ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: March 5, 2019

ClinicalTrials.gov ID: NCT03390166

Study Identification

Unique Protocol ID:	Tri Fluvac Vaccine phase 2/3
Brief Title:	Immunogenicity and Safety of Tri Fluvac, a Seasonal Trivalent Inactivated Influenza Vaccine in Healthy Thai Adults
Official Title:	A Phase II/III Double Blinded, Randomized, Controlled, Non-inferiority Trial to Evaluate the Immunogenicity and Safety of Tri Fluvac, a Seasonal Trivalent Inactivated Split Virion Influenza Vaccine, in Healthy Thai Subjects Aged 18-49 Years
Secondary IDs:	

Study Status

Record Verification:	March 2019
Overall Status:	Completed
Study Start:	July 24, 2017 [Actual]
Primary Completion:	March 31, 2018 [Actual]
Study Completion:	February 12, 2019 [Actual]

Sponsor/Collaborators

Sponsor:	Mahidol University
Responsible Party:	Principal Investigator Investigator: Punnee Pitisuttithum [ppitisuthitham] Official Title: Prof. Affiliation: Mahidol University
Collaborators:	The Government Pharmaceutical Organization World Health Organization

Oversight

U.S. FDA-regulated Drug:	No
U.S. FDA-regulated Device:	No
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: MUTM 2017-020-01 Board Name: Ethics Comittee of the Faculty of Tropical Medicine Board Affiliation: Faculty of Tropical Medicine, Mahidol University Phone: (662) 3069100

Email: pornpimon.ada@mahidol.ac.th
Address:

Faculty of Tropical Medicine, Mahidol University
420/6 Rajvithi road, Ratchathewi, Bangkok 10400
Thailand

Data Monitoring: Yes

FDA Regulated Intervention: No

Study Description

Brief Summary: The study is aim to evaluate the immunogenicity and safety with two groups of participants who will received a seasonal trivalent split, inactivated influenza vaccine (A/H1N1; A/H3N2 and B) or an active comparator (licensed influenza vaccine

Detailed Description: This is a phase II/III, non-inferiority double-blinded, randomized, controlled trial of immunogenicity and safety with two groups of participants who will received a seasonal trivalent split, inactivated influenza vaccine (A/H1N1; A/H3N2 and B) or an active comparator (licensed influenza vaccine).

A total of about 945 healthy Thai male and female adult volunteers 18 through 49 years of age; 630 participants will be randomized to receive the GPO Tri Fluvac and 315 will receive an active comparator (a 2:1 ratio) (inclusion of ~7% lost to follow-up).

Safety will be assessed for all participants through Day 90 after vaccination. Immunogenicity will be assessed in serum samples obtained at baseline and 21 days after vaccination in a subset of at least 586 individuals randomized to study vaccine and 293 active comparator vaccine recipients.

Conditions

Conditions: Influenza

Keywords: GPO Tri Fluvac Vaccine
Tri Fluvac vaccine

Study Design

Study Type: Interventional

Primary Purpose: Prevention

Study Phase: Phase 2/Phase 3

Interventional Study Model: Parallel Assignment
non-inferiority double-blinded, randomized, controlled trial

Number of Arms: 2

Masking: Double (Participant, Investigator)
double blinded

Allocation: Randomized

Enrollment: 945 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: GPO Tri Fluvac vaccine 630 volunteers will receive a single dose of the seasonal trivalent inactivated influenza vaccine (consisting of A/Michigan/45/2015 (H1N1)pdm-09-like virus, A/Hong Kong/4801/2014 (H3N2)-like virus, and B/Brisbane/60/2008-like virus) produced by GPO Thailand. To be administered via the intramuscular route; the preferred injection site will be the deltoid of the non-dominant arm.	Biological/Vaccine: GPO Tri Fluvac vaccine The vaccine will be administered via the intramuscular route; the preferred injection site will be the deltoid of the non-dominant arm.
Active Comparator: Licensed Influenza vaccine 315 volunteers will receive acLicensed Influenza vaccine (seasonal trivalent inactivated split virion influenza vaccine recommended for Southern Hemisphere in 2017 (consisting of A/ Michigan/45/2015 (H1N1)pdm-09-like virus, A/ Hong Kong/4801/2014 (H3N2)-like virus, and B/ Brisbane/60/2008-like virus) 0.5 mL administered intramuscularly (IM) in the deltoid muscle of the non-dominant arm.	Biological/Vaccine: Licensed influenza vaccine The comparator licensed influenza vaccine will be administered via the intramuscular route; the preferred injection site will be the deltoid of the non-dominant arm.

Outcome Measures

Primary Outcome Measure:

1. Primary Immunogenicity Endpoint: Immune responses to the GPO Tri Fluvac and active comparator vaccine at 21 days post-injection.
   null [Time Frame: 21 days post-injection]
2. Primary Safety Endpoints: Number of subjects with all Adverse Events during the study period and % of subjects with all Adverse Events during the study period
   null [Time Frame: upto 90 days]

Eligibility

Minimum Age: 18 Years

Maximum Age: 49 Years

Sex: All

Gender Based:

Accepts Healthy Volunteers: Yes

Criteria: Inclusion Criteria:

- Age 18-49 years old on the day of screening, having Thai ID card or equivalent
- Able to read and write in Thai and sign written informed consent form
- Able to attend all scheduled visits and to comply with all trial procedures.
- Healthy or medically stable, as established by medical history and physical examination. For individuals with medical conditions, symptoms/signs, if present must be stable, under control or unchanged for the past three months. If medication is used to treat the condition, the medication dose must have been stable for at least one month preceding vaccination.
- For female participants:

- Not breast feeding, non-pregnant (based on negative urine pregnancy test) and no plan to become pregnant up to Day 60.
- Women who are not surgically sterile (hysterectomy or tubal ligation) or post-menopausal for more than one year must be willing to use effective contraceptive method to prevent pregnancy until Day 60 after vaccination. Effective methods include intrauterine device, hormonal contraceptives (oral, injectable, patch, implant, ring) or double barrier contraceptives (condom or diaphragm with spermicide). Women with credible history of abstinence may be enrolled at the discretion of the investigator

Exclusion Criteria:

- Participation in another clinical trial involving any therapy within the previous three months or planned enrollment in such a trial during the period of this study.
- Hypersensitivity after previous administration of any vaccine.
- Having a history of H1N1, H3N2 or Flu B infection within 3 months preceding enrollment to the trial
- Vaccination against influenza in the past 6 months preceding enrollment to the trial
- Receipt of any non-study vaccine within four weeks prior to enrollment or refusal to postpone receipt of such vaccines until after the Day 21 visit.
- History of bronchial asthma, chronic lung diseases, chronic rhinitis
- History of immunodeficiency state
- History of immunosuppression < 6 months prior to immunization
- History of anaphylactic or other allergic reactions to influenza vaccine or any vaccine component or excipient (e.g. gentamicin or thimerosal)
- History of Guillain-Barré Syndrome.
- Having acute infection with fever > 38 degree Celsius or noninfectious diseases (within 72 hours) preceding enrollment in the trial
- Volunteers who have been taking immunoglobulin products or have had a blood transfusion during past 3 months before the beginning of the trial or planned receipt of such products prior to the Day 21 visit.
- Current alcohol abuse or drug addiction that might interfere with the ability to comply with trial procedures
- Any condition that in the opinion of the investigator would pose a health risk to the subject if enrolled, or could interfere with the evaluation of the vaccine

Contacts/Locations

Central Contact Person: Punnee Pitisuttithum, Prof.
Telephone: (662) 6435599
Email: punnee.pit@mahidol.ac.th

Central Contact Backup:

Study Officials: Punnee Pitisuttithum, Prof.
Study Principal Investigator
Mahidol University

Locations: **Thailand**

Vaccine Trial Centre, Faculty of Tropical Medicine, Mahidol University
Bangkok, Thailand, 10400
Contact: Punnee Pitisuttithum (662)6435599 punnee.pit@mahidol.ac.th
Principal Investigator: Punnee Pitisuttithum

Vaccine Trial Centre, Faculty of Tropical Medicine, Mahidol University,

Bangkok, Thailand, 10400
Contact: Punnee Pitisuttithum 662-6445599 punnee.pit@mahidol.ac.th
Contact: 662-3549178
Principal Investigator: Punnee Pitisuttithum

IPDSharing

Plan to Share IPD: Undecided

References

Citations:

Links:

Available IPD/Information:

Statistical Analysis Plan (SAP)

For

Government Pharmaceutical Organization (GPO)

A Phase II/III Double Blinded, Randomized, Controlled, Non-inferiority Trial to Evaluate the Immunogenicity and Safety of Tri Fluvac, a Seasonal Trivalent Inactivated Split Virion Influenza Vaccine, in Healthy THAI Subjects Aged 18- 49 years.

Prepare by

Montida Auayporn, Statistician, BIOPHICS

Center of Excellence for Biomedical and Public Health Informatics (BIOPHICS)

Faculty of Tropical Medicine, Mahidol University

Rajavithi Campus, Bangkok 10400

Version 1.0, 12 February 2018

Produced date: 12 Feb 2018

Study Title:	A Phase II/III Double Blinded, Randomized, Controlled, Non-inferiority trial to evaluate the Immunogenicity and Safety of Tri Fluvac, a Seasonal Trivalent Inactivated split virion Influenza vaccine, in healthy THAI subjects aged 18 - 49 years.
Study Protocol:	GPO Tri Fluvac Vaccine (Phase II/ III)
SAP Approval Date:	12 FEB 2018
SAP Version # and Date:	Version 1.0, 12 February 2018

SIGNATURES

SUBMITTED BY: I have authored this document and submit it for approval.

Montida A. **DATE:** 12 FEB 2018

Montida Auayporn

Statistician
BIOPHICS
Center of Excellence for Biomedical and Public Health Informatics

REVIEWED BY: I have reviewed this document and find it to be accurate and acceptable.

DATE: 12 FEB 2018

Saranath Lawpoolsri

Chief of Biomedical Informatics
BIOPHICS
Center of Excellence for Biomedical and Public Health Informatics

Table of Contents

Study Synopsis

Title: A Phase II/III Double Blinded, Randomized, Controlled, Non-inferiority trial to evaluate the Immunogenicity and Safety of Tri Fluvac, a Seasonal Trivalent Inactivated split virion Influenza vaccine, in healthy Thai subjects aged 18 – 49 years.

Protocol #: GPO Tri Fluvac Vaccine Phase II/III

Description of Study Design:

This is a phase II/III, non-inferiority double-blinded, randomized, controlled trial of immunogenicity, safety and preliminary efficacy with two groups of participants who will received a seasonal trivalent split, inactivated influenza vaccine (A/H1N1; A/H3N2 and B) or an active comparator (licensed influenza vaccine).

A total of about 945 healthy Thai male and female adult volunteers 18 through 49 years of age; 630 participants will be randomized to receive vaccine and 315 will receive an active comparator (a 2:1 ratio) (inclusion of ~7% lost to follow-up).

Safety will be assessed for all participants through Day 90 after vaccination. Immunogenicity will be assessed in serum samples obtained at baseline and 21 days after vaccination in a subset of at least 630 individuals randomized to study vaccine and 315 active comparator vaccine recipients.

Study Hypothesis:

Immunogenicity: A single dose of the GPO seasonal trivalent split, inactivated influenza vaccine will induce immune responses measured by HI assay to each of the three vaccine antigens and will be non-inferior to active licensed comparator vaccine.

Safety: A single dose of the GPO seasonal trivalent split, inactivated influenza vaccine will be safe and well tolerated in adults 18 to 49 years of age.

Study Objectives:

Primary objective

Immunogenicity:

To evaluate the immunological non-inferiority seroconversion rate (using HI assay) and Geometric Mean Titre (GMT) of the GPO seasonal trivalent split, inactivated influenza vaccine compared to active comparator vaccine for each of the three vaccine antigens, three weeks after immunization (Day 21) and at the end of follow up period (Day 90).

Safety:

To evaluate the safety profile of a single intramuscular dose of the GPO seasonal trivalent split, inactivated influenza vaccine in adults 18 to 49 years of age. To compare the solicited symptoms, AE and

SAE between subjects who will receive GPO trivalent split, inactivated influenza vaccine and those who will receive active comparator vaccine.

Secondary objective

To evaluate the HI responses at 3 weeks after immunization in participants with or without pre-existing HI antibody.

Study Endpoints and Statistical Analysis:

Primary Immunogenicity Endpoint:

Immune responses to the GPO Tri Fluvac and active comparator vaccine at 21 days post-injection will be analyzed by the following:

- Number and percentage of participants with seroconversion against each of the three vaccine antigens. Seroconversion is defined as a serum HI antibody titer meeting the following four fold rising criteria:

- Pre-vaccination titer <1:10 and a post-vaccination titer measured on Day21 of ≥1:40; or

- Pre-vaccination titer ≥1:10 and at least a four-fold increase in post vaccination measured on Day 21.

- Geometric mean titers (GMTs) of serum HI antibodies pre- (Day 0) and post-vaccination (Day 21) for each of the three vaccine antigens.

Note that titers below the lowest limit of quantitation (i.e., below the starting dilution of assay reported as "< 10") will be set to half that limit (i.e., 10/ 2 = 5). If a titer is reported as greater or equal to the upper limit of the assay, it will be set to that limit. The analyses will be performed on the Total Vaccinated cohort (ITT) and According to Protocol (ATP) cohort for immunogenicity.

- The Total Vaccinated cohort will include all subjects with a documented vaccine administration.

- The ATP cohort for 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 outcome variables were available for antibodies against at least one study vaccine antigen component after vaccination.

Primary Safety Endpoints:

Counts and percentages of subjects with solicited local and systemic reactions during the three days post-injection. In addition, all adverse events (AE) and serious adverse events (SAEs), and new onset of chronic diseases (NOCDs) will be collected for the entire study period. Specifically, the following safety parameters will be monitored and analyzed in terms of the number and proportion of participants reporting the following events will be assessed:

- Solicited local adverse events, including redness/erythema, swelling/induration, pain and limitation of arm movement within 30 minutes of vaccination and over the 3-day period post vaccination (Day 0-3).

- Solicited systemic adverse events, including fever, fatigue/malaise, muscle aches, joint aches, chills, nausea and headache within 30 minutes of vaccination and over the 3-day period post vaccination (Day 0-3).

- Unsolicited adverse events (AEs) occurring within 90 days post vaccination.

- Serious Adverse Events (SAE) occurring during the entire study period (Days 0-90).

Counts of all events will be reported and summarized according to event severity, as "any local AE", or "any systemic AE", and by relationship to administration of study product, as deemed by a blinded study clinician. Percentages of participants experiencing each reaction or event, or at least one reaction or event will be calculated along with two-sided exact 95% CIs. The percentage of participants with solicited AE and SAEs will be compared between vaccine and comparator groups and a two-sided p-value of 0.05 will be considered statistically significant.

Inferential analyses

GMT ratios (GMT active comparator vaccine/GMT GPO TRI FLUVAC) and difference of seroconversion rate (with two-sided 95% CI) related to the comparisons of interest will be computed. Acceptance value of GMT ratios at ≤ 1.5 and/or difference of seroconversion rate at $\leq 10\%$ for the upper bound of the 95% CI will be considered for non-inferiority.

Secondary Immunogenicity Endpoints and analysis:

The secondary immunogenicity endpoints will be analyzed by the following:

- Number and percentage of participants with a HI antibody titer $\geq$1:40 (seroprotective level) to each of the three vaccine antigens measured on Day 21 and Day 90.

- Number and percentage of participants who develop at least a four-fold increase in HI antibody titers to each of the vaccine antigen post-vaccination measured on Day 21 and Day 90 segregated by pre-vaccination HI antibody titers (<1:10 or $\geq$1:10).

- Geometric mean fold rises (GMFRs) of serum HI antibodies (post vaccination/ pre-vaccination) for each of the three vaccine antigens**.**

- GMTs of serum HI antibodies pre- (Day 0) and post-vaccination (Day 21 and Day 90) for each of the three vaccine antigens segregated by pre-vaccination HI antibody titers (<1:10 or $\geq$1:10).

- GMFRs of serum HI antibodies (post-vaccination/pre-vaccination) for each of the three vaccine antigens segregated by pre-vaccination HI antibody titers (<1:10 or $\geq$1:10).

Study Population:

About 945 male and female adults, 18 to 49 years of age

Eligibility Criteria:

Inclusion:

- Age 18-49 years old on the day of screening, having Thai ID card or equivalent
- Able to read and write in Thai and sign written informed consent form
- Able to attend all scheduled visits and to comply with all trial procedures.
- Healthy or medically stable, as established by medical history and physical examination. For individuals with medical conditions, symptoms/signs, if present must be stable under control or unchanged for the past three months. If medication is used to treat the condition, the medication dose must have been stable for at least one month preceding vaccination.

For female participants:

- Not breast feeding, non-pregnant (based on negative urine pregnancy test) and no plan to become pregnant up to Day 60.
- Women who are not surgically sterile (hysterectomy or tubal ligation) or post-menopausal for more than one year must be willing to use effective contraceptive method to prevent pregnancy until Day 60 after vaccination. Effective methods include intrauterine device, hormonal contraceptives (oral, injectable, patch, implant, ring) or double barrier contraceptives (condom or diaphragm with spermicide). Women with credible history of abstinence may be enrolled at the discretion of the investigator.

Exclusion:

- Participation in another clinical trial involving any therapy within the previous three months or planned enrollment in such a trial during the period of this study.
- Hypersensitivity after previous administration of any vaccine.
- Having a history of H1N1, H3N2 or Flu B infection as H1N1, H3N2, or Flu B within 3 months preceding enrollment to the trial
- Vaccination against influenza in the past 6 months preceding enrollment to the trial
- Receipt of any non-study vaccine within four weeks prior to enrollment or refusal to postpone receipt of such vaccines until after the Day 21 visit.
- History of bronchial asthma, chronic lung diseases, chronic rhinitis
- History of immunodeficiency state
- History of immunosuppression < 6 months prior to immunization
- History of anaphylactic or other allergic reactions to influenza vaccine or any vaccine component or excipient (e.g. gentamicin or thimerosal)
- History of Guillain-Barré Syndrome.

- Having acute infection with fever > 38 degree Celsius and noninfectious diseases (within 72 hours) preceding enrollment in the trial

- The volunteers who have been taking immunoglobulin products or have had a blood transfusion during past 3 months before the beginning of the trial or planned receipt of such products prior to the Day 21 visit. Current alcohol abuse or drug addiction that might interfere with the ability to comply with trial procedures

- Any condition that in the opinion of the investigator would pose a health risk to the subject if enrolled, or could interfere with the evaluation of the vaccine

Phase: II/III

Study Duration:

Approximately 1 year

Participation Duration:

About three to four months per participant

Description of Agent or Intervention:

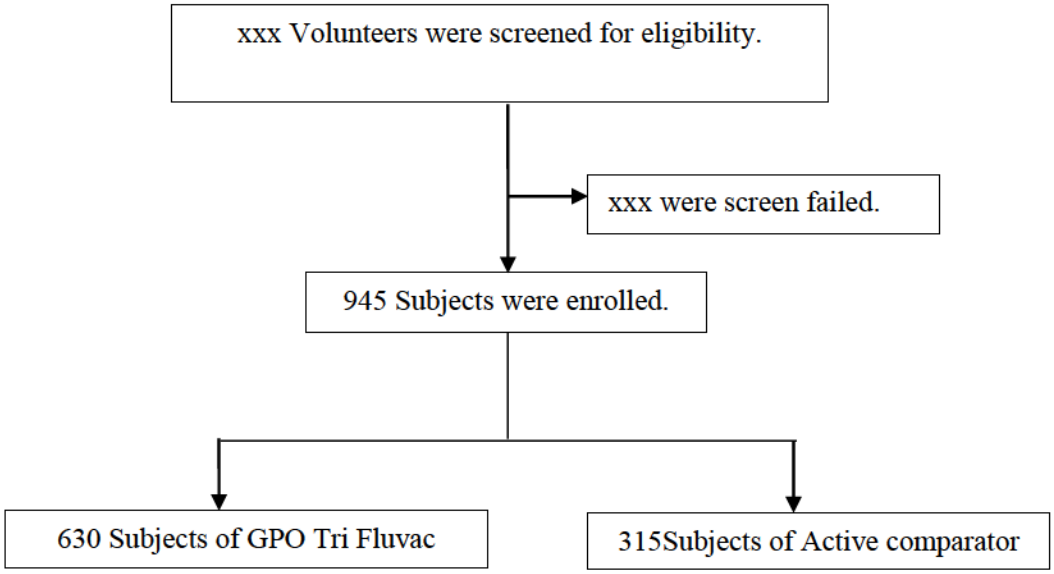
The vaccine is a seasonal trivalent inactivated split virion influenza vaccine recommended for Southern hemisphere in 2017 (consisting of A/Michigan/45/2015(H1N1)pdm-09-like virus, A/Hong Kong/4801/2014 (H3N2)-like virus, and B/Brisbane/60/2008-like virus) produced by The Government Pharmaceutical Organization (GPO), Thailand. Each dose of Tri Fluvac contains a total of 45 micrograms (µg) hemagglutinin (HA) per 0.5 ml dose (15 µg HA per strain per dose), to be administered by intramuscular (IM) injection. Tri Fluvac is manufactured and formulated into a multiple-dose vial vaccine (2 doses) using thimerosal at relatively low concentration as preservative (≤ 7.5 µg mercury/ dose). Each 0.5 ml dose of vaccine may contain residual amounts of ovalbumin (≤ 5.0 µg), formaldehyde (≤ 50 µg), tween 80 (≤ 250 µg), triton x-100 (≤ 5 µg) and gentamicin (not more than 0.05 µg). The vaccine should be administered as a single 0.5ml intramuscular injection, preferably in the region of the deltoid muscle of the upper arm.

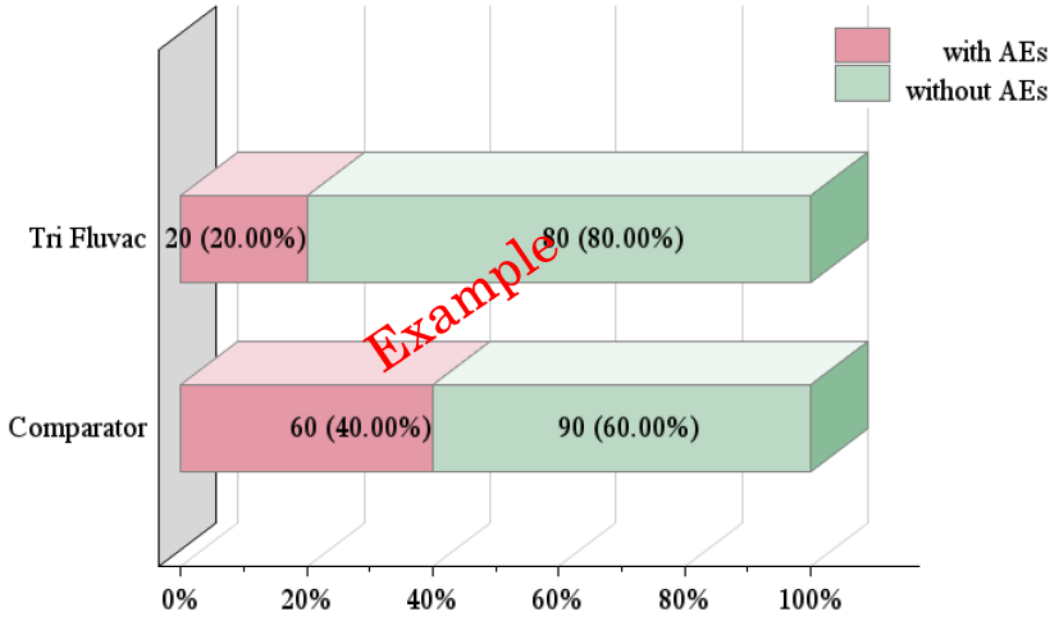
Description of active comparator vaccine:

a Licensed Influenza vaccine (seasonal trivalent inactivated split virion influenza vaccine recommended for Southern hemisphere in 2017 (consisting of A/Michigan/45/2015 (H1N1) pdm-09-like virus, A/Hong Kong/4801/2014 (H3N2) - like virus, and B/Brisbane/60/2008-like virus) 0.5 mL administered intramuscularly (IM) in the deltoid muscle.

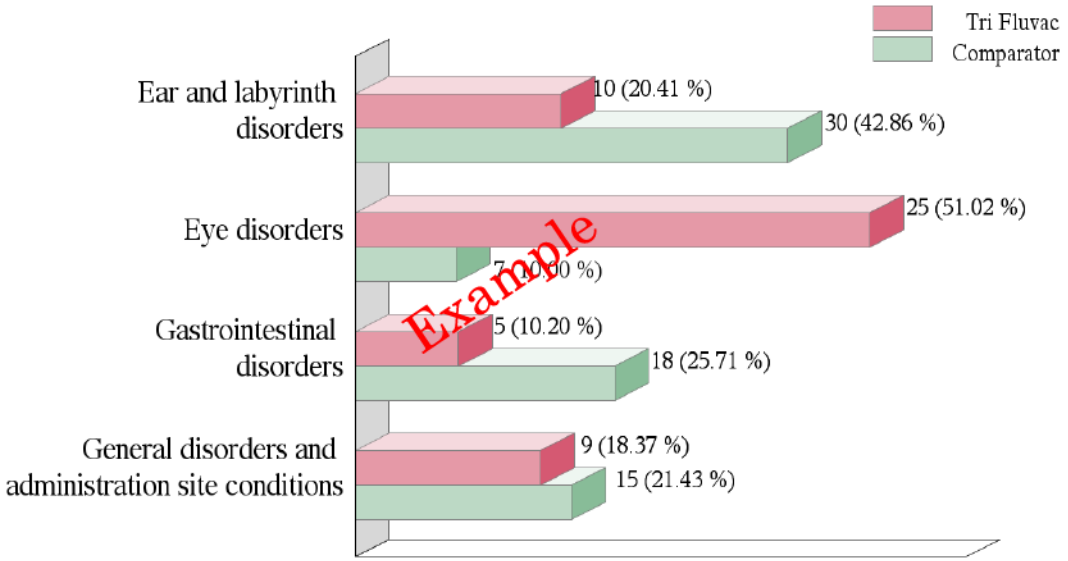
Study Summary

FREF 01: Study Profile

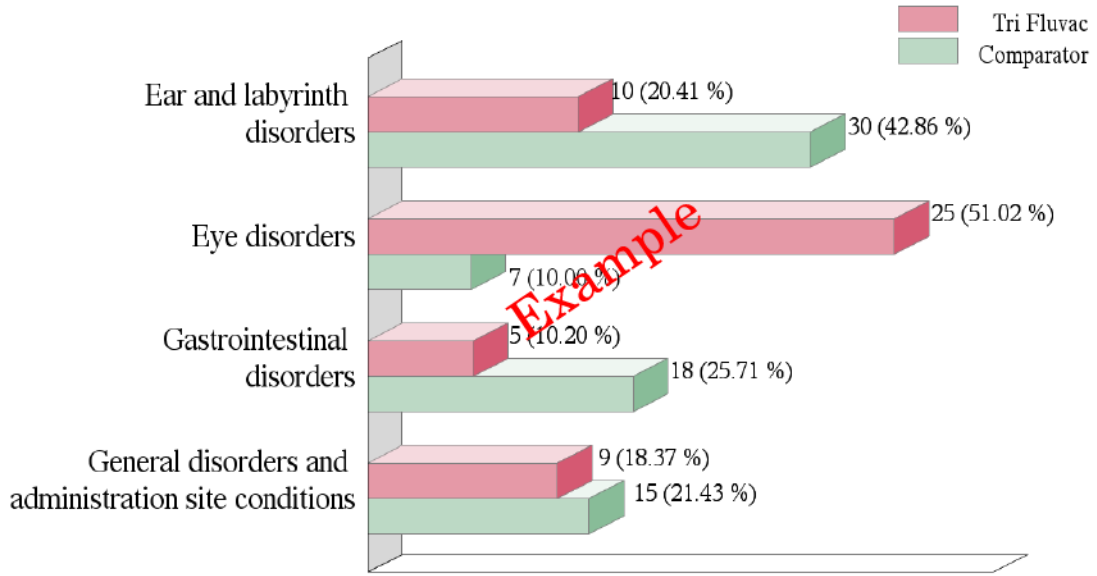




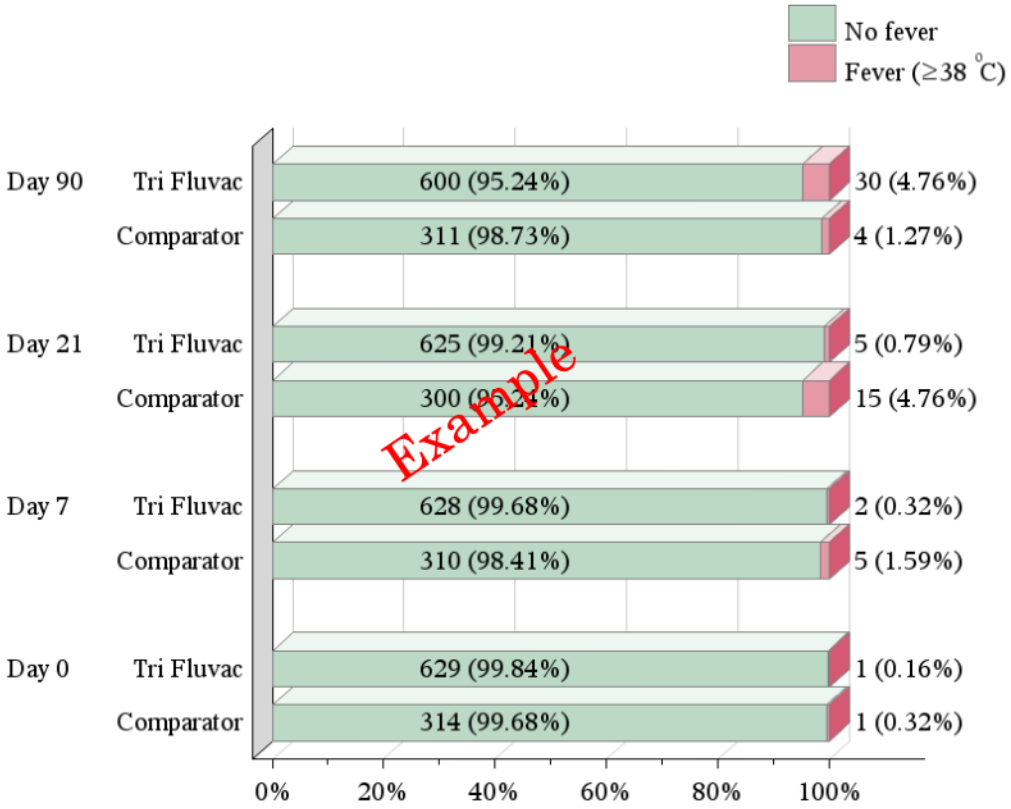
FREF 02: Number and Percentage of Cases with Adverse Events



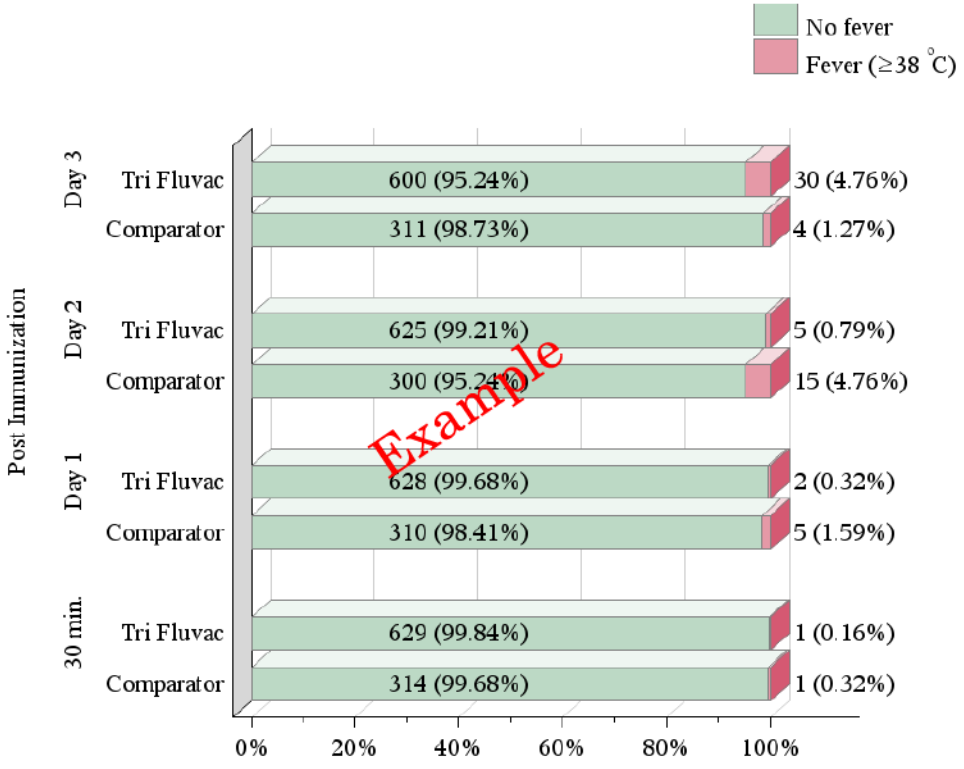
FREF 03: Number and Percentage of Adverse Events by Systemic Organ Class (by Each Group)



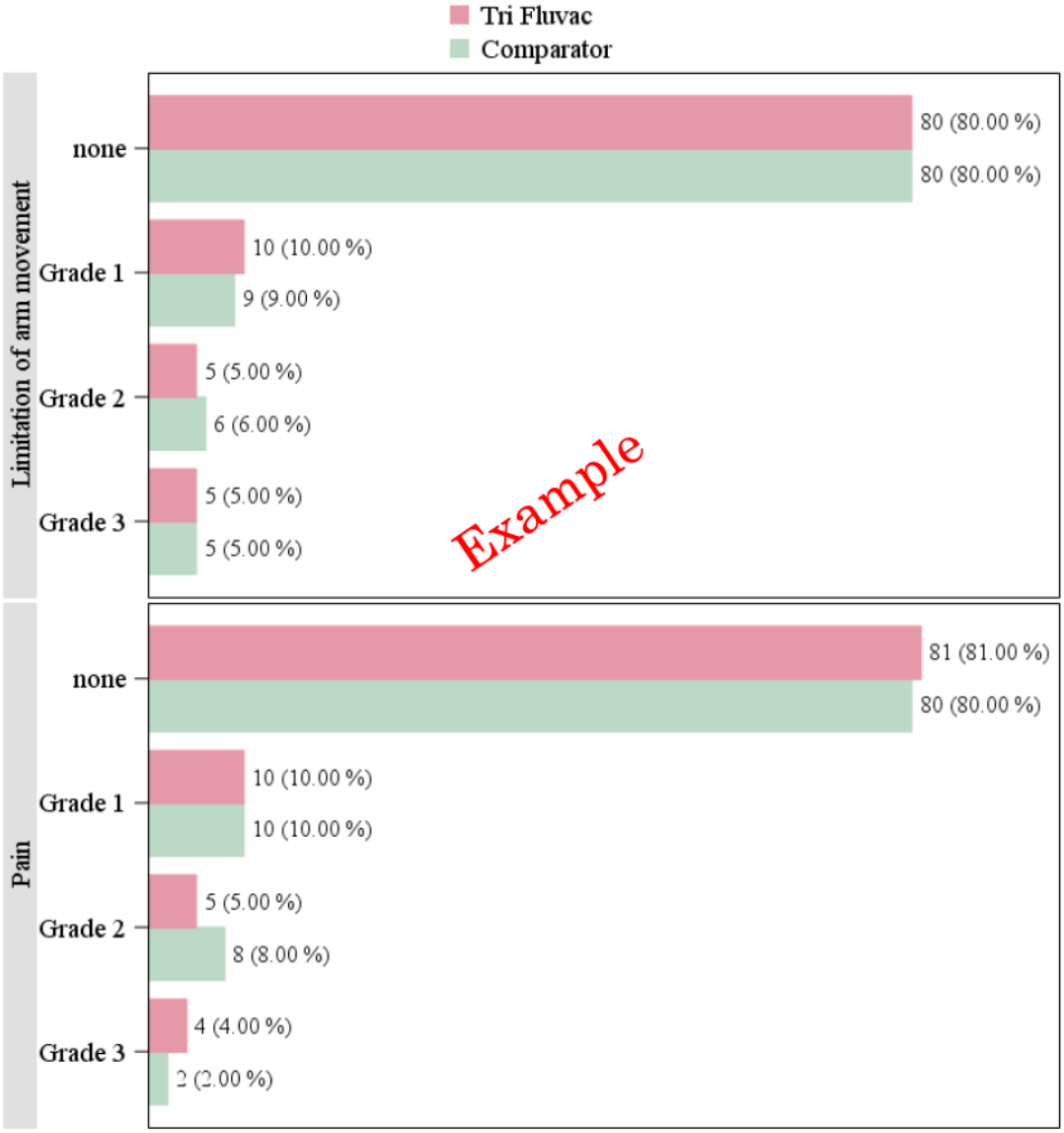
FREF 04: Number and Percentage of Cases with Adverse Events by Systemic Organ Class (by Each Group)



FREF 05: Summary Number and Percentage of Cases by Temperature Grading and Follow up Visit

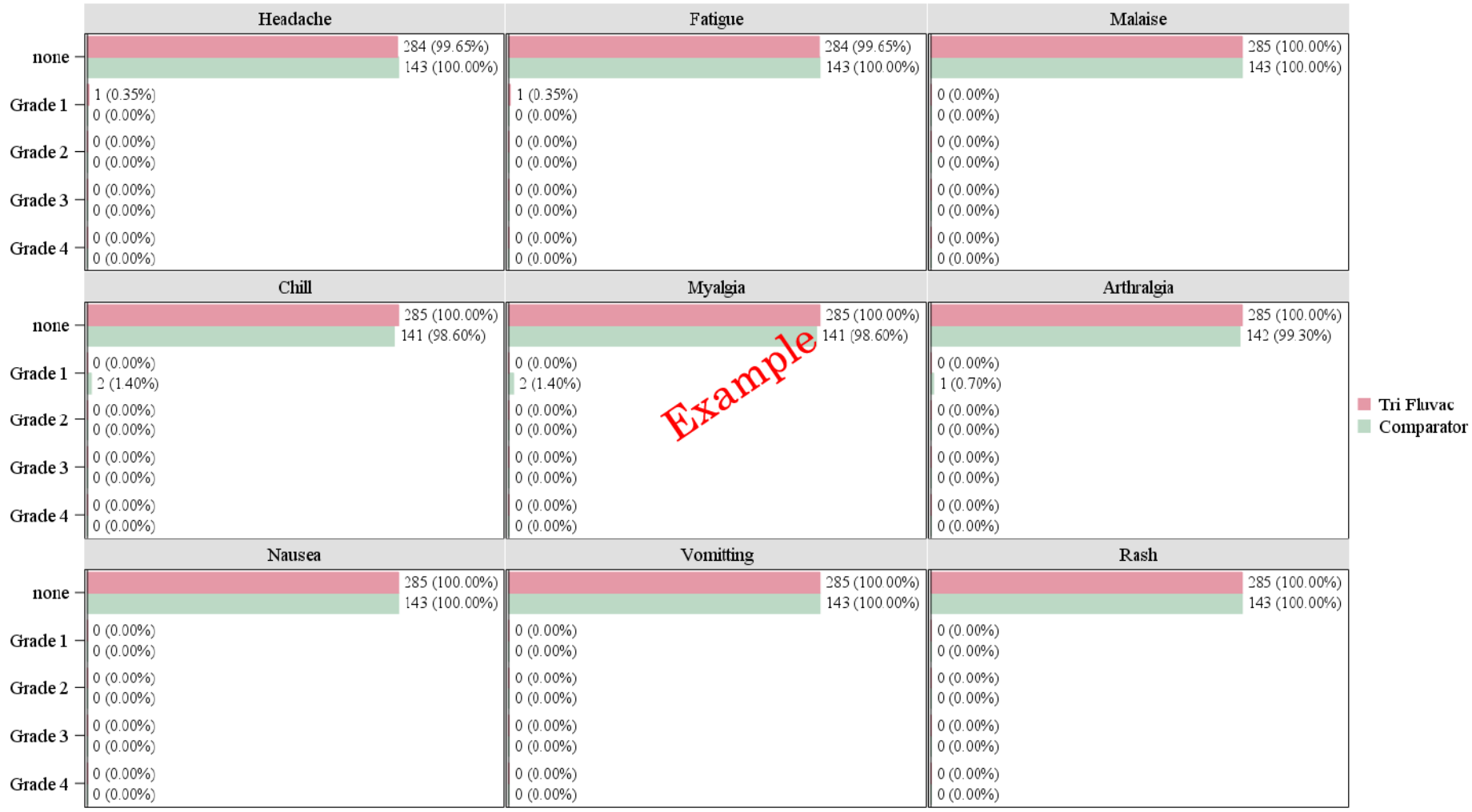


FREF 06: Summary Number and Percentage of Cases by Temperature Grading at Post Immunization



FREF 07: Number and Percentage of Local Reaction Grading at Post Immunization

Note: Erythema and Induration will be not included.



FREF 08: Number and Percentage of Systemic Reaction Grading at Post Immunization

TREF 01: Summary of Sero-conversion, Sero-protection, GMT and GMFRs

Measure	Study Group	HAI Assay		
		Flu A H1 antibody titer	Flu A H3 antibody titer	Flu B antibody titer
Day 21				
Sero-conversion Rate [a]	Tri fluvac (N=)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
	Comparator (N=)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
	P –value =	x.xxxx	x.xxxx	x.xxxx
Sero-protection Rate [b]	Tri fluvac (N=)			
	Comparator (N=)			
	P –value =			
GMT [c]	Tri fluvac (N=)			
	Comparator (N=)			
	P –value =			
GMFRs [d]	Tri fluvac (N=)			
	Comparator (N=)			
Day 90				
Sero-conversion Rate [a]	Tri fluvac (N=			
	Comparator (N=)			
	P –value =			
Sero-protection Rate [b]	Tri fluvac (N=)			
	Comparator (N=)			
	P –value =			

TREF 01: Summary of Sero-conversion, Sero-protection, GMT and GMFRs (Continue)

Measure	Study Group	HAI Assay		
		Flu A H1 antibody titer	Flu A H3 antibody titer	Flu B antibody titer
GMT [c]	Tri fluvac (N=)			
	Comparator (N=)			
	P –value =			
GMFRs [d]	Tri fluvac (N=)			
	Comparator (N=)			

Note: [a] Sero-conversion is defined as 4 fold rising titer from baseline (Day 0). Values are the percent of subjects in each group (with 95% CI).

[b] Sero-protection is defined as a HAI titer ≥ 40; values are the percent of subjects in each group (95% CI) with a HAI titer ≥ 40.

[c] Values are the geometric means titer (GMT) (with 95% CI) for the subjects in each group.

[d] Geometric Mean Fold Rises (GMFR) is the geometric mean of the ratios of post - vaccination to the pre-vaccination (Day 0)

- Seroconversion rate, seroprotection rate and GMTs will be compared between Tri Fluvac and comparator group.

TREF 02: Summary of Non-inferiority Established Based on Seroconversion Rate Differences and GMT Ratios

Measure	Study Group	HAI Assay		
		Flu A H1 antibody titer	Flu A H3 antibody titer	Flu B antibody titer
Day 0				
GMT [c]	Tri Fluvac (N=)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
	Comparator (N=)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
Day 21				
Seroconversion Rate [a]	Tri Fluvac (N=)	xx.xx% (xx.xx%, xx.xx%)	xx.xx% (xx.xx%, xx.xx%)	xx.xx% (xx.xx%, xx.xx%)
	Comparator (N=)	xx.xx% (xx.xx%, xx.xx%)	xx.xx% (xx.xx%, xx.xx%)	xx.xx% (xx.xx%, xx.xx%)
Difference in Seroconversion Rate [b]		xx.xx% (xx.xx%, xx.xx%)	xx.xx% (xx.xx%, xx.xx%)	xx.xx% (xx.xx%, xx.xx%)
GMT [c]	Tri Fluvac (N=)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
	Comparator (N=)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
GMT Ratio [d]		xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)	xx.xx (xx.xx, xx.xx)
Day 90				
Seroconversion Rate [a]	Tri Fluvac (N=)			
	Comparator (N=)			
Difference in Seroconversion Rate [b]				
GMT [c]	Tri Fluvac (N=)			
	Comparator (N=)			
GMT Ratio [d]				

Note: [a] Sero-conversion is defined as 4 fold rising titer from baseline (Day 0). Values are the percent of subjects in each group (with 95% CI).
[b] Percent difference in Seroconversion rate (with 95% CI). Clinical margin ≤ 10 %
[c] Values are the geometric means titer (GMT) (with 95% CI) for the subjects in each group.
[d] Values are the geometric means of the individual at Day 21 and Day 90 of Active comparator vaccine/ GPO Tri Fluvac HAI ratio.
Clinical margin ≤ 1.5
- Non-inferiority criteria based on GMT ratio if the ratio for each HI assay at ≤ 1.5 and / or difference of seroconversion rate at $\leq 10\%$ for the upper bound of the 95% CI.

TREF 03: Summary Immunogenicity Result: GMT Ratio

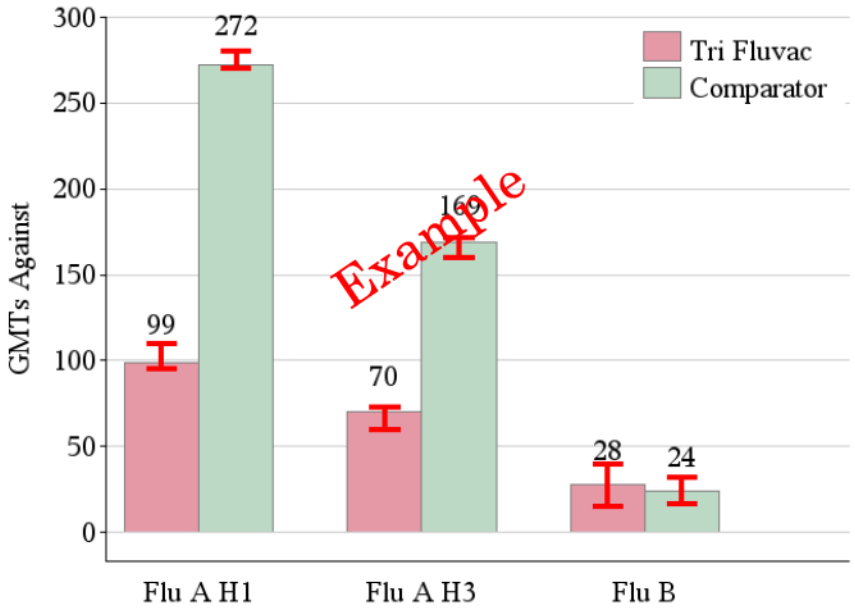
Day	Antibody Titer	GMT Ratio [Comparator/ Tri Fluvac] (95% CI)	Non- inferiority (Upper bound of the two-sided 95% CI of GMT ratio ≤ 1.5)
Day 21	Flu A H1	x.xx (x.xx – x.xx)	Yes / No
	Flu A H3		
	Flu B		
Day 90	Flu A H1		
	Flu A H3		
	Flu B		

Note: Non-inferiority criteria based on GMT ratio if the ratio for each HI assay at ≤ 1.5 and / or difference of sero-conversion rate at ≤ 10% for the upper bound of the 95% CI.

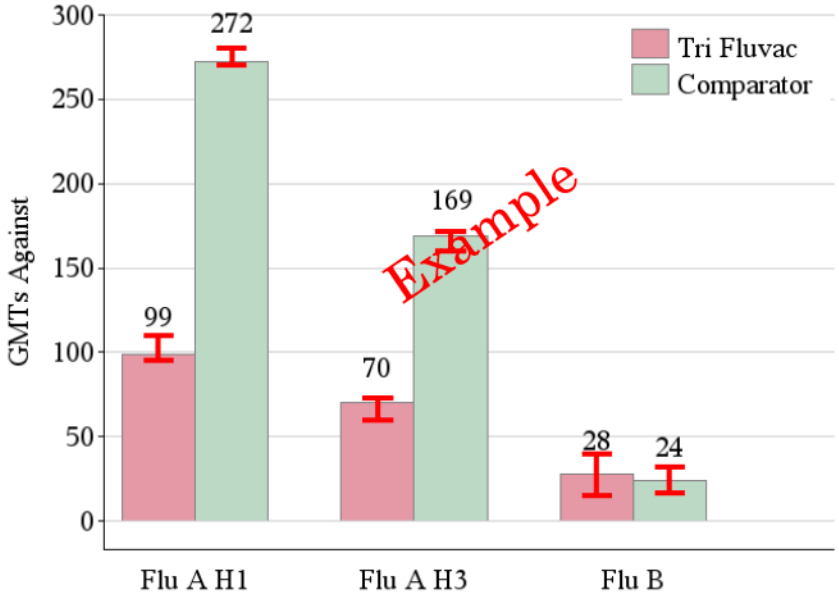
TREF 04: Summary Immunogenicity Result: Sero-conversion Rate (SCR) Difference

Day	Antibody Titer	SCR (%) difference [Comparator-Tri Fluvac] (95% CI)	Non- inferiority (Upper bound of the two-sided 95% CI of SCR Difference ≤ 10%)
Day 21	Flu A H1	x.xx (x.xx – x.xx)	Yes / No
	Flu A H3		
	Flu B		
Day 90	Flu A H1		
	Flu A H3		
	Flu B		

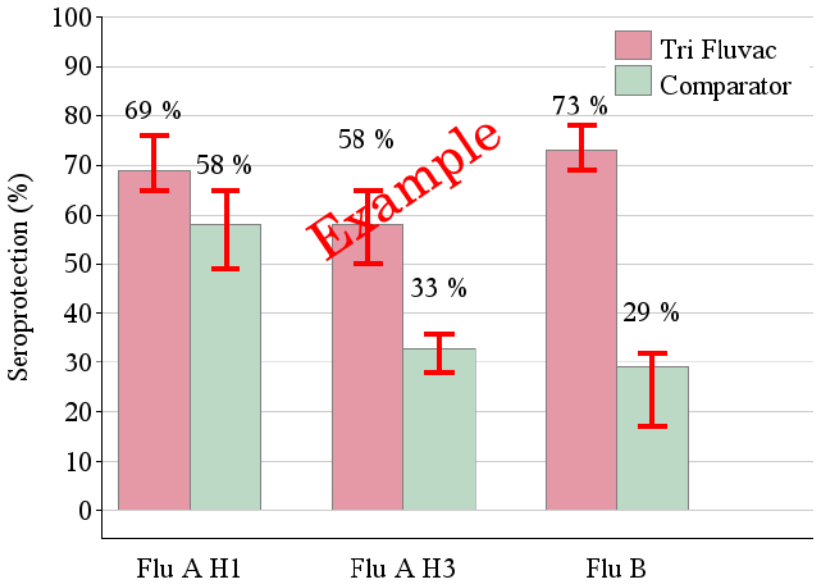
Note: Non-inferiority criteria based on GMT ratio if the ratio for each HI assay at ≤ 1.5 and / or difference of seroconversion rate at ≤ 10% for the upper bound of the 95% CI.



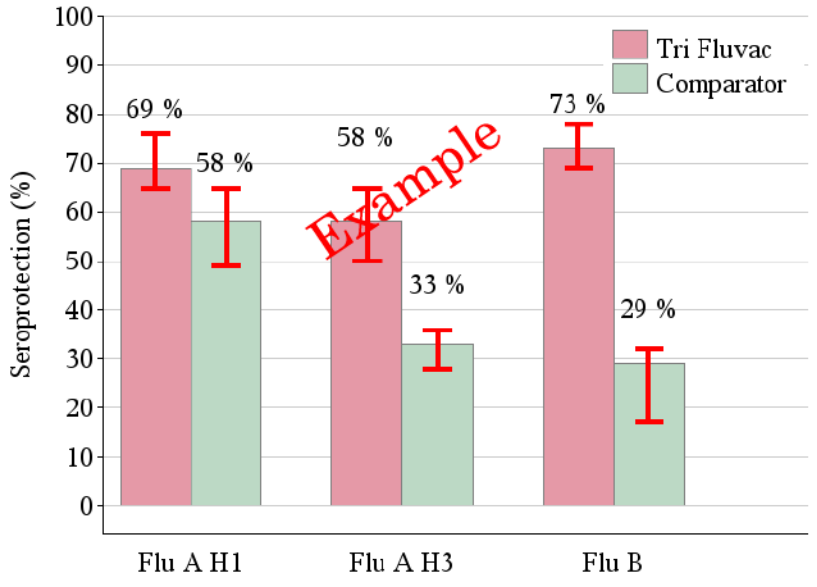
FREF 09: Summary Geometric Mean Titer (GMT) with 95% CI Against Each of Three Vaccine Antigens at Day 21



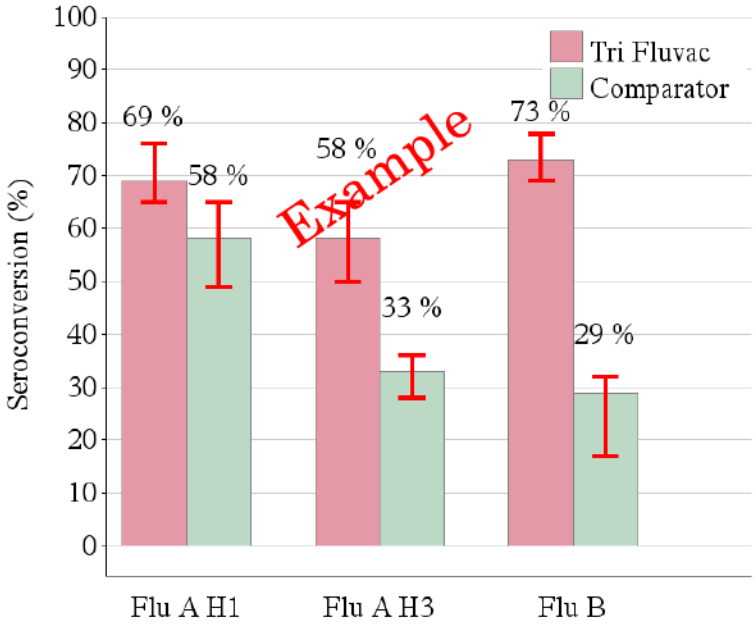
FREF 10: Summary Geometric Mean Titer (GMT) with 95% CI Against Each of Three Vaccine Antigens at Day 90



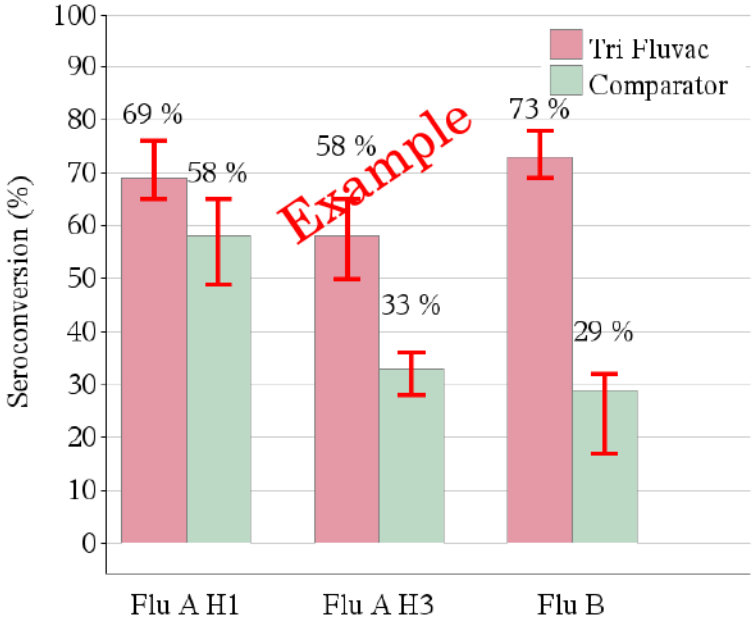
FREF 11: Summary Percentage of Seroprotection with 95% CI Against Each of Three Vaccine Antigens at Day 21



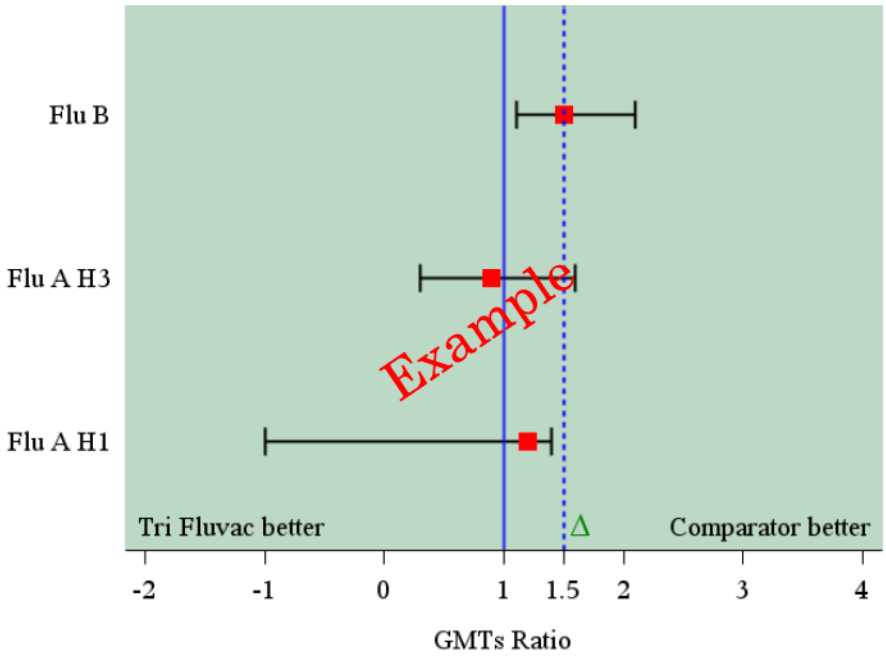
FREF 12: Summary Percentage of Seroprotection with 95% CI Against Each of Three Vaccine Antigens at Day 90



FREF 13: Summary Percentage of Seroconversion with 95% CI Against Each of Three Vaccine Antigens at Day 21



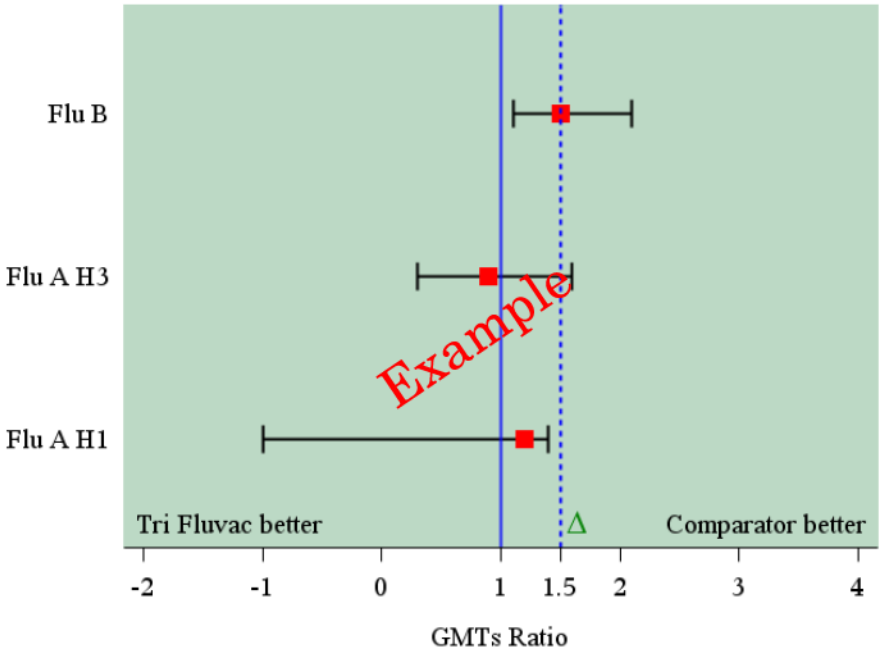
FREF 14: Summary Percentage of Seroconversion with 95% CI Against Each of Three Vaccine Antigens at Day 90



FREF 15: Summary Non-Inferiority Trial of GMTs Ratio and 95% Confidence Interval at Day 21

Note: - Non-inferiority criteria based on GMT ratio if the ratio for each HI assay at ≤ 1.5 and / or difference of seroconversion rate at ≤ 10% for the upper bound of the 95% CI.

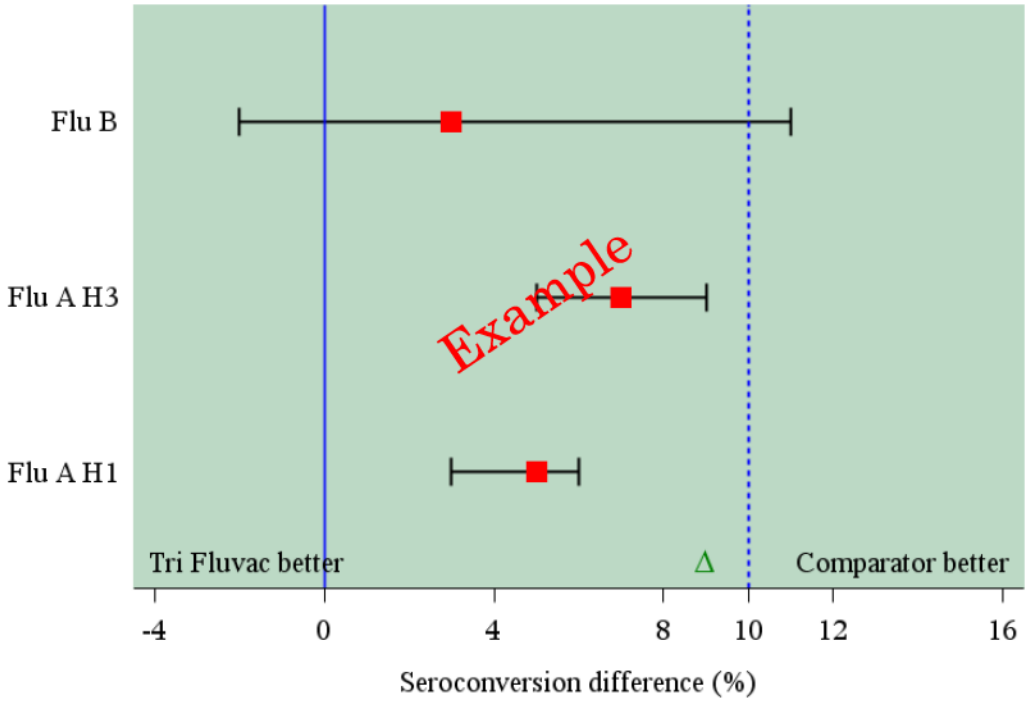
- Δ = margin



FREF 16: Summary Non-Inferiority Trial of GMTs Ratio and 95% Confidence Interval at Day 90

Note: - Non-inferiority criteria based on GMT ratio if the ratio for each HI assay at ≤ 1.5 and / or difference of seroconversion rate at ≤ 10% for the upper bound of the 95% CI.

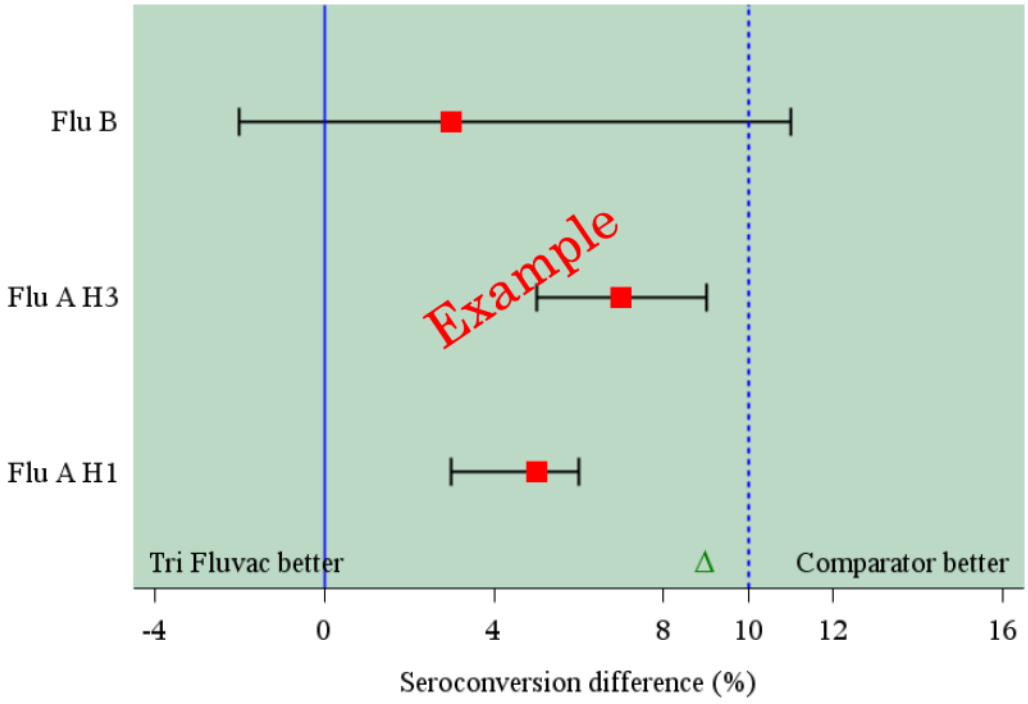
- Δ = margin



FREF 17: Summary Non-Inferiority Trial of Seroconversion Difference (%) and 95% Confidence Interval at Day 21

Note: - Non-inferiority criteria based on GMT ratio if the ratio for each HI assay at ≤ 1.5 and / or difference of seroconversion rate at ≤ 10% for the upper bound of the 95% CI.

- Δ = margin



FREF 18: Summary Non-Inferiority Trial of Seroconversion Difference (%) and 95% Confidence Interval at Day 90

Note: - Non-inferiority criteria based on GMT ratio if the ratio for each HI assay at ≤ 1.5 and / or difference of seroconversion rate at ≤ 10% for the upper bound of the 95% CI.

- Δ = margin

1. General Subject Characteristics at Screening

TREF 1.1: Demographics and Subject Characteristics at Screening by GPO Tri fluvac and Active Comparator Group

TREF 1.2: Medical History at Screening by GPO Tri fluvac and Active Comparator Group

TREF 1.3: Vital Sign at Screening by GPO Tri fluvac and Active Comparator Group

TREF 1.4: Physical Examination at Screening by GPO Tri fluvac and Active Comparator Group

TREF 1.5: Urine Pregnancy Test at Prior Immunization (Day 0)

TREF 1.1: Demographics and Subject Characteristics at Screening by GPO Tri fluvac and Active Comparator Group

				Enrolled	
		All Subjects (N = xx)	**Screen Failed (N = xx)**	**Tri fluvac (N = xx)**	**Comparator (N = xx)**
Sex, n (%)					
Male		xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
Female		xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
P- value =	x.xxxx				
Age (years), n (%)					
n					
Mean(SD)					
Median					
Min, Max					
P- value =					
Birth place, n (%)					
Bangkok and					
Other					
P- value =					
Level of education, n (%)					
No education					
Primary school					
Secondary					
Vocational					
Bachelor degree					
Higher than					
P- value =					
Occupation, n (%)					
No occupation					
Student					
Government					
Employee					
Merchant					
Own business					
Other					
P- value =					

Note: - Enrollment cases will be compared between GPO Tri fluvac and Active Comparator.

TREF 1.2: Medical History at Screening by GPO Tri fluvac and Active Comparator Group

				---------Enrolled---------	
		All Subjects (N=xx)	**Screen Failed (N=xx)**	**Tri fluvac (N = xx)**	**Comparator (N = xx)**
In the last 6 months, past medical history and pre-existing condition, n (%)					
Yes		xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
No		xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
P- value =	x.xxxx				
In the last 6 months, past immunization history, n (%)					
Yes					
No					
P- value =					

Note: - Enrolled cases will be compared between GPO Tri fluvac and Active Comparator.

- Past medical and immunization history will be showed as list in appendix.

TREF 1.3: Vital Sign at Screening by GPO Tri fluvac and Active Comparator Group

	All subjects (N = xx)	Screen Failed (N = xx)	Enrolled	
			Tri fluvac (N = xx)	Comparator (N = xx)
Height (cm.)				
n	xx	xx	xx	xx
Mean(SD)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)	xx.xx (xx.xx)
Median	xx.xx	xx.xx	xx.xx	xx.xx
Min, Max	xx.xx , xx.xx	xx.xx , xx.xx	xx.xx , xx.xx	xx.xx , xx.xx
P- value = x.xxxx				
Weight (kg.)				
n				
Mean(SD)				
Median				
Min, Max				
P- value =				
BMI				
n				
Mean(SD)				
Median				
Min, Max				
P- value =				
Temperature (ºC)				
n				
Mean(SD)				
Median				
Min, Max				
P- value =				
Pulse (Beats per minute)				
n				
Mean(SD)				
Median				
Min, Max				
P- value =				
Blood Pressure				
Systolic (mmHg)				
n				
Mean(SD)				
Median				
Min, Max				
P- value =				

TREF 1.3: Vital Sign at Screening by GPO Tri fluvac and Active Comparator Group (Continue)

	All subjects (N = xx)	Screen Failed (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)
Diastolic				
n				
Mean(SD)				
Median				
Min, Max				
P- value =				

Note: Enrolled cases will be compared between GPO Tri fluvac and Active Comparator.

TREF 1.4: Physical Examination at Screening by GPO Tri fluvac and Active Comparator Group

	All subjects (N=xx)	Screen Failed (N=xx)	---------Enrolled--------- Tri fluvac (N = xx)	Comparator (N = xx)
HEENT, n (%)				
Normal	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
Abnormal	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx				
Lungs, n (%)				
Normal				
Abnormal				
P- value =				
Cardiovascular, n (%)				
Normal				
Abnormal				
P- value =				
Gastrointestinal, n (%)				
Normal				
Abnormal				
P- value =				
Musculoskeletal, n (%)				
Normal				
Abnormal				
P- value =				
Skin, n (%)				
Normal				
Abnormal				
P- value =				
Neurologic, n (%)				
Normal				
Abnormal				
P- value =				
Other……				
Normal				
Abnormal				
p-value =				

Note: - Enrolled cases will be compared between GPO Tri fluvac and Active Comparator.

TREF 1.5: Urine Pregnancy Test at Prior Immunization (Day 0)

	--------- Enrolled ---------	
	Tri fluvac (N=xx)	**Comparator (N=xx)**
Urine Pregnancy Test, n (%)		
Positive		
Negative		
P- value =		

Note: - Enrolled cases will be compared between GPO Tri fluvac and Active Comparator.
- A urine pregnancy test will be done in females on Day 0 prior to vaccination.

2. Safety Assessment

Adverse Event

TREF 2.1.: Summary of Treatment Emergent Adverse Event by GPO Tri fluvac and Active Comparator Group

TREF 2.2: Comparison of Maximum Severity Grade of Adverse Event by GPO Tri fluvac and Active Comparator Group

TREF 2.3: Summary of Adverse Events Classified by MedDRA term

TREF 2.4: Summary of Adverse Events Suspected to be Related to Treatment

TREF 2.5: Summary of Adverse Events with Definitely Related and / or Severe

Illness like Influenza (ILI)

TREF 2.6: Summary Number of Subjects with Illness like Influenza (ILI) by GPO Tri fluvac and Active Comparator Group

TREF 2.7: Vital Sign of Illness like Influenza (ILI) by GPO Tri fluvac and Active Comparator Group

TREF 2.8: Physical Examination of Illness like Influenza (ILI) by GPO Tri fluvac and Active Comparator Group

TREF 2.9: Summary RT- PCR Test for Illness like Influenza (ILI) by GPO Tri fluvac and Active Comparator Group

TREF 2.1: Summary of Treatment Emergent Adverse Events by GPO Tri fluvac and Active Comparator Group

	--------- EVENT ---------		--------- CASE ---------	
	Tri fluvac (N = xx)	**Comparator (N = xx)**	**Tri fluvac (N = xx)**	**Comparator (N = xx)**
Experienced AE, n (%)				
• AE suspected to be not related to Treatment	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
• AE **suspected to be related to Treatment				
Experienced SAE, n (%)				
• SAE suspected to be not related to Treatment				
• SAE **suspected to be related to Treatment				

Note: - Percentage of events will be calculated from all events of AE.
- Percentage of cases will be calculated from all cases.
** suspected to be related treatment = Probably not related ,Probably related, Definitely related

TREF 2.2: Comparison of Maximum Severity Grade of Adverse Event by GPO Tri fluvac and Active Comparator Group

Severity	Tri fluvac (N = xx) n (%)	Comparator (N = xx) n (%)
Mild	xx(xx.xx)	xx(xx.xx)
Moderate		
Severe		
Life-threatening		
P- value = x.xxxx		

Note: Summary by case who had any AEs

TREF 2.3: Summary of Adverse Events Classified by MedDRA term

System Organ Class Term (SOC)	Preferred Term(PT)	---------Event---------		---------Case---------	
		Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)
		n (%)	n (%)	n (%)	n (%)
……..	…….	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)
……..	…….				
…….	…….				

TREF 2.4: Summary of Adverse Events Related to Treatment

System Organ Class Term (SOC)	Preferred Term(PT)	---------Event---------		---------Case---------	
		Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)
		n (%)	n (%)	n (%)	n (%)
…….	……..	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)	xx(xx.xx)

Note: suspected to be related treatment = probably not related, probably related, definitely related

TREF 2.5: Summary of Adverse Events with Definitely Related and / or Severe

Study Number	Study Group	Sex	Age	Adverse Event	Start Date	Stop Date	Medication Taken	Severity	Relation	Outcome	*ILI	Serious
…..	…..	…..	….	……..	……	…..	…..	…..	……	……		…..

*ILI-illness like influenza

TREF 2.6: Summary Number of Subjects with Illness like Influenza (ILI) by GPO Tri fluvac and Active Comparator Group

	Tri fluvac (N = xx)	Comparator (N = xx)
Illness like Influenza (ILI)		
Yes		
No		
p-value = xxx		

Note: This table will be showed number of subjects with and without ILI.

TREF 2.7: Vital Sign of Illness like Influenza (ILI) by GPO Tri fluvac and Active Comparator Group

	Tri fluvac (N = xx)*	Comparator (N = xx)*
Temperature (°C)		
n		
Mean(SD)		
Median		
Min, Max		
P- value =		
Pulse (Beats per minute)		
n		
Mean(SD)		
Median		
Min, Max		
P- value =		
Blood Pressure		
Systolic (mmHg)		
n		
Mean(SD)		
Median		
Min, Max		
P- value =		
Diastolic		
n		
Mean(SD)		
Median		
Min, Max		
P- value =		

Note: - Vital sign will be compared between GPO Tri fluvac and Active Comparator.

- * Number of illness like influenza (ILI) events
- Only subject with of illness like influenza (ILI) will be considered for this table.

TREF 2.8: Physical Examination of Illness like Influenza (ILI) Events by GPO Tri fluvac and Active Comparator Group

	Tri fluvac (N = xx)*	Comparator (N = xx)*
HEENT, n (%)		
Normal	xx(xx.xx)	xx(xx.xx)
Abnormal	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx		
Lungs, n (%)		
Normal		
Abnormal		
P- value =		
Cardiovascular, n (%)		
Normal		
Abnormal		
P- value =		
Gastrointestinal, n (%)		
Normal		
Abnormal		
P- value =		
Musculoskeletal, n (%)		
Normal		
Abnormal		
P- value =		
Skin, n (%)		
Normal		
Abnormal		
P- value =		
Neurologic, n (%)		
Normal		
Abnormal		
P- value =		

Note: - Physical examination will be compared between GPO Tri fluvac and Active Comparator.
- * Number of illness like influenza (ILI) events
- Only subject with of illness like influenza (ILI) will be considered for this table.

TREF 2.9: Summary RT- PCR Test for Illness like Influenza (ILI) Events by GPO Tri fluvac and Active Comparator Group

	Tri fluvac (N = xx)*	Comparator (N = xx)*
Nasal Swab Test Result		
Not done	xx(xx.xx)	xx(xx.xx)
Inconclusive	xx(xx.xx)	xx(xx.xx)
Influenza A		
Positive	xx(xx.xx)	xx(xx.xx)
Negative	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx		
Influenza B		
Positive	xx(xx.xx)	xx(xx.xx)
Negative	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx		
Throat Swab Test Result		
Not done	xx(xx.xx)	xx(xx.xx)
Inconclusive	xx(xx.xx)	xx(xx.xx)
Influenza A		
Positive	xx(xx.xx)	xx(xx.xx)
Negative	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx		
Influenza B		
Positive	xx(xx.xx)	xx(xx.xx)
Negative	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx		
Conclusion of RT-PCR		
Influenza A H1		
Influenza A H3		
Influenza A H5		
Influenza A unspecified		
Influenza B		
Inconclusive test results		
Influenza not detected		
Other ……..		

TREF 2.9: Summary RT- PCR Test for Illness like Influenza (ILI) Events by GPO Tri fluvac and Active Comparator Group (Continue)

	Tri fluvac (N = xx)*	Comparator (N = xx)*
Final Diagnosis		
Influenza		
ILI		
Other……		
P- value = x.xxxx		

Note: - Only subject with of illness like influenza (ILI) will be considered for this table.
- * Number of illness like influenza (ILI) events
- Test result will be compared between GPO Tri fluvac and Active Comparator.

3. Post Immunization Reaction

Temperature Grading

TREF 3.1 Comparison of Temperature Grading at Follow up Visit by GPO Tri Fluvac and Active Comparator Group

TREF 3.2 Comparison of Temperature Grading at Post Immunization by GPO Tri Fluvac and Active Comparator Group

Vital Sign

TREF 3.3: Vital Sign by GPO Tri Fluvac and Active Comparator Group

Physical Examination

TREF 3.4: Physical Examination by GPO Tri Fluvac and Active Comparator Group

Post Immunization Reaction

Local Reaction Post Immunization

TREF 3.5 Comparison of Maximum Grade of Local Reaction at Post Immunization by GPO Tri Fluvac and Active Comparator Group

TREF 3.6 Comparison of Local Reaction at Post Immunization each Follow up Time by GPO Tri Fluvac and Active Comparator Group

TREF 3.7 Comparison of Maximum Grade of Local Reaction by Symptom at Post Immunization by GPO Tri Fluvac and Active Comparator Group

TREF 3.8: Summary Number of Local Reaction Days by Symptom at Post Immunization

TREF 3.9: Summary Number of Local Reaction by Symptom at Post Immunization

Systemic Reaction Post Immunization

TREF 3.10 Comparison of Maximum Grade of Systemic Reaction at Post Immunization by GPO Tri Fluvac and Active Comparator Group

TREF 3.11 Comparison of Systemic Reaction at Post Immunization each Follow up Visit by GPO Tri Fluvac and Active Comparator Group

TREF 3.12 Comparison of Maximum Grade of Systemic Reaction by Symptom at Post Immunization by GPO Tri Fluvac and Active Comparator Group

TREF 3.13: Summary Number of Systemic Reaction Days by Symptom at Post Immunization

TREF 3.14: Summary Number of Systemic Reaction by Symptom at Post Immunization

TREF 3.1: Comparison of Temperature Grading at Follow up Visit by GPO Tri Fluvac and Active Comparator Group

Follow up Visit	Tri fluvac (N = xx) n (%)	Comparator (N = xx) n (%)
Day 0		
- Grade 0	xx(xx.xx)	xx(xx.xx)
- Grade 1	xx(xx.xx)	xx(xx.xx)
- Grade 2	xx(xx.xx)	xx(xx.xx)
- Grade 3	xx(xx.xx)	xx(xx.xx)
- Grade 4	xx(xx.xx)	xx(xx.xx)
p - value = x.xxxx		
Day 7		
- Grade 0		
- Grade 1		
- Grade 2		
- Grade 3		
- Grade 4		
p - value =		
Day 21		
- Grade 0		
- Grade 1		
- Grade 2		
- Grade 3		
- Grade 4		
p - value =		
Day 90		
- Grade 0		
- Grade 1		
- Grade 2		
- Grade 3		
- Grade 4		
p - value =		

Note: Grading of reporting temperature are:
Grade 0: (no) < 38 °C
Grade 1: (mild) 38.0 °C - < 38.6 °C
Grade 2: (moderately high) ≥ 38.6 °C - < 39.3 °C
Grade 3: (high) ≥ 39.3 °C – < 40.0 °C
Grade 4: (Potential Life Threatening) > 40 °C

TREF 3.2: Comparison of Temperature Grading at Post Immunization by GPO Tri Fluvac and Active Comparator Group

Follow up Visit	Tri fluvac (N = xx) n (%)	Comparator (N = xx) n (%)
30 min.		
- Grade 0	xx(xx.xx)	xx(xx.xx)
- Grade 1	xx(xx.xx)	xx(xx.xx)
- Grade 2	xx(xx.xx)	xx(xx.xx)
- Grade 3	xx(xx.xx)	xx(xx.xx)
- Grade 4	xx(xx.xx)	xx(xx.xx)
p - value = x.xxxx		
Day 1		
- Grade 0		
- Grade 1		
- Grade 2		
- Grade 3		
- Grade 4		
p - value =		
Day 2		
- Grade 0		
- Grade 1		
- Grade 2		
- Grade 3		
- Grade 4		
p - value =		
Day 3		
- Grade 0		
- Grade 1		
- Grade 2		
- Grade 3		
- Grade 4		
p - value =		

Note: Grading of reporting temperature are:
Grade 0: (no) < 38 °C
Grade 1: (mild) 38.0 °C - < 38.6 °C
Grade 2: (moderately high) ≥ 38.6 °C - < 39.3 °C
Grade 3: (high) ≥ 39.3 °C – < 40.0 °C
Grade 4: (Potential Life Threatening) > 40 °C

TREF 3.3: Vital Sign at Follow up Visit by GPO Tri Fluvac and Active Comparator Group

Vital Sign	----- Day 0 -----		----- Day 7 -----		----- Day 21 -----		----- Day 90 -----	
	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)
Temperature (ºC)								
n	xx	xx						
Mean(SD)	xx.xx(xx.xx)	xx.xx(xx.xx)						
Median	xx.xx	xx.xx						
Min, Max	xx.xx , xx.xx	xx.xx , xx.xx						
P- value =	x.xxxx							
Pulse (Beats per								
n								
Mean(SD)								
Median								
Min, Max								
P- value =								
Blood Pressure								
Systolic (mmHg)								
n								
Mean(SD)								
Median								
Min, Max								
P- value =								
Diastolic								
n								
Mean(SD)								
Median								

TREF 3.3: Vital Sign at Follow up Visit by GPO Tri Fluvac and Active Comparator Group (Continue)

Vital Sign	----- Day 0 -----		----- Day 7 -----		----- Day 21 -----		----- Day 90 -----	
	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)
Min, Max								
P- value =								

TREF 3.4: Physical Examination by GPO Tri Fluvac and Active Comparator Group

	Day 0		Day 7		Day 21		Day 90	
	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)	Tri fluvac (N = xx)	Comparator (N = xx)
HEENT, n (%)								
Normal	xx(xx.xx)	xx(xx.xx)						
Abnormal	xx(xx.xx)	xx(xx.xx)						
P- value =	x.xxxx							
Lungs, n (%)								
Normal								
Abnormal								
P- value =								
Cardiovascular, n (%)								
Normal								
Abnormal								
P- value =								
Gastrointestinal, n (%)								
Normal								
Abnormal								
P- value =								
Musculoskeletal, n (%)								
Normal								
Abnormal								
P- value =								
Skin, n (%)								
Normal								
Abnormal								
P- value =								

TREF 3.4: Physical Examination by GPO Tri Fluvac and Active Comparator Group (Continue)

	Day 0		Day 7		Day 21		Day 90	
	Tri Fluvac (N = xx)	Comparator (N = xx)	Tri Fluvac (N = xx)	Comparator (N = xx)	Tri Fluvac (N = xx)	Comparator (N = xx)	Tri Fluvac (N = xx)	Comparator (N = xx)
Neurologic, n (%)								
Normal	xx(xx.xx)	xx(xx.xx)						
Abnormal	xx(xx.xx)	xx(xx.xx)						
P- value =	x.xxxx							

TREF 3.5: Comparison of Maximum Grade of Any Local Reaction at Post Immunization by GPO Tri fluvac and Active Comparator Group

Grade	Tri Fluvac (N = xx) n (%)	Comparator (N = xx) n (%)
Grade 0	xx(xx.xx)	xx(xx.xx)
Grade 1	xx(xx.xx)	xx(xx.xx)
Grade 2	xx(xx.xx)	xx(xx.xx)
Grade 3	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx		

Note: - Any local reaction on any day (by case)
- Erythema and Induration will be not included.
- Grading

Grade 0 - none
Grade 1 - mild
Grade 2 - moderate
Grade 3 - severe

TREF 3.6: Comparison of Local Reaction at Post Immunization each Follow up Time by GPO Tri Fluvac and Active Comparator Group

Local Reaction	30 min.		Day 1		Day 2		Day 3	
	Tri Fluvac (N=xx)	Comparator (N=xx)	Tri Fluvac (N=xx)	Comparator (N=xx)	Tri Fluvac (N=xx)	Comparator (N=xx)	Tri Fluvac (N=xx)	Comparator (N=xx)
- **Pain, n (%)**	xx(xx.x)	xx(xx.xx)						
p-value =	x.xxxx							
- **Limitation of arm movement, n (%)**								
p-value =								
- **Erythema (cm.)**								
n								
Mean(SD)								
Median								
Min, Max								
p-value =								
- **Swelling (cm.)**								
n								
Mean(SD)								
Median								
Min, Max								
p-value =								
- **Induration (cm.)**								
n								
Mean(SD)								
Median								
Min, Max								
p-value =								

Note: - Summary by case who had symptoms

TREF 3.7: Comparison of Maximum Grade of Local Reaction by Symptom at Post Immunization by GPO Tri fluvac and Active Comparator Group

Local Reaction	Tri fluvac (N=xx)	Comparator (N=xx)
Pain, n (%)		
Grade 0	xx(xx.xx)	xx(xx.xx)
Grade 1	xx(xx.xx)	xx(xx.xx)
Grade 2	xx(xx.xx)	xx(xx.xx)
Grade 3	xx(xx.xx)	xx(xx.xx)
p-value = x.xxxx		
Limitation of arm movement, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		

Note: - On any day (by cases)

- Grading

Grade 0 - none
Grade 1 - mild
Grade 2 - moderate
Grade 3 - severe

TREF 3.8: Comparison Number of Subject by Number of Local Reaction Days at Post Immunization GPO Tri fluvac and Active Comparator Group

Number of Days by Local Reaction	Tri fluvac (N = xx)	Comparator (N = xx)
Pain		
only 30 min.	xx (xx.xx)	xx (xx.xx)
1 day	xx (xx.xx)	xx (xx.xx)
2 days	xx (xx.xx)	xx (xx.xx)
3 days	xx (xx.xx)	xx (xx.xx)
p-value = x.xxxx		
Limitation of arm movement		
only 30 min.	xx (xx.xx)	xx (xx.xx)
1 day	xx (xx.xx)	xx (xx.xx)
2 days	xx (xx.xx)	xx (xx.xx)
3 days	xx (xx.xx)	xx (xx.xx)
p-value = x.xxxx		

Note: - Subjects who had symptom with local reaction will be considered in this table.
- Number of subjects who had symptom will be compared between Tri fluvac and comparator.
- Percentage will be calculated from total enrollment subject.

TREF 3.9: Comparison Number of Subjects by Number of Local Reaction at Post Immunization GPO Tri fluvac and Active Comparator Group

Number of Local Reaction	Tri fluvac (N = xx)	Comparator (N = xx)
No symptom	xx (xx.xx)	xx (xx.xx)
1 symptom	xx (xx.xx)	xx (xx.xx)
2 symptoms	xx (xx.xx)	xx (xx.xx)
p-value = x.xxxx		

Note: - All enrollment Subjects will be considered in this table.
- Percentage will be calculated from total enrollment subject.

TREF 3.10: Comparison of Maximum Grade of Any Systemic Reaction at Post Immunization by GPO Tri fluvac and Active Comparator Group

Grade	Tri fluvac (N=xx) n (%)	Comparator (N=xx) n (%)
Grade 0	xx(xx.xx)	xx(xx.xx)
Grade 1	xx(xx.xx)	xx(xx.xx)
Grade 2	xx(xx.xx)	xx(xx.xx)
Grade 3	xx(xx.xx)	xx(xx.xx)
P- value = x.xxxx		

Note: Grading

Grade 0 - none
Grade 1 - mild
Grade 2 - moderate
Grade 3 - severe

TREF 3.11: Comparison of Systemic Reaction at Post Immunization each Follow up Time by GPO Tri fluvac and Active Comparator Group

Systemic Reaction	---- 30 min. ----		---- Day 1 ----		---- Day 2 ----		---- Day 3 ----	
	Tri fluvac	Comparator (N=xx)	Tri fluvac (N=xx)	Comparator (N=xx)	Tri fluvac (N=xx)	Comparator (N=xx)	Tri fluvac (N=xx)	Comparator (N=xx)
- **Headache, n (%)**	xx(xx.xx)	xx(xx.xx)						
p-value =		x.xxxx						
- **Fatigue, n (%)**								
p-value =								
- **Malaise, n (%)**								
p-value =								
- **Chills, n (%)**								
p-value =								
- **Myalgia, n (%)**								
p-value =								
- **Arthralgia, n (%)**								
p-value =								
- **Nausea, n (%)**								
p-value =								
- **Vomiting, n (%)**								
p-value =								
- **Rash, n (%)**								
p-value =								

Note: Summary by case who had symptoms

TREF 3.12: Comparison of Maximum Grade of Systemic Reaction by Symptom at Post Immunization by GPO Tri fluvac and Active Comparator Group

Systemic Reaction	Tri fluvac (N=xx)	Comparator (N=xx)
Headache, n (%)		
Grade 0	xx(xx.xx)	xx(xx.xx)
Grade 1	xx(xx.xx)	xx(xx.xx)
Grade 2	xx(xx.xx)	xx(xx.xx)
Grade 3	xx(xx.xx)	xx(xx.xx)
p-value = x.xxxx		
Fatigue, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		
Malaise, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		
Chills, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		
Myalgia, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		
Arthralgia, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		

TREF 3.12: Comparison of Maximum Grade of Systemic Reaction by Symptom at Post Immunization by GPO Tri fluvac and Active Comparator Group (Continue)

Systemic Reaction	Tri fluvac (N=xx)	Comparator (N=xx)
Nausea, n (%)		
Grade 0	xx(xx.xx)	xx(xx.xx)
Grade 1	xx(xx.xx)	xx(xx.xx)
Grade 2	xx(xx.xx)	xx(xx.xx)
Grade 3	xx(xx.xx)	xx(xx.xx)
p-value =		
Vomiting, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		
Rash, n (%)		
Grade 0		
Grade 1		
Grade 2		
Grade 3		
p-value =		

Note: • On any day (by cases)
- Grading
  - Grade 0 - none
  - Grade 1 - mild
  - Grade 2 - moderate
  - Grade 3 - severe

TREF 3.13: Comparison Number of Subject by Number of Systemic Reaction Days at Post Immunization GPO Tri fluvac and Active Comparator Group

Number of Days by Systemic Reaction		Tri fluvac (N=xx)	Comparator (N=xx)
Headache	only 30 min.	xx(xx.xx)	xx(xx.xx)
	1 day	xx(xx.xx)	xx(xx.xx)
	2 days	xx(xx.xx)	xx(xx.xx)
	3 days	xx(xx.xx)	xx(xx.xx)
	4 days	xx(xx.xx)	xx(xx.xx)
	5 days	xx(xx.xx)	xx(xx.xx)
	p-value = x.xxxx		
Fatigue	only 30 min.		
	1 day		
	2 days		
	3 days		
	4 days		
	5 days		
	p-value = x.xxxx		
Malaise	only 30 min.		
	1 day		
	2 days		
	3 days		
	4 days		
	5 days		
	p-value = x.xxxx		
Chills	only 30 min.		
	1 day		
	2 days		
	3 days		
	4 days		
	5 days		
	p-value = x.xxxx		
Myalgia	only 30 min.		
	1 day		
	2 days		
	3 days		
	4 days		
	5 days		
	p-value = x.xxxx		

TREF 3.13: Comparison Number of Subject by Number of Systemic Reaction Days at Post Immunization between GPO Tri fluvac and Active Comparator Group (Continue)

Number of Days by Systemic Reaction		Tri fluvac (N=xx)	Comparator (N=xx)
Arthralgia	only 30 min.	xx(xx.xx)	xx(xx.xx)
	1 day	xx(xx.xx)	xx(xx.xx)
	2 days	xx(xx.xx)	xx(xx.xx)
	3 days	xx(xx.xx)	xx(xx.xx)
	4 days	xx(xx.xx)	xx(xx.xx)
	5 days	xx(xx.xx)	xx(xx.xx)
	p-value = x.xxxx		
Nausea	only 30 min.		
	1 day		
	2 days		
	3 days		
	4 days		
	5 days		
	p-value = x.xxxx		
Vomiting	only 30 min.		
	1 day		
	2 days		
	3 days		
	4 days		
	5 days		
	p-value = x.xxxx		
Rash	only 30 min.		
	1 day		
	2 days		
	3 days		
	4 days		
	5 days		
	p-value = x.xxxx		

Note: - Subjects who had symptom with Systemic reaction will be considered in this table.
- Number of subjects who had symptom will be compared between Tri fluvac and comparator.
- Percentage will be calculated from total enrollment subjects.

TREF 3.14: Comparison Number of Subjects by Number of Systemic Reaction at Post Immunization between GPO Tri fluvac and Active Comparator Group

Number of Local Reaction	Tri fluvac (N=xx)	Comparator (N=xx)
No symptom	xx(xx.xx)	xx(xx.xx)
1 symptom	xx(xx.xx)	xx(xx.xx)
2 symptoms	xx(xx.xx)	xx(xx.xx)
3 symptoms	xx(xx.xx)	xx(xx.xx)
4 symptoms	xx(xx.xx)	xx(xx.xx)
5 symptoms	xx(xx.xx)	xx(xx.xx)
6 symptoms	xx(xx.xx)	xx(xx.xx)
7 symptoms	xx(xx.xx)	xx(xx.xx)
8 symptoms	xx(xx.xx)	xx(xx.xx)
9 symptoms	xx(xx.xx)	xx(xx.xx)

Note: - All enrollment Subjects will be considered in this table.
- Percentage will be calculated from total enrollment subject.

4. Immunogenicity

TREF 4.1: Comparing Seroconversion Rates between GPO Tri fluvac and Active Comparator Group Separated by HI Assay at Day 21 and 90

TREF 4.2: Comparing Seroconversion Rates between GPO Tri fluvac and Active Comparator at Any Day

TREF 4.3: Comparing Seroconversion Rates Separated by HI Assay at Day 21 and 90 in Sub-Group Pre-Vaccination HI Antibody titer < 1:10

TREF 4.4: Comparing Seroconversion Rates Separated by HI Assay at Day 21 and 90 in Sub-Group Pre-Vaccination HI Antibody titer ≥ 1:10

TREF 4.5: Comparing Seroprotective Rates between GPO Tri fluvac and Active Comparator Group Separated by HI Assay at Day 21 and 90

TREF 4.6: Comparing Seroprotective Rates Separated by HI Assay at Day 21 and 90 in Sub-Group Pre-Vaccination HI Antibody titer < 1:10

TREF 4.7: Comparing Seroprotective Rates Separated by HI Assay at Day 21 and 90 in Sub-Group Pre-Vaccination HI Antibody titer ≥ 1:10

TREF 4.8: Geometric Mean Titer (GMTs) of Immune Response by GPO Tri fluvac and Active Comparator Group

TREF 4.9: Geometric Mean Titer (GMTs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer < 1:10

TREF 4.10: Geometric Mean Titer (GMTs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer ≥ 1:10

TREF 4.11: Geometric Mean Fold Rises (GMFRs) of Immune Response by GPO Tri fluvac and Active Comparator Group

TREF 4.12: Geometric Mean Fold Rises (GMFRs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer < 1:10

TREF 4.13: Geometric Mean Fold Rises (GMFRs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer ≥ 1:10

TREF 4.1: Comparing Seroconversion Rates between GPO Tri fluvac and Active Comparator Group Separated by HI Assay at Day 21 and 90

HI Assay	Follow up Day	Study Group	4- fold rising n (%)	Not 4 -fold n (%)
Flu A H1	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu A H3	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu B	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		

Note: Enrollment cases will be compared between GPO Tri fluvac and Active Comparator Group.

TREF 4.2: Comparing Seroconversion Rates between GPO Tri fluvac and Active Comparator at Any Day

HAI Assay	Study Group	4- fold rising n (%)	Not 4 -fold n (%)
H1 Antibody Titer	Tri fluvac (N = xx)	xx.xx(xx.xx)	xx.xx(xx.xx)
	Comparator (N = xx)	xx.xx(xx.xx)	xx.xx(xx.xx)
	p - value = x.xxxx		
H3 Antibody Titer	Tri fluvac (N = xx)		
	Comparator (N = xx)		
	p - value =		
Flu B Antibody Titer	Tri fluvac (N = xx)		
	Comparator (N = xx)		
	p - value =		

TREF 4.3: Comparing Seroconversion Rates Separated by HI Assay at Day 21 and 90 in Sub - Group Pre-Vaccination HI Antibody titer < 1:10

HI Assay	Follow up Day	Study Group		4- fold rising n (%)	Not 4 -fold n (%)
Flu A H1	**Day 21**	Tri fluvac	(N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator	(N=xx)	xx(xx.xx)	xx(xx.xx)
			p - value = x.xxxx		
	Day 90	Tri fluvac	(N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator	(N=xx)	xx(xx.xx)	xx(xx.xx)
			p - value = x.xxxx		
Flu A H3	**Day 21**	Tri fluvac	(N=xx)		
		Comparator	(N=xx)		
			p - value =		
	Day 90	Tri fluvac	(N=xx)		
		Comparator	(N=xx)		
			p - value =		
Flu B	**Day 21**	Tri fluvac	(N=xx)		
		Comparator	(N=xx)		
			p - value =		
	Day 90	Tri fluvac	(N=xx)		
		Comparator	(N=xx)		
			p - value =		

Note: Enrollment cases will be compared between GPO Tri fluvac and Active Comparator Group.

TREF 4.4: Comparing Seroconversion Rates Separated by HI Assay at Day 21 and 90 in Sub-Group Pre-Vaccination HI Antibody titer ≥ 1:10

HI Assay	Follow up Day	Study Group		4- fold rising n (%)	Not 4 -fold n (%)
Flu A H1	**Day 21**	Tri fluvac	(N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator	(N=xx)	xx(xx.xx)	xx(xx.xx)
			p - value = x.xxxx		
	Day 90	Tri fluvac	(N=xx)		
		Comparator	(N=xx)		
			p - value =		
Flu A H3	**Day 21**	Tri fluvac	(N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator	(N=xx)	xx(xx.xx)	xx(xx.xx)
			p - value = x.xxxx		
	Day 90	Tri fluvac	(N=xx)		
		Comparator	(N=xx)		
			p - value =		
Flu B	**Day 21**	Tri fluvac	(N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator	(N=xx)	xx(xx.xx)	xx(xx.xx)
			p - value = x.xxxx		
	Day 90	Tri fluvac	(N=xx)		
		Comparator	(N=xx)		
			p - value =		

Note: Enrollment cases will be compared between GPO Tri fluvac and Active Comparator Group.

TREF 4.5: Comparing Seroprotective Rates between GPO Tri fluvac and Active Comparator Group Separated by HI Assay at Day 21 and 90

HI Assay	Follow up Day	Study Group	Seroprotective n (%)	Non-seroprotective n (%)
Flu A H1	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu A H3	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu B	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		

Note: - Enrollment cases will be compared between GPO Tri fluvac and Active Comparator Group.

- Seroprotective level: HI antibody titer $\geq$ 1:40

TREF 4.6: Comparing Seroprotective Rates Separated by HI Assay at Day 21 and 90 in Sub-Group Pre-Vaccination HI Antibody titer < 1:10

HI Assay	Follow up Day	Study Group	Seroprotective n (%)	Non-seroprotective n (%)
Flu A H1	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu A H3	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu B	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		

TREF 4.7: Comparing Seroprotective Rates Separated by HI Assay at Day 21 and 90 in Sub-Group Pre-Vaccination HI Antibody titer ≥ 1:10

HI Assay	Follow up Day	Study Group	Seroprotective n (%)	Non-seroprotective n (%)
Flu A H1	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu A H3	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		
Flu B	**Day 21**	Tri fluvac (N=xx)	xx(xx.xx)	xx(xx.xx)
		Comparator (N=xx)	xx(xx.xx)	xx(xx.xx)
		p - value = x.xxxx		
	Day 90	Tri fluvac (N=xx)		
		Comparator (N=xx)		
		p - value =		

TREF 4.8: Geometric Mean Titer (GMTs) of Immune Response by GPO Tri fluvac and Active Comparator Group

HAI Assay	Day 0 GMT(95% CI)	Day 21 GMT(95% CI)	Day 90 GMT(95% CI)
Flu A H1 Antibody titer			
Tri fluvac	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
Comparator	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
P - value =	x.xxxx	x.xxxx	x.xxxx
Flu A H3 Antibody titer			
Tri fluvac			
Comparator			
P - value =			
Flu B Antibody titer			
Tri fluvac			
Comparator			
P - value =			

Note: Enrollment cases will be compared between GPO Tri fluvac and Active Comparator.

TREF 4.9: Geometric Mean Titer (GMTs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer < 1:10

HAI Assay	Day 0 GMT(95% CI)	Day 21 GMT(95% CI)	Day 90 GMT(95% CI)
Flu A H1 Antibody titer			
Tri fluvac	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
Comparator	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
P - value =	x.xxxx	x.xxxx	x.xxxx
Flu A H3 Antibody titer			
Tri fluvac			
Comparator			
P - value =			
Flu B Antibody titer			
Tri fluvac			
Comparator			
P - value =			

Note: - Enrollment cases will be compared between GPO Tri fluvac and Active Comparator.
- † For titer reported as < 10, a value of 5 will be assigned when computing GMT

TREF 4.10: Geometric Mean Titer (GMTs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer ≥ 1:10

HAI Assay	Day 0 GMT(95% CI)	Day 21 GMT(95% CI)	Day 90 GMT(95% CI)
Flu A H1 Antibody titer			
Tri fluvac	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
Comparator	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
P - value =	x.xxxx	x.xxxx	x.xxxx
Flu A H3 Antibody titer			
Tri fluvac			
Comparator			
P - value =			
Flu B Antibody titer			
Tri fluvac			
Comparator			
P - value =			

Note: - Enrollment cases will be compared between GPO Tri fluvac and Active Comparator.
- † For titer reported as < 10, a value of 5 will be assigned when computing GMT

TREF 4.11: Geometric Mean Fold Rises (GMFRs) of Immune Response by GPO Tri fluvac and Active Comparator Group

HAI Assay	Tri fluvac (N = xx)	Comparator (N = xx)
Flu A H1 antibody titer		
Day 0		
GMT † (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
Day 21		
GMT† (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
GMFRs	xx.xx	xx.xx
Day 90		
GMT† (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
GMFRs	xx.xx	xx.xx
Flu A H3 antibody titer		
Day 0		
GMT † (95% CI)		
Day 21		
GMT † (95% CI)		
GMFRs‡		
Day 90		
GMT † (95% CI)		
GMFRs‡		
Flu B antibody titer		
Day 0		
GMT † (95% CI)		
Day 21		
GMT † (95% CI)		
GMFRs‡		
Day 90		
GMT † (95% CI)		
GMFRs‡		

Note: - Enrollment cases will be compared between GPO Tri fluvac and Active Comparator.

- † For titer reported as < 10, a value of 5 will be assigned when computing GMT; ‡ GMFR is the geometric mean of the ratios of post - vaccination to the pre-vaccination

TREF 4.12: Geometric Mean Fold Rises (GMFRs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer < 1:10

HAI Assay	Tri fluvac (N = xx)	Comparator (N = xx)
Flu A H1 antibody titer		
Day 0		
GMT † (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
Day 21		
GMT† (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
GMFRs	xx.xx	xx.xx
Day 90		
GMT† (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
GMFRs	xx.xx	xx.xx
Flu A H3 antibody titer		
Day 0		
GMT † (95% CI)		
Day 21		
GMT † (95% CI)		
GMFRs‡		
Day 90		
GMT † (95% CI)		
GMFRs‡		
Flu B antibody titer		
Day 0		
GMT † (95% CI)		
Day 21		
GMT † (95% CI)		
GMFRs‡		
Day 90		
GMT † (95% CI)		
GMFRs‡		

Note: - Enrollment cases will be compared between GPO Tri fluvac and Active Comparator.

- † For titer reported as < 10, a value of 5 will be assigned when computing GMT; ‡ GMFR is the geometric mean of the ratios of post - vaccination to the pre-vaccination

TREF 4.13: Geometric Mean Fold Rises (GMFRs) of Immune Response by GPO Tri fluvac and Active Comparator Group in Sub-Group Pre-Vaccination HI Antibody Titer ≥ 1:10

HAI Assay	Tri fluvac (N = xx)	Comparator (N = xx)
Flu A H1 antibody titer		
Day 0		
GMT † (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
Day 21		
GMT† (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
GMFRs	xx.xx	xx.xx
Day 90		
GMT† (95% CI)	xx.xx(xx.xx - xx.xx)	xx.xx(xx.xx - xx.xx)
GMFRs	xx.xx	xx.xx
Flu A H3 antibody titer		
Day 0		
GMT † (95% CI)		
Day 21		
GMT † (95% CI)		
GMFRs‡		
Day 90		
GMT † (95% CI)		
GMFRs‡		
Flu B antibody titer		
Day 0		
GMT † (95% CI)		
Day 21		
GMT † (95% CI)		
GMFRs‡		
Day 90		
GMT † (95% CI)		
GMFRs‡		

Note: - Enrollment cases will be compared between GPO Tri fluvac and Active Comparator.

- † For titer reported as < 10, a value of 5 will be assigned when computing GMT; ‡ GMFR is the geometric mean of the ratios of post - vaccination to the pre-vaccination

5. Concomitant Medication

TREF 5: Summary of Concomitant Medication According to WHO DD by GPO Tri fluvac and Active Comparator Group

TREF 5: Summary of Concomitant Medication According to WHO DD by GPO Tri fluvac and Active Comparator Group

Anatomical Main Group	Therapeutic Subgroup	Number of Event		Number of Case	
		Tri fluvac (N=xx) n (%)	Comparator (N=xx) n (%)	Tri fluvac (N=xx) n (%)	Comparator (N=xx) n (%)
xxxxxxxxx	xxxxxxxxx	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
xxxxxxxxx	xxxxxxxxx	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)

APPENDICES

Appendix 01: Listing of Subjects were Excluded from Analysis

Observe	Screening Number	Reason for Exclude
1		
2		
3		
…		
…		
…		

Appendix 02: Listing of Past Medical History and Pre-existing Condition in Last 6 Months

Observe	Subject Number	Study Group	Diagnosis /Symptoms /Signs	Month/Year started	Currently active?
1					
2					
3					
…					

Appendix 03: Listing of Past Immunization History in Last 6 Months

Observe	Subject Number	Study Group	Immunization	Month/Year started	Completed?
1					
2					
3					
…					

Appendix 04: Listing of Local Reaction at Post Immunization

Observe	Subject Number	Study Group	Symptom	Follow up Day (Grade)
1				
2				
3				
…				
…				
…				

Appendix 05: Listing of Systemic Reaction at Post Immunization

Observe	Subject Number	Study Group	Symptom	Follow up Day (Grade)
1				
2				
3				
…				
…				

Appendix 06: Listing of Adverse Event

No.	Subject Number	Seq.	Adverse Event	Start Date	End Date	AEs (hrs)	Medication taken?	Severity	Related to Study Vac	Outcome	AE-Serious ?	Date of Immunization	Study Group	#Day at AE started after Immunization
1														
2														
3														

Note: #Day at AE started after immunization date will be calculated from date of immunization to date at AE started.

Appendix 07: Listing of Illness like Influenza (ILI)

No.	Subject Number	ILI Seq.	Specimen Collection Date	Date of Receipt	Time of Receipt	Nasal swab Test	Nasal swab Result Influenza A	Nasal swab Result Influenza B	Throat Swab Test	Throat swab Result Influenza A	Throat swab Result Influenza B	Conclusion of RT-PCR	Related to AE#	Final Diagnosis
1														
2														
3														

Note:

Appendix 08: Listing of Concomitant Medication

No	Subject Number	Study Group	Dose	Unit	Route	Frequency	Start Date	End date	Ongoing	Indication	Date of Immunization	#Day of Conmed started after Immunization
1												
2												
3												

Note: #Day at Conmed started after immunization will be calculated from date of immunization to date of Conmed started.

Appendix 09: List of HAI Assay (Flu A H1 Antigen)

Study number	Day 0	Day 21	Day 90	Study Group
1	xx	xx	xx	xx
2	xx	xx	xx	xx
3	…	…	…	…
…	…	…	…	…

Note: For titer reported as < 10, a value of 5 will be assigned.

Appendix 10: List of HAI Assay (Flu A H3 Antigen)

Study number	Day 0	Day 21	Day 90	Study Group
1	xx	xx	xx	xx
2	xx	xx	xx	xx
3	…	…	…	…
…	…	…	…	…

Note: For titer reported as < 10, a value of 5 will be assigned.

Appendix 11: List of HAI Assay (Flu B Antigen)

Study number	Day 0	Day 21	Day 90	Study Group
1	xx	xx	xx	xx
2	xx	xx	xx	xx
3	…	…	…	…
…	…	…	…	…

Note: For titer reported as < 10, a value of 5 will be assigned.