Environmental and Health Risk Management Plan

1. Institutional Arrangements

Requirements	Current Status	Mitigation Steps
Institutional Bio-Safety Committee (IBSC)	IBSC is approved and active	We are conducting our IBSC meeting every six months / whenever the approval is required for particular activity like PCT protocol / report submission etc.
EHS Team	We have identified EHS team	EHS plays an important role in any organization. We will provide training to all the employees on 1. Fire safety 2. Personal safety 3. Environment protection
Documentation and Record Keeping in reference to the risks mentioned below and quantifiable records of generated waste and compliance measures.	Different levels of documents / records archival system is available	All the records/ data generated during product development, regular batch analysis etc shall be stored in compactors and under custodian of quality assurance.
SOPs related to Environment Compliance e.g Chemical spillage handling, waste segregation etc.	All the chemical spillage, waste segregation shall be handled by SOP	**Procedure for liquid spillage handling** In case of spillage of culture in the Bio-containment area, spray 70% IPA / disinfectant immediately on the spillage and leave for 4-5 minutes. Wipe off the spillage with lint free cloth and collect into a waste beaker. Send the cloth and beaker for decontamination and decontaminate using

		autoclave at 121°C for 30 minutes. Inform the supervisor the incident of spillage of hazardous material. **Procedure for solid waste disposal** Collect the solid waste generated in different areas from the discard bins assigned for solid waste disposal. Collect the Biohazard solid waste from the Biohazard discard bins, decontaminate them by autoclaving at 121°C for 30 minutes and send the waste to effluent treatment plant for further treatment. Discard the waste in proper place assigned for solid waste disposal outside the facility **Procedure for liquid waste disposal** Collect regular liquid waste from different areas and dispose it off in the sink located in washing area which leads to kill tank. Collect decontaminated liquid waste from bio

		contaminant areas and dispose it off in the sink located in the wash area which leads to kill tank. **Procedure for decontamination of Biohazard waste** Collect the biohazard waste into a autoclavable beaker or cover. Cover with aluminum foil or butter paper if it is a beaker. Put them in the autoclave assigned for decontamination and run the cycle for 121°C for 30 minutes. Remove the material from the autoclave and pour them in the drain leading to kill tank. The quantity of water collected in kill tank is seen through the view glass / level indicator present on the kill tank. The steam valve is opened slowly until the temperature reaches to 100 °C and maintain for 60 minutes. When the temperature of the liquid reached to 35 to 40 °C open the value and drain the

		liquid to effluent treatment plant. Disposable plastic ware is used by autoclaving at 121°C for 30 minutes.
General Safety and Storage	General safety and storage mechanism are in place.	Training for general safety mechanisms like fire safety, personal protection measures, record keeping have been imparted to all the employees.

15. Environmental Impact and risk mitigation

Risks	Project Specific Risk	Potential Impact	Mitigation Steps
Air Pollution	minimal risk	There will be no specific air pollution generated from our industry.	The levels of air pollution shall be monitored on monthly and reports shall be submitted to Pollution control board.
Water Pollution and wastewater treatment	There will be no major water pollution generated from industry minimal risk	There will be no major water pollution generated from industry	We will not be using solvents / chemicals in large amounts. All the media / chemicals used are collected into equalization tank where the pH of the water is brought to neutral and then further treated to reduce BOD, COD etc using ion exchangers, sedimentation, drying processes. The treated water shall be used for gardening.
Chemical waste	minimal risk	There will be no major chemical waste	
Biological Waste	Minimal risk Culture generated from fermentation process	Culture generated from fermentation process	All the biological waste generated shall be collected into kill tanks and heated upto 121 °C for 30 minutes. After cooling to room temperature, the same shall be sent to Effluent treatment plant for further treatment.
Heavy metals	Minimal risk	There will be no major heavy metal usage.	There will be very limit of traces of heavy metals (ppm) in our raw materials used.

			These are treated in ETP along with other effluents.
Radiation Waste	Minimal risk	There will be no radiation wastage	There will be no radiation waste as we are not using any radioactive materials etc.
Electronic Waste	minimal risk	There will be no electronic wastage	There will be no much electronic waste immediately as we are not using all new electronic devices which will generally have life of about 7 to 10 years.
Hazardous and C&D Waste	minimal risk	There will be no Hazardous and C&D Waste	There will be no Hazardous and C&D Waste as our is a new facility
Destruction/alteration of surrounding ecosystem	minimal risk	There will be no Destruction/alteration of surrounding ecosystem	Our facility is in the state owned and maintained by Telangana state Industrial Infrastructure corporation where all the necessary steps were taken against destruction / alteration of surrounding ecosystem.

16. Occupational Health and Safety and **risk mitigation**

Risks	Project Specific Risk	Potential Impact	Mitigation Steps
Heat Hazards	minimal risk	project implementation does not cause adverse heat hazards	project implementation does not cause adverse heat hazards
Chemical hazards, including fire and explosions	minimal risk	We will not be using solvents / chemicals in large amounts. All the media / chemicals used are collected into equalization tank where the pH of the water is brought to neutral and then further treated to reduce BOD, COD etc using ion exchangers,	We will not be using solvents / chemicals in large amounts. All the media / chemicals used are collected into equalization tank where the pH of the water is brought to neutral and then further treated to reduce BOD, COD etc using ion exchangers, sedimentation, drying processes. The treated water shall be used for gardening.

		sedimentation, drying processes. The treated water shall be used for gardening	
Pathogenic and biological hazards	minimal risk	All the biological / pathogenic waste generated shall be collected into kill tanks and heated upto 121 °C for 30 minutes. After cooling to room temperature, the same shall be sent to Effluent treatment plant for further treatment.	All the biological / pathogenic waste generated shall be collected into kill tanks and heated upto 121 °C for 30 minutes. After cooling to room temperature, the same shall be sent to Effluent treatment plant for further treatment.
Radiological hazards	minimal risk	There will be no radiation waste as we are not using any radioactive materials etc.	There will be no radiation waste as we are not using any radioactive materials etc.
Electronic Waste	minimal risk	There will be no much electronic waste immediately as we are not using all new electronic devices which will generally have life of about 7 to 10 years.	There will be no much electronic waste immediately as we are not using all new electronic devices which will generally have life of about 7 to 10 years.
Hazardous and C&D Waste	minimal risk	There will be no Hazardous and C&D Waste as our is a new facility	There will be no Hazardous and C&D Waste as our is a new facility
Noise	minimal risk	There will be no noise pollution and we will monitor noise levels on monthly basis and shall report to pollution control board.	There will be no noise pollution and we will monitor noise levels on monthly basis and shall report to pollution control board.
Process safety	minimal risk	The process which we have developed has no major impact	The process which we have developed has no major impact

		as we will not be using solvents at larger scale	as we will not be using solvents at larger scale

17. 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	The solid waste generated after effluent treatment / liquid waste shall be shipped to central treatment plants maintained by Telangana pollution control board / Ramky etc	Special vehicles are available to take all necessary steps to safely transport, treat and dispose.
Emergency preparedness and participation of local authorities and potentially affected communities	Moderate Risk	Health hazards and risk of damage to the property due to incidents of fire or any accident	The building designs have been built with fire safety clearance, provisions for emergency services have been made

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.

EHS Officer details: Mr. M. Srikanth, srikanthm@lazulinebio.com, Mobile no. 9966669070.

Summary of EHS Guidelines

Introduction:

The EHS Guidelines for Pharmaceuticals and Biotechnology Manufacturing include information relevant to pharmaceuticals and biotechnology manufacturing facilities. They cover the production of active pharmaceutical ingredients and secondary processing, including intermediates, formulation, blending, and packaging, and related activities research, including biotechnology research and production.

This guidelines are organized according to the following sections:

Section 1.0 — Industry-Specific Impacts and Management Section

Section 2.0 — Performance Indicators and Monitoring Section

1.0 Industry-Specific Impacts and Management Section

1.1.Environmental:

The following environmental issues are be considered as part of a comprehensive assessment and management program that addresses project-specific risks and potential impacts.

Potential environmental issues associated with pharmaceuticals and biotechnology manufacturing projects include the following:

- Air emissions
- Wastewater
- Solid and hazardous wastes
- Hazardous materials
- Threats to biodiversity
- Bioethics

1.2.Occupation Health and Safety

Facility-specific occupational health and safety hazards are identified based on job safety analysis or comprehensive hazard or risk assessment using established methodologies such as a hazard identification study [HAZID], hazard and operability study [HAZOP], or a scenario-based risk assessment [QRA].

The occupational health and safety issues that may occur during the construction and decommissioning pharmaceutical and biotechnology manufacturing facilities are similar to those of other industrial facilities, the most significant occupational health and safety hazards occur during the operational phase of pharmaceutical and biotechnology facilities and primarily include the following:

Heat hazards

- Chemical hazards including fire and explosions
- Pathogenic and biological hazards
- Radiological hazards
- Noise
- Process safety

1.3.Community Health and Safety

The most significant community health and safety hazards associated with pharmaceutical and biotechnology manufacturing facilities occur during the operation phase and may include the threat from major accidents related to the aforementioned fires and explosions at the facility and potential accidental releases of finished products during their transport outside of the processing facility. The management of these issues shall be covered under Major Hazards below including the Traffic Safety; Transport of Hazardous Materials; and Emergency Preparedness and Response

Major Hazards

The most significant safety impacts are related to the handling and storage of solid, liquid, and gaseous substances. Impacts may include significant exposures to workers and, potentially, to surrounding communities, depending on the quantities and types of accidentally released chemicals and the conditions for reactive or catastrophic events, such as fire and explosion.

Major hazards shall be prevented through the implementation of a Process Safety Management Program which includes

- Facility-wide risk analysis, including a detailed consequence analysis for events with a likelihood above 10^{-6}/year (e.g. HAZOP, HAZID, or QRA);
- Employee training on operational hazards;
- Procedures for management of change in operations, process hazard analysis, maintenance of mechanical integrity, pre-start review, hot work permits, and other essential aspects of process

safety included in the General EHS Guidelines;

- Safety Transportation Management System as noted in the General EHS Guidelines, if the project includes a transportation component for raw or processed materials;
- Procedures for handling and storage of hazardous materials;
- Emergency planning, which should include, at a minimum, the preparation and implementation of an Emergency Management Plan prepared with the participation of local authorities and potentially affected communities.

2.0 Performance Indicators and Monitoring Section

2.1 Environment

These guidelines are achievable under normal operating conditions in appropriately designed and operated facilities through the application of pollution prevention and control techniques discussed in the preceding sections of this document.

Environmental monitoring:

Environmental monitoring programs shall be implemented to address all activities that have been identified to have potentially significant impacts on the environment, during normal operations and upset conditions. Environmental monitoring activities shall be based on direct or indirect indicators of emissions, effluents, and resource use applicable to the particular project. Monitoring data shall be analyzed and reviewed at regular intervals and compared with the operating standards so that any necessary corrective actions can be taken.

2.2 Occupational health and safety:

Occupational health and safety performance should be evaluated against internationally published exposure guidelines of which examples include the Threshold Limit Value (TLV), occupational exposure guidelines and Biological Exposure indices (BEIs) published by American Conference of Governmental Industrial Hygienists (ACGIH), the Pocket guide to Chemical Hazards published by the United States National Institute for Occupational Health and Safety (NIOSH), permissible exposure Limits (PELs) published by the Occupational Safety and Health Administration of the United States (OSHA),[25] Indicative Occupational Exposure Limit Values published by European Union member states.

1.1.1 Biotechnology Manufacturing

Biotechnology can be defined as the application of biological systems to technical and industrial processes. Traditional biotechnology is the result of classic hybridization (i.e., mating or crossing of various organisms to create new organisms used in industrial application, including food industry, pharmaceutical industry, and wastewater treatment). Modern biotechnology combines the principles of chemistry and biological sciences (molecular and cellular biology, genetics, and immunology) with technological disciplines to produce goods and services. It utilizes enzymes to cut and paste genetic information, DNA, from one organism to another outside living cells. The composite DNA is then reintroduced into host cells to determine whether the desired trait is expressed. The resulting cell is called an engineered clone, a recombinant or a genetically manipulated organism (GMO). In general, genetic engineering techniques are therefore used to establish cell lines, which are then used in fermentation processes to produce the biologically active molecules at industrial scale.

The biotechnology industry can be categorized in four main industry sectors:

- Biomedical pharmaceuticals, biologic and medical device products;

- Agricultural foods, transgenic animals, disease resistant and pest resistant plants;
- Genetically enhanced industrial products (e.g., detergent enzymes); and
- Wastewater treatment and decontamination of industrial wastes.

In the biomedical sector, modified cells or organisms are cultivated in monoculture bioreactors. In mammalian cell culture, the protein product is secreted from the cells into the surrounding nutrient medium, and chemical separation methods (e.g., size or affinity chromatography, electrophoresis) may be used to capture and purify the product.

Fermentation using Pichia Pastoris host organisms produces the desired product within the cell membrane. Cells are then physically ruptured in order to harvest the product. Antibiotics may be added to the production media to enhance production or maintain selective pressure on otherwise unstable genetic production elements (plasmids).

Penetrations into the bioreactor vessels are necessary for providing nutrients and oxygen, for off-gassing carbon dioxide, and for monitoring and controlling the system. Sealing and filtration (0.2 micron) is needed for each penetration to prevent contamination of the culture. Exhaust gas filtration is also necessary to protect the working environment and the outside environment from aerosols generated during the culture or fermentation. Depending on the biohazard potential of the system, biological inactivation of liquid effluents (usually by heat, steam, or chemical methods) is standard practice.