Environmental Health Risk Management Plan (EHRMP)
Himedia Laboratories Pvt Ltd

Proposal entitled: "Development and production of affordable serum-free, chemically defined media and feed supplements for therapeutic proteins"

1. Institutional Arrangements

i. Brief description of the proposed activity

We Propose to develop and manufacture Chemically Defined Serum Free Media CDSFM comprised of base media, feeds and growth boosting supplements for a different range of commercialized recombinant mAb and glycoproteins produced by validated certified cell lines such as CHO-S cell lines.

A total of 3 clones will be made available to us by reputed National Biopharma organizations under suitable Confidentiality Disclosure Agreement (CDA) and Material Transfer Agreement (MTA), MOUs and Support Documents for NBM 2019.

Entire two year project is divided into three major objectives –

- Objective 1: To optimize chemically defined animal component free serum free medium and feed for recombinant certified cell lines producing therapeutic proteins.
- Objective 2: Augmentation of production facility at Nashik for commercial scale powdered media and 50 L scale validation facility at Thane Mumbai
- Objective 3: Validation of optimized media at 50 Litre Scale in-house and in commercial setting.

In order to achieve these objectives Hi Media's strategy will be as follows-

Early Phase Development

1. Hi Media will employ design of experiments DOE strategy for media formulations to demonstrate comparable or better growth kinetics and therapeutic protein production of the respective clones in comparison with other commercially available media.
2. Hi Media has a substantial laboratory set up to support this DOE based media development strategy and also has a sterile lab scale production facility. Hi Media proposes to study the substrate utilization and Cell Density Viability CDV and intended therapeutic protein characteristics produced by the respective commercial clone to meet its CQAs, Critical Quality Attributes.
3. Hi Media will carry out spent media analysis for changes in amino acid and water-soluble vitamin levels, glucose/lactate, and selected lipids and cations to support continuous media development.
4. Hi Media will further demonstrate consistency with at least three batches up to 2 L scale in bioreactors.

Upscaling of technology

1. Hi Media will complete early phase development and submit appropriate supporting data. This data will also be shared with clone providing Biopharma partners.
2. Hi Media will demonstrate consistency of media composition and performance with respective recombinant protein producing cell line at a maximum scale of 50 L bioreactor.
3. The Biopharma partners will evaluate the manufactured recombinant protein for its CQAs, its efficacy, safety and other relevant functional attributes necessary for final formulation.
4. Powder Media Facility – Hi Media will augment its serum free media and supplements manufacturing capacities such as blending, dried packing along with scale-up of selected media formulation, cell culture lab to assess the medias/feeds at bioreactor level.
5. Liquid Media Facility – Hi Media will strengthen its capability and facility for sterile media and buffer manufacturing and liquid packing in small volumes in bottles as well as in large volumes in bags and bioprocess containers at various concentrations such as 5X, 10X, 20X, 50X, 100X as needed by the biopharma.
6. Hi Media already has required built-up area to set-up clean room for blending and sterilization of media.
7. Hi Media will provide the required amount of media, manufactured in the newly augmented facility, for validation to the respective CMO to ensure manufacturability, reliability and quality standard as per ISO 9001 and ISO 13485 certified processes and according to current good manufacturing practices cGMP . A consolidated report will be generated.

(i) List of environment related regulatory clearances required for the activity.
Consent to operate under section 26 of the Water (Prevention & Control of Pollution) Act. 1974 & under section 21 of the Air (Prevention & Control of Pollution) Act, 1981 and Authorization / Renewal of Authorization under Rule 5 of Hazardous Wastes (Management, Handling and Trans-boundary Movement) Rules 2008
Consent No.: RO-NASHIK/COSENT/2006000235 dated 5th June 2020

Institutional Arrangement

	Area of Risk	Yes	No	Details	Proposed Plan
1	Is there a designated full-time staff for Environment Health and Safety (EHS) issues?	√		Full time trained staff exists for handling EHA issues	Trained staff will follow EHS guidelines.
2	Does the EHS staff handle the following?			EHS SOP and policy is in place. MPCB consent is in place.	NBM BIRAC Environment Management Framework will be followed as per project requirement https://www.birac.nic.in/nbm/uploads/2019/08/emf.pdf
	Occupational Health and Safety	√			
	Waste Management	√			
	List of consents and regulatory clearances	√			
	Record keeping of accidents and procedures	√			
	EHS trainings for staff	√			
	Environment Management Framework compliance for Innovate in India Project		√		
3	Is there a reporting structure in place regarding EHS issues?	√		Work place site inspection record	Specified record will be maintained throughout the project period
4	Are regular EHS trainings provided to staff?	√		Frequency: quarterly	Periodic training will be scheduled for staff
5	Institutional Bio-Safety Committee (IBSC)	√		IBSC is in place for monitoring of project activities that	Recombinant clones will be procured under MOU and

				involve transfer, usage and disposal of recombinant clones	MTA that are reviewed by IBSC. Experiments will be performed in accordance with the IBSC norms. Meeting frequency = Six monthly
6	Ethics Committee (EC)	√		IEC is not required for this project. IEC is in place for monitoring and review of projects that involve human tissues (isolation of primary cells and stem cells).	This project does not involve human / animal volunteers and tissues taken thereof. Hence IEC will not be required.
General Occupational Health and Safety					
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**
7.	Are there Standard Operating Procedures for accidents, hazards, and other emergencies (chemical spills, heat hazards, fire hazards, radioactive hazards etc.)?	√		EHS SOP is in place.	Mentioned SOP will be followed in case of accidents and emergencies
8.	Are the following in place?			Mentioned safety equipment are located at designated locations	Safety equipment will be immediately used in case of occurrence of adverse events and accidents
	Chemical spill kits	√			
	Eye wash	√			
	Shower stations	√			
	First Aid Kit	√			
	Fire Extinguishers	√			
	Register of accidents and injuries	√			

9.	Are proper signage and storage system in place?	√		Yes. These systems are in place for risk management and safety	All the displayed safety documents and signage will be referred by project members on duty at appropriate time.
	Display of Material Safety Data Sheet (MSDS) where relevant	√			
	Display of emergency numbers and procedures (Person to Contact, Doctor, Ambulance, Fire Emergency, Police) displayed in all critical places	√			
	Signage across the facility (labs, storage, hazardous areas, etc.)	√			
	Are flammable materials appropriately stored to prevent fire hazards?	√			
10.	Are smoke detectors, fire alarms, automatic safety/shut off systems, overflow preventers, etc. in place and regularly maintained?	√		List: AMC for all listed system is done by external authorized agency	Renewal of AMC will be ensured within timelines
11.	Are there control measures for VOC, air emissions, high operating temperatures, pathogens/vectors etc. in place?	√		List: air emission is controlled as per SPCB rules	Control of the mentioned parameters will be ensured as per SPCB rules
12.	Are regular mock drills conducted for emergency preparedness and safety?	√		Frequency (type wise): twice in a year	Regular mock drills will be conducted twice in a year for emergency preparedness and safety
13.	Are staff provided with OHS training?	√		Quarterly training is conducted	Quarterly OHS training will be given to project members
	Biomedical Waste (BMW) –				
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**
14.	Is there generation of biomedical waste (as described in Bio-Medical Waste Management Rules, 2016) in the grantee?	√		If Yes, provide a list of biomedical waste produced in the facility If No, provide a list ofall waste produced in the facility.	This project does not involve any biomedical waste. Procedure for disposal of Biohazard waste material will be followed for disposal of biohazard waste generated. –
15.	Is there trained staff to handle biomedical waste in the grantee?	√		Staff has been trained to handle human primary tissues such as umbilical cord and skin which are used for isolation of stem cells and primary cells	It will be ensured that the trained staff adheres to the procedure for handling and disposal of human tissues. However, this activity does not fall under the scope of this project.
16.	Has the grantee obtained authorization from State Pollution Control Board /Pollution Control	√		SPCB authorization certificate attached	Renewal of authorization will be ensured within timelines

	Committee?					
17.	Is the biomedical waste segregated at point of generation in the facility and stored in suitable containers?	√		Yellow		Biohazard waste will be given to the authorized agency SMS Envoclean and categorization of waste will be performed as per their procedure
				Red	√	
				White	√	
				Blue		
18.	Is the bar code system for the segregated waste in place?		√	Barcoding system does not exist currently		The system will be implemented as per requirement.

19.	Is the biomedical waste being sent to an **authorized** common BMW facility?	√		Biohazard waste is sent to and authorized facility - SMS Envoclean Pvt. Ltd. with agreement of services	Renewal of the agreement will be ensured within timelines
20	Does the grantee have an in-house BMW treatment facility?		√	HiMedia does not have in-house BMW treatment facility. Biohazard wastes are given to SMS Envoclean Pvt. Ltd It is a privately owned organization that operates under jurisdiction of Mumbai	Renewal of the agreement will be ensured within timelines
	Is the treatment facility own (individual)?	√			
	Is the treatment facility a shared facility in an industrial park?		√		
21	Are lab waste, microbiological waste and chemical liquid waste pre-treated before storing and sending to treatment facilities according to guidelines prescribed in BWM, 2016 regulations?	√		Yes the wastes are treated as per SOP	Pre-treatment of the lab waste, microbiological waste and chemical liquid waste will be ensured as per defined SOP.
22	Is the liquid waste checked for active cells before sending to treatment plant?		√	Most liquid wastes are autoclaved before disposal through a separate waste disposal autoclave	Logbook of this activity will be maintained and provided if required
23	Are necessary waste pre-treatment equipment in place?	√		Yes. Pretreatment equipment such as autoclave are in place for in-house pre-treatment.	Periodic validation and calibration of pre-treatment autoclave will be performed.
	Do the equipment adhere to prescribed norms by State Pollution Control Board (SPCB)?	√			
24	Are chlorinated plastic gloves and bags phased out in the grantee?	√		chlorinated plastic gloves and bags are phased out	We will ensure total phase out is done gradually
25	Are grantee's personnel involved in handling BMW provided with regular training?		√	We are not directly involved handling BMW.	BMW and Biohazardous waste are given to SMS Envoclean for disposal

26	Are medical examination provided to personnel involved in BMW waste handling and are they provided with relevant immunization like Hepatitis B and Tetanus?	√		Annual health check-up is organized for all personnel involved in biohazard waste handling and relevant immunizations are also given to them	Annual medical check-up and immunization schedule will be monitored by HR Manager
27	Is a daily register for biomedical waste maintained including accident reporting record?		√	Not currently maintained	We will maintain a register at the onset of the project
28	Are annual reports on BWM submitted to SPCB as per required form (see Bio-Medical Waste Rules 2016)?		√	As BMW and biohazard wastes are submitted to third party, this report is not prepared by HiMedia	HiMedia will ensure submission of such report by third party – SMS Envoclean.
Hazardous Waste (HW) – Manufacturing Site					
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**
29	Is there generation of hazardous waste (as per Hazardous Waste Rules, 2016) in the grantee?	√		Dry ETP sludge	The collection, treatment and disposal of these hazardous waste generated will comply with the Hazardous Waste Rules 2016.
30	Is there trained staff in the facility to identify and handle hazardous waste?	√		AMC is given to external agency	Renewal of AMC will be ensured within timelines.
31	Does the grantee have authorization from SPCB for hazardous waste?	√		SPCB certificate	Renewal and approvals will be done and taken within specified timelines.
32	Is there a secure location for storage of HW with proper signage?	√		Dry ETP sludge stored in gunny bags with proper signage. Current frequency = Six monthly	Disposal of waste within 90 days will be ensured.
	Are hazardous waste stored for more than 90 days in the grantee's premises?	√			
33	Is the hazardous being send to an **authorized** disposal facility or user?	√		Name and address of facility: Maharashtra Enviro Power LTD., Plot No. 56, MIDC Ranjangaon, Tal-Shirur, Dist-Pune-412220	Will ensure that this facility is in place for the entire duration of this Project. Timely renewals of existing vendor's contract will be done.
	Is the disposal facility in house?		√		
	Is the disposal facility external/outsourced?	√			

34	Is a register maintained on production and treatment, and a manifest system followed for transport of hazardous waste from the grantee to treatment facility?		√	Currently not maintained.	We will maintain this register on the onset of project. from June 2020.
E-Waste and Batteries					
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**
35	Does the grantee generate e-waste, produce or manufacture electrical and electronic equipment?	√		E-waste such as instrument used up batteries are generated. But HiMedia does not produce or manufacture electrical and electronic equipment	We will keep a check on generated -waste.
36	Has the grantee obtained SPCB authorization on e-Waste?	√		*SPCB consent attached for reference*	As mentioned in the consent, if E-wastes are generated, they will be disposed by selling to authorized reprocessor
37	Does the grantee channelize the e-waste to **authorized** recycling or disposal facility?		√	Name and address of disposal facility/ Recycler E-wastes are disposed off under buy-back offered by the supplier In-house or outsourced Facility. In house E-waste disposal facility does not exist	Buying-back of the E-waste will be taken care of at the time of new purchase of electronic equipment.
38	Does the manufacturing grantee have Extended Producer Responsibility system and EPR-authorization in place?		√	Describe: - Extended producer responsibility, a practice and a policy approach in which producers take responsibility for management of the disposal of products they produce once those products are designated as no longer useful by consumers.	ERP system will be followed and log books will be maintained as per project requirement

39	Does the grantee practice reduction in the usage of hazardous substances in the manufacture of electrical and electronic equipment and its parts?		√	HiMedia does not manufacture any electrical and electronic equipment and its parts. Hence this point is not applicable	Based on the need of the project, the usage of hazardous substances will be reduced
40	Does the grantee provide detailed information on the constituents of the equipment and their components/spares and declaration of conformation to Reduction in Hazardous Substances in the product user documentation?		√	HiMedia does not manufacture any electrical and electronic equipment and its parts. Hence this point is not applicable	Based on the need of the project, the usage of hazardous substances will be reduced
41	Does the grantee maintain a record of collection, storage, sale and transport of e-waste?		√	Not currently maintained	Record of collection, storage, sale and transport of e-waste will be maintained as per project requirement.
42	Does the grantee submit annual reports on e-waste to SPCB?		√	Currently not submitted	Such reports will be submitted as per project requirements.
43	Is there accident reporting and records in place?	√		Mail records are available for accidents	Records will be maintained if required
44	Are PPEs available to staff?	√		PPEs are available to all staff members and they are used by them while on duty	Use of PPE will be ensured by daily monitoring by authorized personnel.
45	Is the grantee involved in manufacture of batteries?		√	HiMedia does not manufacture any batteries	HiMedia do not have any proposed plan to manufacture batteries in future
46	Does the grantee generate battery waste?	√		Yes the battery wastes are generated from DG Set and inverters	Generated wastes will be returned back to the original seller at the time of new purchase
47	Does the grantee deposit the battery waste to **registered** recycler/dealer/manufacturer/reconditioner/collection center?		√	Name and address of battery waste receiving entity: Green India E-Waste & Recycling OPC Pvt. Ltd.	Generated wastes will be given to the mentioned party
48	In case of manufacturing, does the grantee comply to Battery Management Rules 2000 and ensure collection of old batteries?		√	HiMedia does not manufacture any electronic equipment	Battery Management Rules 2000 will not be applicable
Community Health and Safety and risk mitigation					
		Yes	**No**	**Details**	**Proposed Plan**
49	Safety Transportation Management System (for transport Of hazardous material)	√		MEPL (Maharashtra Enviro Power LTD.) carry transportation by themselves	Will follow the same for the project activities along with ensuring the contract with the outsourced agency is renewed on time.

50.	Emergency preparedness and participation of local authorities and potentially affected communities	√		Contact details are displayed and safety squad is positioned for Emergency preparedness	HiMedia will ensure that a designated person is appointed who would be responsible for constituting the emergency preparedness team and liaison with local authorities.

Other					
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**
52.	Is the lab/room air regularly checked for microbial contamination?	√		Environmental monitoring procedure by contact plate, air sampling and settle plate is in place for checking microbial contamination in lab area	Regular monitoring of the environment a frequency mentioned in SOP will be ensured in order to keep a check on microbial contamination
53	Are there any odor control measures in place?		√	Currently not required	Will be installed based on project need
54.	Are fume hoods and exhausts regularly checked and maintained?	√		Fume hoods do not exist.	Periodic cleaning of exhausts will be done
55.	Does the grantee use DG set > 15 KVA?	√		Consent attached. Frequency: Monthly. Outside agency: Green Envirospace	Monitoring will be done and approvals will be taken within prescribed timeline
	Does the grantee have consent for DG > 15 KVA?	√			
	Are emissions from boilers and DG sets regularly monitored to be within the prescribed norms?	√			
56.	Does the grantee have proper disposal process for solid and plastic waste in compliance to Solid Waste Management Rules, 2016 and Plastic Waste Management Rules, 2016?	√		Solid waste given to SPCB.	Will follow norm given in SPCB consent along with ensuring the consent is renewed on time.
57.	Is wastewater treated separately by the grantee? (Liquid waste from laboratory, chemicals, fluids, solvents, medium and cultures, coolants, etc.)	√		Types of wastewater: 1. Sewage wastewater 2. Effluent waste water Treatment of wastewater: As per procedure Chemical management in wastewater treatment plants: As per procedure	Periodic checks will be done and the treatment plant shall be maintained.
	Are there sludge management and cut off drains in place for wastewater?	√		Sludge management performed as per Doc.	Systems in place will be regulated and monitored
58.	Are necessary provisions for noise cancellation in place?	√		Describe: Noise is measured on DB meter and maintained below 75DB as per factory norms.	Will keep reviewing the noise generated and cap them according to the existing cancellation

					provisions.
59.	Are there any settlements, water bodies, cultivated land, or any other eco-sensitive areas near the grantee's premises?		√	Company is located in Industrial zone. Eco-sensitive areas are not present in near premises.	-
60.	Are there any buffers, fire vehicle routes in the grantee's premises?	√		-	Maintenance as per norms will be ensured.

Notwithstanding the above other risk (relevant to the project activities) that will be identified in the course shall be addressed as per standard mitigation monitoring parameters and manner of records keeping shall be in accordance to the recommendations of the project monitoring committee on subject experts engaged by BIRAC.