Clinical trial results:
A single blind, randomized comparative and multicentre clinical trial of the immunogenicity and safety of booster immunisation with bivalent vaccine against tetanus and diphtheria VACDITE (BIODRUG) and IMOVAX D.T. ADULT (Sanofi Pasteur SA) in healthy adults.

Summary

EudraCT number	2018-001604-10
Trial protocol	SK
Global end of trial date	29 November 2018

Results information

Result version number	v1 (current)
This version publication date	19 June 2019
First version publication date	19 June 2019

Trial information

Trial identification

Sponsor protocol code	TriDiTe2018

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BIODRUG s.r.o.
Sponsor organisation address	Boženy Němcovej 8, Bratislava, Slovakia, 811 04
Public contact	Clinical Trial Information Desk, BIODRUG s.r.o., biodrugpost@gmail.com
Scientific contact	Clinical Trial Information Desk, BIODRUG s.r.o., biodrugpost@gmail.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2018
Global end of trial reached?	Yes
Global end of trial date	29 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective of this trial is to demonstrate non-inferior immunogenicity (represented by seroconversion rate for tetanus and/or diphtheriae) of booster vaccination with the VACDITE vaccine compared to that of the reference vaccine (IMOVAX D.T. ADULT) in healthy adults.

Protection of trial subjects:

The risk to subjects enrolled in this study was not higher than the general risks of adverse reactions after tetanus and diphtheriae vaccination because both commercial vaccines are registered in the Slovakia. Subjects were not exposed to more stress or pain than they are from the vaccination or blood sampling.

Background therapy:

Healthy adults

Evidence for comparator:

The comparator, further called as reference vaccine, was chosen as it was the only one bivalent vaccine against tetanus and dphtheriae available and authorised in the Slovakia. There was no other reason of this selection.

Actual start date of recruitment	12 September 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Slovakia: 200
Worldwide total number of subjects	200
EEA total number of subjects	200

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	200
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In the study was planned to enrol a total of 200 subjects recruited from healthy adults. All patients were selected from outpatient's clinic (clinical sites) according to inclusion and exclusion criteria. In one clinical site, there were planned to enrol a total of 50 subjects.

Pre-assignment

Screening details:

Subjects had have written confirmation on previous immunisation against tetanus and/or diphtheriae not later than 15.9 years and not early than 9.9 years.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

The single blinding was achieved by simple overlapping of subject eyes with a mask before the administration of vaccine. So a subject did not know which vaccine had been administered to him. The single blinding helped especially to objectively assess any adverse events.

Arms

Are arms mutually exclusive?	Yes
Arm title	Test medication

Arm description:

Subjects received one dose of the test vaccine.

Arm type	Experimental
Investigational medicinal product name	VACDITE
Investigational medicinal product code	SUB25254
Other name	DIPHTHERIA AND TETANUS VACCINE (ADSORBED, REDUCED ANTIGEN(S) CONTENT)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly to minimize the occurrence of local adverse reactions as it is recommended by the manufacture. The recommended site of the application was deltoid region in adults.
The vaccine dose was the same for both vaccines, i.e. volume of 0.5 ml. The volume of dose, including the way of administration was in accordance of SmPC of both study vaccines.

Arm title	Reference medication

Arm description:

Subjects received one dose of the reference vaccine.

Arm type	Active comparator
Investigational medicinal product name	IMOVAX D.T. ADULT
Investigational medicinal product code	SUB25254
Other name	DIPHTHERIA AND TETANUS VACCINE (ADSORBED, REDUCED ANTIGEN(S) CONTENT)
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The vaccine was administered intramuscularly to minimize the occurrence of local adverse reactions as it is recommended by the manufacture. The recommended site of the application was deltoid region in

adults.
The vaccine dose was the same for both vaccines, i.e. volume of 0.5 ml. The volume of dose, including the way of administration was in accordance of SmPC of both study vaccines.

Number of subjects in period 1	Test medication	Reference medication
Started	100	100
Completed	100	100

Baseline characteristics

Reporting groups	
Reporting group title	Test medication
Reporting group description:	
Subjects received one dose of the test vaccine.	
Reporting group title	Reference medication
Reporting group description:	
Subjects received one dose of the reference vaccine.	

Reporting group values	Test medication	Reference medication	Total
Number of subjects	100	100	200
Age categorical			
The study stratification was performed on the base of sex and age as follows: 24.1-29.9 years, 30- 49.9 years, 50-64.9 years for both males and females.			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Adults 24.1-29.9	24	24	48
Adults 30-49.9	44	44	88
Adults 50-64.9	32	32	64
Gender categorical			
Units: Subjects			
Female	50	50	100
Male	50	50	100

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The primary objective of proving non-inferiority based on primary analysis of variables was performed on the ITT set (intention-to-treat). It was conservative in approach. This set included all subjects since each subject had the primary endpoint, i.e. the concentration of tetanus-specific and diphtheriae-specific antibodies at the started and completed milestone.	

Reporting group values	ITT		
Number of subjects	200		
Age categorical			
The study stratification was performed on the base of sex and age as follows: 24.1-29.9 years, 30- 49.9 years, 50-64.9 years for both males and females.			

Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Adults 24.1-29.9	48		
Adults 30-49.9	88		
Adults 50-64.9	64		
Gender categorical			
Units: Subjects			
Female	100		
Male	100		

End points

End points reporting groups

Reporting group title	Test medication
Reporting group description:	
Subjects received one dose of the test vaccine.	
Reporting group title	Reference medication
Reporting group description:	
Subjects received one dose of the reference vaccine.	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The primary objective of proving non-inferiority based on primary analysis of variables was performed on the ITT set (intention-to-treat). It was conservative in approach. This set included all subjects since each subject had the primary endpoint, i.e. the concentration of tetanus-specific and diphtheriae-specific antibodies at the started and completed milestone.	

Primary: Seroconversion rate SCR4

End point title	Seroconversion rate SCR4
End point description:	
The seroconversion rate was evaluated positive if the increase in antibody levels is at least 4-fold and the concentration of antibodies was at least 0.4 IU/mL.	
End point type	Primary
End point timeframe:	
Between started and completed milestone (i.e. 28 days)	

End point values	Test medication	Reference medication	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: 100				
tetanus	75	67	142	
diphtheriae	39	30	69	

Statistical analyses

Statistical analysis title	seroconversion rate's difference for tetanus
Statistical analysis description:	
seroconversion rate's difference between test and reference vaccine	
Comparison groups	Reference medication v Test medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.53
upper limit	20.53

Notes:

[1] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Statistical analysis title	seroconversion rate's difference for diphtheriae

Statistical analysis description:

seroconversion rate's difference between test and reference vaccine

Comparison groups	Test medication v Reference medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.12
upper limit	22.12

Notes:

[2] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Secondary: Seroconversion rate SCR2

End point title	Seroconversion rate SCR2

End point description:

The seroconversion rate was evaluated positive if the increase in antibodies was at least 2-fold for pre-vaccination levels ≥1.0 IU/mL or at least 4-fold for pre-vaccination level <1.0 IU/mL and if the concentration of antibodies was at least 0.4 IU/mL.

End point type	Secondary

End point timeframe:

Between started and completed milestone (i.e. 28 days)

End point values	Test medication	Reference medication	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: 100				
tetanus	87	85	172	
diphtheriae	39	30	69	

Statistical analyses

Statistical analysis title	seroconversion rate's difference for tetanus
Statistical analysis description: seroconversion rate's difference between test and reference vaccine	
Comparison groups	Reference medication v Test medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.61
upper limit	11.61

Notes:

[3] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Statistical analysis title	seroconversion rate's difference for diphtheriae
Statistical analysis description: seroconversion rate's difference between test and reference vaccine	
Comparison groups	Test medication v Reference medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.12
upper limit	22.12

Notes:

[4] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Secondary: Seroconversion rate SCR-URL/4

End point title	Seroconversion rate SCR-URL/4

End point description:

The seroconversion rate was evaluated positive if the increase in antibodies was at least 2-fold for pre-vaccination levels > ULR/4 (upper limit of measuring range divided by four) or at least 4-fold for pre-vaccination level < ULR/4 and if the concentration of antibodies was at least 0.4 IU/mL.
URL/4 = 1.75 IU/mL for tetanus antibodies
URL/4 = 0.75 IU/mL for diphtheriae antibodies

End point type	Secondary

End point timeframe:

Between started and completed milestone (i.e. 28 days)

End point values	Test medication	Reference medication	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: 100				
tetanus	82	81	163	
diphtheriae	39	30	69	

Statistical analyses

Statistical analysis title	seroconversion rate's difference for tetanus

Statistical analysis description:

seroconversion rate's difference between test and reference vaccine

Comparison groups	Reference medication v Test medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.76
upper limit	11.76

Notes:

[5] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Statistical analysis title	seroconversion rate's difference for diphtheriae

Statistical analysis description:

seroconversion rate's difference between test and reference vaccine

Comparison groups	Reference medication v Test medication

Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.12
upper limit	22.12

Notes:

[6] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Secondary: Seroconversion rate SCR1

End point title	Seroconversion rate SCR1

End point description:

The seroconversion rate was evaluated positive if the post-vaccination antibodies' levels were at least 1.0 IU/mL.

End point type	Secondary

End point timeframe:

Between started and completed milestone (i.e. 28 days)

End point values	Test medication	Reference medication	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: 100				
tetanus	97	98	195	
diphtheriae	25	22	47	

Statistical analyses

Statistical analysis title	seroconversion rate's difference for tetanus

Statistical analysis description:

seroconversion rate's difference between test and reference vaccine

Comparison groups	Test medication v Reference medication

Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.33
upper limit	3.33

Notes:

[7] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Statistical analysis title	seroconversion rate's difference for diphtheriae

Statistical analysis description:

seroconversion rate's difference between test and reference vaccine

Comparison groups	Test medication v Reference medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.75
upper limit	14.75

Notes:

[8] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Secondary: Seroconversion rate SCR01

End point title	Seroconversion rate SCR01

End point description:

The seroconversion rate was evaluated positive if the post-vaccination antibodies' levels were at least 0.1 IU/mL.

End point type	Secondary

End point timeframe:

Between started and completed milestone (i.e. 28 days)

End point values	Test medication	Reference medication	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: 100				
tetanus	100	100	200	
diphtheriae	81	75	156	

Statistical analyses

Statistical analysis title	seroconversion rate's difference for tetanus
Statistical analysis description: seroconversion rate's difference between test and reference vaccine	
Comparison groups	Reference medication v Test medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0

Notes:

[9] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Statistical analysis title	seroconversion rate's difference for diphtheriae
Statistical analysis description: seroconversion rate's difference between test and reference vaccine	
Comparison groups	Reference medication v Test medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
P-value	< 0.05
Method	Fisher exact
Parameter estimate	Risk difference (RD)
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.45
upper limit	17.45

Notes:

[10] - Fisher's exact test, simple asymptotic interval of difference.
The efficacy objective was met if the seroconversion rate induced with the test vaccine was not worse than 10% compared to reference vaccine-induced seroconversion rate (i.e. seroconversion rates of test minus reference vaccine, including the lower limit of the 95% confidence interval of this difference was not lower than -10%).

Secondary: Geometric means of antibodies

End point title	Geometric means of antibodies

End point description:

Concentrations of antibodies after booster immunisation were expressed with geometric mean (GMC).The ratio of GMCs (test/reference vaccine) was investigated. If the lower limit of 95% confidence interval of this ratio (i.e. [test] / [reference]) was > 0.67 and the two-sided confidence interval contained 1, then the criterion of non-inferiority was met.

End point type	Secondary

End point timeframe:

Between started and completed milestone (i.e. 28 days)

End point values	Test medication	Reference medication	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: IU/mL				
geometric mean (confidence interval 95%)				
tetanus	5.03 (4.40 to 5.75)	5.18 (4.66 to 5.75)	5.10 (4.69 to 5.55)	
diphtheriae	0.33 (0.25 to 0.44)	0.27 (0.21 to 0.35)	0.30 (0.25 to 0.36)	

Statistical analyses

Statistical analysis title	ratio of geometric means for tetanus

Statistical analysis description:

ratio of geometric means - test/reference

Comparison groups	Test medication v Reference medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
P-value	< 0.05
Method	ratio
Parameter estimate	ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.15

Notes:

[11] - It was computed as a difference of logarithms of both geometric means.

Statistical analysis title	ratio of geometric means for diphtheriae

Statistical analysis description:

ratio of geometric means - test/reference

Comparison groups	Test medication v Reference medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
P-value	< 0.05
Method	ratio
Parameter estimate	ratio
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.8

Notes:

[12] - It was computed as a difference of logarithms of both geometric means.

Secondary: Rise in antibodies (RA) for tetanus

End point title	Rise in antibodies (RA) for tetanus

End point description:

The rise in antibodies (RA) was obtained from ratio of the post- and pre-vaccination antibodies' level. The ratio of RA (test/reference vaccine) was investigated. If the lower limit of 95% confidence interval of this ratio (i.e. [test] / [reference]) was > 0.67 and the two-sided confidence interval contained 1, then the criterion of non-inferiority was met.

End point type	Secondary

End point timeframe:

Between started and completed milestone (i.e. 28 days)

End point values	Test medication	Reference medication	ITT	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	100	100	200	
Units: dimensionless				
geometric mean (confidence interval 95%)				
tetanus	7.57 (6.22 to 9.22)	8.00 (6.46 to 9.89)	7.78 (6.74 to 8.98)	
diphtheriae	5.70 (4.41 to 7.36)	5.80 (4.55 to 7.39)	5.75 (4.83 to 6.85)	

Statistical analyses

Statistical analysis title	ratio of rise in antibodies for tetanus
Statistical analysis description: ratio of rise in antibodies - test/reference	
Comparison groups	Test medication v Reference medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
P-value	< 0.05
Method	ratio
Parameter estimate	ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.26

Notes:

[13] - It was computed as a difference of logarithms of both geometric means.

Statistical analysis title	ratio of rise in antibodies for diphtheriae
Statistical analysis description: ratio of rise in antibodies - test/reference	
Comparison groups	Test medication v Reference medication
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	non-inferiority[14]
P-value	< 0.05
Method	ratio
Parameter estimate	ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.39

Notes:

[14] - It was computed as a difference of logarithms of both geometric means.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Between started and completed milestone

Adverse event reporting additional description:

The measures of safety used in this study were routine clinical procedures. They were chosen to capture known undesirable effects of tboth vaccnes from the SmPC. Safety measures were conducted by the investigators. They included close vigilance for reporting of reactions on the day of immunisation and 4 weeks after immunisation.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20

Reporting groups

Reporting group title	test vaccine
Reporting group description: -	
Reporting group title	reference vaccine

Reporting group description: -

Serious adverse events	test vaccine	reference vaccine	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 100 (0.00%)	0 / 100 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	test vaccine	reference vaccine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	24 / 100 (24.00%)	29 / 100 (29.00%)	
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 100 (1.00%)	2 / 100 (2.00%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Pain in extremity	Additional description: Arm/Shoulder pain		

subjects affected / exposed	2 / 100 (2.00%)	8 / 100 (8.00%)	
occurrences (all)	2	8	
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Injection related reaction	Additional description: Bruise, Elevated temperature, Induration, Itching, Pain, Redness, Swelling at injection site		
subjects affected / exposed	18 / 100 (18.00%)	22 / 100 (22.00%)	
occurrences (all)	31	26	
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	1	1	
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 100 (1.00%)	1 / 100 (1.00%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

None

Notes: