Indian Council of Medical Research (ICMR)

Deptartment of Health Research
(Ministry of Health and Family Welfare)

Investigator-Initiated Research Proposals

Date of submission: 28-Apr-2023 11:49:03 AM

Proposal Id: IIRP-2023-4691, **Version Id:** F1, **Proposal Title:** A comparative multicentric non inferiority clinical trial of WHO MBMDT with a new monthly chemotherapy regime containing Rifampicin, Moxifloxacin and Clarithromycin (RMC) on Multibacillary patients from India.

Personal Details of PI

Name of PI (IN BLOCK LETTERS)	DR JOYDEEPA DARLONG	**Designation**	Head
Email	JOYDEEPA.DARLONG@LEPROSYMISSION.IN	**Contact**	9434885198
Date of Birth	28-Oct-1968	**Date of Superannuation**	27-Oct-2028
Nature of Employment	Permanent	**Institute**	The Leprosy Mission Hospital

Proposal Details PART-A

Advertisement	Call for Investigator-Initiated Research Proposals for small extramural grants	**Institute**	The Leprosy Mission Hospital
Institute Type	NGO Darpan ID: 5897	**Valid DSIR Certificate** (Validity)	YES (31-Mar-2025)
Title of the proposed research project	A comparative multicentric non inferiority clinical trial of WHO MBMDT with a new monthly chemotherapy regime containing Rifampicin, Moxifloxacin and Clarithromycin (RMC) on Multibacillary patients from India.		

Summary (up to 250 words): A structured summary should contain the following subheadings: Rationale/ gaps in existing knowledge, Novelty, Objectives, Methods, and Expected outcome.

Rationale/gaps in existing knowledge: Current WHOMDT does not kill 100% bacteria even after a full course of treatment in a subset of patients harboring a large bacterial load thus continuing transmission of the disease responsible for endemicity in some countries. The duration of MDT is long and promotes noncompliance. MDT continues to be controversial with limited evidence support resulting in multiple reformulations since the last 40 years. This calls for a search for newer, more efficacious drugs with shorter duration of action evidenced with well-designed clinical trials. Novelty: Relapse, advocated as the key outcome measure of efficacy of MDT, has its drawbacks. Relapse studies require long years of follow up. The gold standard test for viability was Mouse foot pad studies which is costly and time consuming. Hence, we propose Molecular Viability Assays as outcome measure of efficacy which are newer and better techniques to test viability faster. Objectives: To determine the efficacy of monthly regimen of Rifampicin, Moxifloxacin and Clarithromycin (RMC) regimen as compared to WHO MBMDT regarding clinical cure, lab parameters, immunological reactions, Viability assays, Mouse Foot pad studies and acceptability to the patient in Multibacillary leprosy patients. Methods: It is an open label randomized clinical control trial where in the intervention group monthly supervised regimen of Rifampicin, Moxifloxacin and Clarithromycin will be administered in doses of 600 mg, 400 mg, and 1000 mg respectively and the control arm would be given routine WHO MB MDT. The duration of the treatment in both arms will be 12 months. The random sequence will be generated centrally which will be sent to study centres in opaque envelopes. After consent approved, the envelope will be opened, and patient put on respective arms. The study population will include newly diagnosed, previously untreated MB leprosy patients. Written informed consent will be sought from every subject included in the study. SSS of all the study subjects will be collected at 0-day, 6th, 12th, and 24th month and transported in RNAlater to the SBL. Real Time PCR will be done to quantitate copy numbers of the genes encoding 16S rRNA, hsp18 and esxA specific for M. leprae. Resistance studies will be carried out at 12 months in patients harbouring viable bacilli. Validation of M. leprae growth in mouse foot pad will be performed on participants showing viable load by molecular method at the time of RFT in Schieffelin Institute of Health – Research and Leprosy Centre Karigiri (SIHR&LC), Vellore. Expected outcome: Primary efficacy outcomes: 1. Molecular I. Reduction of copy numbers by MVA II. Complete killing of M. leprae as demonstrated in MFP. 2. Clinical I. Complete clinical cure, defined as full regression of the lesions. II. Clinical improvement of the lesions defined by a clinical criterion 3. Pathological I. Bacillary index (BI) improvement 3. Secondary Efficacy outcomes include: 1. Immunological outcomes Neuritis - if participants reported pain during the interview or when Nerve function impairment is detected on routine test. Type I reaction Type 2 reaction 2. Safety outcomes Severe side effects (defined as a side effect that forced the patient to stop the treatment), mild to moderate side effects. 3. Qualitative outcomes Impact of leprosy treatment on life Perspective towards leprosy treatment

Priority Area: Communicable Diseases	**Priority Area diseases:** One-health	**Area of Research**	Development

Keywords Six keywords separated by comma which best describe your project may be provided.	Leprosy, MDT, alternate regime , clinical trial
Abbrevations Only standard abbreviations should be used in the text. List of abbreviations maximum of ten may be given as a list.	MDT: multidrug therapy MVA: Molecular viability assay MFP: mouse foot pad
Problem Statement (up to 500 words): State the currently available information to present the problem adequately.	Current WHOMDT does not kill 100 % bacteria even after a full course of treatment in a subset of patients harbouring a large bacterial load thus continuing transmission of the disease responsible for endemicity in some countries. The duration of MDT is long and promotes noncompliance.MDT continues to be controversial with limited evidence support resulting in multiple reformulations since the last 40 years. This calls for a search for newer, more efficacious drugs with shorter duration of action evidenced with well-designed clinical trials.
Rationale of the study (up to 250 words) Mention how the research question addresses the critical barrier(s) in scientific knowledge, technical capability, and/or programmatic/ clinical/lab practice and its relevance to local, national and international context with relevant bibliography.	From the few tested drugs, we found fluoroquinolones and macrolides are promising. Fluoroquinolones have proven to be active against Mycobacterium leprae in rodents and in clinical trials in leprosy patients (1,2,3,4). In a murine model of leprosy, moxifloxacin has been demonstrated to be as potent as rifampicin resulting in significant cutaneous clearing and mild side effects, toxicities, and laboratory abnormalities not requiring discontinuation of therapy. Clarithromycin, a semisynthetic macrolide which has significant bactericidal activity against M. leprae that compares with rifampicin (5, 6). The recommendations from the Report of the Global Programme Managers' Meeting on Leprosy Control Strategy 2009 are that a fully supervised, once-monthly regimen be with compounds that have definite bactericidal activity against M. leprae and reasonably well tolerated by patients. A fully supervised, once-monthly regimen is the best possible one that will not overburden health workers (7). An ideal regimen could include rifampicin 600 mg, moxifloxacin 400 mg, and clarithromycin 1000 mg (or minocycline 200 mg) for 12 months. It was suggested that the efficacy and safety of this suggested regimens should be established through long-term, well-designed, and controlled clinical trials. We propose to conduct a Randomized Controlled study comparing WHO MBMDT with a monthly regime consisting of currently most bactericidal and safe drugs of Rifampicin, Moxifloxacin and Clarithromycin in MB leprosy patients. Reference: 1. Gelber, R. H. 1994. Chemotherapy of lepromatous leprosy: recent developments and prospects for the future. Eur. J. Clin. Microbiol. Infect. Dis.13:942–952. 2. Gelber, R. H., A. Iranmanesh, L. Murray, P. Siu, and M. Tsang. 1992. Activities of various quinolone antibiotics against Mycobacterium leprae in infected mice. Antimicrob. Agents Chemother. 36:2544–2547. 3. Grosset, J. H., C. C. Guelpa-Lauras, E. G. Perani, and C. Beoletto. 1988.Activity of ofloxacin against Mycobacterium leprae in the mouse. Int. J. Lepr.Other Mycobact. Dis. 56:259–264. 4. Grosset, J. H., B. Ji, C. C. Guelpa-Lauras, E. G. Perani, and L. NDeli. 1990.Clinical trial of pefloxacin and ofloxacin in the treatment of lepromatous leprosy. Int. J. Lepr. Other Mycobact. Dis. 58:281–295. 5. Chan GP, Garcia-Ignacio BY, Chavez VE, Livelo JB, Jimenez CL,Parrilla ML, et al. Clinical trial of clarithromycin for lepromatous leprosy. Antimicrob Agents Chemother 1994;38:515-7. 6. Ji B, Jamet P, Perani EG, Sow S, Lienhardt C, Petinon C, et al.Bactericidal activity of single dose of clarithromycin plus minocycline,with or without ofloxacin, against Mycobacterium leprae in patients.Antimicrob Agents Chemother 1996;40:2137-41. 7. World Health Organization. Regional Office for South-East Asia. (2009). Report of the global programme managers' meeting on leprosy control strategy. WHO Regional Office for South-East Asia. https://apps.who.int/iris/handle/10665/206250
Hypothesis/ Research question (up to 100 words): Please provide details	Research Question: Is Monthly Rifampicin, Moxifloxacin and Clarithromycin as efficacious and safe as WHO MBMDT in patients affected by multibacillary leprosy?
Study Objectives (up to 25 words/ objective) Define the objectives clearly and in measurable terms; mention as primary and secondary objectives, if necessary. Do not include more than 3-4 objectives.	To determine the efficacy of monthly regimen of Rifampicin, Moxifloxacin and Clarithromycin (RMC) regimen as compared to WHO MBMDT. None None None

Methodology Include objective-wise work plan under the following sub-headings:

#	Study Design	Study Site	Methods (e.g. PICO)	Sample Size	Implementation Strategy	Statistical analysis	Ethical issues
1	It is an open label randomized clinical control non inferiority trial where in the intervention group monthly supervised regimen of Rifampicin, Moxifloxacin and Clarithromycin will be administered in doses of 600 mg, 400 mg, and 1000 mg respectively and the control arm would be given routine WHO MB MDT. The duration of the treatment in booth arms will be 12 months. The random sequence will be generated centrally which will be sent to study centers in opaque envelopes. After consent approved, the envelope will be opened, and patient put on respective arms. The study population will include newly diagnosed, previously untreated MB leprosy patients. Written informed consent will be sought from every subject included in the study. Slit Skin Smears of all the study subjects will be collected at 0-day, 6th, 12th month and	Four tertiary care hospitals from The Leprosy mission Trust India (TLMTI). They are TLM Purulia in West Bengal, TLM Chandkhuri, Chhattisgarh, TLM Shahdara, Delhi and TLM Barabanki, UP. Stanley Browne laboratory of TLMTI located at TLM Shahdara Hospital at Delhi.	Proposed study design It is an open label randomized clinical control non inferiority trial where in the intervention group monthly supervised regimen of Rifampicin, Moxifloxacin and Clarithromycin will be administered in doses of 600 mg, 400 mg, and 1000 mg respectively and the control arm would be given routine WHO MB MDT for 12 months. Research Participants Inclusion Criteria: Never treated, Age 15 and above patients with Multibacillary (MB) leprosy, defined as 5 or more skin lesions or extensive infiltration and /or diffuse skin involvement, classified as borderline tuberculoid, borderline lepromatous or polar lepromatous, as determined using Ridley and Jopling classification system. Exclusion Criteria: History of intolerance to one of the medications. Patients who are not able to come to the clinic every month during their treatment and during follow up. Patients who do not give informed consent or are not capable to give informed consent due to mental impairment. Immunocompromised patients diagnosed with HIV/AIDS and Tuberculosis. Sampling Strategy: Interventional clinical trial where Participants will be randomly allocated to one of the two study arms using randomization tables provided by the statistician, intervention model will be parallel assignment with no	Since there are no previous studies that gives the effectiveness of the new drug Rifampicin, Moxifloxacin and Clarithromycin (RMC) over the standard regimen WHO MBMDT. The sample size will be calculated based on the researcher's clinical experience. Treatment efficacy is measured basedon the reduction in the bacteriological lesions. The sample size needed to estimate the effectiveness of the new drug Rifampicin, Moxifloxacin and Clarithromycin (RMC) , with 80% to 95% reduction in the bacteriological lesions (BL) due to treatment. With alpha-error of 5%, power of 80% and Non-cooperation rate of 10%, and2-sided test was considered. With a risk difference 15% , the required sample size is 140 in each arm .	Data collection will be done at four tertiary care hospitals from The Leprosy mission Trust India (TLMTI). They are TLM Purulia in West Bengal, TLM Chandkhuri, Chhattisgarh, TLM Shahdara, Delhi and TLM Barabanki, UP. Molecular viability assays and resistance testing will be done the Stanley Browne laboratory of TLMTI located at TLM Shahdara Hospital at Delhi. Mouse foot pad analysis will be conducted at SIHR&LC, Karigiri, Vellore. A Trial Management Group (TMG) will be appointed and will be responsible for overseeing the progress of the study. The day-to-day management of the trial will be coordinated through the Study Coordination Centre.	The primary objectives of the statistical analyses are to evaluate the efficacy and safety of the trial drugs. The efficacy analysis will be conducted in the intent-to-treat population, safety analysis will be conducted in the safety population. The independent t test or Mann-Whitney test will be used to compare the outcome between study arms.	Participants will be recruited from TLMTI hospitals, 4 TLM hospitals from Purulia, West Bengal, Chandkhuri, Chattisgarh, Shahdara, Delhi and Barabanki, UP. Informed written consent for participation following the ethical guidelines of the Indian council of Medical Research (ICMR) and the Institutional Ethical Committee of TLMTI, will be sought from all the participants enrolled in the study. All correspondence with ethics committees will be filed at TLMTI by the trial management team in the trial management file. Annual progress reports and notification of end of study will be submitted to all the ethics committees who have granted approval for the study.

Methodology Include objective-wise work plan under the following sub-headings:

#	Study Design	Study Site	Methods (e.g. PICO)	Sample Size	Implementation Strategy	Statistical analysis	Ethical issues
	SBL. Real Time PCR will be done to quantitate copy numbers of the genes encoding 16S rRNA, hsp18 and exsA specific for M. leprae. Resistance studies will be carried out at 12 months in patients harbouring viable bacilli. Validation of M. leprae growth in mouse foot pad will be performed on participants showing viable load by molecular method at the time of RFT in Schieffelin Institute of Health – Research and Leprosy Centre Karigiri (SIHR&LC), Vellore.		primary purpose of treatment. One arm will receive routine WHOMB MDT, and the other arm will receive the RMC (Rifampicin, Moxifloxacin and Clarithromycin) regimen, Purposive sampling for the qualitative aspect of the trial - Participants who both have consented for follow up and who are (a) trending to positive change on the outcome measures AND (b) trending to no change (or negative change on the outcome measures). Sampling these groups across the 2 intervention arms. Therapy Regimen: Arm 1 - WHO MB MDT containing Rifampicin 600 mg, Clofazimine 300 mg once monthly and Clofazimine 50 and Dapsone 100 mg daily x 12 months. Arm 2 - Once a Month supervised regimen containing Rifampicin 600 mg, Moxifloxacin 400 mg, Clarithromycin 1000 mg for 12 months.				
2	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3	N/A	N/A	N/A	N/A	N/A	N/A	N/A
4	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Expected outcome/ Deliverables aligned with research question (up to 100 words):	Primary efficacy outcomes: 1. Molecular I. Reduction of copy numbers by MVA II. Complete killing of M. leprae as demonstrated in MFP. 2. Clinical I. Complete clinical cure, defined as full regression of the lesions. II. Clinical improvement of the lesions defined by a clinical criterion 3. Pathological I. Bacillary index (BI) improvement II. Improved biopsy findings Secondary Efficacy outcomes include: 1. Immunological outcomes Neuritis - if participants reported pain during the interview or when Nerve function impairment is detected on routine test. Type I reaction Type 2 reaction – Incidence and improvement in severity score between the 2 regimes. 2. Safety outcomes Severe side effects (defined as a side effect that forced the patient to stop the treatment), mild to moderate side effects. 3. Qualitative outcomes Impact of leprosy treatment on life Perspective towards leprosy treatment Cost of treatment
Future plan based on expected outcomes	Studies on efficacy of the new drug on immunological reactions and relapses will be undertaken in subsequent studies.
Whether the study is going to generate new intellectual property	None
Timelines with	View

Proposal Details PART-B

Preliminary work done by the PI including the source of funding (up to 250 words):	The PI has undertaken a multicentric clinical trial of azathioprine vs prednisolone in type 1 reactions and neuritis funded by the Welcome trust and partnered with London School of Tropical hygiene and medicine. She is the PI of a current Trial of methotrexate vs prednisolone in type 2 reactions in leprosy.
Skill and experience of the research team Highlight only salient points (along with 5 relevant publications) that provides confidence to reviewers that team can implement the project with quality.	The research team has implemented multiple clinical studies including trials .They have won proposal grants in competitive call for grants , with appropriate registration in ethics board and CTRI. Data is collected on Redcap and all research staff have Good clinical practice certification. Training in data management and ethical principles are mandatory. The hospitals have well equipped lab and impaging facilities with quality medical and surgical and dermatological expertise that can manage adverse events if any. A robust monitoring system is in place with monthly monitoring meetings and face to face mid year and annual reviews for all research projects in the organization. Lockwood DN, Darlong J, Govindharaj P, Kurian R, Sundarrao P, John AS. AZALEP a randomized controlled trial of azathioprine to treat leprosy nerve damage and Type 1 reactions in India: Main findings. PLoS Negl Trop Dis. 2017 Mar 30;11(3):e0005348. doi: 10.1371/journal.pntd.0005348. PMID: 28358815; PMCID: PMC5373510. de Barros B, Lambert SM, Shah M, Pai VV, Darlong J, Rozario BJ, Alinda MD, Sales AM, Doni S, Hagge DA, Shrestha D, Listiawan MY, Yitaye AM, Nery JAC, Neupane KD, Dias VLA, Butlin CR, Nicholls PG, Lockwood D, Walker SL. Methotrexate and prednisolone study in erythema nodosum leprosum (MaPs in ENL) protocol: a double-blind randomised clinical trial. BMJ Open. 2020 Nov 17;10(11):e037700. doi: 10.1136/bmjopen-2020-037700. PMID: 33203627; PMCID: PMC7674097. Walker, S. L., Balagon, M., Darlong, J., Doni, S. N., Hagge, D. A., Halwai, V., ... & Erythema Nodosum Leprosum International STudy Group. (2015). ENLIST 1: an international multi-centre cross-sectional study of the clinical features of erythema nodosum leprosum. PLoS neglected tropical diseases, 9(9), e0004065. Lavania M, Darlong J, Reddy A, Ahuja M, Singh I, Turankar RP, Sengupta U. Successful treatment of rifampicin resistant case of leprosy by WHO recommended ofloxacin and minocycline regimen. Leprosy Review. 2019 Dec 1;90(4):456-9. Lavania M, Singh I, Turankar RP, Ahuja M, Pathak V, Sengupta U, Das L, Kumar A, Darlong J, Nathan R, Maseey A. Molecular detection of multidrug-resistant Mycobacterium leprae from Indian leprosy patients. Journal of global antimicrobial resistance. 2018 Mar 1;12:214-9.
Institutional Support/ Facilities	The activities planned in the study will be conducted at the leprosy mission trust india. There are 14 tertiary care hospitals for leprosy and 4 high burden centres have been chosen to enable timely recruitment and data collection. The Staley Browne lab is the research laboratory with accreditation from the DSIR and has held many ICMR grants including 2 currently. There is a robust system of sample flow from hospitals to the lab for early diagnostic studies and antimicrobial resistance. Reporting is done online and hard copy is posted to the respective centres. There is a whatsapp group of doctors as a community of practice that discusses complicated case management. Each medical officer undergoes a 5 day training program to manage leprosy at The training unit at Naini , Prayagraj ensuring the protocols and management details are learnt by the doctors. The hospitals have lab , physio , counselling , pharmacy , footwear , aids and appliance departments to facilitatae any clinical study.
Laboratory facilities (in-vitro/ in-silico) Institutional resources such as instruments/ equipment and other physical resources available for use in the project proposed animal house etc.	Laboratory is equipped with Biosafety Level cabinets, Tissue culture facility, Qubit, Spectrophotometer, PCR, Real time PCR, Thermocyclers, Deep freezers (-20 and -80), Incubators (Shaking as well), CO2 incubator, Western blotting, SDS PAGE electrophoresis, 2-D gel electrophoresis, Agarose Gel electrophoresis, ELISA Readers, Chemi-Doc as well as other small centrifuges, refrigerators etc.
Conflict of Interest declaration (if any)	None
Duration (in Months)	36 Months

Investigator Details

#	Name	Institute	Designation	Email	Contact No.	Role in Proposal
1	Dr Joydeepa Darlong	The Leprosy Mission Hospital	Head	joydeepa.darlong@leprosymission.in	9434885198	PI
2	Dr Itu Singh	The Leprosy Mission Hospital	Head	itusingh@gmail.com	9717730549	Co-PI
3	Dr Reeta Devi	The Leprosy Mission Hospital	Consultant	rits2gmc@gmail.com	6006203600	Co-PI

Documents consideration

#	Document Name	Uploaded Document	Remarks	Action
1	Revised Budget	View	We have 4 research sites – each site contributing 70 trial participants to be recruited in 12 months . We have budgeted for 3 RA's for 3 sites and the SRF who is the trial coordinator will execute the functions of the RA for 4th site as well as coordinator for all 3 sites. It is very difficult to reduce the number of RA's from any one site – otherwise the implementation of the trial will be stagnated or compromised. Unless one designated staff is present per trial site, quality implementation will be compromised. Hence, we are requesting the budget remain the same.	
2	Declaration & Attestation Form(duly signed by Head of Department/ Director)	View	Declaration form	
3	Additional supplementary information including figures tables flow diagrams etc can be shared as PDF (20-30 KB)	View	Flow diagram of the study	
4	Declaration & Attestation Form(duly signed by Head of Department/ Director)		Declaration	
5	Additional supplementary information including figures tables flow diagrams etc can be shared as PDF (20-30 KB)		work flow	

Budget Details

Year	Institute Name	Manpower	Contingency	Equipment	Travel	Overhead Charges	Total Budget (Rs.)
Year: 1	The Leprosy Mission Hospital	2,378,520.00	770,000.00	0.00	100,000.00	83,340.00	3,331,860.00
Year: 2	The Leprosy Mission Hospital	2,378,520.00	1,570,000.00	0.00	100,000.00	107,340.00	4,155,860.00

Budget Breakup Details (Staff/Manpower)

#	Budget Year	Institute	Designation	No. of Person(nos)	Require Month(nos)	Cost Per Person(Rs.)	Total Cost(Rs.)
1	Year: 1	The Leprosy Mission Hospital	Senior Research Fellow	1	12	44,450	533,400.00
2	Year: 1	The Leprosy Mission Hospital	Project Assistant	4	12	38,440	1,845,120.00
3	Year: 2	The Leprosy Mission Hospital	Senior Research Fellow	1	12	533,400	533,400.00
4	Year: 2	The Leprosy Mission Hospital	Project Assistant	4	12	38,440	1,845,120.00
						Total (Rs.):	**4,757,040.00**

Budget Breakup Details (Contingency)

#	Budget Year	Institute	Contingency Name	Total Cost(Rs.)	Justification
1	Year: 1	The Leprosy Mission Hospital	Mouse Foot Pad test	30,000.00	Mouse foot pad: Gold standard method to find out the viability of M. leprae
2	Year: 1	The Leprosy Mission Hospital	Histopathology	30,000.00	Histopathology: Sections of the skin biopsies will be examined by hematoxylin and eosin (H&E) staining and modified Fite-Faraco technique for M.leprae.
3	Year: 1	The Leprosy Mission Hospital	Real Time PCR test	100,000.00	Real Time PCR reagents: To quantify viable M. leprae.
4	Year: 1	The Leprosy Mission Hospital	Blood test	500,000.00	Blood test will be done for all the study subjects for the study duration.
5	Year: 1	The Leprosy Mission Hospital	Drugs cost	90,000.00	Rifampicin, Clarithromycin and Moxifloxacin for all the study subjects
6	Year: 1	The Leprosy Mission Hospital	Sample collection from TLMTI	20,000.00	Sample collection: RNAlater in which RNA can be stabilized and transported at room temperature from field.
7	Year: 2	The Leprosy Mission Hospital	Drugs cost	82,680.00	Rifampicin, Clarithromycin and Moxifloxacin for all the study subjects
8	Year: 2	The Leprosy Mission Hospital	Sample collection from TLMTI	20,000.00	Sample collection: RNAlater in which RNA can be stabilized and transported at room temperature from field.
			Total (Rs.):	**872,680.00**	

Budget Breakup Details (Equipment)

#	Budget Year	Institute	Equipment Name	Equipment Model	Equipment Manufacturer	Equipment Type	Total Cost(Rs.)	Justification
No Record								

Declaration

I hereby declare that the entries in this form and the additional particulars, if any, furnished herewith are true to the best of my knowledge and belief. I understand that in the event of my information being found false or incorrect at any stage, my project/proposal shall be liable to cancelation / termination without notice or any compensation in lieu thereof.