Himalayan Hemp Industries Pvt. Ltd.
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19-01-2021

Name of the institute: IIT Kanpur

Incubator: SIIC IITK

Faculty: Dr. Sunil D Agarwal

Type of Intervention: Post Vaccination studies

Objective: *Promotion and facilitation of innovative research on phytopharmaceuticals of cannabis for reducing the side-effects post vaccination amongst elderly people*

Background: With reference to the tripartite memorandum of understanding between CSIR (Council of Scientific and Industrial Research), New Delhi, DBT (Department of Bio-technology), New Delhi and ICMR (Indian Council of Medical Research, New Delhi signed on December 31, 2018, we hereby submit the proposal to conduct a two-phased innovation research on phytopharmaceuticals on local indigenous medicinal plant called cannabis. The premises of this memorandum of agreement allows various researchers to conduct phytopharmaceuticals on Cannabis.

Proposal: With reference to the aforementioned MOU, we shall be studying the **phytochemical profile of the cannabis plant** and **observe the profiling of cannabinoids namely THC (Tetrahydrocannabinol), cbd (Cannabidiol), and CBN (Cannabinol)**. In phase 1, HHIPL (Himalayan Hemp Industries Pvt. Ltd.) want to collects samples from all the 12 districts of Himachal Pradesh to carry out the Phytochemical cataloguing of the plants. The results of this analysis may prove beneficial for the government to create a pathway in which a legal framework for medicinal (drug type) and industrial (fiber type) cannabis can be prepared. A research and development partnership agreement (RDPA) can be made between IITK and HHIPL for further perusal.

Phase 1

Time and Scope

Phase 1 will be 12-24 months where cannabis plant samples from all the 12 districts of Himachal Pradesh as given in the table below will be collected and tested for phytochemical research at IITK for their profiling.

Associated Parties

IITK (Indian Institute of Technology, Kanpur), **and HHIPL** (Himalayan Hemp Industries Pvt. Ltd., Kangra, Himachal Pradesh)

Funding and Expectation

We do not seek any funding from IITK for phase 1. However, we wish to utilize the **HPLC machine for phytochemical analysis** of the cannabis plant and expect the appointment of a researcher (Pharmacognosist or

Phytochemist). We are also prepared to involve our own research team as well in case there is any need for it.

Results and Intellectual Property

After the completion of Phase 1, **Conjoined IP sharing** between both parties, IITK and HHIPL.

List of chosen districts is given below:-

District
Kangra
Chamba
Hamirpur
Bilaspur
Mandi
Sirmaur
Una
Shimla
Kinnaur
Kullu
Lahaul and Spiti
Solan

Methodology and Sampling

Phase 1 will be completed in six stages which are given below:-

1) Exploration and collection

2) Characterization and Evaluation

3) Conservation

4) Exchange and utilization

5) Documentation

6) Plant quarantine

We shall focus on “Specific Mission” collection process where we are focusing on specific crops in specific regions.

We shall be collecting plant samples from all the 12 districts. Photos and video evidences of the collection will be maintained. The quantity as mentioned by IITK which fits in the criteria for minimum quantity required for test will be considered.

Type of collection will be base collection for a set of accessions, which in terms of genetic integrity, is as close as possible to the sample provided originally, which is preserved for long term future. We shall follow the **biased sampling process.**

Calculations

After measuring the levels of THC, CBD and CBN in cannabis plants of different districts, recommended methods for the identification and analysis of cannabis and cannabis products given **as per UNODC (United Nations Office on Drugs and Crime) – Page 20 will be utilized to identify the drug type and fiber type cannabis**. Excerpts from the UNODC document page 20 are mentioned below with the formula of calculation and also attached as additional document at the end of this proposal.

The total THC content is used to define fibretype cannabis (cf. the current upper legal limit for industrial hemp of 0.2 per cent THC and 0.3 per cent

THC, respectively, in Europe and Canada). Another simple way of distinguishing between drug-type and fibre-type cannabis is by using the ratio of the main cannabinoids THC, CBN and CBD.

Both CBD and THC, via their acids CBDA and THCA, are derived biosynthetically from CBGA. If the peak area ratio of [THC+CBN] : [CBD] is 1, it is considered a drug-type. Because THC is oxidized partly to CBN after cutting and drying the plant material, the sum of the peak area of THC and CBN is used and divided by the area of CBD.*

$$X = \frac{[THC]+[CBN]}{[CBD]}$$

$[THC]$ Area of THC in the chromatogram
$X > 1$ Drug-type cannabis
$X < 1$ Fibre-type cannabis

Project Monitoring

An open-ended approach can be considered as per the situation. New interventions can be interjected if the need arises.

Confidentiality clause

The MOU signed between both parties will remain confidential and cannot be disclosed to the third party without prior written consent of the concerned parties.

Publishing of results

All the results will be published jointly as collaborative research from both parties.

Phase 2

Scope: After genotypical-phenotypical cataloguing of the medicinal plants, IITK shall provide us an LOI which we shall connect with Department of Bio-technology, New Delhi for further funding to carry out human and animal trials by collaborating further with ICMR for phase-2 research. RIISM/NMPB, Jogindernagar can assist in collecting more plant samples.

Associated Parties

1) IITK

2) **DBT** (Department of Biotechnology, New Delhi)

3) **ICMR** (Indian Council of Medical Research, New Delhi)

4) **RIISM / NMPB** (National Medical Plant Board, Joginder Nagar)

5) HHIPL

Disease / Disorder in Focus

We want to focus on ***reducing the side-effects post vaccination amongst elderly people***

Budget

Responsible Agency	S. No	Name of studies (Recurring expenditure)	Prices (Rs in lakh) per drug
		A	
CSIR, NEW Delhi (IIIM, Jammu)	1	**Cost of Botanical Raw Material (1500 kg) @ Rs. 300/- kg**	004.500
	2	**Extract preparation (GMP batch) @ Rs 40,000/- per batch of 25 kg**	024.000
	3	**CMC studies** Foreign matter, acid in-soluble ash, total ash, pesticide residue, heavy metals, microbial load, aflatoxins, assay of bioactive or phytochemical compounds by HPLC, Chromatographic fingerprinting profile by HPTLC	003.000
	4	**To create a stock of 500 mg of four reference standards to be used as markers**	020.000
	5	**Stability studies as per ICH guidelines** Long time (25°C ± 2°C/60% RH ± 5%) Accelerated (40°C ± 2°C/75% RH ± 5%)	010.000 (for two year data)
	6	**To conduct Pre formulation R&D for developing formulation**	020.000
	7	**Human formulation development including clinical trials batches preparation** Capsule, tablet, oral dosage forms	025.000
	8	**PK studies** PK study/route and Dose escalation study	002.500
		B.	
DBT, New Delhi	9	**Safety Pharmacology studies (GLP)** hERG Assay, Pulmonary functional assessment in Rats, CNS:Irwin test in rats & CVS: Dog Telemetry	060.000
	10	**Regulatory safety studies (GLP)** Single dose study (rat/mice), 28 days repeat dose study in rats including 10 days DRF, 28 Days repeat dose study in Dog, Ames study, In-vitro chromosomal aberration study, Micronucleus assay (*in vivo*) and Male fertility study (Rats)	150.000
		C.	
ICMR, New Delhi	11	**Preparation of IND Dossier & IND filing** **Part 1:** Published scientific reports in respect of safety and pharmacological studies relevant for the phytopharmaceutical drug intended to be marketed, Information on any contraindications, side effects mentioned in traditional medicine or ethno medicine	010.000

		literature or reports on current usage of the formulation etc. **Part 2:** Data generated on Identification, authentication and source of plant used for extraction and fractionation, Process for extraction and subsequent fractionation and purification, Quality specifications and test methods, details of the composition, proportion of the final purified fraction with defined markers of phytopharmaceutical drug per unit dose, name and proportions of all excipients, stabilizers and any other agent used and packaging materials, Manufacturing process of formulation, Stability data, Safety and pharmacological information, Clinical trials for phytopharmaceutical drugs to be conducted as per applicable rules and guidelines for new drugs, clinical trial protocols and investigator information - detailed protocols for proposed clinical studies to assess whether the initial-phase trials will/ will not expose subjects to unnecessary risks) etc.	
	12	**Phase –I trial** Preparation of trial document and outsourcing to CRO	040.000
	13	**Phase –II clinical trial** • Subject expert meeting, • Preparation of Clinical Trial protocol and other documents • Selection of trial sites/investigators and undertaking feasibility studies, • Obtaining codal formalities, submission of ethics committees documents and obtaining institutional ethical approval, • Salaries for trial institutional project staff, • Investigational and laboratory charges, • Cost of minor instruments/equipments, • Site monitoring visits and documentation, • Material and drug transfer charges, • Statistical analysis of data and report preparation, • Clinical Trial Management services	225.000 2.500 0.250 0.500 1.500 95.500 67.500 6.250 6.000 2.500 2.500 40.000
	TOTAL		**594.00**

Expenditure to be incurred on brainstorming sessions, organizing meetings, consultations on respective components will be borne by respective organizations.

Estimated budget for the product will be 5.94 Cr.

Projected Budgetary Responsibilities of three partners are as follows:

Partner	S. No.	Name of study (Responsibility for funding)	Rs. in Crores per drug
CSIR	1	Cost of Botanical Raw Material	1.09
	2	Extract preparation (GMP)	
	3	CMC Studies	
	4	Reference Standards as Markers	
	5	Stability studies as per ICH guidelines	
	6	Human Formulation Development including clinical trial batches	
	7	To conduct Pre formulation R&D for developing formulation	
	8	PK studies	
DBT	9	Safety Pharmacology studies (GLP)	2.10
	10	Regulatory safety studies (GLP)	
ICMR	11	Preparation of IND Dossier & IND filing	2.75
	12	Phase –I trial	
	13	Phase –II clinical trial	

The above figures are only projected budgetary estimates and requirements. The actual expenditure by each partner will subject to availability of budget with them.

Project Monitoring

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Publishing of results

All the results will be published jointly as collaborative research from all parties.

About the organization

Himalayan Hemp Industrial Pvt. Ltd. is a socio-ecological initiative of 26 like-minded individuals joined together as innovators, farmers, agroprenuers, and medical as well as industrial researchers which focus on creating eco-conscious products using the indigenous plants of India. Preserving the local plants for maintaining the biodiversity of the region is one of the major aims of the organization. Organisation has successfully managed to validate rural development products like world's first reusable and biodegradable hemp sanitary pad and India's first N95 test-validated hemp respirator mask. We are also associated with National Institute of Agricultural Marketing, Jaipur.

Submitted

by

Sonam Sodha

MD & COO

Himalayan Hemp Industries Pvt. Ltd.

Haneesh Katnawer

ED & CEO

Himalayan Hemp Industrial Pvt. Ltd.