Environmental Health Risk Management Plan (EHRMP)

M/s Sahajanand Laser Technology Limited

Proposal entitled: "Development of Electroporation device to facilitate the DNA based Covid-19 vaccine candidate"

1. Institutional Arrangements

(i) Brief description of the proposed activity

rAAV have been established for its safety and efficacy in human subjects and rAAV-based gene therapy products Zolgensma and Luxturna have already been approved by US-FDA / EMEA for the treatment of spinal muscular atrophy and retinal disorders, respectively. Therefore, current project aims to develop rAAV-based COVID-19 genetic vaccine by triple-transfection of HEK293T cells using packaging plasmid, helper plasmid and transfer plasmid.

Plasmid production

The competent *E. coli* cells are transformed with individual plasmids encoding the rAAV packaging (rep and cap gene of AAV), helper (E1, E2a, E4 and VA genes of adenovirus) and transfer (antigenic variants of spike protein of SARS-CoV-2 flanked by 5'- and 3-'ITR) vectors. The master microbial cell banks are prepared and characterized. The characterized microbial banks are used for large scale endotoxin-free plasmid preparation. QC for identity, purity and sterility will be done and the produced plasmids will be used for the generation of rAAV.

rAAV generation

Triple-plasmid transfection are used to generate rAAV-COVID-19 vaccines in HEK293T cells.In brief, the HEK293 cells are seeded two day before transfection. On the day of transfection, high quality endotoxin free plasmids and the transfection reagent will mixed at an optimal ratio and added to the cells. After incubation, the supernatant with un-transfected plasmids is removed and a fresh culture medium is added to the cells for rAAV production. Culture is harvested 72 hours post transfection and rAAV is purified using affinity chromatography, ultracentrifugation and buffer exchange. The purified rAAV are stored at -80°C till further usage.

rAAVcharacterization

A functional titer of the rAAV vector is determined by a cell-based assay. A host cell line is used for evaluation of the rAAV's ability to transduce a cell line under specific conditions (transduction units). The titration is performed using the limiting dilution method to transduce the host cells and the titer is measured by real-time polymerase chain reaction (qPCR) quantification of viral genomes in host cell DNA from transduced cells. In brief, the host cells are seeded into 24 well plate and a series of diluted rAAV particles are added to the cells for transduction. Total host cell DNA from each transduced well is extracted and gene specific qPCR are performed to determine the copy number of transfer plasmid in transduced cells. Additionally, purified transfer plasmid alone are used to run standards for the assay. rAAV preparations are also characterized for integrity (SDS-PAGE) and endotoxin. The titer of $5 * 10^9$ TU/ml are used for the QC testing and release criteria.

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(ii) List of environment related regulatory clearances required for the activity.

1. Review Committee on Genetic Manipulation (RCGM)
2. Institutional Biosafety Committee (IBSC)
3. Consent/ authorization from respective PCB for following:
    - Water (Prevention & Control of Pollution) Act, 1974 and Water (Prevention & Control of Pollution) Rules, 1975
    - Air (Prevention & Control of Pollution) Act, 1981.
    - The Environment Protection Act, 1986 and The Environment Protection Rules, 1986.
    - Municipal Solid Waste (Management and Handling) Rules, 2016.
    - The Noise Pollution (Regulation and Control) Rules, 2000.
    - E-Waste Management and Handling Rules, 2016.
    - Bio-medical Waste Management and Handling Rules, 2016.

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?	X		EHS Org Chart in place	Already in place.
2.	Does the EHS staff handle the following?				Currently SLTL admin/HR and respective dept head handles the following. EOHS, Waste management, Consents and regulatory clearances, record keeping of accidents and procedures and EHS training.
	Occupational Health and Safety	X			
	Waste Management	X			
	List of consents and regulatory clearances	X			
	Record keeping of accidents and procedures	X			
	EHS trainings for staff	X			
	Environment Management Framework compliance for Innovate in India Project		X		Environment Management Framework compliance for Innovate in India Project will be followed
3.	Is there a reporting structure in place regarding EHS issues?	X		Already in place. .	Aspects of hierarchy of reporting of accidents and non-compliance be also will be incorporated in the policy
4.	Are regular EHS trainings provided to staff?	X		Frequency:	Already in place. Training records will be provided upon

				Fire Drill: Every year EHS awareness training to staff: Annually. Other Safety Trainings: As per training matrix as per SLTL need	request.
5.	Institutional Bio-Safety Committee (IBSC)		X		IBSC will be formed as and when required
6.	Ethics Committee (EC)		X		EC will be formed as and when 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.)?	X		As per SOP /QCO/080 Standard Operating Procedures for accidents hazards, and other emergencies in place	Already in place.
8.	Are the following in place?			Chemical spill kits Eye wash Shower stations First Aid Kit Fire Extinguishers Register of accidents and injuries are available at the premises.	Proper equipment will be in place and stock will be maintained as per the Institute's guidelines for Environment Health and Safety (EHS).
	Chemical spill kits	X			
	Eye wash	X			
	Shower stations	X			
	First Aid Kit	X			
	Fire Extinguishers	X			
	Register of accidents and injuries	X			
9.	Are proper signage and storage system in place?	X		Biosafety manual Proper signage and storage system are available SLTL at different places MSDS is available with QC team where it is applicable Display of emergency numbers and	These would be regularly updated/ replaced.
	Display of Material Safety Data Sheet (MSDS) where relevant	X			
	Display of emergency numbers and procedures (Person to Contact, Doctor, Ambulance, Fire Emergency, Police) displayed in all critical	X			

	Places			procedures are displayed at all critical places. Signage across the facility (labs, storage, hazardous areas, etc.) are displayed.	
	Signage across the facility (labs, storage, hazardous areas, etc.)	X			
	Are flammable materials appropriately stored to prevent fire hazards?	X		Flammable materials are appropriately stored to prevent fire hazards	
10.	Are smoke detectors, fire alarms, automatic safety/shut off systems, overflow preventors, etc. in place and regularly maintained?	X		Smoke detectors, fire alarms, automatic safety/shutoff systems, overflow preventers are available	Already in place.
11.	Are there control measures for VOC, air emissions, high operating temperatures, pathogens/vectors etc. in place?		X		
12.	Are regular mock drills conducted for emergency preparedness and safety?	X		Frequency (type wise): Fire Drills every year	Records for training are available and will be produced upon request.
13.	Are staff provided with OHS training?	X		Describe: Annual OHS Training program is conducted for all the staff.	Records for training are generated
	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?		X		Any BMW generated will be treated adhering to Bio-Medical Waste Management Rules, 2016.
15.	Is there trained staff to handle biomedical waste in		X		training to staff to handle biomedical waste will be

	the grantee?				provided as and when required
16.	Has the grantee obtained authorization from State Pollution Control Board /Pollution Control Committee?	X		Gujarat pollution control board consent	Authorizations will be renewed from time to time.
17.	Is the biomedical waste segregated at point of generation in the facility and stored in suitable containers?		X		Any BMW generated will be treated adhering to Bio-Medical Waste Management Rules, 2016.
18.	Is the bar code system for the segregated waste in place?		X		The bar code system for the segregated waste will be implemented as and when required
19.	Is the biomedical waste being sent to an **authorized** common BMW facility?		X		If biomedical waste generated it will be sent to authorised common BMW facility
20.	Does the grantee have an in-house BMW treatment facility?		X		
	Is the treatment facility own (individual)?		X		
	Is the treatment facility a shared facility in an industrial park?		X		
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?	X		Treated as per defined SOP	Will ensure compliance of the BMW, 2016 Regulations as and when required.
22.	Is the liquid waste checked for active cells before sending to treatment plant?	X			Will ensure compliance of the BMW, 2016 Regulations as and when required.

23.	Are necessary waste pre-treatment equipment in place?		X		If Bio medical waste generated Pre treatment will be provided to Biomedical Waste before handling over to authorise agency for further treatment. Suitable provision need to be made to pretreat the biomedical waste before handing over to the authorise agency for further treatment.
	Do the equipment adhere to prescribed norms by State Pollution Control Board (SPCB)?		X		
24.	Are chlorinated plastic gloves and bags phased out in the grantee?		X		chlorinated plastic gloves and bags will be phased out
25.	Are grantee's personnel involved in handling BMW provided with regular training?	X		Frequency: Once a Year	Already in place.
26.	Are medical examination provided to personnel involved in BMW waste handling and are they provided with relevant immunization like Hepatitis B and Tetanus?		X	Regular health checkup of all employees are conducted as per SOP	
27.	Is a daily register for biomedical waste maintained including accident reporting record?		X		daily register for biomedical waste will be maintained including accident reporting record if bio medical waste generated
28.	Are annual reports on BWM submitted to SPCB as per required form (see Bio-Medical Waste Rules 2016)?	X		We submit monthly to GPCB	
Hazardous Waste (HW)					
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**

29.	Is there generation of hazardous waste (as per Hazardous Waste Rules, 2016) in the grantee?	X		ETP Sludge	Hazardous waste is generated will be disposed as per Hazardous waste rules 2016.
30.	Is there trained staff in the facility to identify and handle hazardous waste?	X		Yes trained staff available	
31.	Does the grantee have authorization from SPCB for hazardous waste?	X		Valid consent available at site for water, air, hazardous waste from GPCB	Authorizations will be renewed from time to time.
32.	Is there a secure location for storage of HW with proper signage?	X		The HW ETP sludge is stored at a secure location until transported by SPCB authorised CHWTSDF facility.	
	Are hazardous waste stored for more than 90 days in the grantee's premises?		X		
33.	Is the hazardous being send to an **authorized** disposal facility or user?	X		Hazardous waste is sent to E-ColiWaste Management PVT	
	Is the disposal facility in house?		X		
	Is the disposal facility external/outsourced?	X			
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?	X		Yes, Already in place.	
E-Waste and Batteries					
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**
35.	Does the grantee generate e-waste, produce or manufacture	X		E waste such as non working IT equipment's are generated. No other	E waste will be given to authorized recyclers/dismantlers/OEM/vendors only.

	electrical and electronic equipment?			electrical or electronic equipment is produced or manufactured	
36.	Has the grantee obtained SPCB authorization on e-waste?		X		Authorisation will be obtained if required
37.	Does the grantee channelize the e-waste to authorized recycling or disposal facility?	X		Outsourced to R planet Integrated Solution Pvt Ltd	
38.	Does the manufacturing grantee have Extended Producer Responsibility system and EPR-authorization in place?		X		
39.	Does the grantee practice reduction in the usage of hazardous substances in the manufacture of electrical and electronic equipment and its parts?		X		
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?		X		
41.	Does the grantee maintain a record of collection, storage, sale and transport of e-waste?	X		Yes	
42.	Does the grantee submit annual reports on e-waste to SPCB?		X	record is available at premises for ewaste	

43.	Is there accident reporting and records in place?	X		Accident reporting and records in place	
44.	Are PPEs available to staff?	X		PPE provided to staff	Already in place. The stock status of PPEwill be regularly monitored and procurement will be done in time to avoid anysituation of stock out.
45.	Is the grantee involved in manufacture of batteries?		X		
46.	Does the grantee generate battery waste?	X		batteries are returned back to the supplier for disposal	
47.	Does the grantee deposit the battery waste to registered recycler/dealer/manufacturer/reconditioner/collection center?	X		batteries are returned back to the supplier for disposal	
48.	In case of manufacturing, does the grantee comply to Battery Management Rules 2000 and ensure collection of old batteries?		X	NO as the unit does not manufacture batteries.	
Community Health and Safety and risk mitigation					
		Yes	**No**	**Details**	**Proposed Plan**
49.	Safety Transportation Management System (for transport Of hazardous material)		X		Will follow the safety transport managementsystem if required
50.	Emergency preparedness and participation of local authorities and potentially affected communities	X		Emergency response plan available	Emergency preparedness plan will be maintained.
Other					
	Area of Risk	**Yes**	**No**	**Details**	**Proposed Plan**
51.	Does the grantee use any radioactive materials		X	We don't use	

	(isotopes, tracers, radiation equipment, etc)?			radioactive material in our activity	
	Does the grantee have appropriate radioactive material and waste storage and disposal system in place?		X	We don't use radioactive material in our activity	
	Are radioactive warning signs in place?		X	We don't use radioactive material in our activity	
52.	Is the lab/room air regularly checked for microbial contamination?	X		SOPs are there for environment monitoring for medical device facility	
53	Are there any odor control measures in place?		X		odor control measures will be implemented as and when required
54.	Are fume hoods and exhausts regularly checked and maintained?	X		SOP: is there (preventive maintenance of fume hood) at SLTL	Cleaning and maintenance will be done at regular intervals
55.	Does the grantee use DG set > 15 KVA?		X	We have only 3 KVA DG set No boiler is available	DG stack emissions will be monitored as per CPCB rules
	Does the grantee have consent for DG > 15 KVA?		X		
	Are emissions from boilers and DG sets regularly monitored to be within the prescribed norms?		X		
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?	X		Solid & Plastic Waste generated is segregated and handed over to Shree Dav Metals & R planet Intergrated Solution Pvt Ltd SOP no: P-STR-05	

57.	Is wastewater treated separately by the grantee? (Liquid waste from laboratory, chemicals, fluids, solvents, medium and cultures, coolants, etc.)	X		Related chemical waster are Treated in ETP Source: Laboratory waste Outsourced ETP plant for chemical neutalisation is there Related disposal procedure and records are there in place	Waste water treated Separately.
	Are there sludge management and cut off drains in place for wastewater?	X		The mentioned practice is already in place	
58.	Are necessary provisions for noise cancellation in place?	X		Enclosure are built for loud noise Use of PPE such as ear plugs and ear muff. Where required	
59.	Are there any settlements, water bodies, cultivated land, or any other eco-sensitive areas near the grantee's premises?		X		
60.	Are there any buffers, fire vehicle routes in the grantee's premises?	X		, there are vehicle routes in and around the facility accessible to all the buildings within the premises to ensure buffers and safety.	
COVID Precautions & Guidelines Implementation					
61	Guidelines of CPCB/SPCB/GoI for Handling, Treatment, and Disposal of COVID Waste Generated is whether being followed		X		Will follow the guidelines issued by CPCB/SPCB/GoI for COVID waste generation in future also.

62	SOP on preventive measures to contain spread of COVID-19 issued by ICMR/GoI from time to time is whether being followed	X		YES SLTL follows the measures	SOP on preventive measures to contain spread of COVID-19 issued by ICMR/GoI will be followed

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.