Restricted Use of COVAXIN™ Under Clinical Trial Mode

Implementation Plan No: BBIL/COVAXIN™/2021

Version No: 4.0; Date: 11-01-2021

WHILE COVAXIN WAS DEVELOPED THROUGH A COLLABORATION BETWEEN ICMR AND BBIL, THE PROTOCOL DEVELOPED FOR ITS RESTRICTED USE IN EMERGENCY SITUATION RECEIVED INPUTS FROM ICMR, MINISTRY OF HEALTH & FAMILY WELFARE AND BBIL

Title: Restricted use of COVAXIN ™ under clinical trial mode.

Protocol No: BBIL/COVAXIN™/2021

Version No: 3.0; Date: 10-01-2021

Confidentiality Clause: The confidential information in this document is provided to you for review by you and your staff, and any Institutional Review Board/ Independent Ethics Committee member, if applicable. By accepting this document, you agree that the information contained herein will not be disclosed to others, without written authorization from Bharat Biotech International Limited, Hyderabad, India.

Sponsored by:

Bharat Biotech International Limited (BBIL)

Genome Valley, Hyderabad, India.

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Declaration by Responsible Sponsor Representative(s)

Title: Restricted use of COVAXIN ™ under clinical trial mode.

This implementation plan version 4.0 was critically and scientifically reviewed and has been approved by Bharat Biotech International Ltd., the Sponsor of this Implementation Plan. The information it contains is consistent with the current risk/benefit evaluation of the biological investigational medicinal product as well as with the moral, ethical, and scientific principles governing clinical practices as set out in the Declaration of Helsinki, as amended in 64th WMA General Assembly, Fortaleza, Brazil, October 2013 and national and international guidelines on Good Clinical Practice and applicable regulatory requirements.

Signature and Date

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SIGNATURE PAGE

By signing the Implementation Plan, the undersigned confirm our agreement with the contents of the Implementation Plan and our commitment to comply with the procedures contained in the Implementation Plan, with the conditions and principles of GCP, and with all relevant regulatory requirements.

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BACKGROUND:

Bharat Biotech International Limited in collaboration with Indian Council of Medical Research (ICMR) has developed an inactivated whole virion COVID-19 vaccine, COVAXIN™. The COVAXIN™ has been evaluated for its safety, reactogenicity and immunogenicity in phase 1 and 2 clinical trials and the trial reports were submitted to the Central Drugs Standard Control Organization (CDSCO) India. COVAXIN™ has been approved under emergency use authorization with permission number MF/BIO/21/000002, dated 03.01.2021, F. No: BIO/MA/20/000103. This permission is given for restricted use in emergency situation in public interest as an abundant precaution, in clinical trial mode, where COVAXIN™ vaccine will be administered to the vaccine recipients and they will be followed up for safety.

Implementation of activities as delineated in this protocol under clinical trial mode (demarcated from clinical trial by being focused on administration of single pre-decided intervention to selective restricted population with consent and with rigorous monitoring) will be executed through the existing public health program. The shared responsibility pertaining to these activities will rest with Bharat Biotech in terms of supply of vaccines and oversight, with the ministry of health and family welfare for vaccination and with ICMR for providing technical inputs at different stages as well as ensuring ethical conduct throughout. The present dossier is being submitted by Bharat Biotech, on behalf of all the three aforementioned partners in execution.

INTRODUCTION:

The outbreak of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection or Coronavirus disease-2019 (COVID-19) has, as of December 23rd, 2020, spread to over 216 countries across the globe, with a total of ~79 Million confirmed cases and ~1.7 Million deaths. As of 06th Jan, 2021, the number of reported SARS-CoV-2 cases in India is ~10 Million confirmed cases and ~1,50,000 deaths(1). Coronaviruses pose a severe threat to humans and other animals. Earlier other members of the same family coronaviridae, SARS-CoV infected ~8000 people with a death rate of 10% and another member Middle East Respiratory Syndrome (MERS) virus broke out in the Middle East region and infected ~2000 people with 35% fatality rate(2). Porcine epidemic diarrhea coronavirus (PEDV) has swept throughout the United States of America, causing an almost 100% fatality rate in piglets and wiping out more than 10% of America's pig population in less than a year(2).

Coronaviruses are the enveloped positive-stranded RNA viruses that have the largest genome among all RNA viruses with approximately 27 to 32 kb^2. The viral genome is packed inside a helical capsid

formed by the nucleocapsid protein (N) which is surrounded by an envelope. SARS-CoV viral envelope is associated with at least three structural proteins: The membrane protein (M) and the envelope protein (E) are involved in virus assembly, whereas the spike protein (S) mediates virus entry into host cells. Among these structural proteins, the spike forms large protrusions from the virus surface, giving coronaviruses the appearance of having crowns(2). The SARS-CoV-2 virus transmits from person to person mainly through respiratory droplets(3).

The inhaled virus SARS-CoV-2 binds mostly to epithelial cells in the upper respiratory tract and starts replicating following cellular entry. Angiotensin-converting enzyme 2 (ACE2) is the main receptor for both SARS-CoV-2 and SARS-CoV(4,5). There is local propagation of the virus but a limited innate immune response. At this stage, the virus can be detected by nasal swabs. Although the viral burden may be low, these individuals are infectious. The RT-PCR value for the viral RNA might be useful to predict the viral load and the subsequent infectivity and clinical course. The virus propagates and migrates down the respiratory tract, and a more robust innate immune response is triggered. Nasal swabs or sputum should yield the virus (SARS-CoV-2) as well as early markers of the innate immune response(6). The symptoms of SARS-CoV-2 infection appear after an incubation period of ~5 days(7). The period from the onset of SARS-CoV-2 symptoms to death ranged from 6 to 41 days with a median of 14 days. This period is dependent on the age of the patient and the status of the patient's immune system. It was shorter among patients >70 years old compared with those under the age of 70(8). The most common symptoms at the onset of SARS-CoV-2 illness are fever, cough, and fatigue, while other symptoms include sputum production, headache, hemoptysis, diarrhea, dyspnoea, and lymphopenia and in some cases recent onset anosmia and/or ageusia (9,10).

COVAXIN™ DEVELOPMENT:

Bharat Biotech International Limited in partnership with the National Institute of Virology (NIV), a premier institute of ICMR has developed an indigenous whole virion inactivated SARS-CoV-2 virus vaccine (COVAXIN™). The non-clinical toxicity studies to assess the safety of the COVAXIN™ were performed in compliance with the norms of Good Laboratory Practice (GLP). Three animal models Mice, Rats, and Rabbits were used to evaluate the immunogenicity and safety of the COVAXIN™ vaccine and found to be safe and immunogenic in all the animal models. The trial publication is available as pre-print at bioRxiv (doi: https://doi.org/10.1101/2020.09.09.285445)(11). The COVAXIN™ vaccine efficacy has been evaluated in Rhesus macaque (DOI:10.21203/rs.3.rs-65715/v1)(12) and Syrian Hamsters (DOI:10.21203/rs.3.rs-76768/v1)(13) by challenging vaccinated macaques with wild type virus. These studies demonstrate that a two-dose vaccination regimen induced

a significant immune response and provided effective protection in animals challenged with SARS-CoV-2.

The COVAXIN^{TM} vaccine has been evaluated in Phase 1 clinical trial. A total of 375 participants were enrolled in Phase 1 trial and generated excellent safety data without any reactogenicity. COVAXIN^{TM} induced binding and neutralizing antibody responses and with the inclusion of the Algel-IMDG adjuvant, this is the first inactivated SARS-CoV-2 vaccine that has been reported to induce a Th1-biased response. Vaccine-induced neutralizing antibody titers were reported with two divergent SARS-CoV-2 strains (**doi:** https://doi.org/10.1101/2020.12.11.20210419)(14).

COVAXIN^{TM} vaccine has been evaluated in Phase 2 with 380 participants of age between 12 to 65 years. The data showed that all the participants were safe and immunogenic in terms of generating Anti-IgG titers (GMTs) to all epitopes (S1 protein, RBD, and N protein) which increased significantly after the administration of both the doses. COVAXIN^{TM} led to tolerable safety outcomes and enhanced humoral and cell-mediated immune responses. The trial publication is available as pre-print at bioRxiv (**doi:** https://doi.org/10.1101/2020.12.21.20248643)(15).

COVAXIN^{TM} (prepared under Good manufacturing practices, as required under the Drugs and Cosmetics Act, 1940 and the NCDT Rules) has been approved by CDSCO for Restricted Use in Emergency situation in Public Interest as an abundant precaution in Clinical Trial Mode, in India on 3rd January 2021.

RATIONALE:

COVAXIN^{TM} vaccine has been approved with permission number MF/BIO/21/000002, dated 03.01.2021, F. No: BIO/MA/20/000103. This permission is given for restricted use in emergency situation in public interest as an abundant precaution, in clinical trial mode, where COVAXIN^{TM} vaccine will be administered to the adult vaccine recipients and they will be followed up for safety.

OBJECTIVES:

- To evaluate the safety and reactogenicity of COVAXIN^{TM} while rolling out the vaccine in real-life settings under restricted use
- To evaluate the number of RT-PCR positive COVID-19 cases after receipt of COVAXIN^{TM} during stipulated post-vaccination contact days

ELIGIBILITY:

The potential vaccine recipients fulfilling the following criteria will be eligible for vaccination.

- Ability to provide consent.
- Vaccine recipients aged 18 years and above.
- Vaccine recipients with good general health or stable medical conditions as determined by the Vaccinator/Officer supervising vaccination. A stable medical condition is defined as a disease not requiring significant change in therapy or hospitalization or worsening disease during the past 3 months.

The individuals with the following conditions will NOT be eligible for vaccination.

- Have any history of allergies.
- Have fever.
- Have a bleeding disorder or are on a blood thinner.
- Are immunocompromised or are on a medicine that affects their immune system.
- Are pregnant.
- Are breastfeeding.
- Have received another COVID-19 vaccine.
- Any other serious health related issues as determined by the Vaccinator/Officer supervising vaccination.

IMPLEMENTATION PROCEDURE:

While the following sections describe the implementation procedures in brief – detailed activity steps are described later (in section H) in the present protocol (Annexure 4 further provides schematic presentations on the same). The pre-registration process related to COVAXIN administration will follow the operation guideline made available by the Ministry of Health and Family Welfare in the public domain (https://main.mohfw.gov.in/newshighlights-31). This guideline also highlights deployment of adequately trained professionals in the vaccination process. Vaccination officers and other officials will ensure observation of rules on biomedical waste management and compliance with the principle of environmental protection.

A. CONSENT FORM:

Vaccine recipients will be provided information in local language pertaining to the vaccine administration with the help of an Information Sheet (Annexure 1) containing details about COVAXIN™ vaccination. A written consent will be taken from the Vaccine recipient prior to vaccination. The Informed Consent Form is attached as Annexure 2. An Adverse Event Reporting Form (Annexure 3) will be used to record the AEs following each dose of vaccination and each from will be linked with the respective personal identifiers of each Vaccine recipient. Monitoring of 'Adverse Event Following Immunization' (AEFI) scheme followed under the immunization program of the Ministry of Health & Family Welfare, Government of India will be adhered to. The Adverse Events following Immunization (AEFI) Report and the safety monitoring report will be submitted to the National Advisory Committee on Immunization and Causality Assessment Team in the program mode and will be synchronized with the National COVID Implementation program.

B. VACCINATION PROCEDURE:

Visit 1 (Day 0): The Vaccine recipients will be administered with the first dose of the COVAXIN™ via the intramuscular route.

- Following vaccination, Vaccine recipients will remain at the vaccination site for at least 30 minutes of observation to record any adverse event.
- Day 1-7: The Vaccine recipients will be given an adverse event form to record the adverse events (Adverse Event Form is attached as Annexure 3).
- Day 8-27: The Vaccine recipients will inform the vaccination site, if they have encountered any health-related issues or adverse events.
- The Vaccine recipients will return the Adverse Event Form during the visit for the administration of the second dose of vaccine (Day 28).

Visit 2 (Day 28): The Vaccine recipients will be administered the second dose of the COVAXIN™ vaccine via the intramuscular route.

- Following vaccination, Vaccine recipients will remain at the vaccination site for at least 30 minutes of observation to record any adverse event.
- Day 28-35: The Vaccine recipients will be given an adverse event form to record the adverse events. (Adverse Event Form is attached as Annexure 3).

- The Vaccine recipients will inform the site, if they have encountered any health-related issues or adverse events.
- Vaccine recipients will return the filled-in Adverse Event reporting form after completion of 7 days post-vaccination.

All the Vaccine recipients will be followed-up for a period of 3 months after the 2nd dose of vaccination. In case of any adverse events or serious adverse events, the report will be submitted to the designated Immunization officers or Health care workers. Causality assessment of all SAEs, medical management and compensation will be determined by the existing practices under the government immunization program and Central Ethics Committee as appropriate. In case of any adverse events or serious adverse events, Vaccine recipients will be provided medically recognized standard of care in the government designated respective state hospitals. Final outcome of the AEFI monitoring and the compensation to be provided will be based on the recommendation of CDSCO/DCGI.

C. FOLLOW-UP FOR COVID-19:

All the Vaccine recipients need to report to the immunization officers/health care workers/site, if they experience any signs and symptoms of COVID-19 or diagnosed with COVID-19. Upon developing symptoms of COVID-19, Vaccine recipients will be provided medically recognized standard of care in the government designated respective state hospitals. COVID-19 positive outcomes must be documented in Adverse Event Form. Proof of positive RT-PCR should be provided to establish the diagnosis of COVID-19. Vaccine recipient's verbal recall will not confirm the diagnosis.

D. ROLE OF THE SPONSOR:

Sponsor will be responsible for overall implementation of this protocol. Vaccination booths in a district, as identified by the Ministry of Health & Family Welfare, Government of India, for COVAXIN will serve as the implementation sites and sequence of events will follow the steps as depicted below.

E. ANALYSIS:

The descriptive data of the Vaccine recipients will be summarized as counts and proportions. The number of all adverse events and serious adverse events, and the number of COVID-19 cases detected within 3 months post-second dose will be tabulated in number and percentages. Chi-square tests or Fischer tests will be used to assess categorical differences. Collated and analyzed data will be shared at regular intervals with appropriate monitoring bodies and ethics committee for decision making.

F. DATA SAFETY AND MONITORING BOARD (DSMB):

An external DSMB composed of independent vaccine and infectious disease experts and a biostatistician will be established by BBIL to periodically review the cumulative data The DSMB will be responsible for safeguarding the interests of the Vaccine recipients, assessing safety during the implementation plan and provide recommendations for further vaccinations. The reports generated by DSMB will be submitted to both CDSCO as well as CECHR.

G. ETHICS COMMITTEE APPROVAL:

The Implementation Plan as outlined in this document will be submitted to the ICMR – Central Ethics Committee on Human Research (CECHR) for obtaining necessary approval. In addition, the DSMB constituted for the aforementioned implementation will play a complementary role.

H. EXECUTION DESIGN:

At the vaccination sites

1. At each designated session site across the country, hard copies of the 3 documents, as follows, will be made available:

    a. Information sheet on COVAXIN
    b. Informed consent form for each vaccine recipient
    c. Information leaflet for vaccinator

2. The factsheet in regional language will be provided to the vaccine recipient before vaccination and vaccine recipient will be given time to read (in case of inability to read – it will be read out to him/her by vaccination staff) and understand it. Opportunity will be given to the vaccine recipient to ask clarifying questions to the vaccinator. Vaccinator will use the information leaflet to answer the queries raised by the vaccine recipient. Following questions and clarifications, the factsheet will be returned by the vaccine recipient to the vaccinator.

3. If the vaccine recipient agrees to be vaccinated with COVAXIN, he/she will sign an informed consent form (ICF) (in case of inability to write, he/she will put a left thumb impression on the ICF). Only after signing the informed consent, the vaccine recipient will be vaccinated with COVAXIN.

4. The informed consent is required at the time of first dose only. The separate consent is not required for subsequent dose.

5. The vaccine recipient, who refuses to sign the ICF, will not be vaccinated.

6. The signed consent form of each vaccine recipient will be retained by the vaccinator and will be submitted at the end of the day's session to the cold-chain point.

Following administration of the first dose

1. After the first dose of the vaccine is administered (Day 0), the vaccine recipient will be under observation at least for 30 minutes at the session site and then will be allowed to go home.

2. Following instructions will be given to the vaccine recipient before he/she leaves:
    a. The information about expected minor and serious/severe AEFIs will be provided.
    b. On Day 7, the vaccine recipient will be contacted over phone to enquire about any adverse event.
    c. In case of severe / serious adverse event at any given point of time after vaccination, he/she will report to the nearest health facility for treatment and will also inform the designated vaccinator.
    d. He/she will return to the session site on Day 28 or on the date given to him/her for the 2nd dose of COVAXIN.

At the planning unit

1. The designated staff will collate the consent forms obtained on the previous day for record keeping. These will then be kept in files with date of vaccination, session site specifications and planning unit mentioned on it. Daily report of number of consent forms for all session sites under the planning unit on a specific day will be prepared and will be sent to the designated district office by the next day.

At the district level (in sync with the stated objective of the present protocol)

1. A team will be set-up at the district level to telephonically contact and enquire about the adverse events based on grouping of vaccine recipients as follows:

a. Day 7 after dose 1 including symptoms related to Covid-19 and positive RT-PCR test (if any)
b. Day 28 after dose 1 including symptoms related to Covid-19 and positive RT-PCR test (if any)
c. Day 7 after dose 2 including symptoms related to Covid-19 and positive RT-PCR test (if any)
d. Day 28 after dose 2, including symptoms related to Covid-19 and positive RT-PCR test (if any)

2. The list of the vaccine recipients will be generated from Co-WIN on a daily basis with contact numbers.

3. Adverse events and serious adverse events following immunization (AEFI) informed during the aforementioned contacts will be recorded in Co-WIN application against the respective personal identified of a vaccine recipient. Noticeably, monitoring of AEFI under immunization program are done routinely for all vaccines.

4. Grouping of the vaccine recipients in minor, severe and serious adverse event (as the case may be) will be done by District Immunization Officer (DIO) on a daily basis. For all serious and severe cases, the Case Report Form (CRF) will be raised in Co-WIN – SAFE-VAC and the process for further investigation by District AEFI Committee as per AEFI operational guidelines will be initiated.

5. The case details of all serious and severe cases will be entered into Co-WIN – SAFE-VAC as per the operational guidelines.

6. All serious and severe AEFIs reported following COVAXIN will be causally assessed by the Immunization officer / State AEFI Committees. All efforts will be made to collect complete AEFI related data and submit the SAE reports to the CDSCO at the earliest and DCGI will be kept informed about all SAEs on a daily basis.

7. Drug regulators (Drugs Controller General of India, DCGI) will be provided with the collated data for review and assessment on vaccine safety, on a monthly basis.

8. Information about serious and severe cases will be shared with DCGI on a daily basis.

9. The end point and the final outcome of the aforementioned AEFI monitoring related to COVAXIN will be based on the recommendations made by the regulatory authority (DCGI).

10. Vaccination officer 4 (responsibilities described in Annexure 4) will help the vaccine recipients in receiving psychosocial support (as needed) through community influencers / community based organizations as well as immunization program personnel.

ANNEXURES:

1. COVAXIN™ Information Sheet is attached as **Annexure 1**.
2. Consent Form is attached as **Annexure 2.**
3. Adverse Event Reporting Form is attached as **Annexure 3.**
4. Schematic diagram - Implementation Plan and Responsibilities of Vaccination Officers **Annexure 4**

REFERENCES:

1. Coronavirus Death Rate (COVID-19) - Worldometer [Internet]. Available from: https://www.worldometers.info/coronavirus/coronavirus-death-rate/
2. Li F. Structure, Function, and Evolution of Coronavirus Spike Proteins. Annu Rev Virol. 2016 Sep 29;3(1):237–61.
3. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance. Pediatr Med Rodz. 2020 May 20;16(1):9–26.
4. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. J Virol [Internet]. 2020 Mar 17 [cited 2020 Oct 15];94(7). Available from: https://jvi.asm.org/content/94/7/e00127-20

5. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020 16;181(2):271-280.e8.

6. Mason RJ. Pathogenesis of COVID-19 from a cell biology perspective. Eur Respir J [Internet]. 2020 Apr 1 [cited 2020 Oct 15];55(4). Available from: https://erj.ersjournals.com/content/55/4/2000607

7. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med. 2020 Mar 26;382(13):1199–207.

8. Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. J Med Virol. 2020 Apr;92(4):441–7.

9. Carlos WG, Dela Cruz CS, Cao B, Pasnick S, Jamil S. Novel Wuhan (2019-nCoV) Coronavirus. Am J Respir Crit Care Med. 2020 15;201(4):P7–8.

10. Rothan HA, Byrareddy SN. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun. 2020;109:102433.

11. Ganneru B, Jogdand H, Dharam VK, Molugu NR, Prasad SD, Vellimudu S, et al. Evaluation of Safety and Immunogenicity of an Adjuvanted, TH-1 Skewed, Whole Virion InactivatedSARS-CoV-2 Vaccine - BBV152. bioRxiv. 2020 Sep 12;2020.09.09.285445.

12. Remarkable immunogenicity and protective efficacy of BBV152, an inactivated SARS-CoV-2 vaccine in rhesus macaques. 2020 Sep 10 [cited 2021 Jan 5]; Available from: https://www.researchsquare.com/article/rs-65715/v1

13. Immunogenicity and protective efficacy of BBV152: a whole virion inactivated SARS CoV-2 vaccine in the Syrian hamster model. 2020 Sep 16 [cited 2021 Jan 5]; Available from: https://www.researchsquare.com/article/rs-76768/v1

14. A Phase 1: Safety and Immunogenicity Trial of an Inactivated SARS-CoV-2 Vaccine-BBV152 | medRxiv [Internet]. [cited 2021 Jan 5]. Available from: https://www.medrxiv.org/content/10.1101/2020.12.11.20210419v1

15. Ella R, Reddy S, Jogdand H, Sarangi V, Ganneru B, Prasad S, et al. Safety and immunogenicity clinical trial of an inactivated SARS-CoV-2 vaccine, BBV152 (a phase 2, double-blind, randomised controlled trial) and the persistence of immune responses from a phase 1 follow-up report. medRxiv. 2020 Dec 22;2020.12.21.20248643.

ANNEXURE 1

INFORMATION SHEET FOR VACCINE RECIPIENTS AND CAREGIVERS

Restricted Use of COVAXIN™ under Clinical Trial Mode

THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) TO PREVENT CORONAVIRUS DISEASE 2019 (COVID-19)

PRIORITIZED GROUPS OF INDIVIDUALS WHO ARE 18 YEARS OF AGE AND OLDER AND WHO HAVE BEEN INFORMED BY THE MINISTRY OF HEALTH & FAMILY WELFARE TO ATTEND A BOOTH SPECIFIED FOR COVAXIN BASED VACCINATION

You are being offered the Bharat Biotech COVID-19 Vaccine **(COVAXIN™)** to prevent Coronavirus Disease 2019 (COVID-19) caused by SARS-CoV-2. This Information Sheet contains information to help you understand the risks and benefits of the Bharat Biotech COVID-19 Vaccine **(COVAXIN™)**, which you may receive because there is currently a pandemic of COVID-19.

Reporting of side effects

As with any new medicine, this vaccine will be closely monitored to allow quick identification of new safety information. You can help by reporting any side effects you may get after vaccination to Bharat Biotech who is the manufacturer of COVAXIN™ vaccine on 24x7 Toll-Free Number: +9118001022245 or atpvg@bharatbiotech.com.For more information, read this Information Sheet carefully.

The Bharat Biotech COVID-19 Vaccine **(COVAXIN™)** may prevent you from getting infected COVID-19.

Read this Information Sheet for information about the Bharat Biotech COVID-19 Vaccine (COVAXIN™). Talk to Vaccinator/ Officer supervising your vaccination if you have any questions. It is your choice to receive the Bharat Biotech COVID-19 Vaccine (COVAXIN™).

The Bharat Biotech COVID-19 Vaccine (COVAXIN™) is administered as a 2-dose series, 4 weeks apart, into the deltoid muscle of the upper arm.

WHAT IS COVID-19?

COVID-19 disease is caused by a Coronavirus called SARS-CoV-2. This type of Coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. It is predominantly a respiratory illness that can affect other organs. People with COVID-19 may experience wide range of symptoms of mild to severe category. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; loss of taste or smell of recent onset; sore throat; congestion or runny nose; nausea or vomiting; diarrhea.

WHAT IS THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™)?

The Bharat Biotech COVID-19 Vaccine **(COVAXIN™)** is a vaccine with approval for restricted use in emergency situation that may prevent COVID-19. The Central Licensing Authority has granted permission for the sale or distribution of Covaxin for restricted use in emergency situation in public

interest as an abundant precaution, in clinical trial mode. It has also completed the phase of trial where COVAXIN's ability to produce immunity against COVID-19 has been examined and established. However, the efficacy of COVAXIN is still being studied in clinical trials. As the clinical efficacy is currently being examined for COVAXIN through phase-III trial, it is important to appreciate that receiving the vaccine does not mean that other precautions related to Covid-19 need not be observed.

WHERE WILL MY VACCINATION INFORMATION BE RECORDED?

The Vaccinator/ Officer supervising your vaccination may include your vaccination information in your state/National Immunization Information System or another designated system. This will ensure that you receive the same vaccine when you return for the second dose. Please also note that privacy and confidentiality pertaining to any information provided by you and archived in the National Immunization Information System will be maintained.

WHAT IS AN EMERGENCY USE AUTHORIZATION (EUA)?

The Central Drugs Standard Control Organisation (CDSCO) has made the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)** available under an emergency access mechanism called an emergency use authorization (EUA). The EUA for the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)** is in effect for the duration of the COVID-19 EUA declaration justifying emergency use of the products unless terminated or revoked (after which the products may no longer be used).

WHAT IS RESTRICTED USE IN EMERGENCY SITUATION?

Restricted use in emergency situation means that the vaccine offered under this plan will be offered to the restricted prioritized groups only. As you fell under this category, you have been invited to this booth for administration of COVAXIN. This administration will take place under clinical trial mode, which is different from clinical trial as effect of COVAXIN will not be examined against any other intervention through this effort. You will however be monitored for any adverse event under this clinical trial mode and supported for medical care under the existing public health program.

WHAT SHOULD YOU MENTION TO YOUR VACCINATION PROVIDER BEFORE YOU GET THE COVAXIN™ COVID-19 VACCINE?

Tell the Vaccinator/ Officer supervising your vaccination about all of your medical conditions, including if you:

- Are you on regular medication for any illness? If yes, for how long and for which condition?

- Have any allergies
- Have fever
- Have a bleeding disorder or are on a blood thinner
- Are immunocompromised or are you on a medicine that affects your immune system
- Are pregnant
- Are breastfeeding
- Have received another COVID-19 vaccine

It is advisable not to take the vaccine in any of these conditions

WHO IS ELIGIBLE TO GET THE BHARAT BIOTECH COVID-19 VACCINE?

CDSCO has authorized the Restricted Use of COVAXIN™ under Clinical Trial Mode. Individuals who are 18 years of age and older and have been prioritized under the public health program of the Ministry of Health & Family Welfare, Government of India will be covered under this endeavor. Informing the individuals about the offer for vaccination with COVAXIN will rest with the respective Government Program Officials. Those offered COVAXIN at pre-specified booths will have the options to receive or reject administration of the vaccine. No alternative vaccine will be offered at the booth as this protocol provides for administration of single type of vaccine (COVAXIN) only at a pre-specified designated vaccination booth.

WHO SHOULD NOT GET BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™)?

You should not get the BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) if you:

- Have any history of allergies.
- Have fever.
- Have a bleeding disorder or are on a blood thinner.
- Are immune-compromised or are on a medicine that affects *your* immune system
- Are pregnant.
- Are breastfeeding.
- Have received another COVID-19 vaccine.
- Any other serious health related issues, as determined by the Vaccinator/Officer supervising vaccination.

WHAT ARE THE INGREDIENTS IN THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™)?

The BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) includes the following ingredients: COVAXIN™ contains 6µg of whole-virion inactivated SARS-CoV-2 antigen (Strain: NIV-2020-770), and the other inactive ingredients such as aluminum hydroxide gel (250 µg), TLR 7/8 agonist (imidazoquinolinone) 15 µg, 2-phenoxyethanol 2.5 mg, and phosphate buffer saline up to 0.5 ml.

The vaccine (COVAXIN™) thus has been developed by using inactivated/killed virus (which in non-activated state carries the potential to cause COVID-19) along with the aforementioned chemicals.

HOW IS THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) GIVEN?

The BHARAT BIOTECH COVID-19 VACCINE will be given to you as an injection into the deltoid muscle of the upper arm. The BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)** vaccination series is 2 doses given 4 weeks apart.

HAS BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) BEEN USED BEFORE?

The Central Licensing Authority has granted permission for the sale or distribution of Covaxin for restricted use in emergency situation in public interest as an abundant precaution, in clinical trial mode. In phase 1 and Phase 2 clinical trials, about 680 (300 in Phase 1, and 380 in Phase 2) were administered with 2-doses of COVAXIN™, and in phase 3 clinical trial, approximately 12,900 individuals of age ≥ 18 years and older have received at least 1 dose of the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)** Vaccine. About 75 participants in phase 1 and 12,900

participants in phase 3 received a placebo for comparing the vaccine effect in the study.

WHAT ARE THE BENEFITS OF BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™)?

In an ongoing clinical trial, the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)** has been shown to generate an immune response that may be suggestive of protection towards preventing COVID-19 following 2 doses given 4 weeks apart. The duration of protection against COVID-19 is currently being examined. The efficacy of COVAXIN is still being studied in phase III clinical trial.

WHAT ARE THE RISKS OF BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™)?

Side effects that have been reported with the BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) include:

- Injection site pain
- Injection site swelling
- Injection site redness
- Injection site itching
- Stiffness in the upper arm
- Weakness in injection arm
- Body ache
- Headache
- Fever
- Malaise
- Weakness
- Rashes
- Nausea
- Vomiting

There is a remote chance that the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)** could cause a severe allergic reaction. A severe allergic reaction may very rarely occur after getting a dose of the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)**. For this reason, your vaccination provider will ask you to stay for 30 minutes after each dose of vaccination at the place where you received your vaccine for monitoring after vaccination. Signs of a severe allergic reaction can include:

- Difficulty in breathing
- Swelling of your face and throat
- A fast heart beat
- Rash all over your body
- Dizziness and weakness

These may not be all the possible side effects of the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)**. Serious and unexpected side effects may occur. BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™)** is still being studied in clinical trials.

WHAT SHOULD I DO ABOUT SIDE EFFECTS?

If you experience any side effect(s), please contact/visit your health provider/Vaccinator/ Officer supervising your vaccination or immediately go to the nearest hospital.

WHAT IF I DECIDE NOT TO GET THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™)?

It is your choice to receive or not to receive the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™**).Should you decide not to receive it, it will not change your standard of medical care.

ARE OTHER CHOICES AVAILABLE FOR PREVENTING COVID-19 BESIDES BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™)? If you choose not to receive the Bharat Biotech Covid-19 Vaccine COVAXIN, you will not receive another vaccine instead at this time. There will be no consequences at the workplace for refusing to take the vaccine

Another vaccine (COVISHIELD) developed by the Serum Institute of India has also been approved under emergency use authorization to prevent COVID-19 in India, which is currently being provided in other booths or districts. However, invitation received by you to attend this booth for vaccination against COVID-19 pertains to COVAXIN only. We can therefore offer you administering COVAXIN only, which you could opt to receive or reject. It is your choice to receive or not to receive the BHARAT BIOTECH COVID-19 VACCINE (COVAXINTM). Should you decide not to receive it, it will not change your standard of medical care.

CAN I RECEIVE THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) WITH OTHER VACCINES?

There is no scientific information yet available on the appropriateness of use of the BHARAT BIOTECH COVID-19 VACCINE **(COVAXIN™**) with other vaccines. Hence, the Vaccine recipients who receive the first dose of COVAXIN™ should not take another COVID-19 vaccine developed by a different vaccine platform such as COVISHIELD.

WHAT IF I AM PREGNANT OR BREASTFEEDING?

If you are pregnant or breastfeeding, you should not get the vaccine as the effect of the vaccine has not been studied in pregnant women and nursing mothers.

WILL THE BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) GIVE ME COVID-19?

No. BHARAT BIOTECH COVID-19 VACCINE (COVAXIN™) is an inactivated (killed) vaccine, and hence, there is no chance of getting COVID-19 because of COVAXIN™ vaccination.

HOW LONG WILL I HAVE TO PARTICPATE IN THIS PROGRAM?

All the Vaccine recipients will be followed-up for a period of 3 months after the 2nd dose of vaccination. In case of any adverse events or serious adverse events (same as with the side effects described above), reports of SAEs (prepared by the district level vaccination officers) will be submitted to the Central Ethics Committee on Human Research, which will determine whether the SAE is related to the administration of Covaxin. If it is determined that the SAE is related to the administration of Covaxin, compensation will be provided in accordance with the procedure in Rule 42 of the NCDT Rules. In case of any adverse events or serious adverse events, Vaccine-recipients will be provided medically recognized standard of care in the government designated respective state hospitals.

All the recipients need to report to the health care provider/site/sponsor, if they are having signs and symptoms of COVID-19 or diagnosed with COVID-19. If any Vaccine recipient develops symptoms of COVID-19, Vaccine recipient will be provided medically recognized standard of care in the government designated respective state hospitals. COVID-19 Positive outcomes must be documented

in Adverse Event Form. Proof of positive RT-PCR (tests conducted under the existing government program and from approved laboratories) should be provided to establish the diagnosis of COVID-19. Vaccine recipient's verbal recall will not confirm the diagnosis.

ANNEXURE 2

COVID-19 VACCINATION (COVAXIN™)
SCREENING & CONSENT FORM

The Covid-19 Vaccine, COVAXIN, is being offered to you as part of a vaccination drive by the Ministry of Health and Family Welfare under restricted use in emergency situation. COVAXIN is being offered at this booth in this district. The other vaccine that is being made available at other booths is Covishield

The Central Licensing Authority has granted permission for administration of Covaxin for restricted use in emergency situation in public interest as an abundant precaution, in clinical trial mode. This does not mean that you are being offered the vaccine as part of a clinical trial. However, you are entitled to medical management and compensation for serious adverse events related to the administration of this vaccine in the manner set out in this form and the Fact Sheet

HOW CAN YOU LEARN MORE IF YOU WISH BEFORE PROVIDING CONSENT?

- Ask the Vaccinator/ Officer supervising your vaccination.
- Visit at https://www.mygov.in/covid-19/

I FUTHER EMPHASIZE THAT ANY INFORMATION THAT YOU PROVIDE PRIOR TO TAKING THE VACCINE WILL BE ARCHIVED IN THE DATABASE MAINTAINED BY THE IMMUNIZATION PROGRAM OF THE GOVERNMENT & PRIVACY AS WELL AS CONFIDENTIALITY OF THE INFORMATION PROVIDED BY YOU WILL BE MAINTAINED

Recipient Name:		
DOB: Age:	Gender: Male……..Female……..Third Gender…..	Marital Status:
Address of the recipient: Mobile/Phone Number:		
Name: Mobile/Phone Number:		
Name and Address of Clinic/Office Site Where Vaccine is Administered:		
Name and contact mobile number of the Vaccinator/ Officer supervising your vaccination:		

SCREENING COMPONENT

S. No.	**Questionnaire**			
1.	Are you feeling sick today?	□ Yes	□ No	
2.	In the last 14 days, have you had a COVID-19 test or been told by a health care provider or health department to isolate or quarantine at home due to COVID-19 infection or exposure?	□ Yes	□ No	□ Unknown
3.	Have you been treated with antibody therapy for COVID-19 in the past 90 days (3 months)? If yes, when did you receive the last dose as furnished on document? …….....(please tell me)	□ Yes	□ No	□ Unknown
4.	Have you ever had a serious allergic reaction?	□ Yes	□ No	□ Unknown
5.	Have you had any vaccines in the past 28 days (4 weeks)? If yes, how long ago was your most recent vaccine? …….....(please tell me)	□ Yes	□ No	□ Unknown
6.	Are you pregnant or considering becoming pregnant?	□ Yes	□ No	□ Unknown
7.	Are you a nursing mother?	□ Yes	□ No	□ Unknown
8.	Are you on any medication for a long standing disease? a) If yes please tell me the name of the disease …….	□ Yes	□ No	□ Unknown
9.	Are you taking radiotherapy?	□ Yes	□ No	□ Unknown

INFORMED CONSENT

I have been provided and have read, or had explained to me, the Information sheet about the COVID-19 vaccination. I have read the information sheet. I understand that this vaccine requires two doses for it to be effective and two doses need to be administered (given). I have been allowed to ask questions which were answered to my satisfaction. I understand the benefits and risks of the vaccination as described. I request that the COVID-19 vaccination be given to me.

Name	Vaccine recipient (Signature)	Date/Time

Area Below to be Completed by Vaccinator					
Vaccine Name	Vaccine Dose	Date of administration	Time of Administration	Route of Administration	Manufacturer & Lot Number
COVAXIN™	□ First Dose				
	□ Second Dose				

Administration Site:	□ Left Deltoid	□ Right Deltoid
Dosage:	□ 0.5ml	

- I have reviewed the details of side effects with the vaccine recipient.

- I confirm that the vaccine recipient was allowed to ask questions about the vaccination, and all the questions asked by the vaccine recipient have been answered correctly, and to the best of my ability.

Name of the Vaccinator: _____

Vaccinator Signature: _____

Location Name (Vaccination Site): _____

Please contact your vaccination supervising officer at this number ……and your vaccinator (contact number ……..) in case of any need related to vaccination or difficulty faced even after going back home following vaccination.

ANNEXURE 3

ADVERSE EVENT REPORTING FORM	Date Received: _____

I. INFORMATION OF THE INDIVIDUAL

1. Initials of the Individual	2. DOB (DD/MM/YYYY) /Age:	3. Gender	4. Weight
			_____ Kgs

II. DETAILS OF ADMINISTERED VACCINE (DOSE 1)

Vaccine	Current Dose	Route/site	Manufacturer	Batch number	Place of vaccination	Date of Vaccination: (DD/MM/YYYY)	Time : (AM/PM)
	Dose 1						

2. ANY OTHER VACCINATION RECEIVED IN THE LAST 4 WEEKS OF DOSE 1 & DOSE 2 (If yes; please mention below)

Vaccine	Current Dose	Route/site	Manufacturer	Batch number	Place of vaccination	Date of Vaccination: (DD/MM/YYYY)	Time: (AM/PM)

Follow-up for Adverse Event(s):

Was there any immediate adverse event(s) within 30 minutes after Dose 1: □Yes □No

If yes; Please mention:_____

Was there any adverse event within 7 Days after administration of Dose 1? If yes; Please mention below:

S.No	Symptom	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1	Pain							
2	Fever							
3	Redness							
4	Itching							
5	Weakness in Right Arm							
6	Stiffness in the upper arm							
7	Bodyache							
8	Malaise							
9	Weakness							
10	Rashes							
11	Headache							
12	Any other symptom (Specify)							
13	Any other symptom (Specify)							
14	Any other symptom (Specify)							

Did you use any medication for any of the above symptoms? □Yes □No
If yes, please indicate the name of the symptom and medication:_____
The outcome of the event: □ Recovered □ Recovering □ Recovered with sequelae
Date of recovery(DD/MM/YYYY): _____/_____/_____

DETAILS OF ADMINISTERED VACCINE (DOSE 2)

Vaccine	Current Dose	Route/site	Manufacturer	Batch number	Place of vaccination	Date of Vaccination: (DD/MM/YYYY)	Time : (AM/PM)
	Dose 2						

ANY OTHER VACCINATION RECEIVED IN THE LAST 4 WEEKS OF DOSE 1 & DOSE 2 (If yes; please mention below)

Vaccine	Current Dose	Route/site	Manufacturer	Batch number	Place of vaccination	Date of Vaccination: (DD/MM/YYYY)	Time:

Follow-up for Adverse Event(s):

Was there any immediate adverse event(s) within 30 minutes after Dose 2: □Yes □No

If Yes; Please mention:_____

Was there any adverse event within 7 Days after administration of Dose 2? If yes; Please mention below:

S.No	Symptom	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
1	Pain							
2	Fever							
3	Redness							
4	Itching							
5	Weakness in Right Arm							
6	Stiffness in the upper arm							
7	Bodyache							
8	Malaise							
9	Weakness							
10	Rashes							
11	Headache							
12	Any other symptom (Specify)							
13	Any other symptom (Specify)							
14	Any other symptom (Specify)							

Did you use any medication for any of the above symptoms? □Yes □No
If yes, please indicate the name of the symptom and medication:_____
The outcome of the event: □ Recovered □ Recovering □ Recovered with sequelae
Date of recovery(DD/MM/YYYY): _____/_____/_____

Was the event serious? □Yes □No (If yes; Please mention the seriousness criteria below):
Seriousness criteria (Please Tick):
□ Death (DD/MM/YYYY): □ Hospitalization/Prolonged □ Disability □ Life-threatening
□ Permanent impairment/Damage □ Others (specify :)

3. Description of Serious adverse event (symptoms, sign, time course) and treatment, if any:

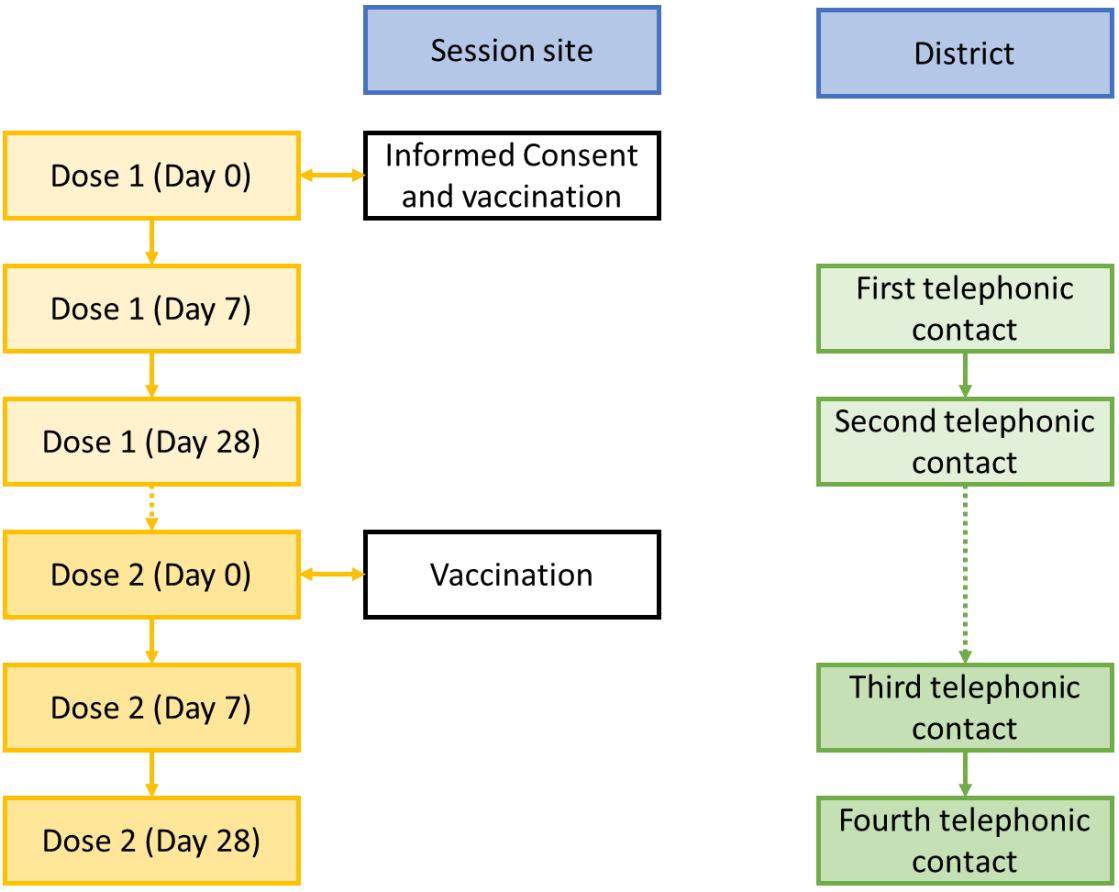
IV.OTHER DETAILS	
1.Relevant diagnostic tests/laboratory data	2. Pre-existing physician-diagnosed allergies, birth defects, medical conditions (please specify)
3.Illness at the time of vaccination and treatment if any:	
Illness:_____ Medications:_____	
4. COVID-19 Diagnosis, if any (This box should be filled only if any vaccine recipient complains of COVID-19 after vaccination)	
Laboratory Test used for Diagnosis of COVID-19: □ RT-PCR Test □ Any other method (Please specify here): Date of onset of COVID-19 symptoms (DD/MM/YYYY): Date of Sample Collection (DD/MM/YYYY): Reporting Date: (DD/MM/YYYY): Type of Treatment: □ In-patient Hospital Based Treatment □ OPD (Home Quarantine) based treatment Name of the Hospital (if hospitalized): Outcome: □Recovered □ Recovering □ Recovered with sequelae □ Fatal Date of Hospital Discharge (DD/MM/YYYY): Date of Hospital Discharge (DD/MM/YYYY): (A copy of Lab. test report must be attached with this Adverse Event Form; Please attach a copy of Hospital Discharge Sheet, if the vaccine recipient is hospitalized) (Please note that vaccine recipient's verbal recall will not be considered for COVID-19 diagnosis).	
V.REPORTER	
Name and professional Address:	
Pin code: Email:	
Tel.No (with STD code):	
Occupation: Signature/Date:	

Signature of the Vaccine recipient: _____

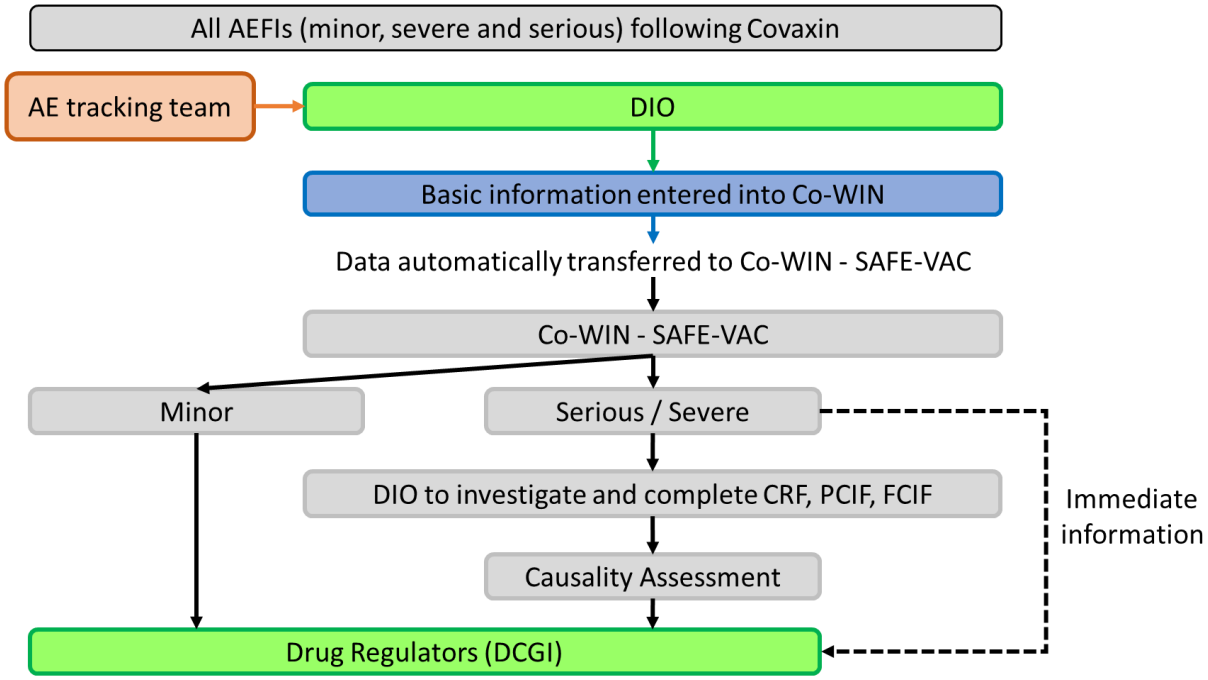
Adverse Event form returned on: _____ (DD/MM/YYYY)

ANNEXURE 4

AEFI protocol for Covaxin

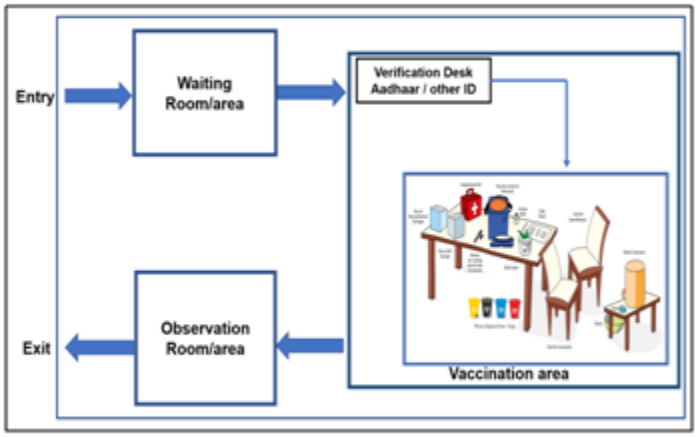


DATA FLOW


All AEFIs (minor, severe and serious) following Covaxin
AE tracking team
DIO
Basic information entered into Co-WIN
Data automatically transferred to Co-WIN - SAFE-VAC
Co-WIN - SAFE-VAC
Minor
Serious / Severe
DIO to investigate and complete CRF, PCIF, FCIF
Causality Assessment
Drug Regulators (DCGI)
Immediate information

Layout for Vaccination Site

- **3 separate rooms or areas**
  - Waiting room
  - Vaccination Room
  - Observation Room
- **Separate entry and exit** if possible
- **Adequate physical distance** between chairs/ seats in waiting rooms
- **Avoid criss-cross movement** of beneficiaries at session site
- Friendly to people with special needs
- Arrangement of drinking water for beneficiaries at session site



All SOPs related to Infection Prevention & Control are to be followed

Role of Vaccination Officer - 1

- May belong to police/home guard/NCC/others
- Stationed at the entry gate
- Will identify the beneficiary based on available list and message received by beneficiary
- Ask beneficiary to wash or sanitize hands before entry
- Ensure that beneficiaries follow COVID appropriate behaviour
  - ✓ Wear mask/ face cover
  - ✓ Maintain physical distance from each other
- Be mindful of cultural sensitivities like purdah/hijab
  - ✓ Take need based support from female teammates

Role of Vaccination Officer - 2

- Cross check the name of the beneficiary in the CoWIN application
- Will verify the identity of the beneficiary through
  - ✓ Aadhaar Card
  - ✓ Other Govt photo ID
  - ✓ Service ID/ Proof of employment of healthcare worker
  - ✓ Other ID cards listed in Operational Guidelines/FAQs
- Allow only one beneficiary at a time for vaccination

Role of Vaccination Officer - 3

- Will be available in observation room at all times
- Ensure that the beneficiaries maintain physical distance
- Ensure that each beneficiary is under observation for 30 minutes
- Inform vaccinator in case any beneficiary has adverse event
- Support vaccinator to manage the AEFI and inform the Medical Officer

Role of Vaccination Officer - 4

- Ensure COVID Vaccine IEC are displayed at the site
- Ensure beneficiaries are called for the session as per the given time
- Ensure one influencer to be present at the venue to support the activity
- Inform the beneficiaries that they will be contacted with information on the subsequent dose/ vaccination day and time
- Provide the contact details of ANM/ASHA/ Medical Officer to beneficiary for any support post vaccination, if required