In the last few days, we have received several queries from the media about the ongoing Phase III Covaxin trial. As we have announced two days ago, we have achieved the recruitment target of 25,800 on January 7, 2021 and express our deep appreciation to all our partners for their dedication and commitment to this ongoing study. Most of all, we express our appreciation to all the volunteers in our study whose participation in the study will help us move forward with the development of an effective vaccine against COVID-19. The Covaxin Phase III study is being conducted across 26 sites in India in compliance with the study protocol, GCP guidelines and all the regulatory provisions that apply to the conduct of clinical trials in India, including the New Drugs and Clinical Trials Rules, 2019. At the heart of all of this is a focus on ethics, patient safety and quality. Given the queries we have received, we would like to clarify a few basic facts.

Payment made to participants in the study

Under the Indian Good Clinical Practice (GCP) guidelines, which seek to protect the rights of human subjects and authenticity of biomedical data generated in all biomedical research in India at all stages of drug development, clause 2.4.5 deals with **Compensation for Participation**. The clause states, "*Subjects may be paid for the inconvenience and time present, and should be reimbursed for expenses incurred, in connection with their participation in research. They may also receive free medical services. However, payments should not be so large or the medical services so extensive as to induce prospective subjects to consent to participate in research against their better judgement (inducement). All payments, reimbursement and medical services to be provided to research subjects should be approved by the IEC*." The decision taken for the Covaxin Phase III study was to reimburse all participants at the rate of Rs 750/- for each study visit. The reimbursement amount was approved by every Institutional Ethics Committee (IEC) at the study sites. The reimbursement of Rs 750/- to study participants is therefore guided by the Indian GCP and approved by Institutional Ethics Committees. It is NOT an inducement.

Informed Consent

The process of Informed Consent for participants in Clinical Trials is covered under Section 2 of the New Drugs and Clinical Trials Rules, 2018. It is a process whereby a potential clinical trial participant is informed by the study team conducting the clinical trial of all the details of the study prior to participation. The Rules clearly lay down the process to be followed for consenting a participant in a clinical trial, including participants who are not able to read/write. The Informed Consent Form must be signed by the trial participant and investigator prior to the subject's participation in a study. The process to be followed by participants who are illiterate is mentioned in the Rules. We can confirm that the Informed Consent Form, as defined in the study protocol and approved by Institutional Ethics Committee, and the Informed Consent process as defined in the New Drugs and Clinical Trials Rules, 2019, were followed for all participants of the Covaxin Phase III study. These are documented and all copies are with the site.

Clinical Trial Participants

Participation in a clinical trial is purely voluntary. Every clinical trial has well defined inclusion and exclusion criteria to determine who is eligible to participate in a clinical trial. Only eligible participants are enrolled in a study after a careful assessment of their various health parameters. These participants may

come from various strata of society and are a representation of different socio-economic demographics to ensure that there is a diversified representation as required.

Adverse Events and Serious Adverse Events

An Adverse Event (AE) is defined in the New Drugs and Clinical Trials Rules, 2019, as "any untoward medical occurrence (including a symptom or disease or an abnormal laboratory finding) during treatment with an investigational drug or a pharmaceutical product in a patient or a trial subject that does not necessarily have a relationship with the treatment being given." A Serious Adverse Event (SAE) is defined in the same Rules as "an untoward medical occurrence during clinical trial resulting in death or permanent disability, or hospitalization of the trial subject where the trial subject is an outdoor patient or a healthy person, prolongation of hospitalization where the trial subject is an indoor-patient, persistent or significant disability or incapacity, congenital anomaly, birth defect or life threatening event."

Indian GCP guidelines mandate that all AEs and SAEs must be reported to the Ethics Committee and Central Licensing Authority, whether study related or not. This could include all and any AEs or SAEs, including an unrelated serious illness a patient may develop, an accident on the road, an age-related disorder or even death as a natural progression of a disease. They have to be reported, whether likely related to the study medication or not. Therefore, an AE or SAE in a clinical trial cannot be assumed to be due to the clinical trial study medicine and could be due to various other unrelated factors. Not all AEs and SAEs in a clinical trial are due to a clinical trial.

The Rules lay down the process to be followed in reporting SAEs (both related and not related) to the Ethics Committees and Central Licensing Authority and the process followed to determine causality.

All SAEs (related and not related) in the Covaxin Phase III trial have been reported to the regulator and Ethics Committees in accordance with the New Drugs and Clinical Trials Rules, 2019.

Deaths are routinely recorded and reported in human clinical trials, especially in large clinical trials with diverse population demographics, and with older age groups. The current rate of death in India is ~ 7.3 deaths / 1000, we would expect to see a rate far lower in our phase III trials. The most important criteria are detailed investigations and causality assessments between the adverse event and the test item.

Monitoring of Participants

All participants in a clinical trial are monitored on an ongoing basis as per the study protocol. Various studies the world over have proven that the quality of care and attention that participants in a clinical trial receive are far higher than in regular clinical practice. The protocol outlines the kind of tests and check-ups that are required on an ongoing basis, often much after the study is completed. In the Covaxin Phase III trial, we can confirm that all participants are being followed up on and monitored on an ongoing basis as per the study protocol to ensure the safety of all participants.

Finally, we would like to state that the development of Covaxin is a matter of great pride to us, not just at Bharat Biotech but also for India, and indeed the rest of the world. Our constant focus during the development of the vaccine and the clinical trials has been on ensuring patient safety and ensuring that the study is done to the requirements of all the relevant and applicable rules and guidelines, and that the data generated is of the highest quality and valid. We would not do anything that would compromise either the scientific rigor of what we do or the lives of patients. We ask the media's support to ensure that what is communicated to the public at large are the facts and that no information seeks to compromise the integrity and dignity of clinical trial participants to whom we owe a lot.

Clinical Trial Data Reporting

The routine process for reporting clinical trial data is carried out in the following order,

- Data is gathered and analysed, with the approved statistical plan,
- Data is submitted to CDSCO and Subject Expert Committees,
- Data is submitted to peer reviewed journals for acceptance and publication,
- Generally acceptance and publication of data by peer reviewed journals is required prior to public disclosure of data,

Clinical Trial Adverse Events Reporting

The routine process for reporting adverse events is carried out in the following order,

- AE's are reported to the Trial sites and Principle investigators (PI),
- They are immediately reported to the DSMB, CDSCO and the sponsor, by the PI,
- The PI, DSMB and sites, thoroughly investigate the AE to determine causality, and a detailed report is submitted to ethics committees and CDSCO,
- due to patient confidentiality and human ethics related disclosure issues, information regarding AE's are not disclosed in the public domain,
- Generally acceptance and publication of data by peer reviewed journals is required prior to public disclosure of data

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