)	28.5 (8.82)	28.9 (8.90)	28.7 (9.02)	28.8 (8.96)
Median	26.1	25.6	25.8	25.9	25.6	25.8	26.2	25.8	26.0
Min, Max	18, 64	18, 63	18, 64	18, 64	18, 63	18, 64	18, 64	18, 63	18, 64
Gender									
Female, n (%)	553 (55)	539 (53)	1092 (54)	503 (55)	488 (54)	991 (54)	449 (55)	439 (53)	888 (54)
Male, n (%)	461 (46)	479 (47)	940 (46)	418 (45)	424 (47)	842 (46)	372 (45)	384 (47)	756 (46)
Race									
Caucasian, n (%)	935 (92)	945 (93)	1880 (93)	854 (93)	849 (93)	1703 (93)	763 (93)	766 (93)	1529 (93)
Asian, n (%)	48 (5)	43 (4)	91 (5)	40 (4)	36 (4)	76 (4)	34 (4)	33 (4)	67 (4)
Black, n (%)	23 (2)	13 (1)	36 (2)	19 (2)	12 (1)	31 (2)	16 (2)	12 (2)	28 (2)
Other, n (%)	8 (<1)	17 (2)	25 (1)	8 (<1)	15 (2)	23 (1)	8 (1)	12 (2)	20 (1)
Ethnicity									
Not Hispanic or Latino, n (%)	995 (98)	992 (97)	1987 (98)	905 (98)	889 (98)	1794 (98)	807 (98)	802 (97)	1609 (98)
Hispanic or Latino, n (%)	19 (2)	26 (3)	45 (2)	16 (2)	23 (3)	39 (2)	14 (2)	21 (3)	35 (2)

	Safety Population [1]			mITT Population [2]			PPP [3]		
	Group 1 (37.5□g LT) N=1014	Group 2 (Placebo) N=1018	Overall N=2032	Group 1 (37.5□g LT) N=921	Group 2 (Placebo) N=912	Overall N=1833	Group 1 (37.5□g LT) N=821	Group 2 (Placebo) N=823	Overall N=1644
Weight (kg)									
Mean (SD)	72.37 (14.140)	71.70 (14.160)	72.03 (14.151)	72.57 (14.391)	71.81 (14.297)	72.19 (14.345)	72.31 (14.089)	71.83 (14.419)	72.07 (14.253)
Median	71.90	70.00	71.00	72.00	70.00	71.00	71.35	70.00	70.90
Min, Max	42.7, 160.0	39.8, 175.0	39.8, 175.0	42.7, 160.0	39.8, 175.0	39.8, 175.0	42.7, 152.4	39.8, 175.0	39.8, 175.0
Height (cm)									
Mean (SD)	174.4 (9.74)	174.0 (10.01)	174.2 (9.88)	174.5 (9.79)	174.2 (10.18)	174.3 (9.99)	174.4 (9.71)	174.2 (10.36)	174.3 (10.04)
Median	175.0	174.0	174.5	175.0	174.0	175.0	175.0	174.0	175.0
Min, Max [5]	145, 205	64, 199	64, 205	145, 205	64, 199	64, 205	149, 205	64, 199	64, 205

Note: All percentages are based on the number of subjects in the specified population.

[1] All subjects who received at least one vaccination (active or placebo) as randomized.

[2] All consented, randomized subjects who entered the DC within the study period.

[3] All subjects who were consented, randomized, received both study vaccinations as randomized, arrived in the DC, successfully attended the DC Check-in and Study Progress Visits, and completed the Surveillance Phase Diary information for each day up through the date of completion of the Study Progress Visit.

[4] Age was calculated as an integer value indicating the number of full years passed since birth.

[5] Subsequent to database lock for the final analysis, it was determined that the height for Subject 2070106 was incorrectly entered as 64 cm when in actuality the subject's height was 164 cm. This error was documented in a Note to File and was not changed in the database, as the impact on the results is nominal.

mITT=Modified Intent-to-Treat; PPP=Per Protocol Population; N=Number of subjects in the specified population per group; n=Number of subjects in the category indicated per group; kg=Kilogram; cm=Centimeter;

Country of Origin and Destination City, Safety Population

	Safety Population [1]		
	Group 1 (37.5□g LT) N=1014	Group 2 (Placebo) N=1018	Overall N=2032
	n (%)	n (%)	n (%)
Country of Origin (CO)			
United Kingdom	575 (57)	577 (57)	1152 (57)
Germany	439 (43)	441 (43)	880 (43)
Destination Country (DC)			
Mexico	630 (62)	628 (62)	1258 (62)
Guatemala	290 (29)	283 (28)	573 (28)
Did not travel	94 (9)	107 (11)	201 (10)
Destination City [1]			
Mexico City	362 (36)	372 (37)	734 (36)
Antigua	179 (18)	167 (16)	346 (17)
Oaxaca	118 (12)	113 (11)	231 (11)
Cuernavaca	89 (9)	73 (7)	162 (8)
Guatemala City	68 (7)	71 (7)	139 (7)
Guadalajara	54 (5)	60 (6)	114 (6)
Panajachel	32 (3)	38 (4)	70 (3)
Quetzaltenango	11 (1)	7 (<1)	18 (<1)
San Miguel	7 (<1)	10 (1)	17 (<1)

Note: Percentages are based on the number of subjects in the specified analysis population
N=Number of subjects in the specified analysis population per group; n=Number of subjects in the category indicated per group.
[1] The destination city refers to the city in which the DC Check-in Visit took place. Subjects frequently traveled throughout Latin America and were seen at multiple DC study sites.

Duration (Hours) of Patch Exposure

	Safety Population [1]		mITT Population [2]		PPP [3]	
	Group 1 (37.5□g LT) N=1014	Group 2 (Placebo) N=1018	Group 1 (37.5□g LT) N=921	Group 2 (Placebo) N=912	Group 1 (37.5□g LT) N=821	Group 2 (Placebo) N=823
Vaccination 1						
Subjects Vaccinated, n	1014	1018	921	912	821	823
Patch Exposure (Hours)						
Mean (SD)	6.2 (0.88)	6.2 (0.58)	6.2 (0.46)	6.2 (0.56)	6.2 (0.42)	6.2 (0.54)
Median	6.1	6.0	6.1	6.0	6.1	6.0
Min, Max	4, 30	2, 17	4, 10	2, 17	5, 9	5, 17
Vaccination 2						
Subjects Vaccinated	965	974	911	910	821	823
Patch Exposure (Hours)						
Mean (SD)	6.2 (0.65)	6.3 (0.78)	6.2 (0.60)	6.3 (0.79)	6.3 (0.57)	6.3 (0.77)
Median	6.0	6.1	6.0	6.1	6.0	6.1
Min, Max	3, 14	2, 17	3, 11	2, 17	5, 11	5, 17

Note: Only subjects with patch application and removal data are included.
[1] All subjects who received at least one vaccination (active or placebo) as randomized.
[2] All consented, randomized subjects who entered the DC within the study period.
[3] All subjects who were consented, randomized, received both study vaccinations as randomized, arrived in the DC, successfully attended the DC Check-in and Study Progress Visits, and completed the Surveillance Phase Diary information for each day up through the date of completion of the Study Progress Visit.
mITT=Modified Intent-to-Treat; PPP=Per Protocol Population; SD=Standard deviation; Min=Minimum; Max=Maximum; N=Number of subjects in the specified analysis population per group.

Primary Endpoint: Incidence of Vaccine Preventable Outcome [1] Diarrheal Episodes Experienced during the Surveillance Phase (First Episode Experienced), Per Protocol and mITT Populations

	Group 1 (37.5□g LT)		Group 2 (Placebo)		VE% [2]	VE 95% CI [3]	p-value [4]
Analysis Population	n/N (%)	95% CI	n/N (%)	95% CI			
Per Protocol Population	30/821 (3.7)	2.5, 5.2	46/823 (5.6)	4.1, 7.4	34.60	-2.20, 58.90	0.0621
mITT Population	35/921 (3.8)	2.7, 5.2	48/912 (5.3)	3.9, 6.9	27.80	-10.50, 53.30	0.1332

Note: All percentages are based on the number of subjects in the specified analysis population per group.
[1] All moderate/severe diarrheal cases (those with four or more unformed stools as the greatest frequency observed in any consecutive 24-hour period during a diarrheal episode) in which LT, LT and ST or ST toxins were detected by either PCR or DNA hybridization from diarrheal stool samples that were passed during the first diarrheal episode and were otherwise pathogen-free.
[2] Vaccine Efficacy defined as 100*(1-Pt/Pc) where Pt=fraction of cases in the LT Patch group and Pc=fraction of cases in the Placebo Patch group.
[3] Vaccine Efficacy 95% confidence interval for the ratio of two binomial proportions.
[4] Exact unconditional test of treatment equality (Barnard's).
CI=Confidence interval; mITT=Modified Intent-to-Treat; VE=Vaccine efficacy; N=Number of subjects in the specified analysis population per group; n= Number of subjects with one or more VPO diarrheal episode per group.

This study failed to meet the primary endpoint. VPO incidence was low in both treatment groups, with a slightly lower incidence in the LT Group as compared to the Placebo Group in each analysis population (PPP: 3.7% in LT Group, 5.6% in Placebo Group; mITT Population: 3.8% in LT Group, 5.3% in Placebo Group). Vaccine efficacy (VE) was 34.60% (VE 95% CI: -2.20%, 58.90%; p=0.0621) for the PPP and 27.80% (VE 95% CI: -10.50%, 53.30%; p=0.1332) for the mITT Population.

Overall Summary of All Adverse Events, Safety Population

	Group 1 (37.5□g LT) N=1014	Group 2 (Placebo) N=1018	Overall N=2032	p-value [1]
	n (%)	n (%)	n (%)	
Any Adverse Events [2]				
Number of adverse events	12659	4550	17209	---
Subjects with at least one adverse event	981 (97)	864 (85)	1845 (91)	---
Subjects with an adverse event related to study drug [3]	951 (94)	637 (63)	1588 (78)	---
Subjects with a serious adverse event	14 (1)	11 (1)	25 (1)	---
Subjects with an adverse event leading to study withdrawal	3 (<1)	0 (0)	3 (<1)	---

Any Local Adverse Events [4]				
Number of adverse events	9333	1444	10777	---
Subjects with at least one adverse event	943 (93)	574 (56)	1517 (75)	**<0.0001**
Subjects with an adverse event related to study drug [3]	941 (93)	567 (56)	1508 (74)	**<0.0001**
Subjects with a serious adverse event	0 (0)	0 (0)	0 (0)	NA
Subjects with an adverse event leading to study withdrawal	0 (0)	0 (0)	0 (0)	---
Any Systemic Adverse Events [5]				
Number of adverse events	3326	3106	6432	---
Subjects with at least one adverse event	765 (75)	750 (74)	1515 (75)	0.3866
Subjects with an adverse event related to study drug [2]	278 (27)	211 (21)	489 (24)	**0.0005**
Subjects with a serious adverse event	14 (1)	11 (1)	25 (1)	0.5540
Subjects with an adverse event leading to study withdrawal	3 (<1)	0 (0)	3 (<1)	---

Note: Percentages are based on the number of subjects in the Safety Population.
Note: Only treatment-emergent adverse events are summarized
[1] Fisher's Exact Test
[2] Local and Systemic AEs
[3] Includes those adverse events considered possibly, probably, or definitely related to study drug by the Investigator.
[4] Local adverse events were those events that occurred at the site of patch application.
[5] Systemic adverse events were those events that occurred outside the site of patch application.
N=Number of subjects per group in the Safety Population; n=Number of subjects meeting the specified criteria; NA=Not applicable

Incidence of Non-Solicited Systemic Adverse Events Reported in ≥2% of Subjects by Vaccination, Study Phase and Preferred Term, Safety Population

	Group 1 (37.5□g LT)	Group 2 (Placebo)
Preferred Term	**n (%)**	**n (%)**
Vaccination Phase - Vaccination 1 [1]	**N=1014**	**N=1018**
Any non-solicited systemic adverse event	263 (26)	206 (20)
Headache	63 (6)	56 (6)
Nasopharyngitis	23 (2)	18 (2)
Vaccination Phase - Vaccination 2 [2]	**N=965**	**N=974**
Any non-solicited systemic adverse event	231 (24)	192 (20)
Headache	65 (7)	68 (7)
Nasopharyngitis	24 (3)	22 (2)
Surveillance Phase [3]	**N=920**	**N=911**
Any non-solicited systemic adverse event	507 (55)	518 (57)
Diarrhoea	400 (44)	426 (47)
Abdominal Pain	108 (12)	108 (12)
Headache	111 (12)	111 (12)
Fecal Urgency	91 (10)	97 (11)
Nausea	66 (7)	79 (9)
Vomiting	34 (4)	34 (4)
Pyrexia	27 (3)	23 (3)

Preferred Term	Group 1 (37.5□g LT) n (%)	Group 2 (Placebo) n (%)
Follow-up Phase [4]	**N=887**	**N=870**
Any non-solicited systemic adverse event	75 (9)	58 (7)

Note: Percentages are based on the number of subjects in the Safety Population who were in the study during the specified phase. A subject is counted only once per category.

[1] Systemic adverse events that occurred following Vaccination 1 prior to Vaccination 2. Events of fever, malaise, headache, and unformed stools/diarrheal episodes were considered unsolicited events when reported more than seven days post-vaccination.

[2] Systemic adverse events that occurred following Vaccination 2 prior to the start of the Surveillance Phase. Events of fever, malaise, headache, and unformed stools/diarrheal episodes were considered unsolicited events when reported more than seven days post-vaccination.

[3] Systemic adverse events that occurred within the Surveillance Phase prior to the start of the Follow-up Phase.

[4] Systemic adverse events that occurred within the Follow-up Phase prior to the end of the study.

N=Number of subjects in the Safety Population who were in the study during the specified phase; n = Number of subjects meeting the specified criteria.

Incidence of Solicited Local Adverse Events by Vaccination, Safety Population

Local Adverse Event	Group 1 (37.5□g LT) n (%)	Group 2 (Placebo) n (%)
Vaccination 1[1]		
Subjects Vaccinated:	**N=1014**	**N=1018**
Erythema	802 (79)	438 (43)
Rash	812 (80)	91 (9)
Pruritus	705 (70)	66 (7)
Hyperpigmentation	462 (46)	19 (2)
Pain	189 (19)	49 (5)
Hypopigmentation	22 (2)	6 (<1)
Edema	21 (2)	4 (<1)
Vaccination 2[2]		
Subjects Vaccinated:	**N=965**	**N=974**
Erythema	771 (80)	347 (36)
Rash	766 (79)	67 (7)
Pruritus	643 (67)	33 (3)
Hyperpigmentation	260 (27)	18 (2)
Pain	122 (13)	19 (2)
Hypopigmentation	37 (4)	3 (<1)
Edema	20 (2)	1 (<1)

Note: Percentages are based on the number of subjects in the Safety Population who were in the study during the specified phase.

[1] Local events occurring at the Vaccination 1 application site.

[2] Local events occurring at the Vaccination 2 application site.

N=Number of subjects per group in the Safety Population; n=Number of subjects meeting the specified criteria

Incidence of Solicited Systemic Adverse Events by Vaccination, Safety Population

Systemic Adverse Event	Group 1 (37.5□g LT) n (%)	Group 2 (Placebo) n (%)
Vaccination 1[1]	**N=1014**	**N=1018**
Headache	177 (18)	175 (17)
Diarrhea [2]	109 (11)	94 (9)
Malaise	102 (10)	70 (7)
Fever	11 (1)	7 (<1)
Vaccination 2[3]	**N=965**	**N=974**
Headache	117 (12)	107 (11)
Diarrhea[2]	78 (8)	63 (7)
Malaise	66 (7)	61 (6)
Fever	4 (<1)	5 (<1)

Note: Percentages are based on the number of subjects in the Safety Population who were in the study during the specified phase.

[1] Solicited systemic events reported within the first seven days after Vaccination 1.

[2] For the purposes of this analysis, diarrhea was defined as three or more loose stools in 24 hours.

[3] Solicited systemic events reported within the first seven days after Vaccination 2.

N = Number of subjects in the Safety Population who were in the study during the phase; n = Number of subjects with at least one AE, per category. A subject is counted only once per category.

Overall Summary of All Serious Adverse Events by System Organ Class and Preferred Term, Safety Population

System Organ Class Preferred Term	Group 1 LT Patch (37.5 µg) (N=1014) n (%)	Group 2 Placebo Patch (N=1018) n (%)	Overall (N=2032) n (%)
No Serious Adverse Events	1000 (98.6%)	1006 (98.8%)	2006 (98.7%)
All Serious Adverse Events	14 (1.4%)	12 (1.2%)	26 (1.3%)
Infections and infestations	4 (0.4%)	4 (0.4%)	8 (0.4%)
Appendicitis	1 (0.1%)	0 (0.0%)	1 (0.0%)
Bronchitis	1 (0.1%)	0 (0.0%)	1 (0.0%)
Erysipelas	0 (0.0%)	1 (0.1%)	1 (0.0%)
Infectious mononucleosis	0 (0.0%)	1 (0.1%)	1 (0.0%)
Pyelonephritis	0 (0.0%)	1 (0.1%)	1 (0.0%)
Sepsis	1 (0.1%)	0 (0.0%)	1 (0.0%)
Tonsillitis	0 (0.0%)	1 (0.1%)	1 (0.0%)
Viral infection	1 (0.1%)	0 (0.0%)	1 (0.0%)
Injury, poisoning and procedural complications	4 (0.4%)	1 (0.1%)	5 (0.2%)
Facial bones fracture	1 (0.1%)	0 (0.0%)	1 (0.0%)
Fibula fracture	1 (0.1%)	0 (0.0%)	1 (0.0%)
Ligament rupture	1 (0.1%)	0 (0.0%)	1 (0.0%)
Mountain sickness acute	0 (0.0%)	1 (0.1%)	1 (0.0%)
Splenic rupture	1 (0.1%)	0 (0.0%)	1 (0.0%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3 (0.3%)	0 (0.0%)	3 (0.1%)
Breast cancer recurrent	1 (0.1%)	0 (0.0%)	1 (0.0%)
Gastrointestinal carcinoma	1 (0.1%)	0 (0.0%)	1 (0.0%)

Metastatic neoplasm	1 (0.1%)	0 (0.0%)	1 (0.0%)
Gastrointestinal disorders	0 (0.0%)	2 (0.2%)	2 (0.1%)
Gastric ulcer haemorrhage	0 (0.0%)	1 (0.1%)	1 (0.0%)
Ileus	0 (0.0%)	1 (0.1%)	1 (0.0%)
General disorders and administration site conditions	2 (0.2%)	0 (0.0%)	2 (0.1%)
Accidental death	2 (0.2%)	0 (0.0%)	2 (0.1%)
Musculoskeletal and connective tissue disorders	1 (0.1%)	1 (0.1%)	2 (0.1%)
Musculoskeletal pain	0 (0.0%)	1 (0.1%)	1 (0.0%)
Osteoarthritis	1 (0.1%)	0 (0.0%)	1 (0.0%)
Nervous system disorders	0 (0.0%)	2 (0.2%)	2 (0.1%)
Headache	0 (0.0%)	1 (0.1%)	1 (0.0%)
Partial seizures with secondary generalisation	0 (0.0%)	1 (0.1%)	1 (0.0%)
Pregnancy, puerperium and perinatal conditions	0 (0.0%)	1 (0.1%)	1 (0.0%)
Pregnancy	0 (0.0%)	1 (0.1%)	1 (0.0%)
Reproductive system and breast disorders	0 (0.0%)	1 (0.1%)	1 (0.0%)
Endometriosis	0 (0.0%)	1 (0.1%)	1 (0.0%)
Respiratory, thoracic and mediastinal disorders	1 (0.1%)	0 (0.0%)	1 (0.0%)
Nasal septum deviation	1 (0.1%)	0 (0.0%)	1 (0.0%)

Note: Percentages are based on the number of subjects in the Safety Population in each group.