A Novel Vaccine for Chikungunya Virus Infection

Bharat Biotech International Limited

Environmental and Health Risk Management Plan

1. Environmental Impact and risk mitigation

Risks	Project Specific Risk	Potential Impact	Mitigation Steps
Air Pollution	Minimal Risk	Running of generators during power failure	Monthly monitoring by Ministry of Environment and Forests, Govt. of India, authorized testing laboratory and complying with parameters prescribed in Air act, 1981. Annual reports are prepared as per IFC guidelines and submitted to IFC-WBG every year.
Water Pollution and Waste water treatment	Minimal Risk	Bharat Biotech international limited has its own waste water treatment plant and there is no release of waste water in to municipal drainage.	**Water pollution** - Monthly monitoring by Ministry of Environment and Forests, Govt. of India, authorized testing laboratory, and complying with the parameters prescribed in water act, 1974 and IFC –WBG requirements. **Waste water treatment –** Bharat Biotech international limited has its own waste water treatment plant for treating the process and utilities releases (BBIL SOP No. EHD/002) and complies with the requirements of the Central/Sate Pollution Control Board. Annual report is prepared as per IFC guidelines and submitted to IFC-WBG.
Chemical waste	Minimal Risk	Chemical waste is disposed as per the guidelines of the Ministry of Environment and Forests	Bharat biotech international limited is handling chemical waste via segregation, treatment and safe disposal as per the guidelines of the Ministry of Environment and Forests, Govt. of India and complies with the hazardous waste management rules, 2016.

Biological Waste	Minimal Risk	Biological waste handling is via segregation, treatment and disposal as per BBIL SOP No. EHD/015.	Biological waste handling is via segregation, treatment and disposal as per BBIL SOP No. EHD/015. The Company has permission from State Pollution control Board and complies with the Rules, 2016 of the Ministry of Environment and Forests, Govt. of India. Annual report is submitted to IFC-WBG.
Heavy metals	Minimal Risk	Project implementation will not cause any adverse heavy metal waste	Project implementation will not cause any adverse heavy metal waste.
Radiation Waste	Minimal Risk	Project implementation will not cause any adverse radiation waste	Project implementation will not cause any adverse radiation waste.
Destruction/alteration of surrounding ecosystem	Minimal Risk	BBIL SOP No.EHD/020 for destruction and disposal procedure is followed.	BBIL SOP No.EHD/020 for destruction and disposal procedure is followed. Solid – By autoclaving, incineration Liquid – Treatment with sodium hypo chlorite solution prior to disposal as per national and international guidelines on biological waste management.

2. Occupational Health and Safety and Risk Mitigation

Risks	Project Specific Risk	Potential Impact	Mitigation Steps
Heat Hazards	Minimal Risk	Injuries	Heat hazards will be controlled by proper personal protective equipment's and adequate training.
Chemical hazards, including fire and explosions	Minimal Risk	Project implementation will not cause any adverse Chemical hazards including fire and explosions	Project implementation will not cause any adverse Chemical hazards including fire and explosions.

Pathogenic and biological hazards	Moderate	There will be exposure to pathogens.	Handling under controlling environment like use of biological safety cabinets, use of suitable personal protective equipment's and adequate employee training.
Radiological hazards	Minimal Risk	Project implementation will not cause any adverse radiological hazards	Project implementation will not cause any adverse radiological hazards
Noise	Minimal Risk	Hearing loss	Wearing of personal protective equipment at high noise areas.
Process safety	Minimal Risk	Equipment maintenance shall be undertaken as per SOP.	Process safety rules will be adhered to and adequate training shall be provided.

3. Community Health and Safety and Risk Mitigation

Risks	Project Specific Risk	Potential Impact	Mitigation Steps
Safety Transportation Management System (for transport of hazardous material)	Minimal Risk	Spills of lab chemical can cause contamination of air, soil and ground water.	No hazardous material is used in the manufacture of the vaccine. The handling of the virus within the manufacturing facility will be according to the biosafety guidelines. Inactivated vaccine is potentially harmless to personnel and material. Transportation vehicle shall be tracked through GPS, if required.
Emergency preparedness and participation of local authorities and potentially affected communities	Minimal Risk	Localized	**Emergency preparedness -** BBIL is having on site emergency management and biosafety plan and annually, report is submitted to IFC-WBG.

In case your organization already has **EHS guideline**, please summarise the same. If not, please describe the impact because of hazardous material, release of chemicals, biological, management of catastrophic events like fire/explosion

Biological waste

Bharat Biotech is handling biological waste via segregation, treatment and disposal as per BBIL SOP No. EHD/015. Bharat Biotech is Telangana State Pollution control Board certified organization for handling biological waste and disposal to authorized agency. The Company adheres to rules on biomedical waste management stipulated by the Ministry of Environment and Forests. Bharat Biotech manufactures biological like vaccines and bio-therapeutics that does not involve the use of hazardous chemicals.

Management of catastrophic events like fire/explosion:

Bharat Biotech has adequate measures to control accidental fires in its premises. As part of the safety measures implemented in the Company, an emergency response team (ERT) has been constituted in March 2018 involving nominees from all the departments. The members are trained in all safety aspects such fire safety including live demonstration of different classes of fire, first aid and rescue operations as an emergency response. All ERT members will act as safety representatives in case of any emergency and have been adequately trained for the purpose. The employees are trained as per the BBIL SOP EHD/016.

Fire Extinguishers are placed in all the facilities in the campus and shall be monitored once in 3 months. The employees are trained as per BBIL SOP NO EHD/016 on safety operations.

Clinical Trial Risk Management Plan

Clinical and Regulatory			
S.No	**Area of Risk**	**Monitoring Parameters**	**Mitigation Measures**
1	Production of CT material	As CHIKV vaccine is manufactured under GMP, manufacturing and quality operations are monitored as per GMP guidelines.	As GMP procedures and guidelines, Quality Management System (QMS).

2	Protocol design and scientific validity ensuring favourable risk-benefit ratio	The study protocol is designed by experienced medical writer(s), immunologists, clinical development specialist(s) and infectious disease experts. A Subject Advisory Committee has been constituted for this project.	The timeline for review of CT application (Form 44) is 180 days. During the 180 days of review, SEC meeting is expected, during which the study protocol is reviewed and experts provide their opinion. Any suggestions or requirements shall be added or modified in the study protocol Quick turnaround of response to CDSCO suggestions.
3	Regulatory approvals	The clinical trial(s) shall be conducted after appropriate Regulatory (CDSCO) approvals.	Monitoring as per GCP requirements
4	Ethics approvals	All sites shall submit the required study related documents to their respective Institutional Ethics Committee (IEC) for approval. There will be no site initiation without CDSCO and IEC approvals.	BBIL/ CRO shall submit all requirements as per IEC/CDSCO norms.
5	Ensuring appropriate informed consent process and respect for human subjects	Informed consent process is mandated for subject recruitment. Regular clinical monitoring will ensure stringent implementation.	BBIL/ CRO study monitor(s) shall regularly verify source data with CRFs, ICFs, Lab Reports, etc. Site auditswill be conducted regularly.

6	Capacity of the sponsor	Bharat Biotech has a full-fledged Medical Affairs department for clinical management and has the experience of conducting over 50 vaccine trials in the country. The trials are proposed to be outsourced to a reputed CRO who will conduct it as per the GCP guidelines Bharat Biotech as sponsor has financially supported the project from inception until completion of phase 1 clinical trials.	Site audits will be conducted regularly. Bharat Biotech has the experience of conducting phase Ito phase IV clinical trials for various vaccines. The prior experience will help in monitoring and smooth conduct of CHIKV trials.
7	Staff at the trial site and Investigator responsibilities	All study staff shall be appropriately trained inGCP guidelines, and tasks shall be delegated according to their experience.	The chosen site investigator shall be educated, trained and experienced in infectious diseases. The site team shall be trained on the study protocol The Study Monitor(s)s shall be trained on the study protocol Study Monitor shall verify at each visit the Task Delegation Log for any changes. GCP guidelines shall be adhered to throughout the study.
8	Recruitment of study subjects and fair subject selection	Clinical study will be conducted strictly as per GCP guidelines. Regular clinical monitoringwill be in place.	BBIL/ CRO Study Monitor(s) shall regularly verify source data with CRFs, ICFs, Lab Reports, etc. This process will check each subject's eligibility to be enrolled in the study.

9	Safety Management (AE and SAE)	The study protocol shall describe safety management including adverse and serious adverse events, and the method of reporting to Sponsor and the Investigator. All adverse and serious adverse events will be investigated promptly and appropriate measures shall be taken to ensure safety of the subjects.	The study protocol shall describe safety management, provide data collection instrument (AE & SAE Forms), and stipulatetimelines for reporting to stakeholders (Investigators & sponsor) and reporting timelines to CDSCO).
10	Costs and reimbursements to subjects	All reimbursements (travel and wages) shall be compensated appropriately to the subjects wherever required.	All payments shall be documented.
11	Compensation and Insurance	Compensation for SAE (trial related injuries) as per directions of CDSCO, and medical management costs shall be paid by the Sponsor through clinical trial insurance	A clinical trial insurance for the study period for all subjects shall be obtained from local insurance Company to cover for medical/ surgical expenses, compensation for death (as per CDSCO decision) and indemnity for those involved in the clinical trial process - BBIL, CRO, Site, IEC, and others.
12	Breach of confidentiality and protocol violations	Any breach of confidentiality will be handled by legal department as per the terms of mutually signed Non-disclosure agreement.	NDA between all the stakeholders and sites involved in the study shall be executed and any dispute arising thereafter will be dealt legally as per the mutually accepted terms in the executed NDA. Any serious violation of protocol will be brought to the notice of the Sponsor by the Investigator or CRO. Sponsor will report the protocol

			violations to DCG (I).

13	Audit and independent reviews	Site audits shall be conducted by BBIL or outsourced to a third-party expert in GCP.	Audits shall be conducted by BBIL or third-party GCP expert. Prompt corrective measures will be taken in case of adverse reports.
14	Logistics and Data quality	All shipments, including study documents, investigational material and biological samples shall be transported/ handled by reputed agencies. Cold chain requirements of the samples will be followed and shipment temperature will be monitored using data loggers.	All shipments, including study documents, INV and biological samples shall be transported/ handled by reputed agencies. All temperature logs for transport in cold chain shall be checked and filed.
15	Serology / efficacy	Serology assays ($PRNT_{50}$) shall be outsourced to a NABL accredited laboratory. If required, technology transfer of the method will be done by the sponsor to the CRO. The CRO will perform the assays only as per validated protocols with appropriate controls.	Periodic monitoring and site audits by the sponsor will be carried out to ensure GLP in data capture and analyses by the CRO.