Statistical Analysis Plan

Final Analysis

DOUBLE BLINDED, RANDOMIZED, PRIORIX®- AND PLACEBO-CONTROLLED TRIAL TO EVALUATE THE OPTIMAL DOSE OF MV-CHIK VACCINE (AGAINST CHIKUNGUNYA VIRUS) IN REGARD TO IMMUNOGENICITY, SAFETY AND TOLERABILITY IN HEALTHY VOLUNTEERS

Protocol: MV-CHIK-202

Confidential

Sponsor: Themis Bioscience GmbH, Vienna, Austria

Based on:
STAT03_A Statistical Analysis Plan
Version 5.0, Effective Date 16-Dec-2016

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Revision History and Approval

Revision History

Version	Date
Final 1.0	24-Jul-2017
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Final 3.0	09-May-2018

Approval

Function	Name	Signature	Date
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List of Abbreviations

AE	Adverse event
ALT	Alanine Aminotransferase
ANOVA	Analysis of variance
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical (classification system)
BDRM	Blind data review meeting
CI	Confidence interval
CHIKF	Chikungunya fever
CHIKV	Chikungunya virus
CFR	Case fatality ratio
CSP	Clinical Study protocol
DMP	Data management plan
DSMB	Data safety monitoring board
eCRF	Electronic case report form
e.g.	For example
ELISA	Enzyme-linked immunosorbent assay
ET	Early termination
HIV	Human immunodeficiency virus
G/L	Giga per liter
GMT	Geometric mean titer
i.e.	This is
i.m.	Intramuscularly
imp	Investigational medicinal product
iTT	Intention to treat
Log 10	Logarithm to base 10
MedDRA	Medical dictionary for regulatory activities
mL	Milliliter
µmol/L	Micromole per liter
mITT	Modified intention to treat
MV	Measles virus
PD	Protocol deviation
PP	Per protocol
$PRNT_{50}$	Plaque reduction neutralization test 50%
PT	Preferred term

PT	Prothrombin time
Q1	Quartil1
Q3	Quartil3
s	Seconds
SAE	Serious adverse event
SAP	Statistical analysis plan
SCR	Seroconversion rate
SOC	System organ class
SD	Standard deviation
T/L	Tera per liter
TCID	Tissue culture infection dose
TEAE	Treatment emergent adverse event
U/L	Unit per liter
vs.	versus
WHO	World health organization

1. OVERVIEW

Chikungunya virus (CHIKV), a mosquito-borne pathogen that causes Chikungunya fever (CHIKF), has been spreading throughout Asia, Africa, and parts of Europe in recent times. Formerly indigenous to tropical Africa, recent large outbreaks have been reported in parts of South East Asia and due to global travel, the risk of spreading CHIKV in non-endemic regions, such as Europe and the United States, has increased.

CHIKV is transmitted to humans primarily by Aedes aegypti and Ae.albopictus, which are common in many non-tropic urban areas. Transmission of the virus can occur in an urban cycle whereby the mosquito spreads the disease from an infected human to an uninfected human, following an epidemiological pattern similar to dengue fever. Even vertical transmission of CHIKV from mother to fetus, causing congenital illness and fetal death, seems possible.

Most individuals will present with symptomatic disease after an incubation period of three to seven days (range, 2-12 days). Not all individuals infected with the virus will develop symptoms, approximately 3%-25% of persons with antibodies to Chikungunya virus have asymptomatic infections. However, individuals acutely infected with Chikungunya virus, whether clinically apparent or asymptomatic, can contribute to the transmission of the disease if active vectors are present.

Acute disease is mostly characterized by the acute onset of high fever (>102°F/ 39°C). The fevers typically last from several days up to two weeks. Other signs and symptoms may include, headache, diffuse back pain, myalgias, nausea, vomiting, polyarthritis, rash, and conjunctivitis. After the onset of fever, the majority of infected persons develop severe, often debilitating polyarthralgia. Joint symptoms are usually symmetric and occur most commonly in wrists, elbows, fingers, knees, and ankles but also more proximal joints. The lower extremity arthralgias can be severely disabling resulting in slow, broad based, halting gait, which can persist for months. The patients suffer from severe pain, tenderness, swelling and stiffness and they cannot perform normal tasks or go to work.

During the La Reunion Epidemic a number of unusual clinical presentations were observed, including hepatitis, autoimmune neurologic pathologies (Guillain-Barré), cardiologic manifestations and death. The case fatality ratio (CFR) during the 2006 La Reunion epidemic has been estimated to be 1:1000 (0.1%), with most deaths occurring in neonates, adults with underlying medical conditions and older people (>65 years). During an epidemic in Mauritius (2005-2006) and India (2006) a CFR of 4.5% and 4.9% was reported. The difference in fatality rates can be explained by difference in pathogenicity of the viral strains causing the epidemic, but also by the difference in medical care of infected patients. Calculated estimates from annualized averages over combined epidemic and interepidemic periods suggest 33 to 26K deaths annually attributed to Chikungunya fever. Up to 46K patients per year can develop a chronic infection.

The vaccine includes a backbone of measles virus (Schwarz Vaccine strain), which has been developed at the Institute Pasteur. Chikungunya Virus structural proteins have been inserted into the MV genome (MV-CHIK) and are expressed as the vaccine antigens. The backbone has already been tested in previous trials of MV-HIV

construct. A detailed description of the vaccine construct and mechanism of action can be found in the investigators' brochure.

1.1 Study Objectives

1.1.1 Primary Objective

- To investigate the immunogenicity and safety of MV-CHIK 28 days after primary immunization regimen, comprising one or two vaccinations

1.1.2 Secondary Objectives

- To investigate the immunogenicity, safety and tolerability of MV-CHIK booster dose 24 weeks after primary immunization.
- To investigate the immunogenicity, safety and tolerability of MV-CHIK during the vaccination period up to 28 days after the last vaccination (i.e. after three or five vaccinations).
- To identify dose and schedule of MV-CHIK to forward to Phase 3 clinical development

1.2 Study Design

The MV-CHIK-202 study is a double blinded, randomized, Priorix® and placebo-controlled, dose finding, multi-center phase 2 trial in 320 healthy volunteer subjects will be randomized to one of six treatment groups (A, B, C, D, M1 or M2) differing in dosage and scheduling of vaccinations.

Treatment plan:

- Group A + B: two doses of 0.3 mL MV-CHIK low dose $5x10^4$ (± 0.5 log) $TCID_{50}$/ dose vs. two doses of 0.5 mL control vaccine (e.g. Priorix®)
- Group C + D: two doses of 0.3 mL MV-CHIK high dose $5x10^5$ (± 0.5 log) $TCID_{50}$/ dose vs. two doses of 0.5 mL control vaccine
- AUT: Group M1 + M2: after one dose of 0.5 mL control vaccine, two doses of 0.3 mL MV-CHIK low dose $5x10^4$ (± 0.5 log) $TCID_{50}$/ dose at different time points
- GER: Group M1 + M2: after one dose of 0.5 mL control vaccine, two doses of 0.3 mL MV-CHIK high dose $5x10^5$ (± 0.5 log) $TCID_{50}$/ dose at different time points

Group	Vaccine	Vaccine on day	Placebo on day
A	MV-CHIK low dose or	0 + 28	196
	control vaccine		
B	MV-CHIK low dose or	28 + 196	0
	control vaccine		
C	MV-CHIK high dose or	0 + 28	196
	control vaccine		

D	MV-CHIK high dose or	28 + 196	0
	control vaccine		
M1 AUT/GER	control vaccine and	- 28	168 + 196
	MV-CHIK low/high dose	0 + 28	
M2 AUT/GER	control vaccine and	-28	0 + 28
	MV-CHIK low/high dose	168 + 196	

All subjects of group A, B, C and D will receive three i.m. injections on study day 0, 28 and 196. Subjects of group A and B will receive MV-CHIK low dose or control-vaccine Priorix® (or equivalent measles vaccine) and subjects of group C and D will be treated with MV-CHIK high dose or control-vaccine (Priorix® or equivalent measles vaccine).

All subjects of group A, B, C and D additionally will be randomized to one of two treatment sequences: group A and C will receive MV-CHIK or control-vaccine Priorix® on study day 0 and 28, followed by placebo on day 196, and group B and D receive placebo on day 0 and MV-CHIK or Priorix® on day 28, followed by an additional vaccination of the same product on day 196 (boosting vaccination).

All subjects of the measles booster group M1 and M2 will receive five i.m. injections on study day -28, 0, 28, 168 and 196. The first vaccination will be Priorix® or equivalent measles vaccine on study day -28. Group M1 will receive MV-CHIK low/high dose vaccinations on day 0 and day 28 and placebo on day 168 and 196. Group M2 will receive placebo on day 0 and 28 and MV-CHIK low/high dose on day 168 and on day 196.

Group A, B, C and D will be merged into a first category labeled as Group A/B/C/D. Group M1 and M2 will be merged into a second category labeled as Group M1/M2.

All subjects will be followed for safety and immunogenicity evaluation until day 224. The estimated study duration per subject will be 33-37 weeks (~8 months), respectively. Overall study duration is estimated to be 3 years from study initiation until reporting.

1.3 Endpoints

1.3.1 Primary Endpoint

Immunogenicity on Day 56 confirmed by the presence of functional anti-chikungunya antibodies as determined by the plaque reduction neutralization test ($PRNT_{50}$)

1.3.2 Secondary Endpoints

- Immunogenicity on Day 0, 28, 196 and 224; additionally for group M1 and M2 on Day -28 and 168 as confirmed by the presence of functional anti-chikungunya antibodies as determined by the plaque reduction neutralization test ($PRNT_{50}$) and by ELISA.

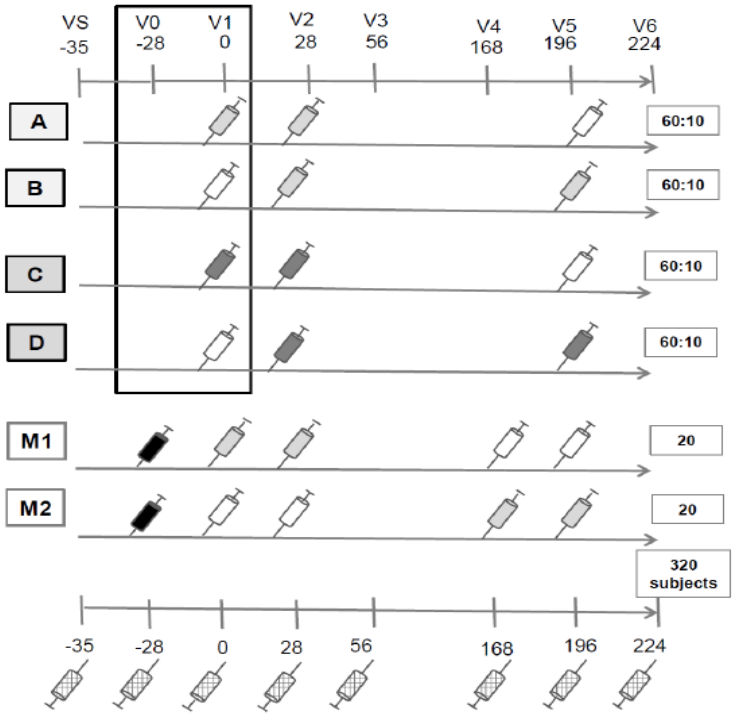
- Measurement of anti-measles antibodies on day 0, 28, and 56; additionally for group M1 and M2 on day -28 as determined by ELISA.
- Solicited local and systemic adverse events (AEs)
- Serious adverse events (SAEs)
- Rate of AEs during the 28 day post-vaccination period
- Safety laboratory parameters (hematology, serum chemistry, urinalysis)
- Shedding of live recombinant virus until day 196 (subset of subjects)
- Induction of a Chikungunya virus specific T cell responses (subset of subjects)
- Pre-existing anti-vector immunity:
    - Immunogenicity of Chikungunya vaccine in the presence of recently boosted measles immunity (measles booster groups M1 and M2).
    - Relation of post-vaccination anti-chikungunya plaque reduction neutralization titers ($PRNT_{50}$) and baseline anti-measles ELISA titers (all treatment groups).

1.4 Sample Size Calculation

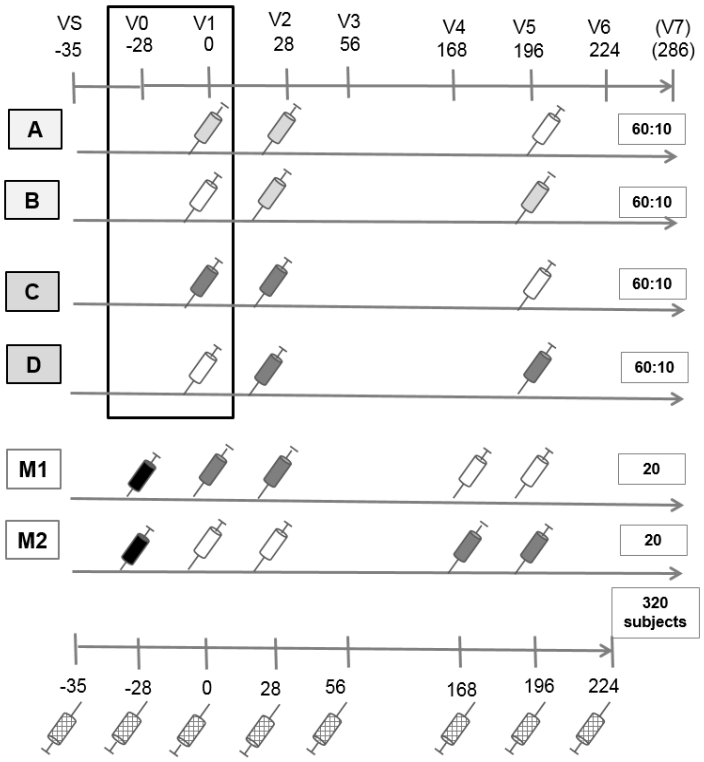
No formal sample size calculation was performed. Sample size for this study was determined on grounds of feasibility and common practice in similar trials. Number of subjects planned is 320. Results of the predecessor study MV-CHIK-101 allow to assess the usefulness of the chosen sample size.

1.5 Flowchart

1.5.1 Treatment Schedule for Austria:



1.5.2 Treatment Schedule for Germany:



1.5.3 Austria

	Screening Visit*	Visit 0	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Early
Study Day	Day -35*	Day -28	Day 0	Day 28	Day 56	Day 168	Day 196	Day 224	Termination
Time windows / treatment groups	M1+M2: -35 to -29 A-D: -7 to -1	M1+M2: ±5 days **A-D -28 is study day 0	M1+M2 day 0 = V0+V1 at once on d	±5 days all groups	± 5 days all groups	±10 days only M1+M2	± 10 days all groups	± 10 days all groups	
Informed consent	X								
Inclusion/exclusion criteria (1)	X	X	X (14)	X	X	X (14)	X		
HIV, hepatitis B/C, [blood: 8-10 mL]	X								
Demographic data	X								
Physical examination	X								
Vaccination history	X								
Hematology blood sample [3-5 mL] (6)	X				X			X	X
Coagulation parameter [blood: 3-5 mL] (7)	X				X			X	X
Clinical chemistry serum [8-10 mL] (8)	X				X			X	X
Urinalysis (10)	X				X			X	X
Medical history	X	X (2)							
Concomitant medications	X	X	X (14)	X	X	X (14)	X	X	X
Assessment of arthralgia	X	X	X (14)	X	X	X (14)	X	X	X
Symptom-directed physical exam (3)		X	X (14)	X	X	X (14)	X	X	X
Vital signs (4)	X	X	X (14)	X	X	X (14)	X	X	X
Urine pregnancy test (9)	X	X	X (14)	X	X	X (14)	X	X	X
Randomization		M1+M2 X A B C D							
Study treatment: vaccination		X (14)	X	X		X (14)	X		
Immunogenicity 1: serum [blood: 16-20 mL]		X (14)	X	X	X	X (14)	X	X	X
Immunogenicity 2 (5.1): [blood: 16-20 mL]		X (14)	X	X	X	X (14)	X	X	X
Measles antibody titer [no additional blood]		X (14)	X	X	X				X
T- cell analysis (5.2): [blood: 24-30 mL]			X	X	X	X (14)	X	X	X
Measles virus shedding (13): [blood: 2-3 mL, urine and saliva]			X (13)	X (13)			X (13)		
Local tolerability (12)		X (14)	X	X	X	X (14)	X	X	X
Dispense subject diary (11)		X (14)	X	X		X (14)	X		
Collect subject diary (11)			X (14)	X	X		X (14)	X	X
Adverse events		X (14, 2)	X (2)	X	X	X (14)	X	X	X

* Screening visit within 7 days before randomization
(1) After randomization, only exclusion criteria which could influence the subject's eligibility throughout the study will be checked. The following exclusion criteria are concerned: 1, 7, 8, 10. 19, 20, 21, 22 and 23
(2) Symptoms noted prior to randomization are not considered adverse events but will be recorded as medical history
(3) Including system-based assessment if necessary according to symptom-directed physical examination. (section 11.2.2)
(4) Systolic and diastolic blood pressure, body temperature and pulse
(5.1) Sites outside of Vienna: serum samples (blood 2x 8-10 mL) to be collected for additional immunogenicity analyses (cross neutralization and passive transfer)
(5.2) Vienna sites only: PBMCs will be isolated from fresh blood (blood 24-30 mL and once at V3 48-60 mL). (section 8.3.2)
(6) Hemoglobin, hematocrit, erythrocyte count, differential white blood count, platelets (EDTA blood: 3-5 mL)
(7) Prothrombin time, aPTT, fibrinogen (blood: 3-5mL)
(8) Creatinine, sodium, potassium, calcium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, bilirubin (blood 8-10 mL),
(9) Pregnancy test will be performed for women of childbearing potential. (section 8.3.6)
(10) Glucose, protein, pH, erythrocytes, leucocytes, nitrite, ketones, urobilinogen, bilirubin and specific gravity
(11) The subjects will assess local tolerability and systemic reactions themselves over a period of 7 consecutive days after each injection. (section 11.2.5)
(12) Investigation of injection site reaction 1 hour after vaccination and additionally before each subsequent vaccination. (section 11.2.4)
(13) Shedding: only in AKH Vienna, only in a subset of group A-D, on day 0, 28, 196 and additional shedding sampling visits on day 7, 10 and 14 after the first vaccination on day 0. (section 8.3.1)
(14) Only measles booster group M1 and M2
** Group A, B, C, and D will perform Visit 0 and Visit 1 procedures on one day, group M1 and M2 will perform V0 and V1 on two days (28 days apart)

1.5.4 *Germany*

	Screening Visit*	Visit 0	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Early
Study Day	Day -35*	Day -28	Day 0	Day 28	Day 56	Day 168	Day 196	Day 224	Day 286	Termination
Time windows / treatment groups	M1+M2: -35 to -29 A-D: -7 to -1	M1+M2: ±5 days **A-D -28 is study day 0	M1+M2 day 0 = V0+V1 at once on d 0	±5 days all groups	± 5 days all groups	±10 days only M1+M2	± 10 days all groups	± 10 days all groups	± 10 days all groups	
Informed consent	X									
Inclusion/exclusion criteria (1)	X	X	X (14)	X	X	X (14)	X			
HIV, hepatitis B/C, [blood: 8-10 mL]	X									
Demographic data	X									
Physical examination	X									
Vaccination history	X									
Hematology blood sample [3-5 mL] (6)	X				X			X		X
Coagulation parameter [blood: 3-5 mL] (7)	X				X			X		X
Clinical chemistry serum [8-10 mL] (8)	X				X			X		X
Urinalysis (10)	X				X			X		X
Medical history	X	X (2)								
Concomitant medications	X	X	X (14)	X	X	X (14)	X	X		X
Assessment of arthralgia	X	X	X (14)	X	X	X (14)	X	X		X
Symptom-directed physical exam (3)		X	X (14)	X	X	X (14)	X	X		X
Vital signs (4)	X	X	X (14)	X	X	X (14)	X	X		X
Urine pregnancy test (9)	X	X	X (14)	X	X	X (14)	X	X	(15)	X
Randomization		M1+M2 X	A B C D							
Study treatment: vaccination		X (14)	X	X		X (14)	X			
Immunogenicity 1: serum [blood: 2x 8-10 mL]		X (14)	X	X	X	X (14)	X	X		X
Immunogenicity 2 (5.1): [blood: 16-20 mL]		X (14)	X	X	X	X (14)	X	X		X
Measles antibody titer [no additional blood sample]		X (14)	X	X	X					X
T- cell analysis (5.2): [blood: 24-30 mL]			X	X	X	X (14)	X	X		X
Measles virus shedding (13): [blood: 2-3 mL, urine and saliva]			X (13)	X (13)			X (13)			
Local tolerability (12)		X (14)	X	X	X	X (14)	X	X		X
Dispense subject diary (11)		X (14)	X	X		X (14)	X			
Collect subject diary (11)			X (14)	X	X		X (14)	X		X
Adverse events		X (14,2)	X (2)	X	X	X (14)	X	X		X

* Screening visit within 7 days before randomization

(1) After randomization only exclusion criteria, which could influence the subject's eligibility throughout the study will be checked. The following exclusion criteria are concerned: 1, 7, 8, 10, 19, 20, 21, 22 and 23

(2) Symptoms noted prior to randomization are not considered as adverse events but will be recorded as medical history

(3) Including system-based assessment if necessary according to symptom-directed physical examination. (section 11.2.2)

(4) Systolic and diastolic blood pressure, body temperature and pulse

(5.1) Sites outside of Vienna: serum samples (blood 2x 8-10 mL) to be collected for additional immunogenicity analyses (cross neutralization and passive transfer)

(5.2) Vienna sites only: PBMCs will be isolated from fresh blood (blood 24-30 mL and once at V3 48-60 mL). (section 8.3.2)

(6) Hemoglobin, hematocrit, erythrocyte count, differential white blood count, platelets (EDTA blood: 3-5 mL)

(7) Prothrombin time, aPTT, fibrinogen (blood: 3-5mL)

(8) Creatinine, sodium, potassium, calcium, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, bilirubin (blood 8-10 mL),

(9) Pregnancy test will be performed for women of childbearing potential. (section 8.3.6)

(10) Glucose, protein, pH, erythrocytes, leucocytes, nitrite, ketones, urobilinogen, bilirubin and specific gravity

(11) The subjects will assess local tolerability and systemic reactions themselves over a period of 7 consecutive days after each injection. (section 11.2.5)

(12) Investigation of injection site reaction 1 hour after vaccination and additionally before each subsequent vaccination. (section 11.2.4)

(13) Shedding: only in AKH Vienna, only in a subset of group A-D, on day 0, 28, 196 and additional shedding sampling visits on day 7, 10 and 14 (±1 day each) after the first vaccination on day 0. (section 8.3.1)

(14) Only measles booster group M1 and M2

(15) women of childbearing potential will be followed up by a phone call, to ensure no pregnancy occurred 3 months after the last vaccination

** Group A, B, C, and D will perform Visit 0 and Visit 1 procedures on one day, group M1 and M2 will perform V0 and V1 on two days (28 days apart)

2. GENERAL CONSIDERATIONS

The Statistical Analysis Plan (SAP) is based on the final study protocols for Austria (Version 1.5; 24-Nov-2016) and Germany (Version 1.6; 19-Apr-2017). The present Statistical Analysis Plan (SAP) has been prepared in order to pre-specify and describe the statistical analyses that will be performed for the DSMB Analysis, the Preliminary Analysis and the Final Analysis. The analysis plan will be signed off before database snapshot for the DSMB Analysis.

2.1 Rationale

This Phase 2 trial is designed to investigate the immunogenicity, safety and tolerability of MV-CHIK.
Two different doses of MV-CHIK at a concentration of $5x10^4$ (± 0.5 log) $TCID_{50}$/ dose and $5x10^5$ (± 0.5 log) $TCID_{50}$/ dose per 0.3 mL will be assessed to healthy adults for the induction of functional anti-chikungunya neutralizing antibodies. In addition, the direct effect of the pre-existing vector immunity will be addressed by the immunization of a small subset of subjects with Priorix® prior immunization with two doses of MV-CHIK.

2.2 Conduct of Analysis

2.2.1 Preliminary Analysis

A preliminary analysis including safety and immunogenicity data will be performed in August 2017. The analysis was initially planned to be conducted after all subjects completed Visit 3 (Day 56) but was re-scheduled due to unforeseen delays to enable further vaccine development progress. The goal of this analysis is to provide highly valuable data of the novel Chikungunya vaccine for further development. Results from this analysis will have no impact on the study design and treatment of the subjects in this study.
All tables and listings marked with an "x" in column "IA" in section 10.1 and 10.1 will be generated for this Preliminary Analysis.

2.2.2 Final Analysis

The final analysis will be conducted once the last subject has completed the study.
All tables and listings marked with an "x" in column "FA" in section 10.1 and 10.1 will be generated for this Final Analysis.

2.3 Treatment Groups

For tables the groups M1 and M2 are not stratified by country (Austria, Germany):

- M1 of Austria (low dose) and M1 of Germany (high dose) are summarized in one group M1
- M2 of Austria (low dose) and M2 of Germany (high dose) are summarized in one group M2

Following treatment groups will be used in the analysis:

1. Group CV1: control vaccine on Day 0 and 28

2. Group CV2: control vaccine on Day 28 and 196
3. Group A: MV-CHIK low dose on Day 0 and 28
4. Group B: MV-CHIK low dose Day 28 and 196
5. Group C: MV-CHIK high dose on Day 0 and 28
6. Group D: MV-CHIK high dose Day 28 and 196
7. Group M1: MV-CHIK on Day 0 and 28
8. Group M2: MV-CHIK on Day 168 and 196

Further, tables will show one total column for

9. all MV-CHIK serum groups (i.e. total of A, B, C, D, M1 and M2)
10. all control vaccines (i.e. total of CV1 and CV2)

2.4 Statistical Software and Quality Control

All statistical analyses will be performed using SAS® version 9.3. Tables, figures and data listings will be generated in Microsoft® Word® as well as PDF® format.

Quality control of SAS® programs will include a review of the whole process of result generation:

- Review of all analysis SAS® programs
- Review of SAS® log for errors, uninitialized variables and warnings
- Review of all tables, listings and figures for completeness and correctness

2.5 Blinding and Randomization

This study is conducted in a double-blind manner in regard to assignment to treatment groups A, B, C or D. An assignment to the measles booster groups M1 and M2 will be apparent to both subject and study personnel, but the vaccination sequence will also be kept double-blind (the allocation to M1 or to M2 is unknown). The vaccine will be prepared by authorized personnel otherwise not involved in the conduct of the study or in the assessment of safety or efficacy after randomization.

At Visit 0, eligible subjects will be assigned to one of six treatment groups in timely order and received a three-digit randomization number using randomization envelopes provided by data management. The site will also be provided with emergency envelopes for unblinding in case of emergency and if knowledge of the treatment assignment is mandatory for emergency treatment.

2.6 Descriptive Analyses

Descriptive analyses of continuous variables (summary statistics) will be performed with the number of non-missing observations (N), arithmetic mean, standard deviation (±SD), median, quartiles (Q1 and Q3) and range (minimum and maximum).

Categorical variables (frequency statistics) will be described with the number of non-missing observations and percentages (%). Percentages will be calculated within each stratum on the total number of non-missing observations.

2.7 Inferential Analyses

Inferential analysis on immunogenicity endpoints will only be performed on the PP and ITT population. The significance level will be 0.05. All p-values will be two-sided and rounded to four decimal places.

GMTs and GMT ratios will be estimated by applying an analysis of variance (ANOVA) by using log-10 transformed data and taking the anti-log of the resulting point estimates for the least squares means, least squares means differences and the corresponding 2-sided 95% CIs. Pairwise comparisons for multiple comparisons will be adjusted according to Tukey-Kramer. For the definition of the baseline percentiles treatment groups A, B, C and D will be used.

2.7.1 Inferential Analysis for the Primary Endpoint

The primary immunogenicity analysis will compare the $PRNT_{50}$ antibody geometric mean titer (GMT) on Day 56 between the treatment groups (CV1, CV2, A, B, C, D, M1, M2).

GMTs and GMT ratios will be estimated with including the factor vaccination group. GMTs for the MV-CHIK groups will be compared pairwise.

2.7.2 Inferential Analysis for the Secondary Immunogenicity Endpoints

- An ANOVA with the fixed factors treatment group (CV1, CV2, A, B, C, D, M1, M2) will be used to compare PRNT functional antibody geometric mean titers (GMT) per visit (incl. Day -28).
- An ANOVA with the fixed factors treatment group (CV1, CV2, A, B, C, D, M1, M2) will be used to compare ELISA functional antibody geometric mean titers (GMT) per visit (incl. Day -28).
- Seroconversion rates (SCR) will be compared between treatment groups. Seroconversion will be defined as anti-Chikungunya $PRNT_{50}$ titers ≥10.
- The CHIKV PRNT50 GMT 28 days after first vaccination (i.e. Day 28 for group A and C; Day 56 for group B and D), between the four baseline (Day 0) measles titer groups, defined by baseline percentiles (0 to <25%, 25 to < 50%, 50 to <75%, 75 to 100%), will be compared by an ANOVA with fixed factors baseline measles titer group. No stratification by dose groups is intended.
- An ANOVA with the fixed factors treatment group (CV1, CV2, A, B, C, D, M1, M2) will be used to compare T-cells (geometric mean values) per visit.

And additionally for Final Analysis:

- The CHIKV $PRNT_{50}$ GMT 28 days after second vaccination (i.e. Day 56 for group A and C; Day 224 for group B and D), between the four baseline (Day 0) measles titer groups, defined by baseline percentiles (0 to <25%, 25 to < 50%, 50 to <75%, 75 to 100%), will be compared by an ANOVA with fixed factor baseline measles titer group. No stratification by dose groups is intended.

- An ANOVA with the fixed factors treatment group will be used to compare PRNT antibody geometric mean titers (GMT) 4 weeks after second vaccination between group A and B (i.e. comparing the GMT for A at Day 56 with the GMT of group B at Day 224).
- An ANOVA with the fixed factors treatment group will be used to compare PRNT antibody geometric mean titers (GMT) 4 weeks after second vaccination between group C and D (i.e. comparing the GMT for C at Day 56 with the GMT of group D at Day 224).
- An ANOVA with the fixed factors treatment group will be used to compare PRNT antibody geometric mean titers (GMT) 4 weeks after second MV-CHIK vaccination between group M1 and M2 (i.e. comparing the GMT for M1 at Day 56 with the GMT of group M2 at Day 224).

2.7.3 Inferential Analysis for the Safety Analysis

A Fisher's exact test will be provided to compare the AE rates for MV-CHIK vs. Priorix®. P-values will also be provided to compare AE rates between treatment groups (pairwise comparisons). No adjustment for multiple testing will be performed.

2.8 Center and Country Effect

This study is a multicentre study and conducted in three Austrian and one German site.

As the M1 an M2 dose is different in both countries (cp. Section 1.2) a stratification by countries will be prepared only for listings. No stratification by centers inside the country will be done.

2.9 Drop-outs

If "early termination" was ticked on the eCRF page "Study end page" the subjects was considered as early termination. If the study was terminated early a reason has to be indicated (i.e. subject withdrew consent, protocol, deviation, adverse event, failure to comply with protocol requirements, lost to follow-up, discretion of the investigator or other reason).

2.10 Screening Failures

All subjects who signed the informed consent were registered in the eCRF. If the question "Is subject eligible for the study" was answered with "no" or the question "Has the subject been randomized" was answered with "no", the subject was considered a screening failure.

2.11 Handling Missing Data

In general, missing data will not be imputed. However, for adverse events missing assessments for severity, causality and seriousness will be imputed with the worst case (severity=severe, causality=definitely and seriousness=yes).

2.13 Local/systemic tolerability symptoms (diary evaluation)

Local/systemic tolerability symptoms will be recorded by the study subjects at each diary day and diary period (for a period of 7 consecutive days after each vaccination).

Diary periods are defined as follows:

2. diary period 1 is after vaccination 1 (on Visit 0; only for measles booster group M1 and M2)
3. diary period 2 is after vaccination 2 (on Visit 1 - Day 0)
4. diary period 3 is after vaccination 3 (on Visit 2 - Day 28)
5. diary period 4 is after vaccination 4 (on Visit 4 - Day 168; only for measles booster group M1 and M2)
6. diary period 5 is after vaccination 5 (on Visit 5 - Day 196)

2.13.1 Local tolerability symptoms

- Symptoms: injection side pain (pain without touching), tenderness (pain upon touching), itching (pruritus), redness (erythema), hardening (induration) and swelling (edema)
- If symptoms are present, the investigator interprets the subject entries:
    - (mild/moderate/severe) for injection side pain (pain without touching), tenderness (pain upon touching) and itching (pruritus) as grade 1 (mild), grade 2 (moderate), grade 3 (severe) or grade 4 (potentially life threatening).
    - (circle A to circle E) for redness (erythema), swelling (edema) and hardening (induration) as grade 1, grade 2 grade 3 or grade 4.

2.13.2 Systemic tolerability symptoms

- Symptoms: headache, body temperature (fever), joint pain (arthralgia), flu-like symptoms, nausea, vomiting, rash, limb discomfort, myalgia and excessive fatigue
- If symptoms are present, the investigator interprets the subject entries:
    - (mild/moderate/severe) for headache, muscle pain, joint pain (arthralgia), flu-like symptoms, nausea, vomiting, rash, vomiting and excessive fatigue as grade 1 (mild), grade 2 (moderate), grade 3 (severe) or grade 4 (potentially life threatening).
    - (°C) for body temperature (fever) as grade 1, grade 2, grade 3 or grade 4.

For summarizing local/systemic severity symptoms the outcome is set to the worst severity. The order for severity is grade 1 to grade 4, where grade 4 is the worst severity.

2.14 Protocol Deviations

Protocol deviations will be collected only for the final analysis from the study database. The listing of protocol deviations will be prepared by Assign Data Management and Biostatistics GmbH using information from the eCRF documentation as well as from monitoring.

Protocol deviations will be identified during a Blind Data Review Meeting (BDRM) attended by Assign Data Management and Biostatistics GmbH and Themis Bioscience GmbH (sponsor).

The BDRM will take place after all outstanding queries have been resolved. Protocol deviations will be classified into major or minor protocol deviations based on their possible impact to the study results. Protocol deviations are defined as "major" if they are likely to affect the outcome of the study (e.g. effect on target variables). During the course of the study unforeseen events may occur or new scientific knowledge may become available, therefore final decisions on all protocol deviations for this analysis will be made on a case by case decision in the BDRM.

Subjects with major protocol deviations will be part of the Safety Population and mITT Population, but not part of the Per-Protocol Population (PP Population). Minor protocol violations will be regarded as fully evaluable and, therefore, will be part of the PP Population.

2.15 Medical Coding

Adverse events and medical history will be coded using MedDRA. Concomitant medications will be coded using WHO Drug Dictionary. Coding will be reviewed internally for consistency and will be approved by the sponsor prior to database snapshot and prior to database closure. For details to medical coding and the used coding dictionary versions, please refer to the Coding Guideline in DMP (Appendix 8; Version: Final 2.0; 05-May-2017).

2.16 Analysis Populations

Three analysis populations will be used in this analysis:

- **Modified Intent-to-Treat (mITT) Population**
  The exploratory immunogenicity analyses will be based on the modified ITT population. The modified Intent-to-treat (mITT) analysis population is defined to include all subjects randomized who receive at least one vaccination. Subjects will be analyzed according to the treatment group to which they are randomized to, rather than by the actual treatment they received.
- **Safety Population (Final Analysis only)**
  All safety analyses will be based on the Safety population, which is defined to include all subjects who entered into the study and receive at least one vaccination. All analysis based on the Safety population will be carried out using the actual treatment received.
- **Per-Protocol (PP) Population (Final Analysis only)**
  The Per-Protocol population is defined as mITT population excluding those subjects with at least one major protocol deviation. The PP population will exclude an enrolled subject if one of the following criteria is met:
    - Immunosuppressive drugs: Use of corticosteroids (excluding topical preparations) or immunosuppressive drugs within 30 days prior to vaccination, or anticipated use during the trial.
    - Subjects with any confirmed immunosuppressive or immunodeficient condition, including human immunodeficiency virus (HIV), hepatitis A, B or C infection or a family history of congenital or hereditary immunodeficiency
    - Subjects who received the wrong or no study medication
    - Subjects with other major protocol deviations

These criteria for potential protocol violation were identified at the time of planning the study. However, during the course of the trial unforeseen events may occur or new scientific knowledge may become available, therefore final decisions on whether any protocol violation could impact immune response and thus lead to exclusion from the PP population will be made by the sponsor on a case by case basis in a data review meeting. Sample testing issues may also lead to exclusion from the PP population for particular time points.

2.17 Changes in the Conduct of the Study or Planned Analysis

The statistical analysis plan is based on the final study protocols for Austria (Version 1.5; 24-Nov-2016) and Germany (Version 1.6; 19-Apr-2017). No changes in the conduct of the planned analysis as described in the CSP are intended.

However, the time point of the Preliminary Analysis was moved forward to August 2017. The Preliminary Analysis was initially planned to take place after all subjects completed Visit 3.

3. OVERALL STUDY INFORMATION

Treatment groups for the preliminary analysis as well the final analysis are defined in section 2.3. Overall study information analysis will be prepared for the:

- Preliminary analysis: mITT population.
- Final analysis: Safety, mITT and PP population.

3.1 Patient Disposition

The following tables will be provided:

- The number of subjects per analysis population and study site (frequency statistics)
- The number of subjects by treatment group and overall
- The number of subjects by study visit, treatment group and overall (frequency statistics)
- The number of major protocol deviations by treatment group and overall (Final Analysis only)

The following listings will be provided:

- Analysis population details (incl. reason not in analysis population)
- Attended study visits (incl. planned date and actual date)
- Protocol deviations (Final Analysis only)

3.2 Screening Failures and Drop-Outs

Following tables will be provided:

- The number of screening failures (frequency statistics)
- Early terminations by treatment group and overall (frequency statistics)
- Reason for early termination by treatment group and overall (frequency statistics)

The following listings will be provided:

- Screening failure with reason
- Early terminations with reason

4. BASELINE EVALUATION

Treatment groups were defined in section 2.3. For the Preliminary Analysis baseline evaluation tables will be produced for the mITT population. In the Final Analysis the tables will be repeated for the PP population.

4.1 Demographic Aspects

The following tables / listing will be provided:

- Age (calculated as difference in years between year of birth and year of informed consent) will be tabulated by treatment group and overall (summary statistics).
- Gender by treatment group and overall (frequency statistics)
- Ethnicity will be tabulated by treatment group and overall (frequency statistics)
- A data listing of all demographic data will be prepared (subject number, treatment group, date of birth, date of informed consent, age, gender and ethnicity).

4.2 Physical Examination

The following tables / listing will be provided:

- The results (normal / abnormal / not done) of the physical examination of ten body systems at screening will be tabulated by body system ("General appearance and skin", "Head/Eyes/Ears/Nose/Throat", "Cardiovascular System", "Respiratory System", "Abdominal and Gastrointestinal System", "Musculoskeletal System", "Neurological System", "Lymph nodes", "Other")
- A data listing of physical examinations at screening (including description of abnormal findings) will be prepared.

4.3 Vital Signs

The following tables / listing will be provided:

- Blood pressure (systolic and diastolic, in mmHg), pulse rate (in beats/min) and body temperature (in °C) and at baseline will be tabulated by treatment group and overall (summary statistics).
- A data listing of vital signs (patient number, treatment group, date of assessment, blood pressure systolic, blood pressure diastolic, pulse rate, body temperature) will be prepared.

4.4 Virology

A data listing of virology details (patient number, treatment group, sampling date, test parameter, result) will be prepared.

4.5 Pregnancy Test

A data listing of pregnancy test details at screening (patient number, treatment group, pregnancy test performed: yes/no/not applicable, date, result) will be prepared.

4.6 Medical History

Medical history entries will be coded using the Medical Dictionary for Regulatory Activities (MedDRA, cp. section 2.15). The version which will actually be used will also be indicated in the respective tables and listing.

The following tables / listings will be provided:

- The number and proportion of subjects with at least one medical history entry as well as the total number of medical history entries will be tabulated.
- Additionally, the number and proportion of subjects with at least one medical history entry will be tabulated by System Organ Class (SOC) and Preferred Term (PT) (frequency statistics). The table will be sorted by relative frequency of SOCs and by relative frequency of PTs within SOCs.
- A data listing will be provided for all medical history entries.

4.7 Vaccination History

Vaccination history covers the last three years prior to screening.

A data listing of vaccination history details will be provided.

4.8 Prior and Concomitant Medications

All medications entered in the concomitant medication-log of the eCRF will be coded using the WHO Dictionary (cp. section 2.15).

Medications stopped clearly prior (<) to the date of first study treatment will be considered prior medication, all other medications are considered to be concomitant. Medications with a missing stop date or an incomplete stop date where it cannot clearly be decided if the stop date was before or after the date of first study treatment or if "currently ongoing", "ongoing at final examination" or "dosage changed" is ticked will be considered concomitant.

The following tables/listings will be provided:

- The number and proportion of subjects with at least one concomitant medication as well as the total number of concomitant medications will be tabulated.
- Additionally, the number and proportion of subjects with at least one concomitant medication will be tabulated by ATC level 2. The table will be sorted by relative frequency of ATC level 2.
- A data listing will be provided for all prior medications (incl. medication, ATC level 2, start date, stop date, dose/unit/frequency, route of administration, indication)
- A data listing will be provided for all concomitant medications (incl. medication, ATC level 2, start date, stop date, ongoing, dose/unit/frequency, route of administration, indication)

5. EFFICACY ANALYSIS

Not applicable for this study.

6. IMMUNOGENICITY ANALYSIS

Immunogenicity analysis will be presented for the mITT and PP population for the Final Analysis, whereas the Preliminary Analysis is presented for the mITT population only. Analysis are stratified by treatment group (defined in subsection 2.3) and overall.

For statistics in tables only actual numbers can be used. Therefore the following substitution rules will apply:

Actual $PRNT_{50}$ value (used for listings)	Derived $PRNT_{50}$ value used for tables
Number (greater or equal 10)	number (greater or equal 10)
"< 10"	5
"> 1280"	1280
"MISSING"	missing

Actual ELISA (CHIK) value (used for listings)	Derived ELISA (CHIK) value used for tables
Number (greater or equal 2)	number (greater or equal 2)
"< 2"	1
"MISSING"	missing

Actual ELISA (Measles) value (used for listings)	Derived ELISA (Measles) value used for tables
Number (greater or equal 50)	number (greater or equal 50)
"< 50"	25
"> 5000"	5000
"MISSING"	missing

Seroconversion rates (PRNT_SC) will be calculated as follows:

- Case 1: If $PRNT_{50}$ value ≥ 10, then seroconversion PRNT_SC is set to “YES”,
- Case 2: If $PRNT_{50}$ value< 10, then seroconversion PRNT_SC is set to “NO”.
- Case 3: If the $PRNT_{50}$ value is missing then seroconversion PRNT_SC is set to “missing”
- Case 4: If $PRNT_{50}$ is “> 1280”, then seroconversion PRNT_SC is set to “YES”.

Seroconversion rates (ELISA_SC) will be calculated as follows:

- Case 1: If ELISA (CHIK) value ≥ 16, then seroconversion ELISA_SC is set to “YES”,
- Case 2: If ELISA (CHIK) value < 16, then seroconversion ELISA_SC is set to “NO”.
- Case 3: If the ELISA (CHIK) value is missing then seroconversion ELISA_SC is set to “missing”

6.1 Primary Endpoint

The primary immunogenicity endpoint is the immunogenicity on Day 56 in the mITT population confirmed by the presence of functional antibodies as determined by the plaque reduction neutralization test ($PRNT_{50}$).

Following tables will be provided:

- Number of functional antibodies blood samples drawn (yes/no) will be tabulated by treatment group and overall (frequency statistics).
- The geometric mean titer (GMT) of the functional antibodies by $PRNT_{50}$ will be tabulated by treatment group and overall (summary statistics).

Statistical analysis will be performed as described in section 2.7.1.

6.2 Functional Antibodies Assessment

6.2.1 Preliminary Analysis

For the Preliminary Analysis immunogenicity blood samples are taken at Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), ET visit (if ET up to Day 56) and for M1 and M2 additionally at Visit 0 (Day -28).

Following tables will be provided:

- Number of functional antibodies blood samples drawn (yes/no) will be tabulated by visit, treatment group and overall (frequency statistics).
- The geometric mean titer (GMT) of the functional antibodies by $PRNT_{50}$ will be tabulated by visit treatment group and overall (summary statistics).
- The seroconversion rate PRNT_SC by visit, treatment group and overall (frequency statistics).
- The geometric mean titer (GMT) of the functional antibodies by ELISA will be tabulated by visit treatment group and overall (summary statistics).

Following listing will be provided:

- A data listing of functional antibodies PRNT details will be provided (incl. visits).
- A data listing of functional antibodies ELISA details will be provided (incl. visits).

Statistical analysis will be performed as described in section 2.7.2.

6.2.2 Final Analysis

Immunogenicity blood samples for the final analysis are statistically analyzed for Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), Visit 5 (Day 196), Visit 6 (Day 224) and ET visit. Additionally for treatment groups M1 and M2 samples are taken at Visit 0 (Day -28), Visit 4 (Day 168).

Following tables will be provided:

- Number of functional antibodies blood samples drawn (yes/no) will be tabulated by visit, treatment group and overall (frequency statistics).
- The geometric mean titer (GMT) of the functional antibodies by $PRNT_{50}$ will be tabulated by visit treatment group and overall (summary statistics).
- The geometric mean titer (GMT) of the functional antibodies by ELISA will be tabulated by visit treatment group and overall (summary statistics).
- The seroconversion rate PRNT_SC by visit, treatment group and overall (frequency statistics).
- The seroconversion rate ELISA_SC by visit, treatment group and overall (frequency statistics)

Following listings will be provided:

- A data listing of functional antibodies PRNT details will be provided by visits.
- A data listing of functional antibodies ELISA details will be provided by visits.

Statistical analysis will be performed as described in section 2.7.2

6.4 Measles Antibodies Assessment

Measles antibody titers are taken at, at Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), and for M1 and M2 additionally at Visit 0 (Day -28) and ET visit if applicable.

Following tables/listing will be provided for the Preliminary and Final Analysis:

- The number of measles antibody titer samples drawn (yes/no) will be tabulated by visit, treatment group and overall (frequency statistics).
- The geometric mean titer (GMT) for the variable measles antibodies by ELISA will be tabulated by visit, treatment group and overall (summary statistics).
- A data listing of measles antibody results will be provided by visits.

6.5 T-cell Analysis

6.5.1 Preliminary Analysis

Samples of a subset of subjects (only in Vienna) will be analyzed for T cell immune response. Chikungunya virus specific T cells will be analyzed on Visit 3 (Day 56).

Following tables/listing will be provided:

- The number of functional Chikungunya virus specific T cells at Visit 3 by treatment group and overall (summary statistics).
- The geometric mean value for T cell immune response by treatment group and overall (summary statistics).
- A data listing of T-cell details will be provided.

Statistical analysis for T-cells will be performed as described in section 2.7.2

6.5.2 Final Analysis

Samples of a subset of subjects (only in Vienna) will be analyzed for T cell immune response at Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), Visit 5 (Day 196) and Visit 6 (Day 224) and additionally on Visit 4 (Day 168) for treatment group M1 and M2 and ET visit if applicable.

Following tables/listing will be provided:

- The number of functional, Chikungunya virus specific T cells by visit, treatment group and overall (summary statistics).
- The geometric mean value for T cell immune response tabulated by visit, treatment group and overall (summary statistics).
- A data listing of T-cell details will be provided by visits.

Statistical analysis for T-cells will be performed as described in section 2.7.2

6.7 Measles Virus shedding

Measles virus shedding will be analyzed in a subset of subjects randomized to treatment group A, B, C or D in the study center of AKH Vienna only at Visit 1 (Day 0), Visit 2 (Day 28) and Visit (Day 196). Besides the regular visits, subjects additionally will return to the study site on Day 7, 10, and 14 after the first injection.

Following tables/listing will be provided for the Final Analysis:

- The number of subjects participating in measles virus shedding (frequency statistics).
- The number of sample performed by visit and treatment group (frequency statistics).
- A data listing of measles virus shedding details (incl. date of separate informed consent and samples obtained: urine/saliva/whole blood, sample results: urine/saliva).
- The number of subjects with positive shedding results (value ≥ 20) in urine by visit and treatment group (frequency statistics).
- The number of subjects with positive shedding results (value ≥ 20) in saliva by visit and treatment group (frequency statistics).

7. PHARMACOKINETICS / PHARMACODYNAMICS ANALYSIS

Not applicable for this study.

8. SAFETY ANALYSIS

The mITT population will be used for the Preliminary Analysis, whereas the Safety population will be used for the Final Analysis. Analysis will be stratified by treatment group and overall. Safety analysis will be done except section 8.3 (Adverse event) for the Final Analysis only.

8.1 Extent of Exposure

The treatment duration (in days) and the study duration (in days) will be calculated as follows:

- date of last administered vaccine – date of first vaccination + 1
- date of last attended visit – date of signed Informed consent + 1

The treatment duration as well as the study duration will be tabulated (summary statistics). A data listing will be provided.

8.2 Study medication

The study medication will be prepared at site and administered during the study visits. Each treatment will be documented in the subject's charts, the eCRF and an IMP Inventory Log (CSP section 5.8). A data listing of study medication details will be provided.

8.3 Adverse Events

Adverse Events are statistically analyzed once for the Preliminary Analysis up to Visit 3 and once for the final analysis.

The Preliminary Analysis includes all Adverse Events with a start date which is at of before the date of Visit 3.

Adverse Events will be coded using the Medical Dictionary for Regulatory Activities (cp. section 2.15)

Solicited AEs comprise reactions at the injection site or systemic reactions that are typical for vaccinations:

- Solicited local AEs (injection site reactions) are the following: injection site pain, tenderness, pruritus, erythema (redness), edema, induration (hardening)
- Solicited systemic AEs are the following: headache, fever, myalgia, limb discomfort, arthralgia, flu-like symptoms, nausea, vomiting, rash and excessive fatigue.

For solicited local and systemic AEs were summarized for a 7 day period. Solicited AEs will not be coded into MedDRA and no assessment of relatedness was performed.

An AE is considered to be related to study drug if the "Causal relationship to study treatment" was considered "definite", "probable", "possible" or the classification is missing.

For solicited local and systemic AEs the following tables will be tabulated:

- at least one AE
- at least one serious AE
- at least one severe AE

- at least one AE by severity

An AE is considered to be a treatment-emergent AE (TEAE) if, and only if, first onset or worsening is simultaneous with or after first vaccination (AE start date is greater or equal first vaccination date). AEs for which it cannot be clearly decided if the start date was before or on/after first vaccination will be considered treatment-emergent, following a worst case approach.

For unsolicited AEs the following tables will be tabulated:

- at least one TEAE
- at least one severe TEAE
- at least one serious TEAE
- at least one TEAE related to study drug
- at least one medically attended TEAE
- at least one TEAE where an action was taken (i.e. no action taken was NOT ticked)
- at least one TEAE of special interest (arthritis)

The same tables grouped by SOC and PT will be provided.

Statistical analysis will be performed as described in section 2.7.3.

The following further summary tables will be provided:

- Number of subjects with solicited adverse event by symptom and severity -- MV-CHIK vs. control
- Number of subjects with unsolicited adverse event by symptom and severity -- MV-CHIK vs. control, for the five most frequent adverse events

The following listings will be provided:

- All AEs (including information if local/ systemic solicited, unsolicited)
- Solicited local adverse events
- Systemic adverse events
- Unsolicited adverse events
- Serious adverse events (SAEs)
- AEs leading to death

The following figures will be provided:

- Bar chart for number of subjects with solicited adverse event by event and maximum severity
- Bar chart for number of subjects with unsolicited adverse event by preferred term and maximum severity, where only the five most frequent terms will be included

8.4 Laboratory Parameters

The following laboratory parameters are analyzed throughout the study at Screening, Visit 3 (Day 56), Visit 6 (Day 224) and ET visit. The laboratory parameters will be converted to the standard units provided in the table below:

Type	Parameter	Standard Unit
Hematology	Hemoglobin	g/L
Hematology	Hematocrit	%
Hematology	Erythrocytes	T/L
Hematology	Leukocytes	G/L
Hematology	Platelets	G/L
Hematology	Neutrophils	G/L
Hematology	Basophils	G/L
Hematology	Lymphocytes	G/L
Hematology	Monocytes	G/L
Hematology	Eosinophils	G/L
Hematology	Eosinophils	G/L
Hematology	Neutrophils/Leukocytes	%
Hematology	Lymphocytes/Leukocytes	%
Hematology	Monocytes/Leukocytes	%
Hematology	Eosinophils/Leukocytes	%
Hematology	Basophils/Leukocytes	%
Clinical chemistry	Bilirubin	µmol/L
Clinical chemistry	Creatinine	µmol/L
Clinical chemistry	Alanine Aminotransferase (ALT)	U/L
Clinical chemistry	Aspartate Aminotransferase (AST)	U/L
Clinical chemistry	Sodium	mmol/L
Clinical chemistry	Calcium	mmol/L
Clinical chemistry	Potassium	mmol/L
Clinical chemistry	Alkaline phosphatase	U/L
Coagulation	Prothrombin time (PT)	%

Type	Parameter	Standard Unit
Coagulation	Activated partial thromboplastin time (aPTT)	s
Coagulation	Prothrombin Time absolute	s
Coagulation	Fibrinogen	g/L

8.4.1 Tables of Hematology, Clinical chemistry and Coagulation

The following tables will be provided:

- Separate tables will be provided for hematology, clinical chemistry and coagulation.
- The number of available samples as documented in the eCRF (item "Has blood sample been drawn" is set to “yes”) will be tabulated separately by parameter and by visit (frequency statistics).
- Absolute values for all laboratory parameters will be tabulated by visit (summary statistics).
- Absolute changes from screening (difference: value after screening – value at screening) for all laboratory parameters will be tabulated by visit (summary statistics).

8.4.2 Listings of Hematology, Clinical chemistry and Coagulation

- Separate listings will be provided for hematology, clinical chemistry and coagulation parameters.
- Data listings will be prepared for all laboratory parameters outside normal limits. In these listings the values will be presented in the units in which they have been determined and in the standard units provided above, the sampling date, the clinical relevance (yes/no) as well as causa relationship if clinically relevant.

8.5 Urinalysis

Laboratory parameters are analyzed at Screening, Visit 3 (Day 56), Visit 6 (Day 224) and ET visit. The following tables/listing will be provided:

- The number of available samples as documented in the eCRF (item "Has urine sample been taken" is set to “yes”) will be tabulated separately by parameter and by visit (frequency statistics).
- The value for pH and specific gravity (in g/ml) will be tabulated by visit (summary statistics).
- The results (outcome: negative/1+/2+/3+/4+/not available for nitrite, protein, glucose, ketones, urobilinogen, bilirubin and erythrocytes (white blood cells) will be tabulated by visit (frequency statistics).
- A data listing of urinalysis details (including sampling date, age, clinical relevance (yes/no) as well as the specification if relevant) will be prepared.

8.6 Vital Signs

Vital signs are investigated at Screening, Visit 0 (Day 0), Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), Visit 4 (Day 168), Visit 5 (Day 196), Visit 6 (Day 224) and ET visit. The following tables / listing will be provided:

- Blood pressures (systolic/diastolic, in mmHg) and pulse rate (in beats/min) will be tabulated by visit (summary statistics).
- A data listing with vital signs at screening (subject number, time of assessment, blood pressure and pulse rate) will be provided.

8.7 Symptom-directed physical examination

Symptom-directed physical exam is investigated at Visit 0, Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), Visit 4 (Day 168), Visit 5 (Day 196), Visit 6 (Day 224) and ET visit. The following tables / listing will be provided:

- The presence (yes / no / not assessed) of symptom-directed physical exams of ten symptoms will be tabulated by symptom (headache, fever, myalgia, limb discomfort, joint pain (arthralgia), flu-like symptoms, nausea, vomiting, rash, excessive fatigue, other).
- A data listing of symptom-directed physical exams details will be prepared.

8.8 Local tolerability

The investigator's assessments of local tolerability of previous injection site: injection side pain (pain without touching), tenderness (pain upon touching), itching (pruritus), redness (erythema), hardening (induration) and swelling (edema) will be analyzed at Visit 0, Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), Visit 4 (Day 168), Visit 5 (Day 196), Visit 6 (Day 224) and ET visit by time-points (before vaccination (previous injection site) / 1 hour after vaccination). The following tables / listing will be provided:

- The results (yes/no/not assessed) will be tabulated by local tolerability symptom, visit and time-point (frequency statistics).
- A data listing of local tolerability of previous injection site symptoms will be prepared.

8.9 System-based physical assessment

System-based assessment is investigated at Visit 0, Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), Visit 4 (Day 168), Visit 5 (Day 196), Visit 6 (Day 224) and ET visit. The following tables / listing will be provided:

- The results (normal / abnormal / not done) of system-based assessments will be tabulated by body system (general appearance and skin; head/eyes/ears/nose/throat; cardiovascular system; respiratory system; abdominal and gastrointestinal system; musculoskeletal system; neurological system; lymph nodes; other).
- A data listing of system-based assessments (including date of examination, clinical relevance and description of abnormal findings) will be prepared.

8.10 Pregnancy Test

Urine pregnancy test are performed at Screening, Visit 0, Visit 1 (Day 0), Visit 2 (Day 28), Visit 3 (Day 56), Visit 4 (Day 168), Visit 5 (Day 196), Visit 6 (Day 224) and ET visit. The following tables / listing will be provided:

- The result of the pregnancy test (outcome: negative, positive, not applicable) will be tabulated by visit for female subjects (frequency statistics).
- A data listing of pregnancy test details (date of pregnancy test, result, test performed) will be prepared.

9. CONVERSION FACTORS FOR LABORATORY PARAMETERS

Conversion of laboratory parameters from a study site specific laboratory unit into the standard unit is performed via the following formula:

- Value in standard unit = value in study site specific unit * conversion factor

The following values will be used for conversion factors.

Parameter	Standard Unit	Site Unit	Conversion Factor
Alanine Aminotransferase	U/L	mU/mL	1
Alkaline Phosphatase	U/L	mU/mL	1
Aspartate Aminotransferase	U/L	mU/mL	1
Bilirubin	µmol/L	mg/dL	17.1
Creatinine	µmol/L	mg/dL	88.4025
Erythrocytes	T/L	Tera/L	1
Fibrinogen	g/L	mg/dL	0.01
Hematocrit	%	L/L	100
Hemoglobin	g/L	g/dL	10
Leukocytes	G/L	Giga/L	1
Platelets	G/L	Giga/L	1
Potassium	mmol/L	mval/L	1
Sodium	mmol/L	mval/L	1
Specific Gravity (Urine)	g/L	g/ml	1000

10. LIST OF TABLES, DATA LISTINGS AND FIGURES

10.1 List of Tables

No	IA	FA	Legend	Content
			Overall Study Information	
1.1	x	x	Number of subjects in each analysis population by study site and overall	
1.2	x	x	Number of subjects in each analysis population by treatment group and overall	
1.3	x	x	Number of screening failures	
1.4		x	Number of subjects by visit (incl. early terminations) by treatment group and overall (Safety population)	
1.5	x	x	Number of subjects by visit (incl. early terminations) by treatment group and overall (mITT population)	
1.6		x	Number of subjects by visit (incl. early terminations) by treatment group and overall (PP population)	
1.7		x	Early terminations and reasons by treatment group and overall (Safety population)	
1.8	x	x	Early terminations and reasons by treatment group and overall (mITT population)	
1.9		x	Early terminations and reasons by treatment group and overall (PP population)	
1.10		x	Number of major protocol deviations by treatment group and overall (Safety population)	
1.11		x	Number of major protocol deviations by treatment group and overall (mITT population)	
			Baseline Data	
2.1.1	x	x	Demography and baseline characteristics (mITT Population)	Age, gender, ethnic group
2.1.2	x	x	Physical examination results at screening by body system treatment group and overall (mITT population)	
2.1.3	x	x	Vital signs (mITT Population)	Systolic/diastolic blood pressure, pulse rate, body temperature
2.1.4	x	x	Medical history and concomitant medication by treatment group and overall (mITT Population)	Medical history, concomitant medication
2.1.5	x	x	Medical history by SOC and PT (mITT Population)	
2.1.6	x	x	Concomitant medication by ATC level 2 (mITT Population)	
2.2.1 - 2.2.6		x	Repeat tables for the Safety population	
2.3.1 - 2.3.6		x	Repeat tables for the PP population	
			Immunogenicity Analysis	
Primary Endpoint				
3.1.1	x	x	Number of subjects with functional antibody blood samples drawn at Day 56, treatment group and overall (mITT population)	
3.1.2	x	x	Primary Endpoint: GMT of functional antibodies by PRNT at Day 56 by treatment group and overall (mITT population)	
3.1.3	x	x	Primary Endpoint: ANOVA with fixed factor treatment group for GMT of functional antibodies by PRNT at Day 56 (mITT population)	

Functional Antibodies				
3.1.4	x	x	Number of subjects with functional antibody blood samples drawn by visit, treatment group and overall (mITT population)	
3.1.5	x	x	GMT of functional antibodies by PRNT by visit, treatment group and overall (mITT population)	
3.1.6	x	x	ANOVA with fixed factor treatment group for GMT of functional antibodies by PRNT by visit (mITT population)	
3.1.7		x	ANOVA with fixed factors treatment group for GMT of functional antibodies by PRNT between group A and B - 28 days after second vaccination (mITT population)	
3.1.8		x	ANOVA with fixed factors treatment group for GMT of functional antibodies by PRNT between group C and D - 28 days after second vaccination (mITT population)	
3.1.9		x	ANOVA with fixed factors treatment group for GMT of functional antibodies by PRNT between group M1 and M2 - 28 days after second vaccination (mITT population)	
3.1.10	x		GMT of functional antibodies by PRNT - 28 days after first vaccination by baseline measles titer group and overall (mITT population)	
3.1.11	x		ANOVA with fixed factor baseline measles titer group for GMT of functional antibodies by PRNT - 28 days after first vaccination (mITT population)	
3.1.12		x	GMT of functional antibodies by PRNT - 28 days after second vaccination by baseline measles titer group and overall (mITT population)	
3.1.13		x	ANOVA with fixed factor baseline measles titer group for GMT of functional antibodies by PRNT - 28 days after second vaccination (mITT population)	
3.1.14	x	x	Seroconversion rate PRNT_SC by visit, treatment group and overall (mITT population)	
3.1.15	x	x	GMT of functional antibodies by ELISA by visit, treatment group and overall (mITT population)	
3.1.16	x	x	ANOVA with fixed factor treatment group for GMT of functional antibodies by ELISA by visit (mITT population)	
3.1.17	x	x	Seroconversion rate ELISA_SC by visit, treatment group and overall (mITT population)	
Measles Antibodies				
3.1.18	x	x	Number and proportion of subjects with measles antibody titer samples drawn by visit, treatment group and overall (mITT population)	
3.1.19	x	x	GMT for ELISA measles antibodies by visit, treatment group and overall (mITT population)	
T-cell Analysis				
3.1.20	x	x	Number of subjects of functional Chikungunya virus specific T cells by visit, treatment group and overall (mITT population)	
3.1.21	x	x	GMT for T cell immune by visit, treatment group and overall (mITT population)	
3.1.22	x	x	ANOVA with fixed factor treatment group for T-cells by visit (mITT population)	
Measles Virus Shedding				
3.1.23		x	Number of subjects participating in measles virus shedding by treatment group and overall (mITT population)	
3.1.24		x	Number of sample performed by visit, treatment group and overall (mITT population)	

3.1.25		x	Number of subjects with positive shedding results in urine by visit, treatment group and overall (mITT population)	
3.1.26		x	Number of subjects with positive shedding results in saliva by visit, treatment group and overall (mITT population)	
3.2.1 - 3.2.26		x	Repeat the tables for the PP population	
			Safety Analysis	
4.1		x	Extent of Exposure (Safety population)	Study duration, Treatment duration
4.2	x	x	Solicited Adverse Events ('Analysis' population)	AE, serious AE, severe AE, AE by severity
4.3	x	x	Unsolicited Adverse Events ('Analysis' population)	TEAE, serious TEAE, severe TEAE, TEAE related to study drug, medically attended TEAE, TEAE where an action was taken, TEAE of special interest (arthritis)
4.4	x	x	At least one unsolicited TEAE by SOC, PT, treatment group ('Analysis' population)	
4.5	x	x	At least one severe unsolicited TEAE by SOC, PT, treatment group ('Analysis' population)	
4.6	x	x	At least one serious unsolicited TEAE by SOC, PT, treatment group ('Analysis' population)	
4.7	x	x	At least one unsolicited TEAE related to study drug by SOC, PT, treatment group ('Analysis' population)	
4.8	x	x	At least one medically attended unsolicited TEAE by SOC, PT, treatment group ('Analysis' population)	
4.9	x	x	At least one unsolicited TEAE where an action was taken SOC, PT, treatment group ('Analysis' population)	
4.10	x	x	At least one unsolicited TEAE of special interest by SOC, PT, treatment group ('Analysis' population)	
4.11	x	x	At least one unsolicited TEAE related to study drug by SOC, PT, treatment group ('Analysis' population)	
4.2 - 4.11	x		Use in tables 4.2 - 4.11 the mITT population as 'Analysis' population	
4.2 - 4.11		x	Use in tables 4.2 - 4.11 the Safety population as 'Analysis' population	
4.12		x	Number of subjects with laboratory samples drawn by category, visit, treatment group (Safety population)	
4.13		x	Hematology laboratory: absolute values by parameter, visit, treatment group (Safety population)	
4.14		x	Clinical chemistry laboratory: absolute values by parameter, visit, treatment group (Safety population)	
4.15		x	Coagulation laboratory: absolute values by parameter, visit, treatment group (Safety population)	
4.16		x	Hematology laboratory: absolute changes from screening by parameter, visit, treatment group (Safety population)	
4.17		x	Clinical chemistry laboratory: absolute changes from screening by parameter, visit, treatment group (Safety population)	
4.18		x	Coagulation laboratory: absolute changes from screening by parameter, visit, treatment group (Safety population)	
4.19		x	Number of subjects with urine samples drawn by category, visit, treatment group (Safety population)	
4.20		x	Quantitative urinalysis by parameter, visit, treatment group (Safety	

			population)	
4.21		x	Qualitative urinalysis by parameter, visit, treatment group (Safety population)	

4.22		x	Systolic blood pressure by visit, treatment group (Safety population)	
4.23		x	Diastolic blood pressure by visit, treatment group (Safety population)	
4.24		x	Pulse rate by visit, treatment group (Safety population)	
4.25		x	Body temperature by visit, treatment group (Safety population)	
4.26		x	Presence of symptom-directed physical examination by symptom, visit, treatment group (Safety population)	
4.27		x	Local tolerability by symptom, visit and time-point, treatment group (Safety population)	
4.28		x	Presence of any local tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.29		x	Presence of any local tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.30		x	Presence of each local tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.31		x	Presence of each local tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.32		x	Severity of any local tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.33		x	Severity of any local tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.34		x	Severity of each local tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.35		x	Severity of each local tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.36		x	Size of affected areas for redness (erythema), swelling (edema) and hardening (induration), by time-point, treatment group (Subject Diary, Safety population)	
4.37		x	Presence of any systemic tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.38		x	Presence of any systemic tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.39		x	Presence of each systemic tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.40		x	Presence of each systemic tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.41		x	Severity of any systemic tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.42		x	Severity of any systemic tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.43		x	Severity of each systemic tolerability symptom by time-point, treatment group (Subject Diary, Safety population)	
4.44		x	Severity of each systemic tolerability symptom by diary period and overall by treatment group (Subject Diary, Safety population)	
4.45		x	Body temperature by time-point, treatment group (Safety population)	
4.46		x	System-based assessment results by body system, visit, treatment group (Safety population)	
4.47		x	Result of pregnancy test by visit, treatment group (Safety population)	

10.2 List of Data Listings

No	IA	FA	Legend	Content
			Overall Study Information	
1.1	x	x	Analysis population details	Subject number, Country, Site, Treatment group, Safety population, Reason for not Safety, mITT population, Reason for not mITT, PP population, Reason for not PP
1.2	x	x	Screening failures with reason	Subject number, Country, Date of informed consent, Reason for screening failure
1.3		x	Protocol deviations	Subject number, Country, Treatment group, Deviation type, Deviation, Severity
1.4	x	x	Early terminations with reason (Randomized subjects)	Subject number, Country, Treatment group, Date of study end, Reason, Visit attendance status
1.5	x	x	Attended visits (Randomized subjects)	Subject number, Country, Treatment group, Visit, Date of Visit, Reason if out of time window
			Baseline Data	
2.1	x	x	Demographic data (Randomized subjects)	Subject number, Country, Treatment group, Year of birth, Date of IC, Age [years], Gender, Ethnic origin, Other origin
2.2	x	x	Physical examination (Randomized subjects)	Subject number, Country, Treatment group, Body system, Specification other body system, Result, Specification of Abnormality
2.3	x	x	Vital signs (Randomized subjects)	Subject number, Country, Treatment group, Systolic blood pressure [mmHg], Diastolic blood pressure [mmHg], Pulse rate [b/min], Body temperature [°C]
2.4	x	x	Virology (Randomized subjects)	Subject number, Country, Treatment group, Date of sample drawn, Parameter, Result
2.5	x	x	Pregnancy test (Randomized subjects)	Subject number, Country, Treatment group, Urine pregnancy test performed, Date of of pregnancy test, Result
2.6	x	x	Medical history (Randomized subjects)	Subject number, Country, Treatment group, Condition, MedDRA Preferred Term, System organ class, Start date, End date, Ongoing
2.7	x	x	Vaccination history (Randomized subjects)	Subject, Treatment group, Date of last measles vaccination, Any vaccinations within 3 years prior screening, Date of vaccination, Trade name
2.8	x	x	Prior medications (Randomized subjects)	Subject number, Country, Treatment group, Medication, ATC (level 2), Start date, End date, Dose frequency, Route of administration, Indication
2.9	x	x	Concomitant medications (Randomized subjects)	Subject number, Country, Treatment group, Medication, ATC (level 2), Start date, End date, Ongoing, Dose frequency, Route of administration, Indication

			Immunogenicity Analysis	
3.1	x	x	Functional Antibodies Assessment (PRNT) (Randomized subjects)	Subject number, Country, Treatment group, Visit, Functional antibody titer sample drawn, Date of sample, Time of sample, Titer [IU/ml]
3.2	x	x	Functional Antibodies Assessment (ELISA) (Randomized subjects)	Subject number, Country, Treatment group, Visit, Functional antibody titer sample drawn, Date of sample, Time of sample, Titer [IU/ml]
3.3	x	x	Measles Antibodies Assessment (Randomized subjects)	Subject number, Country, Treatment group, Visit, Measles antibody titer sample drawn, Date of sample, Time of sample, Titer [IU/ml], negative (no quantit. result available), Reason not drawn
3.4	x	x	T-cell details (Randomized subjects)	Subject number, Country, Treatment group, Visit, Functional antibody titer sample drawn, Date of sample, Time of sample, Number of spots
3.5		x	Measles Virus shedding (Randomized subjects)	Subject number, Country, Treatment group, Measles virus shedding observation, Date of separate IC, Visit/Day, Date, Urine sample obtained, Saliva sample obtained, Whole Blood sample obtained, urine result, saliva result,
			Safety Analysis	
4.1		x	Extent of exposure (Randomized subjects)	Subject number, Treatment group, Date informed consent, Date of first vaccination, Date of last vaccination, Date of last attended visit, Treatment duration [days], Study duration [days]
4.2		x	Study medication details (Randomized subjects)	Subject number, Country, Treatment group, Vaccination been performed, Date/time, Medication, Reason not vaccinated
	x	x	Adverse Events (Randomized subjects)	Subject number, Treatment group, AE term,
4.3				Part 1: Country , Type (local solicited, systemic solicited, unsolicited), MedDRA Preferred Term, System organ class Start date, End date, Medically attended
4.4				Part 2: , Severity, Serious AE,Causality, Action taken in general, Action taken on the investigational product, Outcome
	x	x	Solicited local AEs (Randomized subjects)	Subject number, Country, Treatment group, AE term,
4.5.				Part 1: Start date, End date, Medically attended, Severity, Serious AE
4.6				Part 2: Causality, Action taken in general, Action taken on the investigational product, Outcome
	x	x	Systemic AEs (Randomized subjects)	Subject number, Country, Treatment group, AE term,
4.7				Part 1: Start date, End date, Medically attended, Severity, Serious AE
4.8				Part 2: Causality, Action taken in general, Action taken on the investigational product, Outcome
	x	x	Unsolicited AEs (Randomized subjects)	Subject number, Treatment group, AE term,
4.9				Part 1: Country, MedDRA Preferred Term, System organ class, Start date, End date, Medically attended
4.10				Part 2: Severity, Serious AE, Causality, Action taken in general, Action taken on the

				investigational product, Outcome
	x	x	Serious AEs (Randomized subjects)	Subject number, Treatment group, AE term,
4.11				Part 1: Country, MedDRA Preferred Term, System organ class, Start date, End date, Medically attended
4.12				Part 2: Severity, Serious AE, Causality, Action taken in general, Action taken on the investigational product, Outcome
	x	x	AEs leading to death (Randomized subjects)	Subject number, Treatment group, AE term,
4.13				Part 1: MedDRA Preferred Term, System organ class, Start date, End date, Medically attended
4.14				Part 2: Severity, Serious AE, Causality, Action taken in general, Action taken on the investigational product, Outcome
4.15		x	Hematology laboratory parameter (Randomized subjects)	Subject ID, Country, Treatment group, Visit, Date, Parameter, Value (site), Unit (site), Normal range, Clinical relevance, Causal relationship, Value (standard), Unit (standard), Change from screening
4.16		x	Clinical chemistry laboratory parameter (Randomized subjects)	Subject ID, Country, Treatment group, Visit, Date, Parameter, Value (site), Unit (site), Normal range, Clinical relevance, Causal relationship, Value (standard), Unit (standard), Change from screening
4.17		x	Coagulation laboratory parameter (Randomized subjects)	Subject ID, Country, Treatment group, Visit, Date, Parameter, Value (site), Unit (site), Normal range, Clinical relevance, Causal relationship, Value (standard), Unit (standard), Change from screening
4.18		x	Urinalysis (Randomized subjects)	Subject ID, Country, Treatment group, Visit, Date, Parameter, Value/Result, Unit, Normal range, Clinical relevance, Causal relationship, Specification
4.19		x	Vital signs (Randomized subjects)	Subject number, Country, Treatment group, Visit, Date, Systolic blood pressure [mmHg], Diastolic blood pressure [mmHg], Pulse rate [b/min], Body temperature [°C]
4.20		x	Symptom-directed physical exam (Randomized subjects)	Subject number, Country, Treatment group, Visit, Symptom, Symptom present
4.21		x	Local tolerability (Randomized subjects)	Subject number, Country, Treatment group, Visit, Time-point, Date and time, Symptom, Symptom present
4.22		x	System-based assessment (Physical examination, Randomized subjects)	Subject number, Country, Treatment group, Visit, Assessment necessary, Body system, Result, Specification
4.23		x	Pregnancy test (Randomized subjects)	Subject number, Country, Treatment group, Visit, Urine pregnancy test performed, Date of of pregnancy test, Result

10.3 List of Figures

No	IA	FA	Legend
			Safety Evaluation
4.1	x	x	Bar chart for number of subjects with local solicited adverse event by symptom and severity -- MV-CHIK vs. control (safety population)
4.2	x	x	Bar chart for number of subjects with systemic solicited adverse event by symptom and severity -- MV-CHIK vs. control (safety population)
4.3	x	x	Bar chart for number of subjects with unsolicited adverse event by symptom and severity for the five most frequent unsolicited adverse events -- MV-CHIK vs. control (safety population)