SUMMARY OF AMENDMENTS IN PROTOCOL AND INFORMED CONSENT FORM

Protocol Number: BBIL/BBV152A/2020

Protocol Title: An Adaptive, Seamless Phase 1, Followed by Phase 2 Randomized, Double-blind, Multicenter Study to Evaluate the Safety, Reactogenicity, Tolerability and Immunogenicity of the Whole-Virion Inactivated SARS-CoV-2 Vaccine (BBV152) in Healthy Volunteers

Changes in Study Protocol (BBIL/BBV152A/2020)			
S. No.	**Protocol version : 3.0; Date: 17-08-2020**	**Amendments proposed in the protocol version 5.0; Date: 02-09-2020**	**Rationale for the proposed amendments**
1.	**Short Title:** Safety, Reactogenicity, Tolerability, and Immunogenicity of Whole-Virion Inactivated SARS-CoV-2 Virus Vaccine, BBV152 in Healthy Volunteers. Pg. No. 16 of 73	**Short Title:** Phase 1/2 study to evaluate the Safety, Reactogenicity, Tolerability, and Immunogenicity of Whole-Virion Inactivated SARS-CoV-2 Virus Vaccine, BBV152 in Healthy Volunteers. Pg. No. 17 of 78	The section is updated to expedite the phase 2 trial
2.		**Clinical Trial Strategy:** The phase 1 part of this clinical trial has completed, 375 subjects were recruited, and the the safety data of 3 vaccine formulations was analyzed post 7 days of second dose and an interim report was prepared and submitted to CDSCO. Based on the Phase 1 study safety data and non-human primate challenge study results, the BBV152-A, BBV152-B formulations are selected to continue the Phase 2 study. The Clinical Trial Strategy is depicted in the Schematic, given in Annex 1. Pg. No. 17 of 78	The section is updated to expedite the phase 2 trial

3.	**Study Objective:** **Phase 2:** To evaluate the safety and immunogenicity of two selected formulations of BBV152 (Whole-Virion Inactivated SARS-CoV-2 virus vaccine). Pg. No. 16 and 41 of 73	**Study Objective:** **Phase 2:** To evaluate the safety and immunogenicity of selected formulations (BBV152-A and BBV152-B) (Whole-Virion Inactivated SARS-CoV-2 virus vaccine). Pg. No. 17 and 45 of 78	The section is updated to expedite the phase 2 trial
4.	**Population** A total sample size of 1125 healthy volunteers, with 375 ages ≥18-≤55 in the phase 1 study and 750 ages ≥12 - ≤65 years in phase 2 study (4:1 test and placebo). Pg. No. 16 of 73	**Population** A total sample size of 755 healthy volunteers, with 375 ages ≥18-≤55 in the phase 1 study (4:1 test and placebo) and 380 ages ≥12 - ≤65 years in phase 2 study (1:1 test groups). Pg. No. 18 of 78	The section is updated to expedite the phase 2 trial
5.	**Study Purpose** This study will be conducted in a dose escalatory manner with a two-dose regimen fourteen days apart in Phase 1 and two selected formulations will be further evaluated in Phase 2. This study will be conducted in a dose escalatory manner with a two-dose regimen fourteen days apart in Phase 1 and selected formulations will be further evaluated in Phase 2. Pg. No. 16 and 40 of 73	**Study Purpose** This study will be conducted in a dose escalatory manner with a two-dose regimen fourteen days apart in Phase 1 and selected formulation (BBV152-A and BBV152-B) will be further evaluated in Phase 2. This study will be conducted in a dose escalatory manner with a two-dose regimen fourteen days apart in Phase 1 and selected formulations will be further evaluated in Phase 2 study with routine dosage schedule on day 0 and day 28 Pg. No. 18 and 44 of 78	The section is updated to expedite the phase 2 trial
6.	**Investigational Product** Whole-Virion Inactivated SARS-CoV-2 vaccine (BBV152) with three formulations, BBV152A, BBV152B and BBV152C. Any of these three formulations will beadministered as intramuscular injection. Pg. No. 16 of 73	**Investigational Product** Whole-Virion Inactivated SARS-CoV-2 vaccine (BBV152) with three formulations, BBV152A, BBV152B and BBV152C were used in phase 1 and BBV152-A and BBV152-B is selected for phase 2 study. Pg. No. 18 of 78	The section is updated to expedite the phase 2 trial

7.		**Rationale for BBV152-A & BBV152-B selection and dosage schedule change: (Added Additionally)** The vaccine formulation BBV152-A and BBV152-B are selected for the phase 2 study based on the safety data of the 3 formulations in the phase 1 study and the non-human primate animal challenge study results. **Phase 1 safety data:** In this adaptive, seamless study of Whole-Virion Inactivated SARS-CoV-2 Vaccine (BBV152), subject recruitment for Phase 1 study was initiated on 15th July 2020. A total of 897 subjects have undergone screening. A total of 133 subjects have been found to be SAS-CoV-2 positive by RT-PCR testing and/or ELISA testing, and a total of 153 subjects had abnormal lab values. A total of 402 subjects have been enrolled for the 1st dose. A total of 394 subjects have been administered the 2nd dose, after 8 subject dropouts. No immediate adverse events were reported within 2 hours of vaccine administration. Among the 402 subjects who were administered the 1st dose, a total of 76 adverse events have been recorded, and among the 394 subjects who were administered the 2nd dose, a total of 17 adverse events have been recorded. Most of the adverse effects were mild in nature and resolved without any sequelae. One serious adverse event was reported where the	The section is updated to expedite the phase 2 trial

		subject was hospitalized with viral pneumonitis and has recovered. **Non-human Primate Animal Challenge Study:** Based on the immunogenicity data from the challenge studies of Hamster and Rhesus macaque monkeys conducted at NIV, Pune, we have identified the 1 desired formulation for the Phase 2 clinical trial. Data from this study is available to review by DCGI and which will ensure that appropriate formulation (BBV152-A) is selected for Phase 2. **Dosage Schedule:** In the phase 1 study, vaccine was administered as two doses at 14 days interval (Accelerated dosage schedule), in phase 2 we would like to go with conventional (0, 28 days) dosage schedule to compare the immunogenicity between two arms. Pg. No. 20 and 21 of 78	
8.	**Study Endpoints** **Phase 2:** **Primary** 1. To evaluate the immunogenicity in terms of GMT and four-fold seroconversion rate amongst the two selected BBV152 vaccine formulations from baseline to days 14+2, 28±2,42±2, 104±7 and 194±7, in two arms.	**Study Endpoints** **Phase 2:** **Primary** 1. To evaluate the immunogenicity in terms of GMT and four-fold seroconversion rate of NAbs specific to SARS-CoV-2 virus in subjects administered with the selected BBV152-A and BBV152-B vaccine formulation from baseline to	The section is updated to expedite the phase 2 trial

	Pg. No. 19 and 41of 73	days 28+2,42±2, 56±2, 118±7 and 208±7, in two arms. Pg. No. 21 and 45 of 78	
9.	**Study Design:** **Phase 2 study** The study is designed to evaluate the safety, reactogenicity, tolerability, and immunogenicity of three arms of healthy volunteers who receive two intramuscular doses of BBV152 vaccine formulations (X1 and X2) selected from phase 1 study and placebo will be administered in 4:1 ratio among these three Arms. Since the age group is differs from the Phase 1, upon completion of the enrolment and vaccination of 50 participants among these three arms [Arm 1 (X1), Arm 2 (X2) and Arm 3 (placebo)] as per randomization, DSMB safety assessment will be conducted three days after vaccination. If the study product is deemed safe based on the DSMB review, participants will be further enrolled. **Arm 1:** A total of 300 subjects will be enrolled in this arm 1 and will receive two intramuscular doses of X1 . The two doses will be administered 14 days apart. **Arm 2:** A total of 300 subjects will be enrolled in this arm and will receive two intramuscular doses of X2 . The two doses will be administered 14 days apart. **Arm 3:** A total of 150 subjects will be enrolled in this arm and will receive two intramuscular doses of placebo. The two doses will be administered 14 days apart. After completion of Day 28, immunogenicity & safety in arms 1, 2 and 3 will be reviewed by Data Safety Monitoring Board (DSMB) and interim report will submitted to CDSCO. All subjects will be followed up to day 194 for safety and immunogenicity.	**Study Design:** **Phase 2 study** The study is designed to evaluate the safety, reactogenicity, tolerability, and immunogenicity of three arms of healthy volunteers who receive two intramuscular doses of BBV152 vaccine formulations (BBV152-A & BBV152-B) selected from phase 1 study will be administered in 1:1 ratio. **Arm 1:** A total of 190 subjects will be enrolled in this arm 1 and will receive two intramuscular doses of BBV152-A vaccine. The two doses will be administered 28 days apart. **Arm 2:** A total of 190 subjects will be enrolled in this arm and will receive two intramuscular doses of BBV152-B vaccine. The two doses will be administered 28 days apart. Data will be unblinded and an interim analysis will be performed at day 42 & 56 for Immunogenicity and safety Pg. No. 23 and 47 of 78	The section is updated to expedite the phase 2 trial

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10.	**Sample Collection :** **Phase 2**: **Immunogenicity analysis:** A total of 5 ml of blood is collected at day **0**, **14+2, 28±2, 42±2, 104±7 and 194±7**. **Pregnancy test:** By using rapid test kit. SARS-CoV-2 at the time of base line using RT-PCR and/or ELISA method. Pg. No. 27 of 73	**Sample Collection :** **Phase 2**: Immunogenicity analysis: A total of 5 ml of blood is collected at day 0, 28+2, 42±2, 56±2, 118±7 and 208±7. Blood (10 mL) will be collected on Day 0, 4, 14, 28, 42, 56, 118 and 208 from the subjects who are willing to provide for the isolation of PBMCs to assess the cell mediate immunity. Pregnancy test: By using rapid test kit. SARS-CoV-2 at the time of Screening using RT-PCR and ELISA method. Pg. No. 29 of 78	The section is updated to expedite the phase 2 trial
11.	**Study Procedure:** **Visit 2: (Day 14+2)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19. Blood samples will be withdrawn prior to vaccination for immunogenicity test. A study vaccine/placebo will be administered.	**Study Procedure:** **Visit 1: Baseline (Day 0)** If eligible, study participants will attend the OPD for physical, general examination, and specific symptoms for COVID-19. When no clinically significant abnormalities are detected, blood samples will be withdrawn prior to vaccination. A	The section is updated to expedite the phase 2 trial

	Following vaccination, participants will remain at the study site for at least 2 hours of observation to record any adverse event. Day 15-21: The study participants will be telephonically followed up by the site or first seven days post-vaccination to know their current health status **Visit 3: (Day 28±2)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19 and laboratory investigation. Blood samples will be withdrawn to assess clinical laboratory safety and immunogenicity for inactivated (COVID-19) vaccine. **Visit 4: (Day 42±2)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19 and laboratory investigation. Blood samples will be withdrawn to assess immunogenicity for inactivated (COVID-19) vaccine. **Visit 5: (Day 104±7)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19. Blood samples will be withdrawn on to assess immunogenicity for inactivated (COVID-19) vaccine. **Visit 6: (Day 194±7)** Study participants will return to the OPD for physical, general examination and specific symptoms for COVID-19. Blood samples will be withdrawn on to assess immunogenicity for inactivated (COVID-19) vaccine. Pg. No. 27 and 28 and 48 of 73	study vaccine/placebo will be administered. Following vaccination, participants will remain at the study site for at least 2 hours of observation to record any adverse event. **Day 1-7:** The study participants will be telephonically followed up by the site for the first seven days post-vaccination to know their current health status. **Visit 2: (Day 28+2)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19. Blood samples will be withdrawn prior to vaccination for immunogenicity test. A study vaccine/placebo will be administered. Following vaccination, participants will remain at the study site for at least 2 hours of observation to record any adverse event. **Phase 2: Day 29-36;** The study participants will be telephonically followed up by the site or first seven days post-vaccination to know their current health status. **Visit 3: (Day 42+2)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19 and laboratory investigation. Blood samples will be withdrawn to assess clinical laboratory safety and immunogenicity for inactivated (COVID-19)	

		vaccine. **Visit 4: (Day 56±2)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19 and laboratory investigation. Blood samples will be withdrawn to assess immunogenicity for inactivated (COVID-19) vaccine. **Visit 5: (Day 118±7)** Study participants will return to the OPD for physical, general examination, and specific symptoms for COVID-19. Blood samples will be withdrawn on to assess immunogenicity for inactivated (COVID-19) vaccine. **Visit 6: (Day 208±7)** Study participants will return to the OPD for physical, general examination and specific symptoms for COVID-19. Blood samples will be withdrawn on to assess immunogenicity for inactivated (COVID-19) vaccine. Pg. No. 31, 32, 53 and 54 of 78	

12.	**DSMB & Interim report** **Phase 2:** Since the age group is differs from the Phase 1, upon completion of the enrolment and vaccination of 50 participants among these three arms [Arm 1 (X1), Arm 2 (X2) and Arm 3 (placebo)] as per randomization, DSMB safety assessment will be conducted three days after vaccination. If the study product is deemed safe based on the DSMB review, participants will be further enrolled. Pg. No. 29 of 73	**DSMB & Interim report** **Phase 2:** Arm 1: Data will be unblinded at day 42 and an interim report on day 42 and 56 based on the safety and immunogenicity of the BBV152-A and BBV152-B will be prepared and notified to CDSCO. This interim report will contain a detailed analysis of the data based on the primary and secondary objectives on Day 42 and 56 (Immunogenicity & Safety). Pg. No. 33 of 78	The section is updated to expedite the phase 2 trial
13.	**Randomization** **Phase 2:** The Block Randomization will be generated for 750 subjects in the age group of ≥12-≤65 using the SAS PROC PLAN procedure in the ratio of 4:1 of Test & placebo arm. Pg. No. 30 of 73	**Randomization** **Phase 2:** The Block Randomization will be generated for 380 subjects in the age group of ≥12-≤65 using the SAS PROC PLAN procedure in the ratio of 1:1 of Test groups. Pg. No. 34 of 78	The section is updated to expedite the phase 2 trial
14.	**Safety Assessment** **Phase 2:** **1.** 5 mL of the sample will be collected for immunogenicity at baseline, Days 14+2, 28±2, 42±2, 104±7 and 194±7 **2.** Pregnancy test with rapid test kit.	**Safety Assessment** **Phase 2:** 1. **Arm 1:** 5 mL of the sample will be collected for immunogenicity at baseline, Days 28+2, 42±2, 56±2 118±7 and 208±7 2. **Arm 2:** 5 mL of the sample will be	The section is updated to expedite the phase 2 trial

	Pg. No. 30 of 73	collected for immunogenicity at baseline, 28+2, 42±2, 104±7 and 194±7 3. Pregnancy test with rapid test kit. Blood (10 mL) will be collected on Day 0, 4, 14, 28, 42, 56, 118 and 208 from the subset of subjects who are willing to provide for the isolation of PBMCs to assess the cell mediate immunity. Pg. No. 35 of 78	
15.	**Sample Size:** A total sample size of 1125 healthy volunteers, with 375 ages ≥18-≤55 in the phase 1 study and 750 ages ≥12-≤65 in phase 2 study (4:1 test and placebo). We assume immunogenicity data will be available for 90% of randomized study participants, resulting in sample sizes for analysis of 90 BBV152 recipients per formulation in Phase 1 and 270 per formulation in Phase 2. The table below gives the statistical power to find a significant difference at the twosided 5% significance level between SC rates with different formulations for various combinations of true underlying SC rates, using a normal approximation test of differences in proportions. Pg. No. 32 and 64 of 73	**Sample Size:** A total sample size of 755 healthy volunteers, with 375 ages ≥18-≤55 in the phase 1 study and 380 ages ≥12-≤65 in phase 2 study (1:1 test and placebo). We assume immunogenicity data will be available for 90% of randomized study participants, resulting in sample sizes for analysis of 90 BBV152 recipients per formulation in Phase 1, and 180 per Arm 1 dosage schedule and 180 per Arm 2 dosage schedule in Phase 2. Pg. No. 35 and 66 of 78	The section is updated to expedite the phase 2 trial
16.	**Statistical Analysis Plan:** **Phase 2:** Data will be unblinded upon completion of visit 3 by all participants in Arm1 and Arm 2. Safety analysis of all vaccine-related events would be conducted up to Day 28 to examine the acceptability of the vaccine. Immunology data of BBV152 vaccine titers will be compared to Arm	**Statistical Analysis Plan:** **Phase 2:** **Arm 1:** Data will be unblinded at day 42 and an interim report will be prepared on day 42 and 56 based on the safety and immunogenicity of the BBV152-A will be prepared and notified to	The section is updated to expedite the phase 2 trial

	3 (placebo) titers i.e., baseline (Day 0) vs. Day 14 and Day 28 data. A clinical study report will be generated for the interim analysis data for licensure. Pg. No. 32 of 73	CDSCO. **Arm 2:** Data will be unblinded on day 42 interim report will be prepared on day 42, 56 and notified to the CDSCO, India, for further progressing the clinical development of the vaccine. Pg. No. 36 of 78	
17.	**Table 1: Study Design chart** Pg. No. 34 of 73	**Table 1: Study Design chart** Changed based on all above mentioned changes. Pg. No. 38 of 78	The section is updated to expedite the phase 2 trial
18.	**Table 3: Study Flow Chart of Phase 2 Study** Pg. No. 36 of 73	**Table 3: Study Flow Chart of Phase 2 Study** Changed based on all above mentioned changes. Pg. No. 40 of 78	The section is updated to expedite the phase 2 trial.
19.	**Annexure 1:** Pg. No. 37 of 73	**Annexure 1:** Changed based on all above mentioned changes. Pg. No. 41 of 78	The section is updated to expedite the phase 2 trial
Changes in Informed Consent Document (BBIL/BBV152A/2020)			
S. No.	**Informed Consent Form version : 3.0; Date: 17-08-2020**	**Amendments proposed in the Informed Consent Form version 5.0; Date: 02-09-2020**	**Rationale for the proposed amendments**
	STUDY PARTICIPATION AND PROCEDURES A total of 375 (4:1) healthy volunteer subjects of 18 to 55 years of age will participate in the study. 125 subjects	**STUDY PARTICIPATION AND PROCEDURES** A total of 380 (1:1) healthy volunteer subjects of _12 to _65 years of age will participate in the study.	The section is updated as per the changes in the protocol.

	will be enrolled in Arm 1, 125 subjects will be enrolled in Arm 2 and 125 subjects will be enrolled in Arm 3. You will be screened for selection to take part in the study. If you are eligible and decide to participate in the study, you may be put in test arm or placebo arm in Phase 1 study. Two arms, test and placebo the subjects will receive either 3µg/6µg dose strength of BBV 152 (0.5mL) vaccine in the test arm and placebo in placebo arm. Vaccine formulations BBV152A, BBV152B, and BBV152C of test vaccine will be administered intramuscularly. Enrolment of all the Arms will be done in parallel. Pg. No. 2 of 11	190 subjects will be enrolled in Arm 1 and 190 subjects will be enrolled in Arm 2. You will be screened for selection to take part in the study. If you are eligible and decide to participate in the study, you may be randomized either in Arm1 or Arm 2. **Arm 1:** A total of 190 subjects will be enrolled in this Arm 1 and will receive two intramuscular doses of BBV152-A vaccine. The two doses will be administered 28 days apart. **Arm 2:** A total of 190 subjects will be enrolled in this Arm 2 and will receive two intramuscular doses of BBV152-B vaccine. The two doses will be administered 28 days apart. Pg. No. 2 of 11	
	Study Procedure: Visit 3: (Day 14+2) • Physical and general examination will be performed and also checked for COVID-19 specific symptoms. • 15 mL of blood will be collected for routine laboratory investigations including hematology, biochemistry, liver and kidney function tests , serology (HIV & Hep B), urine analysis and and diagnosis for SARS-CoV-2. • 5 mL blood will be collected for Immunogenicity analysis. • Urine pregnancy test will be performed in case of potential child bearing women.	**Study Procedure:** • Urine pregnancy test will be performed in case of potential child bearing women and eligible subjects will be enrolled. • Blood (10 mL) will be collected at time points (Day 0, Day 4, Day 14, Day 28, Day 42, Day 56, Day 118, Day 208) from the subset of subjects who are willing to provide for the isolation of PBMC's to assess the cell mediated immunity. Blood sample for PBMCs will be collected from NIMS, Hyderabad and AIIMS, New Delhi. **Visit 2: (Day 28±2)** • Physical and general examination will be	The section is updated as per the changes in the protocol.

	Pg. No. 3 of 11	performed and also checked for COVID-19 specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis. • Administration of 0.5 mL of test vaccine. • Following vaccination, you will be observed for at least 2 hrs for any adverse events • Diary card will be reviewed to record adverse events. You will receive calls from the site staff for first seven days of post vaccination to check if you have any adverse events following the vaccination and his/her current health status • All the adverse events should be recorded by you in the subject diary card provided and brought to the clinic for the study doctor's review. You should contact the study doctor for immediate medical assistance throughout the study period. • Urine pregnancy test will be performed in case of potential child bearing women. **Visit 3: (Day 42±2)** • Physical and general examination will be performed and also checked for COVID-19 specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis. • Urine pregnancy test will be performed in case of potential child bearing women. **Visit 5: (Day 118±7)** • Physical and general examination will be	

		performed and also checked for COVID-19 specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis. **Visit 6: (Day208±7)** • Physical and general examination will be performed and also checked for COVID-19 specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis Pg. No. 2, 3 and 4 of 11	
Changes in Case Report Form (BBIL/BBV152A/2020)			
S. No.	**Case Report Form version**: **3.0; Date: 17-08-2020. This should be CRF.**	**Amendments proposed in the Case Report Form version 5.0; Date: 02-09-2020**	**Rationale for the proposed amendments**
		Dosage schedule is changed – Day 28 Pg. No. 34 to 37 of 47	The section is updated as per the changes in the protocol.
Assent Form (BBIL/BBV152A/2020)			
	Assent Form version: 2**.0; Date: 17-08-2020 ICD Repeated. This should be CRF.**	**Amendments proposed in the Assent form version 3.0; Date: 28-08-2020**	**Rationale for the proposed amendments**
	STUDY PARTICIPATION AND PROCEDURES A total of 375 (4:1) healthy volunteer subjects of 18 to 55 years of age will participate in the study. 125 subjects	STUDY PARTICIPATION AND PROCEDURES A total of 380 (1:1) healthy volunteer subjects of _12 to _65 years of age will participate in the study.	The section is updated as per the changes in the protocol.

	will be enrolled in Arm 1, 125 subjects will be enrolled in Arm 2 and 125 subjects will be enrolled in Arm 3. You will be screened for selection to take part in the study. If you are eligible and decide to participate in the study, you may be put in test arm or placebo arm in Phase 1 study. Two arms, test and placebo the subjects will receive either 3µg/6µg dose strength of BBV 152 (0.5mL) vaccine in the test arm and placebo in placebo arm. Vaccine formulations BBV152A, BBV152B, and BBV152C of test vaccine will be administered intramuscularly. Enrolment of all the Arms will be done in parallel. Pg. No. 2 of 9	190 subjects will be enrolled in Arm 1 and 190 subjects will be enrolled in Arm 2. You will be screened for selection to take part in the study. If you are eligible and decide to participate in Phase 2 study. Arm 1: A total of 190 subjects will be enrolled in this Arm 1 and will receive two intramuscular doses of BBV152-A vaccine. The two doses will be administered 28 days apart. Arm 2: A total of 190 subjects will be enrolled in this Arm 2 and will receive two intramuscular doses of BBV152-B vaccine. The two doses will be administered 28 days apart. Pg. No. 2 of 9	
	Visit 3: (Day 28±2) • Physical and general examination will be performed and also checked for COVID-19 specific symptoms. • 15 mL of blood will be collected for routine laboratory investigations including hematology, biochemistry, liver and kidney function tests , serology (HIV & Hep B), urine analysis and and diagnosis for SARS-CoV-2. • 5 mL blood will be collected for Immunogenicity analysis. • Urine pregnancy test will be performed in case of potential child bearing women. Pg. No. 3 of 9	**Study Procedure:** • Urine pregnancy test will be performed in case of potential child bearing women and eligible subjects will be enrolled. • Blood (10 mL) will be collected at time points (Day 0, Day 4, Day 14, Day 28, Day 42, Day 56, Day 118, Day 208) from the subset of subjects who are willing to provide for the isolation of PBMC's to assess the cell mediated immunity. Blood sample for PBMCs will be collected from NIMS, Hyderabad and AIIMS, New Delhi. **Visit 2: (Day 28±2)** • Physical and general examination will be All the adverse events should be recorded	The section is updated as per the changes in the protocol.

		by you in the subject diary card provided and brought to the clinic for the study doctor's review. You should contact the study doctor for immediate medical assistance throughout the study period. • Urine pregnancy test will be performed in case of potential child bearing women. • performed and also checked for COVID-19 specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis. • Administration of 0.5 mL of test vaccine. • Following vaccination, you will be observed for at least 2 hrs for any adverse events • Diary card will be reviewed to record adverse events. You will receive calls from the site staff for first seven days of post vaccination to check if you have any adverse events following the vaccination and his/her current health status • All the adverse events should be recorded by you in the subject diary card provided and brought to the clinic for the study doctor's review. You should contact the study doctor for immediate medical assistance throughout the study period. • Urine pregnancy test will be performed in case of potential child bearing women. **Visit 3: (Day 42±2)** • Physical and general examination will be performed and also checked for COVID-19	

		specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis. • Urine pregnancy test will be performed in case of potential child bearing women. **Visit 5: (Day 118±7)** • Physical and general examination will be performed and also checked for COVID-19 specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis. **Visit 6: (Day208±7)** • Physical and general examination will be performed and also checked for COVID-19 specific symptoms. • 5 mL blood will be collected for Immunogenicity analysis Pg. No. 3 and 4 of 9	