GlaxoSmithKline	Study RAP	
Study Id: 108706	**Abbreviated Title:** PRO HIV-005	
Version: ☐ Draft version	☒ Final	**Date:** 26SEP 2008

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Study Reporting and Analysis Plan

HIV Prophylactic Vaccine

PRO HIV-005 (108706)

GlaxoSmithKline Biologicals

Global Clinical Research & Development

Study Reporting and Analysis Plan Approval

Title:	Dose-ranging study to evaluate the safety and immunogenicity of GSK Biologicals' HIV vaccine 732461, adjuvanted or not, when administered as a 3 2-dose schedule to healthy adult HIV seronegative volunteers, aged 18 to 40 years.
eTrack study number	108706
eTrack abbreviated title	PRO HIV-005
Scope:	All Final data pertaining to the above study
Date:	11 MAR 2008 **(amendment 1)**
Co-ordinating author:	PPD (4Clinics), PPD (Amendment 1) PPD (Amendment 2)
Others author(s):	

Approved by:

	Name	Signature	dd-mmm-yyyy
Worldwide Project Clinical Development Manager	PPD		
Project Statistician	PPD		
Statistical Manager	PPD		

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LIST OF ABBREVIATIONS

AE	Adverse event
ATP	According to Protocol
BCSP	Biologicals clinical safety and pharmacovigilance
CD40L	Immune cells that carry a marker on its surface known as Cluster of Differentiation 40L Immune cells that carry a marker on its surface known as Cluster of Differentiation 40L
CI	Confidence Interval
CMI	Cell-mediated immunity
ELISA	Enzyme Linked Immunosorbent Assay
GCRD	Global clinical research and developpement
GMT	Geometric mean titer
GSK	GlaxoSmithKline
MedDRA	Medical Dictionary for Regulatory Activities
RAP	Report analysis plan
SAE	Serious adverse event
SRT	Safety review team

1. INTRODUCTION

The purpose of this document is to describe (on the basis of protocol/amendment dated 08 October 2007):

- criteria for evaluation of objectives in terms of endpoints, study cohorts, derived data, group description and interim analysis (paragraph 2);
- statistical methodology and planned analyses (paragraph 3);
- change(s) from protocol (paragraph 4);
- individual listings, list of tables and template tables (paragraph 5).

Any planned modification of the statistical analyses should be documented by an amendment to the RAP (Table 1).

Table 1. List of amendments to the RAP

Date	Description
28 JAN 2008	First version
18 FEB 2008	Amendment 1 cut-off definition for CD4/CD8 modification of CD8 exploratory endpoints Correction of grading for exploratory safety analysis N definition for CMI responders
26SEP2008	Amendement 2 Precisions for final analysis (month 12 data available): ATP cohort definition clarified Group order has been modified to account for the order actually used in the presentations

2. CRITERIA FOR EVALUATION OF OBJECTIVES

2.1. Objectives

2.1.1. Primary objectives

- To evaluate the reactogenicity and safety of the candidate vaccine F4co (p24-RT-Nef-p17) with or without AS01B adjuvant at three different doses (10-30-90 µg).
- To evaluate the CD4+ T-cell response to the candidate vaccine F4co (p24-RT-Nef-p17) with or without AS01B at three different doses (10-30-90 µg) in terms of proportion of responders to at least 1, 2, 3 antigens and to all 4 antigens determined two weeks after the second vaccination.

2.1.2. Secondary Objectives

- To evaluate the CD4+ T-cell immune response to the candidate vaccine F4co (p24-RT-Nef-p17) with or without AS01B at three different doses (10-30-90 µg) after two vaccinations.
- To evaluate the serological response to the candidate vaccine F4co (p24-RT-Nef-p17) with or without AS01B at three different doses (10-30-90 µg) after two vaccinations
- To evaluate the persistence of cell-mediated and serological responses to the candidate vaccine F4co (p24-RT-Nef-p17) with or without AS01B at three different doses (10-30-90 µg).

2.1.3. Exploratory Objectives

- To evaluate the cross clades reactivity determined by ICS 2 weeks and/or 1 month after the second vaccination.
- To evaluate the CD8+ T-cells immune response to the candidate vaccine F4co (p24-RT-Nef-p17) with or without AS01B at three different doses (10-30-90 µg).

2.2. Endpoints

2.2.1. Primary endpoints

Reactogenicity and safety

- Occurrence, intensity and relationship to vaccination of solicited local and general symptoms during a 7-day (Day 0 to Day 6) follow-up period after each vaccination.
- Occurrence, intensity and relationship to vaccination of unsolicited symptoms during a 30-day (Day 0 to Day 29) follow-up period after each vaccination.

- Occurrence and relationship to vaccination of serious adverse events during the whole study period.
- Haematological and biochemical levels at months 0, 1, 2, 6, 9, 12 and at Day 44 (two weeks after the second vaccination) in all subjects.

Immunogenicity

- Frequency of CD4+ T cells expressing at least two cytokines including IL-2 equal or above the cut-off to at least 1, 2, 3 antigens and to all 4 antigens at Day 44 (two weeks after the second vaccination).

2.2.2. Secondary endpoints

- Frequency of p17, p24, Nef and RT-specific CD4+ T cells expressing IL-2 and/or TNF-α and/or IFN-γ and/or CD40-L, as determined by ICS at Months 0, 2, 6, 12 and at Day 44 (two weeks after the second vaccination).
- Frequency of p17, p24, Nef and RT-specific CD4+ T cells expressing at least 2 cytokines including IL-2 equal or above the cut-off at Months 0, 2, 6, 12 and at Day 44 (two weeks after the second vaccination).
- Antibody titers to p17, p24, Nef, RT and F4co as measured by ELISA at Months 0, 2, 6, 12 and at Day 44 (two weeks after the second vaccination).

2.2.3. Exploratory endpoints

- Frequency of p17, p24, Nef and RT-specific CD4+ T cells to other HIV clades expressing IL-2 and/or TNF-α and/or IFN-γ and/or CD40-L, as determined by ICS at Day 44 (two weeks after the second vaccination) and/or at Month 2.
- Frequency of p17, p24, Nef and RT-specific CD8+ T cells expressing ~~**IL-2 and/or**~~ TNF-α and/or IFN-γ ~~**and/or CD40-L**~~, as determined by ICS at Months 0, 2, 6, 12 and at Day 44 (two weeks after the second vaccination) **(amendment 1)**.
- Frequency of p17, p24, Nef and RT-specific CD8+ T cells expressing at least 2 cytokines (~~**IL-2 and/or**~~ TNF-α and/or IFN-γ ~~**and/or CD40-L**~~) equal or above the cutoff at Months 0, 2, 6, 12 and at Day 44 (two weeks after the second vaccination) **(amendment 1)**.

2.3. Study cohorts

Three cohorts will be evaluated, as described below.

2.3.1. Total Vaccinated cohort

The Total Vaccinated cohort will include all vaccinated subjects.

Thus, the Total Vaccinated cohort for analysis of safety will include all subjects with at least one vaccine administration documented. This is valid for both Month 2 and Month12 analyses

The Total Vaccinated cohort for analysis of immunogenicity will include vaccinated subjects for whom data concerning immunogenicity endpoint measures are available. This is valid for both Month 2 and Month12 analyses

The Total Vaccinated cohort analysis will be performed per treatment actually administered. This is valid for both Month 2 and Month12 analyses

2.3.2. According-To-Protocol (ATP) cohort for analysis of safety

The ATP cohort will include all vaccinated subjects

- who have received at least one dose of study vaccine according to their random assignment.
- with sufficient data to perform an analysis of safety (at least one dose with safety follow-up).
- for whom administration route of study vaccines is known.
- who have not received a vaccine not specified or forbidden in the protocol. This criterion would potentially lead to a different ATP cohort for Month 2 and for Month 12 analyses.
- for whom the randomization code has not been broken. This criterion would potentially lead to a different ATP cohort for Month 2 and for Month 12 analyses.

It has been decided to present the results for Month 6 and Month 12 based on the Month 12 cohort definition, while all results produced at Month 2 analysis will be based on Month 2 cohort.

2.3.3. According-To-Protocol (ATP) cohort for analysis of immunogenicity

The ATP cohort for analysis of immunogenicity will include all evaluable subjects, (i.e., those meeting all eligibility criteria, complying with the procedures and intervals defined in the protocol, with no elimination criteria during the study) for whom data concerning immunogenicity endpoint measures are available. This definition would potentially lead to a different ATP cohort for Month 2 and for Month 12 analyses.

It has been decided to present the results for Month 6 and Month 12 based on the Month 12 cohort definition, while all results produced at Month 2 analysis will be based on Month 2 cohort

2.4. Group description

The following group description will be used for the demography, reactogenicity and immunogenicity analyses.

Group order in tables	Group label in tables (8 characters only)	Group definition for footnote
1	F4co10W	F4co 10 µg + WFI
2	F4co30W	F4co 30 µg + WFI
3	F4co90W	F4co 90 µg + WFI
4	F4co10A	F4co 10 µg + AS01B
5	F4co30A	F4co 30 µg + AS01B
6	F4co90A	F4co 90 µg + AS01B

2.5. Interim safety analysis

Six interim analyses were planned for safety evaluation (see Section 5.6).

These analyses have been performed at the end of the 7-day follow-up period (Days 7 and 37) after each vaccine injection in a subset of 12 subjects and for each vaccine dose (10, 30 and 90 µg).

Analysis has been done on uncleaned and blinded data. Individual data listings of the demographic and safety data (solicited/unsolicited AE, SAE, haematology and biochemistry values) have been provided to the SRT. Tables with the number of subjects responding to each stopping rules have been also provided.

No clinical report has been written.

As interim safety analyses have been already performed, description of tables and template will be not be part of a RAP.

Protocol forwarded that Final analysis would be performed in 2 steps:

- A first analysis was performed on all data up to and including month 2. These analyses were based on amendment 2 of the present document.
- A second analysis was planned for the report to be written at the end of the study (month 12). The analyses to be covered are detailed in this version of the RAP.

3. STATISTICAL METHODOLOGY AND ANALYSIS

3.1. Study cohorts and demography analysis

3.1.1. Study cohorts

The number and percentage of subjects included in each of the study cohorts, for both the Month 2 and thre Month 12 analyses, as well as the reason(s) for elimination will be presented.

The number of subjects who attended each study visit and the identification numbers of subjects who dropped out from the study along with the reason for withdrawal will be displayed per group for both study conclusions (month 2 and month 12). From an analysis perspective, a “drop-out” is any subject who did not come back for the concluding visit/contact foreseen in the protocol. A subject who returns for the concluding visit/contact foreseen in the protocol is considered to have completed the study. Reasons for drop-out from the study will also be summarised by group.

The age at the first vaccination and the intervals between visits defined in the protocol should be followed as closely as possible. Subjects falling outside of these intervals will be reviewed and eventually excluded from the According-To-Protocol immunogenicity analysis:

Interval	Length of interval (Days)
Visit 2 → Visit 3	14 ± 2
Visit 2 → Visit 4	30 - 34
Visit 1 → Visit 5	180 ± 14
Visit 5 → Visit 7	180 ± 14

The number and percentage of subjects out of these defined limits for the age and/or the intervals between visits will be described. The denominator used to calculate the percentage is the number of subjects present at the considered visits.

An overview of the number of vaccine doses received will be displayed (only for Month 2 analysis).

For each activity, the minimum and maximum dates over all vaccinated subjects will be presented.

3.1.2. Analysis of demographics/baseline characteristics

Demographic characteristics (age, gender, race) of each study cohort , for both the Month 2 and thre Month 12 analyses, will be tabulated.

The mean age (plus range and standard deviation) by gender of the enrolled subjects, as a whole, and per group, will be calculated , (only for Month 2 analysis).

3.2. Reactogenicity

3.2.1. Cohorts

The primary analysis will be based on the total vaccinated cohort. If the percent of enrolled subjects excluded from the ATP cohort for analysis of safety is more than 5%, a second analysis based on this ATP cohort will be performed to complement the Total analysis.

3.2.2. Handling of missing data

For the analysis of solicited symptoms, missing or non-evaluable measurements will not be replaced. Therefore the analysis of the solicited symptoms based on the

totalvaccinated cohort will include only subjects/doses with documented safety data (i.e.symptom screen/sheet completed).

For the analysis of unsolicited adverse events/serious adverse event/concomitant medication, all vaccinated subjects will be considered and subjects who did not report an event will be considered as subjects without an event.

3.2.3. Compliance

This analysis will be performed for Month 2 only.

The number of doses injected, the number of doses not given according-to-protocol, the number of symptom sheets (SS) transcribed for local and general symptoms and, the compliance for local and general symptoms will be tabulated. Compliance (%) is defined as the number of (local/general) symptom sheets completed divided by the number of doses administered for a specified group. The number of doses not given according-to-protocol is the number of doses administered at wrong site and/or side, or administered using a wrong route as compared to the protocol specifications.

3.2.4. All symptoms

This analysis will be performed for Month 2 only.

The percentage of subjects with at least one local AE (solicited and unsolicited), with at least one general AE (solicited and unsolicited) and with any AE during the solicited follow-up period (Day 0 to Day 6) will be tabulated with exact 95% confidence interval (CI) after each vaccine injection and overall.

The percentage of vaccine injections followed by at least one local AE (solicited and unsolicited), by at least one general AE (solicited and unsolicited) and by any AE will be tabulated, overall vaccination course, with exact 95% CI.

3.2.5. Solicited symptoms

This analysis will be performed for Month 2 only.

The number and percentage of subjects reporting each individual solicited local and general AE during the solicited follow-up period will be tabulated with exact 95% CI.

The number and percentage of vaccine injections followed by each individual solicited local and general AE will be tabulated, overall vaccination course, with exact 95% CI.

The maximum intensity of fever and local injection site redness/swelling will be scored as follows:

Symptoms	Grade	Scale
Fever (Oral or Axillary temperature)	0	] 37.5°C
	1	[37.5°C – 38°C]
	2	] 38°C – 39°C]
	3	[39°C
Redness/Swelling	0	0 mmm
	1	[20 mm
	2	]20 mm – 50 mm]
	3	] 50 mm

The same tabulations will be done for grade 3 adverse events and/or for adverse events with relationship to vaccination.

The number and percentage of of subjects reporting a solicited symptom will be also presented by duration (≤ 2 days or > 2 days).

For fever, temperatures will be also summarized in 0.5°C increments.

The number of days with a solicited symptom during the solicited follow-up period will be aslo presented. The same tabulations will be done for grade 3 adverse events and/or for adverse events with relationship to vaccination.

3.2.6. Unsolicited symptoms

This analysis will be performed for Month 2 only.

The proportion of subjects with at least one report of unsolicited AE classified by the Medical Dictionary for Regulatory Activities (MedDRA) and reported up to 30 days after vaccination will be tabulated with exact 95% CI.

The same tabulations will be done for grade 3 adverse events and/or for adverse events with relationship to vaccination.

3.2.7. Serious adverse events

Serious AEs and withdrawal due to AEs will be described in detail for both the Month 2 and thre Month 12 analyses.

3.2.8. Haematological and biochemical parameters

The frequency distribution of values below, within and above normal ranges will be tabulated per treatment group at each scheduled time point. In addition, change from baseline will be also tabulated.

Cleaning for these data for the month 12 analysis will only performed in a second step. This has no impact on the other analyses to be performed, as these data will not impact on the cohort definition.

3.2.9. Concomitant medication

This analysis will be performed for Month 2 only.

The number and percentage of subjects with concomitant medication(s), with antipyretics, with antibiotics and with immunosuppressant within 30 days post-vaccination will be tabulated with exact 95% CI. Concomitant medications will be classified in antipyretics, antibiotics and immunosuppressant according to the WHO drug dictionary.

3.2.10. Exploratory analyses

Analyses of solicited symptoms will be also performed with the following grading to facilitate comparisons with other GSK studies:

Symptoms	Grade	Scale
Fever (Oral or Axillary temperature)	0	] 38°C
	1	[38°C – 38.5°C [
	2	[38.5°C – 39°C [
	3	[39°C – 40°C [
	4	[40°C
Redness/Swelling	0	≤ 20~~0~~ mm **(amendment 1)**
	1	]20 mm – 50 mm]
	2	]50 mm – 100 mm]
	3	] 100 mm

3.3. Immunogenicity

3.3.1. Cohorts and stratification

The primary analysis will be based on the ATP cohort for analysis of immunogenicity. If the percent of enrolled subjects excluded from this ATP cohort is more than 5%, a second analysis based on the Total Vaccinated cohort will be performed to complement the ATP analysis.

It has been decided to present the results for Month 6 and Month 12 based on the Month 12 cohort definition, while all results produced at Month 2 analysis will be based on Month 2 cohort. For clarity purposes, Month 12 analyses which include only descriptive summaries will be presented in separate tables with only the relevant time points included (Month 6 and Month 12).

3.3.2. Derived and transformed data

Serology data

- The cut-off values for antibody titers will be defined by the laboratory before the analysis.
- A seronegative subject is a subject whose titer is below the cut-off value.
- A seropositive subject is a subject whose titer is greater than or equal to the cut-off value.
- The seropositivity rate is defined as the percentage of seropositive subjects.
- The Geometric Mean Titers (GMTs) calculations will be performed by taking the anti-log of the mean of the log titer transformations. Antibody titers below the cut-off of the assay will be given an arbitrary value of half the cut-off for the purpose of GMT calculation.

ICS data

- ICS data will be expressed as antigen-specific CD4+/CD8+ T-cells per million respectively of CD4+ or CD8+ T-cells.

- The cut-off will be choosen on the basis of pre-vaccination response for all subjects, by examining percentiles (95th percentile included) of the different antigens ~~**and the different cytokines**~~ **(amendment 1). A 95th percentile will be determined for each antigen on the CD4 expressing at least two cytokines (all doubles) for CD4 responses and on the CD8 expressing at least one cytokine for CD8 responses.**

The cut-off will be defined as the rounded (superior hundred) maximum 95th percentile among the 4 antigens (amendment 1).

- A responder is a subject with antigen-specific CD4+/CD8+ T-cells response greater than or equal to the cut-off value.
- Frequency of CD4+/CD8+ T-cells expressing cytokines to the fusion protein F4co (all antigens) will be estimated by adding individual frequencies of CD4+/CD8+ T-cells to each 4 antigens (p17, p24, Nef, RT).

3.3.3. Lab assays for immunogenicity

The following table describes the lab assays that will be analyzed for immune response:

Assay	Assay method	Test kit/ Manufacturer	Assay unit	Assay cut-off or Limit of detection	Laboratory
Anti-p17,-24,-RT,-Nef, -F4co antibodies	ELISA	In-house ELISA	EU/mL	To be determined	CEVAC, Belgium
p17-,24-,RT-,Nef-specific effector T-cells	Flow Cytometry, ICS	In-house ICS	Number of cytokine(s) positive cells per 10^6 cells	To be determined	*CEVAC, Belgium

* Or GSK Biologicals,

3.3.4. Handling of missing data

For a given subject and a given immunogenicity measurement, missing or non-evaluable measurements will not be replaced.

For the calculation of percentage of responders to 1, 2, 3 and all 4 antigens, subjects with missing data to at least one of the concerned antigen(s) will not be taken into account.

3.3.5. Cell-mediated immune response

3.3.5.1. Within group assessment

CD4+ ~~and CD8+~~ T-cells response

For cell-mediated immune response, the following parameters will be tabulated by vaccine groups at months 0, 2, 6, 12 and at day 44 (two weeks after the second vaccination):

- descriptive statistics of the frequency of CD4+~~/CD8+~~ T cell expressing at least two different cytokines (IFN-γ, IL-2, TNF-α,CD40L) to each antigen and to all antigens;
- descriptive statistics of the frequency of CD4+~~/CD8+~~ T cell expressing at least IFN-γ and another cytokine (IL-2, TNF-α,CD40L) to each antigen and to all antigens;
- descriptive statistics of the frequency of CD4+~~/CD8+~~ T cell expressing at least IL-2 and another cytokine (IFN-γ, TNF-α,CD40L) to each antigen and to all antigens;
- descriptive statistics of the frequency of CD4+~~/CD8+~~ T cell expressing at least TNF-α and another cytokine (IFN-γ, IL-2,CD40L) to each antigen and to all antigens;
- descriptive statistics of the frequency of CD4+ T cell expressing at least CD40L and another cytokine (IFN-γ, IL-2, TNF-α) to each antigen and to all antigens.

CD4+ T-cells expressing IL-2 and another cytokine

For CD4+ T-cells expressing IL-2 and another cytokine response, the following parameters will be tabulated by vaccine groups at months 0, 2, 6, 12 and at day 44 (two weeks after the second vaccination):

- percentage of responders to each antigen (p17, p24, Nef, RT);
- percentage of responders to at least one antigen (p17, p24, Nef or RT);
- percentage of responders to at least two antigens;
- percentage of responders to at least three antigens;
- percentage of responders to all four antigens (p17, p24, Nef and RT).

In addition, percentage of responders to one, two, three and four antigens will be tabulated, with and without specification of antigens.

CD8+ T-cells ~~expressing at least 2 cytokines~~ **(~~IL-2 and/or~~** TNF-α and/or IFN-γ **~~and/or CD40 L~~) (amendment 1)**

For CD8+ T-cells, the following parameters will be tabulated by vaccine groups at months 0, 2, 6, 12 and at day 44 (two weeks after the second vaccination):

- **descriptive statistics of the frequency of CD8+ T cell expressing at least one cytokine (IFN-γ and/or TNF-α) to each antigen and to all antigens**
- **descriptive statistics of the frequency of CD8+ T cell expressing only TNF-α to each antigen and to all antigens**
- **descriptive statistics of the frequency of CD8+ T cell expressing only IFN-γ to each antigen and to all antigens**
- **descriptive statistics of the frequency of CD8+ T cell expressing IFN-γ and TNF-α to each antigen and to all antigens**
- **for CD8+ T-cells expressing at least one cytokine, percentage of responders to each antigen (p17, p24, Nef, RT) (amendment 1)**

3.3.5.2. Between group assessment

For the following analyses, statistically significant differences (p-value ≤ 0.05) should be interpreted with caution as adjustment for multiplicity of endpoints and clinical relevance of the difference will not considered.

Analysis of frequency of CD4+ T-cells

A two-way ANOVA test will be performed on frequency of CD4+ T-cells expressing at least IL-2 to compare three doses of antigen F4Co with or without adjuvant two weeks after the second vaccination. The ANOVA model will include the doses (10 µg, 30 µg and 90 µg) and the "adjuvants" (AS01B and WFI) as fixed effects.

If requires, the analysis will be performed on log10 frequency of CD4+ T-cells.

If interaction between doses and "adjuvant" is significant (p-value ≤ 0.05), comparison of doses will be done by "adjuvant" factor.

If difference between the three doses is significant (p-value ≤ 0.05), multiple comparisons will be performed and relationship between doses and CD4+ T-cell response will be also assessed.

ANOVA analyses will be done for each antigen (p17, p24, RT, Nef) and for the fusion protein F4Co.

Analysis of responders in terms of CD4+ T-cells

A logistic regression will be performed on occurrence of responders in terms of CD4+ T-cells expressing at least IL-2 (dichotomous response, 0 or 1) to compare three doses of antigen F4Co with or without adjuvant two weeks after the second vaccination. Doses, "adjuvant" and interaction will be included in the logistic model.

If interaction between doses and "adjuvant" is significant (p-value ≤ 0.05), a logistic regression will be applied by "adjuvant" factor.

Logisitic regressions will be done for responders to at least one, two, three and 4 antigens (p17, p24, RT or/and Nef).

3.3.6. Humoral response

3.3.6.1. Within group assessment

For humoral immune response, the following parameters will be tabulated by vaccine groups for each antigen (p17, p24, Nef, RT and F4co) at months 0, 2, 6~~, 7~~, 12 and at day 44 (two weeks after the second vaccination) :

- Geometric mean titers (GMTs) with 95% confidence intervals (CIs);
- Seropositivity rates with exact 95% CIs.

3.4. Methodology for computing CI

All CI will be 2 sided 95% CI.

- The exact 95% CIs for a proportion within a group will be calculated from Proc StatXact [Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of binomial. *Biometrika.* 1934;26:404-413].
- The 95% CI for geometric mean titers/concentrations (GMTs/GMCs) will be obtained within each group separately. The 95% CI for the mean of log-transformed titer/concentration will be first obtained assuming that log-transformed values were normally distributed with unknown variance. The 95% CI for the GMTs/GMCs will be then obtained by exponential-transformation of the 95% CI for the mean of log-transformed titer/concentration.

4. CHANGE FROM PROTOCOL

The cut-off will be choosen on the basis of pre-vaccination response for all subjects, by examining percentiles (95th percentile included) of the different antigens ~~**and the different cytokines**~~ **(amendment 1). A 95th percentile will be determined for each antigen on the CD4 expressing at least two cytokines (all doubles) for CD4 responses and on the CD8 expressing at least one cytokine for CD8 responses. The cut-off will be defined as the rounded (superior hundred) maximum 95th percentile among the 4 antigens (amendment 1).**
~~**To avoid a bias of analyses, cut-off will be determined for each antigens and each cytokines before the start of immunogenicity analyses (i.e, at the time of the pre-analysis meeting) on the basis of pre-vaccination blinded data**~~ **(amendement 1).**

In addition to analyses described in the protocol for CD4+ T-cells expressing IL-2 and another cytokine:

- percentage of responders to one, two, three and four antigens will be tabulated, with and without specification of antigens;
- a between assessment group will be performed (see section 3.3.5.2)

Cytokines measured for CD8+ T-cells response have been reduced to TNF-α and/or IFN-γ (amendment 1).

The stepwise nature of the final analysis implied the use of a different cohort (called month 12 cohort) for the time points Month 6 and month 12 to account for the elimination of subjects between month 2 and month 12. It was agreed to use this Month 12 cohort for the SAE description and for the descriptive immunogenciity analysis. For this last type of analysis (immunogenciity), to avoid any possible confusion, tables for these month6 and month 12 time points will be separate as those presented for the month 2 analysis for all preceding tilme points.

5. INDIVIDUAL LISTINGS AND TABLES

5.1. Individual listings

Appendix Table I.A - Elimination codes

Appendix Table I.B - Demography

Appendix Table I.Ci - Dates of birth, Informed consent, Vaccination and blood sampling, Contact

Appendix Table I.Cii - Reason for visit not done

Appendix Table I.D - General medical history

Appendix Table I.E - Study conclusion

Appendix Table I.I - Reason for non administration of vaccine

Appendix Table II.A - Solicited local symptoms

Appendix Table II.B - Solicited general symptoms

Appendix Table II.Ci - Unsolicited adverse events within 31 days post-vaccination

Appendix Table II.Cii - Unsolicited adverse events after 31 days post-vaccination

Appendix Table II.Di - Concomitant medication

Appendix Table II.Dii - Concomitant vaccination

Appendix Table III.A - Immunogenicity (antibody response)

Appendix Table III.B - Immunogenicity (Cell-mediated immune response)

Appendix Table IV.A - Haematology

Appendix Table IV.B - Biochemistry

5.2. List of tables

The following table summarizes all tables that will be produced for the planned interim (x for first interim analysis, xx for second interim analysis) and final analyses (see previous sections for detazils of cohort/analysis and time points):

Denomination	Template table	Total vaccinated cohort	ATP cohort for immunogenicity	Macro
Parameter setting in stat batches		Elim = 9	Elim = 2	
1. Study cohorts and demography analysis				
1.1. Study cohorts				
Table D - 1 Number of subjects enrolled into the study as well as the number excluded from ATP analyses with reasons for exclusion.	Template Table D - 1	Table D.0-1 *(Elim = 0)*		%ELIMLIST
Table D - 2 Number of subjects at each visit and list of withdrawn subjects	Template Table D - 2	Supplementary Table D.9-2		%DROPOUT
Table D - 3 Number of subjects vaccinated, completed and withdrawn with reason for withdrawal	Template Table D - 3	Table D.9-3		%DROP_SUM
Table D - 4 Minimum and maximum activity dates	Template Table D - 4	Working Table D.9-4		%DATE
Table D - 5 Number and percentage of subjects who received vaccine dose(s)	Template Table D - 5	Table D.9-5		%EXPO
Table D - 6 Deviations from specifications for age and intervals between study visits	Template Table D - 6	Supplementary Table D.9-6		%INT_VAL
1.2. Demographic characteristics				
Table D – 7 Summary of demographic characteristics	Template Table D - 7	Table D.9-7	Table D.9-8b	%DEMOGRA

Denomination	Template table	Total vaccinated cohort	ATP cohort for immunogenicity	Macro
2. Reactogenicity/safety analysis				
2.1. Compliance				
Table R - 1 Compliance in returning symptom sheets	Template Table R - 1	Working Table R.9-1		%COMPLI
Table R - 2 Compliance to data capture	Template Table R - 2	Table R.9-2		%CAPTURE
2.2. All symptoms				
Table R – 3.1 Incidence and nature of symptoms (solicited and unsolicited) reported during the 7 days (Days 0-6) follow-up period after each dose and overall	Template Table R - 3	Table R.9-3.1		%LOCGEN
Table R – 3.2 Incidence and nature of **grade 3** symptoms (solicited and unsolicited) reported during the 7 days (Days 0-6) follow-up period after each dose and overall	Template Table R - 3	Table R.9-3.2		%LOCGEN
Table R – 3.3 Incidence and nature of symptoms (solicited and unsolicited) **with causal relationship** to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall	Template Table R - 3	Supplementary Table R.9-3.3		%LOCGEN
Table R – 3.4 Incidence and nature of **grade 3** symptoms (solicited and unsolicited) **with causal relationship** to vaccination, reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall	Template Table R - 3	Supplementary Table R.9-3.4		%LOCGEN
2.3. Solicited symptoms				
Table R – 4 Incidence of solicited **local** symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall	Template Table R - 4	Table R.9-4		%FREQ
Table R – 5 Incidence of solicited **general** symptoms reported during the 7-day (Days 0-6) post-vaccination period following each dose and overall	Template Table R - 5	Table R.9-5		%FREQ
Table R – 6.1 Number of days with symptoms during the solicited post-vaccination period	Template Table R - 6	Table R.9-6.1		%SYMPDUR
Table R – 6.2 Number of days with **grade 3** symptoms during the solicited post-vaccination period	Template Table R - 6	Table R.9-6.2		%SYMPDUR
Table R – 6.3 Number of days with **related** symptoms during the solicited post-vaccination period	Template Table R - 6	Supplementary Table R.9-6.3		%SYMPDUR
Table R – 6.4 Number of days with **Related grade 3** symptoms during the solicited post-vaccination period	Template Table R - 6	Supplementary Table R.9-6.4		%SYMPDUR
Table R – 7 Maximum temperature per dose, overall doses, overall subject (0.5° increments)	Template Table R - 7	Table R.9-7		%FREQ

Denomination	Template table	Total vaccinated cohort	ATP cohort for immunogenicity	Macro
2.4. Unsolicited symptoms				
Table R – 8.1 Percentage of **subjects** reporting the occurrence of unsolicited symptoms classified by MEDDRA Primary System Organ Class and Preferred Term, within the 30-day (Days 0-29) post-vaccination period	Template Table R - 8	Table R.9-8.1		%UNSOL
Table R – 8.2 Percentage of **doses** with unsolicited symptoms classified by MEDDRA Primary System Organ Class and Preferred Term, within the 30-day (Days 0-29) post-vaccination period	Template Table R - 9	Table R.9-8.2		%UNSOL
Table R – 8.3 **Global Summary** of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period	Template Table R - 10	Table R.9-8.3		%UNSOL
Table R – 9.1 Percentage of **subjects** reporting the occurrence of **grade 3** unsolicited symptoms classified by MEDDRA Primary System Organ Class and Preferred Term, within the 30-day (Days 0-29) post-vaccination period	Template Table R - 8	Table R.9-9.1		%UNSOL
Table R – 9.2 Percentage of **doses** with **grade 3** unsolicited symptoms classified by MEDDRA Primary System Organ Class and Preferred Term, within the 30-day (Days 0-29) post-vaccination period	Template Table R - 9	Table R.9-9.2		%UNSOL
Table R – 9.3 **Global Summary** of **grade 3** unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period	Template Table R - 10	Table R.9-9.3		%UNSOL
Table R – 10.1 Percentage of **subjects** reporting the occurrence of unsolicited symptoms classified by MEDDRA Primary System Organ Class and Preferred Term **with causal relationship** to vaccination, within the 30-day (Days 0-29) post-vaccination period	Template Table R - 8	Supplementary Table R.9-10.1		%UNSOL
Table R – 10.2 Percentage of **doses** with unsolicited symptoms classified by MEDDRA Primary System Organ Class and Preferred Term **with causal relationship** to vaccination, within the 30-day (Days 0-29) post-vaccination period	Template Table R - 9	Supplementary Table R.9-10.2		%UNSOL
Table R – 10.3 **Global Summary** of unsolicited signs and symptoms reported **with causal relationship** to vaccination, within the 30-day (Days 0-29) post-vaccination period	Template Table R - 10	Supplementary Table R.9-10.3		%UNSOL
2.5. Serious adverse events				
Table R – 11 Listing of SAEs reported during the whole study period	Template Table R - 11	Table R.9-11		%SAE
2.6. Haematology and biochemistry				
Table R – 12.1 Distribution of haematology and biochemistry with respect to normal laboratory ranges	Template Table R - 12	Supplementary Table R.9-12.1		%LAB_RW

Denomination	Template table	Total vaccinated cohort	ATP cohort for immunogenicity	Macro
Table R – 12.2 Change from baseline in haematological and biochemical levels with respect to normal ranges	Template Table R - 1	Supplementary Table R.9-12.2		
2.7. Concomitant medication				
Table R – 13 Incidence of concomitant medication during the 30-day (Days 0-29) post-vaccination period by dose and overall	Template Table R - 14	Supplementary Table R.9-13		%CMED_INC
3. Immunogenicity tables				
3.1. CD4+/CD8+ T-cells response by ICS				
Table I – 1a Frequency of **CD4+** T-cells expressing cytokines (by ICS) at pre-vaccination: percentiles **(amendment 1)**	Template Table I - 1		Working Table I.2-1a	Specific
3.1.1. Primary objective				
Table I – 2 CD4+ T cells expressing at least 2 cytokines including IL-2 : Number and percentage of responders to at least one, two, three and all 4 antigens	Template Table I - 2		Table I.2-2	Specific
3.1.2. Secondary objectives				
Table I – 3 CD4+ T cells expressing at least 2 cytokines including IL-2 : Descriptive statistics	Template Table I - 3		Table I.2-3	%CMI
Table I – 4 CD4+ T cells expressing at least 2 cytokines including IL-2 : Number and percentage of responders per antigen	Template Table I - 4		Table I.2-4	specific
Table I – 5 CD4+ T cells expressing at least 2 cytokines including IL-2 : Number and percentage of responders to one, two, three or four antigens	Template Table I - 5		Table I.2-5	specific
Table I – 6 CD4+ T cells expressing at least 2 cytokines including IL-2 : Number and percentage of responders to one, two, three or four antigens with specification of antigens	Template Table I - 6		Supplementary Table I.2-6	specific
Table I – 7 CD4+ T cells expressing at least 2 cytokines including TNF-α : Descriptive statistics	Template Table I - 3		Supplementary Table I.2-7	%CMI
Table I – 8 CD4+ T cells expressing at least 2 cytokines including IFN-γ : Descriptive statistics	Template Table I - 3		Supplementary Table I.2-8	%CMI
Table I – 9 CD4+ T cells expressing at least 2 cytokines including CD40-L : Descriptive statistics	Template Table I - 3		Supplementary Table I.2-9	%CMI
Table I – 10 CD4+ T cells expressing at least 2 cytokines : Descriptive statistics	Template Table I - 3		Supplementary Table I.2-10	%CMI
3.1.3. Exploratory objectives				
Table I – 1b Frequency of **CD8+** T-cells expressing cytokines (by ICS) at pre-vaccination: percentiles **(amendment 1)**	Template Table I - 1		Working Table I.2-1b	Specific
Table I – 11 CD8+ T cells expressing at least **one** cytokine **(TNF-α and/or IFN-γ)** : Descriptive statistics **(amendment 1)**	Template Table I - 3		Supplementary Table I.2-11	%CMI
Table I – 12 CD8+ T cells expressing **only TNF-α** : Descriptive statistics **(amendment 1)**	Template Table I - 3		Supplementary Table I.2-12	%CMI

Denomination	Template table	Total vaccinated cohort	ATP cohort for immunogenicity	Macro
Table I – 13 CD8+ T cells expressing **only IFN-γ** : Descriptive statistics **(amendment 1)**	Template Table I - 3		Supplementary Table I.2-13	%CMI
Table I – 14 CD8+ T cells expressing **TNF-α and IFN-γ** : Descriptive statistics **(amendment 1)**	Template Table I - 3		Supplementary Table I.2-14	%CMI
Table I – 16 CD8+ T cells expressing at least **one** cytokine **(TNF-α and/or IFN-γ)** : Number and percentage of responders per antigen **(amendment 1)**	Template Table I - 4		Table I.2-16	Specific
Table I – 17 CD4+ T cells expressing at least 2 cytokines including IL-2 (stimulaled with other HIV clade antigens) : Descriptive statistics	Template Table I - 3		Table I.2-17	%CMI
Table I – 18 CD4+ T cells expressing at least 2 cytokines including TNF-α (stimulaled with other HIV clade antigens): Descriptive statistics	Template Table I - 3		Supplementary Table I.2-18	%CMI
Table I – 19 CD4+ T cells expressing at least 2 cytokines including IFN-γ (stimulaled with other HIV clade antigens): Descriptive statistics	Template Table I - 3		Supplementary Table I.2-19	%CMI
Table I – 20 CD4+ T cells expressing at least 2 cytokines including CD40-L (stimulaled with other HIV clade Table I.2-4.antigens): Descriptive statistics	Template Table I - 3		Supplementary Table I.2-20	%CMI
Table I – 21 CD4+ T cells expressing at least 2 cytokines (stimulaled with other HIV clade antigens): Descriptive statistics	Template Table I - 3		Supplementary Table I.2-21	%CMI
3.2. Antibodies by Elisa				
Table I - 22 Seroposivity rates and GMTs for antibodies	Template Table I - 7		Table I.2-22	%GMT

5.3. Template of tables

5.3.1. Study cohorts and demography analysis

5.3.1.1. Study cohorts

Template Table D - 1 **Number of subjects enrolled into the study as well as the number of subjects excluded from ATP analyses with reasons for exclusion**

Title	Total			[Each group]	
	n	S	%	n	s
Total enrolled cohort					
… (code XXXX)					
Total vaccinated cohort					
… (code XXXX)					
ATP safety cohort					
… (code XXXX)					
ATP immunogenicity cohort					

Note: Subjects may have more than one elimination code assigned
n = number of subjects with the elimination code assigned excluding subjects who have been assigned a lower elimination code number
s = number of subjects with the elimination code assigned
% = percentage of subjects in the considered ATP cohort relative to the Total vaccinated cohort
Data source = Appendix table IA

Template Table D - 2 **Number of subjects at each visit and list of withdrawn subjects**

Group	VISIT	N	Withdrawn Subject numbers	Reason for withdrawal
[Each group]	VISIT 1			
	VISIT 2			
	VISIT 3			
	VISIT 4			
	VISIT 5			
	VISIT 6			
	VISIT 7			
	VISIT 8			
	VISIT 9			
	VISIT 10			

Data source = Appendix table IC, Appendix table IEi

Template Table D - 3 **Number of subjects vaccinated, completed and withdrawn with reason for withdrawal**

	[Each group]	Total
Number of subjects enrolled		
Number of subjects completed		
Number of subjects withdrawn		
Reasons for withdraw:		
Serious Adverse Event		
Non-serious adverse event		
Protocol violation		
Consent withdrawal (not due to an adverse event)		
Migrated/moved from study area		
Lost to follow-up (subjects with incomplete vaccination course)		
Lost to follow-up (subjects with complete vaccination course)		
Others		

Vaccinated = number of subjects who were vaccinated in the study
Completed = number of subjects who completed last study visit
Withdrawn = number of subjects who did not come for the last visit
Data source = Appendix table IEi

Template Table D - 4 **Minimum and maximum activity dates**

Activity number		Minimum date	Maximum date
[Each activity]	[Each visit]	DDMMMYYYY	DDMMMYYYY
…		DDMMMYYYY	DDMMMYYYY

Template Table D - 5 **Number and percentage of subjects who received the vaccine dose(s)**

	[Each group] (N =)		Total (N =)	
	n	%	n	%
1				
2				
Any				

N = number of subjects in each group or in total included in the considered cohort
n/% = number/percentage of subjects receiving the specified total number of doses in each group or in total
Any = number and percentage of subjects receiving at least one dose
Data source = Appendix table IG, Appendix table IIA, Appendix table IIB

Template Table D - 6 **Deviations from specifications for age and intervals between study visits**

		Age	VISIT 1 – VISIT 2	[Other intervals]
Group		Protocol	Protocol	Protocol
		from xx to xx	From 0 to 0 days	from xx to xx days
[Each group]	N			
	n			
	%			
	range			

Adapted = interval used for defining the ATP cohorts for immunogenicity
N = total number of subjects with available results
n/% = number / percentage of subjects with results outside of the interval
range = minimum-maximum for age and intervals
Data source = Appendix table IB, Appendix table ICi

5.3.1.2. Demographic characteristics

Template Table D - 7 **Summary of demographic characteristics**

Characteristics	Parameters or Categories	[Each group] N=		Total N=	
		Value or n	%	Value or n	%
Age(Years)	Mean SD Median Minimum Maximum				
Gender	Female Male				
Race	African Heritage / African American American Indian or Alaskan Native Asian – Central / South Asian Heritage Asian – East Asian Heritage Asian – Japanese Heritage Asian – South East Asian Heritage Native Hawaiian or Other Pacific Islander White – Arabic / North African Heritage White – Caucasian / European Heritage Other				

N = number of subjects
n = number of subjects in a given category
Value = value of the considered parameter
% = n/Number of subjects with available results x 100
Data source = Appendix table IB

5.3.2. Reactogenicity/Safety

5.3.2.1. Compliance with respect to documenting safety

Template Table R - 1 Compliance in returning symptom sheets

Dose	Group	Number Of Doses	Doses NOT according to protocol	Number Of General SS	Compliance % general	Number Of Local SS	Compliance % Local
1 2 Total	[Each group]						

SS = Symptom sheets used for the collection of local and general solicited AEs
Compliance % = (number of doses with symptom sheet returned / number of administered doses) X 100
Data source = Appendix table IG, Appendix table IIA, Appendix table IIB

Template Table R - 2 Compliance to data capture

Group	Criteria	[Each dose]		All doses		Per subject	
		n	%	n	%	n	%
[Each group]	With visit done With dose received With local solicited data available With general solicited data available						
Total	With visit done With dose received With local solicited data available With general solicited data available						

n = for each dose: number of subjects enrolled in the considered cohort and fulfilling specific criteria for the considered dose
for all doses : sum of n from individual doses
per subject : number of subjects enrolled in the considered cohort and fulfilling specific criteria for at least one dose
% = percentage of doses with solicited/unsolicited data available among the number of administered doses
Data source = Appendix table IG

5.3.2.2. All symptoms

Template Table R - 3 **Incidence and nature of symptoms reported during the 7-day (Days 0-6) post-vaccination period**

	Group	Any Symptom					General symptoms					Local symptoms				
		N	n	%	95% CI		N	n	%	95% CI		N	n	%	95% CI	
					LL	UL				LL	UL				LL	UL
Dose 1	[Each group]															
Dose 2	[Each group]															
Overall/dose	[Each group]															
Overall/subj	[Each group]															

For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects presenting at least one type of symptom whatever the study vaccine administered
For overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom whatever the study vaccine administered
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IIA, Appendix table IIB

5.3.2.3. Solicited symptoms

Template Table R - 4 **Incidence of solicited local symptoms reported during the 7-day (Days 0-6) post-vaccination period**

			[Each group]				
						95 % CI	
Symptom	Follow-up	Type	N	n	%	LL	UL
(Each dose)/Overall dose/Overall subject							
Pain	<= 2 days	All					
		Grade 3					
	> 2 days	All					
		Grade 3					
	Total	All					
		Grade 3					
Redness (mm)	<= 2 days	All					
		> 20					
	> 2 days	All					
		> 20					
	Total	All					
		> 20					
Swelling (mm)	<= 2 days	All					
		> 20					
	> 2 days	All					
		> 20					
	Total	All					
		> 20					

For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting at least once the symptom
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Data source = Appendix table IIA

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Template Table R - 5 **Incidence of solicited general symptoms reported during the 7-day (Days 0-6) post-vaccination period**

			[Each group]				
						95 % CI	
Symptom	Follow-up	Type	N	n	%	LL	UL
			[Each dose]/Overall dose/Overall subject				
(Each symptom)	<= 2 days	All					
		Grade 3					
		Rel					
		Rel*Grade 3					
	> 2 days	All					
		Grade 3					
		Rel					
		Rel*Grade 3					
	Total	All					
		Grade 3					
		Rel					
		Rel*Grade 3					

For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting at least once the symptom
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Data source = Appendix table IIB

Template Table R - 6 **Number of days with symptoms during the solicited post-vaccination period**

Solicited symptom	Dose	Group	N	Mean	Min	Q1	Median	Q3	Max
(Each symptom)	(Each dose) [Overall/dose]	[Each Group]							

N = number of doses with the symptom
Q1 = 25th percentile
Q3 = 75th percentile
Data source = Appendix table IIA, Appendix table IIB

CONFIDENTIAL

Template Table R - 7 **Maximum temperature per dose, overall doses, overall subject (0.5° increments)**

		[Each group]				
					95 % CI	
Symptom	**Type**	**N**	**n**	**%**	**LL**	**UL**
	(Each dose)/Overall dose/Overall subject					
Fever	All					
	37.5 - 38.0°C					
	38.1 - 38.5°C					
	38.6 - 39.0°C					
	39.1 - 39.5°C					
	39.6 - 40.0°C					
	40.1°C +					
	Rel*[37.5 - 38.0°C[					
	Rel* [38.1 - 38.5°C[					
	Rel* [38.6 - 39.0°C[					
	Rel* [39.1 - 39.5°C[					
	Rel* [39.6 - 40.0°C[					
	Rel* [40.1°C ...[					

For each dose and overall/subject:
N= number of subjects with at least one documented dose
n/%= number/percentage of subjects reporting at least once the symptom
For Overall/dose:
N= number of documented doses
n/%= number/percentage of doses followed by at least one type of symptom
95%CI= Exact 95% confidence interval; LL = lower limit, UL = upper limit
Data source = Appendix table IIB

5.3.2.4. Unsolicited symptoms

Template Table R - 8 **Percentage of subjects reporting the occurrence of unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term within the 30-day (Days 0-29) post-vaccination period**

System Organ Class (CODE)	Preferred Term (CODE)	[Each group] (N=)			
		n	%	95%CI LL	UL
At least one symptom					
[Each SOC]	[Each preferred term]				

At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IICi

Template Table R - 9 **Percentage of doses with unsolicited symptoms classified by MedDRA Primary System Organ Class and Preferred Term, within the 30-day (Days 0-29) post-vaccination period**

System Organ Class (CODE)	Preferred Term (CODE)	[Each group] (N=)			
		n	%	95%CI LL	UL
At least one symptom					
[Each SOC]	[Each preferred term]				

At least one symptom = at least one symptom experienced (regardless of the MedDRA Preferred Term)
N = number of administered doses
n/% = number/percentage of doses with the symptom
95% CI= exact 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IICi

Template Table R - 10 **Global Summary of unsolicited signs and symptoms reported within the 30-day (Days 0-29) post-vaccination period**

	[Each group]	Total
Number of subjects with at least one unsolicited symptom reported		
Number of doses followed by at least one unsolicited symptom		
Number of unsolicited symptoms classified by MEDDRA Preferred Term*		
Number of unsolicited symptoms reported		

* Symptoms reported by a subject after a given dose and classified by the same Preferred Term are counted once
Data source = Appendix table IICi

5.3.2.5. Serious adverse events

Template Table R - 11 Listing of SAEs

Group	Sub. No.	Case Id	Age at onset (Year)	Sex	Verbatim	Preferred term	System Organ Class	MA type	Dose	Day of onset	Duration	Causality	Outcome

* = SAEs available in OCEAN but not in Clinical Data Base
????????? = SAEs available in Clinical Data Base but not in OCEAN

5.3.2.6. Haematology and biochemistry

Template Table R - 12 Distribution of haematology and biochemistry with respect to normal laboratory ranges

		[Each group]								
			-Unk.-		-Below-		-Within-		-Above-	
Laboratory parameter	Timing	N	n	%	n	%	n	%	n	%
[Each parameter]	[Each timing]									

Unk. = Laboratory value unknown
% = Percentage of subjects based on N
N = total number of subjects with available results
n = Number of subjects in the appropriate category
Data source = Appendix table IV.a, IV.B

Template Table R - 13 Change from baseline in hematological and biochemical levels with respect to normal ranges

			[Each group]								
				-Below-		-Within-		-Above-		-Alert-	
Laboratory parameter	Timing	Baseline Assessment	N	n	%	n	%	n	%	n	%
[Each laboratory parameter]	[Each timing]	Below									
		Within									
		Above									
		Alert									

N = number of subjects with available results
n/% = number/percentage of subjects in the specified category
Data source = Appendix table IV.a, IV.B

5.3.2.7. Concomitant medications

Template Table R - 14 **Incidence of concomitant medication during the 30-day (Days 0-29) post-vaccination period**

	[Each group]				
				95% CI	
	N	n	%	LL	UL
[Each dose] [Overall/dose] [Overall/subject]					
Any					
Any antibiotic					
Any antipyretic					
Any immunosuppressant					

For each dose and overall/subject:
N= number of subjects with at least one administered dose
n/%= number/percentage of subjects who started to take the specified concomitant medication at least once during the mentioned period
For overall/dose:
N= number of administered doses
n/%= number/percentage of doses after which the specified concomitant medication was started at least once during the mentioned period
95% CI = exact 95% confidence interval, LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IIDi

5.3.3. Immunogenicity

5.3.3.1. CD4+/CD8+ T-cells response by ICS

Template Table I - 1 **Frequency of CD4+/CD8+ T-cells expressing cytokines (by ICS) at pre-vaccination : Percentiles**

Type of T-cells	Antigen	Cytokines	Percentiles			
			90%	95%	99%	100%
[CD4+ or CD8+]	[p17 or p24 or Nef or Tat or F4Co]					

Data source = Appendix table IIIB

Template Table I - 2 **Frequency of CD4+/CD8+ T-cells expressing cytokines (ICS) : Number and percentage of responders to at least one, two, three and all 4 antigens**

Group	Timing	Number of antigens	N	n	%	95% CI	
						LL	UL
[Each group]	[Each Timing]	At least 1 antigen					
		At least 2 antigens					
		At least 3 antigens					
		All 4 antigens					

N = number of subjects with available results **for all 4 antigens (amendment 1)**
n/% = number/percentage of subjects in the specified category
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IIIB

Template Table I - 3 **Frequency of CD4+/CD8+ T-cells expressing cytokines (ICS) : Descriptive statistics**

Stimulating Ag	Study Group	Activity	N	Mean	SD	Min	Q1	Median	Q3	Max
[Each stimulation]	[Each group]	[Each timing]								

N = number of subjects with available results
SD= standard deviation
Q1/Q3 = first/third quartile
MIN/MAX = Minimum/Maximum
Data source = Appendix IIIB

Template Table I - 4 **Frequency of CD4+/CD8+ T-cells expressing cytokines (ICS) : Number and percentage of responders per antigen**

Group	Timing	Antigens	N	n	%	95% CI	
						LL	UL
[Each group]	[Each Timing]	p17					
		p24					
		Nef					
		RT					

N = number of subjects with available results
n/% = number/percentage of subjects in the specified category
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IIIB

Template Table I - 5 **Frequency of CD4+/CD8+ T-cells expressing cytokines (ICS) : Number and percentage of responders to one, two, three or four antigens**

Group	Timing	Number of antigens	N	n	%	95% CI	
						LL	UL
[Each group]	[Each Timing]	None					
		1 antigen					
		2 antigens					
		3 antigens					
		4 antigens					

N = number of subjects with available results **for all 4 antigens (amendment 1)**
n/% = number/percentage of subjects in the specified category
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IIIB

Template Table I - 6 **Frequency of CD4+/CD8+ T-cells expressing cytokines (ICS) : Number and percentage of responders to one, two, three or four antigens with specification of antigens**

Group	Timing	Number of antigens	Ag Stimulation	N	n	%	95% CI	
							LL	UL
[Each group]	[Each timing]	None	None					
		1 antigen	Any					
			p17					
			[other]					
		2 antigens	Any					
			p17+p24					
			[other]					
		3 antigens	Any					
			p17+p24+Nef					
			[other]					
		4 antigens	p17+p24+Nef+RT					

N = number of subjects with available results **for all 4 antigens (amendment 1)**
n/% = number/percentage of subjects with a number of expressed cells above or equal the cut-off
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
Data source = Appendix table IIIB

5.3.3.2. Antibodies

Template Table I - 7 **Seropositivity rates and GMT for each antibody**

				>=cut-off				GMT				
					95% CI				95% CI			
Antibody	Group	Timing	N	n	%	LL	UL	value	LL	UL	Min	Max
[Each antibody]	[Each group]	[Each timing]										

GMT = geometric mean antibody titre calculated on all subjects
N = number of subjects with available results
n/% = number/percentage of subjects with concentration within the specified range
95% CI = 95% confidence interval; LL = Lower Limit, UL = Upper Limit
MIN/MAX = Minimum/Maximum
Data source = Appendix table IIIA