High yielding cell line development of a Factor VIII Biosimilar with a novel purification strategy"

AMTHERA Life Sciences Pvt. Ltd

Environmental and Health Risk Management Plan

1. Institutional Arrangements

Requirements	Current Status	Mitigation Steps
Institutional Bio-Safety Committee (IBSC)	AMTHERA is in the process of making the application to constitute the IBSC to DBT. *As a required first step, Company registration through the RCGM website & Consent Letters from 3 external experts is completed.*	IBSC suggestions and recommendations will be followed.
EHS Team	Not Existing	Recommendations of EHS will be followed
Documentation and Record Keeping in reference to the risks mentioned below and quantifiable records of generated waste and compliance measures.	Existing	IBSC recommendations are followed
SOPs related to Environment Compliance e.g Chemical spillage handling, waste segregation etc.	Existing *Handling& Storage of Chemicals Handling & Disposal of Hazardous Chemicals & Biological Waste*	The SOPs are provided to researchers in the laboratory.
General Safety and Storage	Standard practise followed Project staff and students are provided adequate training and provided with a manual having standard operating procedures.	Any inadequacy/accidents are reported to IBSC; appropriate measure are taken to avert further damages to individuals and for the property

2. Environmental Impact and risk mitigation

Risks	Project Specific Risk	Potential Impact	Mitigation Steps
Air Pollution	-Minimal Risk	Project implementation will not create any adverse air pollution.	Project implementation will not create any adverse air pollution.
Water Pollution and Waste water treatment	Minimal Risk	Project implementation will not create adverse water pollution.	Project implementation will not create adverse water pollution.
Chemical waste	Flammable chemicals are used with appropriate protection in the certified hood. All chemicals are disposed off as per the norms established by by Pollution Control Board of Govt. Of Karnataka	The risk will be minimum and adequate protection will be taken as solvents such as methanol, acetonitrile will be used in the work. The solvent waste bottles will be covered with caps and kept in certified hoods and handed over to solvent waste management team for disposal	Hazardous/flammable chemicals are used with appropriate protection in the certified hood. Fire extinguishers placed near the entrance of the laboratory to dose off fire in case of fire accidents. All chemicals are disposed of as per the norms established by Pollution Control Board of Govt. Of Karnataka
Biological Waste	Biological wastes are mainly from bacteria, yeast and mammalian cells. All the biological plastic wares and tissue culture wares are collected in biohazard bags and autoclaved and	The impact is minimal as safety measures are in place as per IBSC regulations. All the biological wastes such as plastics or other materials autoclaved and	Biological wastes are mainly from bacteria, yeast and mammalian cells. All the biological plastic wares and tissue culture wares are collected in biohazard bags and autoclaved and discarded

	discarded through **Medicare Environmental Management Pvt. Ltd., Bengaluru,** which is a certified third party vendor.While the spent media is treated with 4% Sodium hypochlorite and discarded in specified locations at AMTHERA. All the biological wastes are managed as per the norms IBSC. All waste of Amthera are disposed off by **Medicare Environmental Management Pvt. Ltd., Bengaluru,** which is a certified third party vendor to collect the biological wastes for disposal.	disposed according to Biosafety guidelines.	through **Medicare Environmental Management Pvt. Ltd.** which is a certified third party vendor. While the spent media is treated with 4% Sodium hypochlorite and discarded in specified locations AMTHERA. All the biological wastes are managed as per the norms of IBSC. All waste are disposed off by **Medicare Environmental Management Pvt. Ltd. Bengaluru,** which is a certified third party vendor to collect the biological wastes for disposal.
Heavy metals	Minimal Risk	Project implementation will not create any adverse heavy metal waste.	Project implementation will not create any heavy metal waste.
Radiation Waste	-Minimal Risk	Project implementation will not create any adverse radiation waste.	Project implementation will not create any adverse radiation waste.

Electronic Waste	Minimal Risk	Project implementation will not create any adverse electronic waste	Project implementation will not create any adverse electronic waste
Hazardous and C&D Waste	Minimal Risk	Chemicals which comes under the category of carcinogenic agents will be minimally used with appropriate protection including using masks, safety googles, protective dress etc.	Project personnel are trained to use chemicals in the certified hood with protective clothing, gloves, safety goggles, masks. The facilities are in place.
Destruction/alteration of surrounding ecosystem	Minimal Risk	Project implementation will not create any adverse Destruction/alteration of surrounding ecosystem	Project implementation will not create any adverse Destruction/alteration of surrounding ecosystem

3. Occupational Health and Safety and risk mitigation

Risks	Project Specific Risk	Potential Impact	Mitigation Steps
Heat Hazards	No direct contact with fire is done in the work. Autoclaves are used for sterilization purposes for both exerpimental requirements and post experimental sterlizations	Minimal; Periodically proper functioning of the autoclaves and are monitored	Autoclaves are kept in an isolated and secured room. They are periodically inspected for the quality of gasket, pressure valves. Etc. Any accidents, security and safety personnel will be

			invited to assess the situation and assistance will be sought from medical practioners to provide immediate primary health care to affected indivuals. Estate office and to depute service maintenance staff to rectify any anamolies.
Chemical hazards, including fire and explosions	All the hazardous and flammable chemicals will be handled in certified chemical hoods All chemicals are disposed off by certified third party vendors	Risk is Minimal	In case of accidents; rooms/regions will be isolated and blocked. Any accidents, security and safety personnel will be invited to assess the situation and assistance will be sought from medical practioners to provide immediate primary health care to affected individuals. Estate office and to depute service maintenance staff to rectify any anomalies.
Pathogenic and biological hazards	All waste are disposed off by certified third party vendors as per the norms of IBSC	Risk is minimal as pathogenic and infectious organisms are not used in the proposed work. Biological solid wastes will be autoclaved biohazard bags and disposed through Biolink Vendors.	IBSC SOPs are followed. They are displayed in the laboratory as a guideline. Researchers are also trained for BioSafety compliance as IBSC

		Liquid wastes are treated with 4% Sodium hypochlorite and discarded in specific meant for disposal	
Radiological hazards	Not used in work	NIL	NIL
Electronic Waste	Very minimal waste will produced	Minimal Risk	Minimal Risk
Hazardous and C&D Waste	Hazardous and C & D chemicals are kept in certified shelves and used in hood	NIL	NIL
Noise	The proposed work generates minimal noise.	Minimal impact	If any equipments found to be noisy,; Immediately, the equipments will be turned off. Authorized company service personnel will be invited to rectify the problems
Process safety	The process producing the rBDDFVIII molecule is done authorized rooms. The cabinets and incubators will be checked periodically. The maximum volume that will be used in the study is 0.5 Lits	Risk is minimal	IBSC protocol for cleaning and disposal will be followed which includes both solid and liquid wastes produced during the process
others	NIL	NIL	NIL

4. Community Health and Safety and risk mitigation

Risks	Project Specific Risk	Potential Impact	Mitigation Steps

Safety Transportation Management System (for transport of hazardous material)	Hazardous chemicals/reagents will not be transported. Biologicals samples will be transported which includes plasmid constructs, CHO cells, cell culture media expressing rBDDFVIII (10ml, 50ml, 100ml and 500 ml containers)and purified rBDDFVIII.	Hazardous chemicals/reagents will not be transported. Biological materials such as plasmid construct, CHO Cells, rBDDFVIII containing CHO cell media, purified factor VIII are not hazardous. Minimal impact due to spillage	The intended biological samples well packed and sealed containers or tubes according to volume. In addition, the samples will also be kept with cold packs or dry ice if necessary in appropriate cardboard boxes and covered and labelled as per the norms. They will be transported either in a car in secured manner or professional vendors who transport biological samples
Emergency preparedness and participation of local authorities and potentially affected communities	Emergency preparedness and participation of local authorities may not be required as No hazardous chemicals will be transported. Regarding biological samples, they are non-hazardous and in addition they will not harbour any pathogens or infectious agents which will affect the local communities Since, volume of the samples transported will be small (upto	Very Minimal Risk	The intended biological samples well packed in sealed containers or tubes according to volume (10 ml to 500 ml). In addition, the samples will also be kept with cold packs or dry ice if necessary in appropriate cardboard boxes and covered and labelled as per the norms. They will be transported either in a car in a secured manner. Alternatively, services of professional vendors

	500 ml) in sealed containers and packed boxes, the impact of any spillage will be very minimal. Moreover, the biological samples transported are for laboratory research purposes only .		who transports such materials will be utilized.
In case your organization already has **EHS guideline**, please summarise the same. Also, share details of the **EHS Officer/ Contact Person** of the organization. If not, please describe the impact because of hazardous material, release of chemicals, biologicals, management of catastrophic events like fire/explosion**.**			

Annexure - 3

Clinical Trial Risk Management Plan (if applicable)

NOT APPLICABLE. As this project proposal does not involve any human clinical trial

Clinical and Regulatory		
Area of Risk	**Monitoring Parameters**	**Mitigation Measures**
Production of CT material	NIL	NIL
Protocol design and scientific validity ensuring Favourable risk-benefit ratio	NIL	NIL
Regulatory approvals	NIL	NIL
Ethics approvals	NIL	NIL
Ensuring appropriate informed consent process and respect for human subjects	NIL	NIL
Capacity of the sponsor	NIL	NIL
Staff at the trial site and Investigator responsibilities	NIL	NIL
Recruitment of study subjects and fair subject selection	NIL	NIL
Safety Management (AE and SAE)	NIL	NIL
Costs and reimbursements to subjects	NIL	NIL
Compensation and Insurance	NIL	NIL
Breach of confidentiality and protocol violations	NIL	NIL
Audit and independent reviews	NIL	NIL
Logistics and Data quality	NIL	NIL

Serology / efficacy	NIL	NIL
Post- trial access issues (if applicable)	NIL	NIL