WORK PLAN AND METHODOLOGY:

A flow of work would be in following direction:

1. Literature review
   Literature search for related information will be a continuous process from starting till the finalization of the research activity. The sources would be Books, Standards references like IP, USP, Ph.Eur, BP, WHO guidelines etc., Journals including National and International, Patent applications and published patent and Internet.

2. Design of strategy & Intellectual Property Clearance
   Based on the literature search, all the available related formulation designs will be critically studied and will be designed out of scope generic economic modified release formulation having defined therapeutic benefit to the targeted patients.

3. Procurement of actives, raw material, Packaging Material
   Reliable sources for all the raw materials, active pharmaceutical ingredients (API) and packaging materials will be identified to get Pharmacopoeial standard materials and will be store in the proper temperature and humidity condition maintained storage area.

4. Preformulation studies
   Preformulation studies will be planned with an intention to get the critical information about the API, Raw materials characteristics and their interaction at stress condition. This experiment is planned to predict the stability of the product on long-term storage condition in real time situation.

5. Development of analytical methods
   Quality of the finished product is always depends on the accurate, precise and stability indicating analytical test method for that product. So, at the initial stages of formulation development, all the required critical analytical test methods such as Assay, Related substances and Biorelevant multimedia dissolution and quality control (QC) dissolution test methods will be developed.
6. **Formulation development trials (Bench scale development)**

Based on the Intellectual Property Clearance, various out of scope formulation design strategy will be planned. Then formulation development trials will be taken as per the design plan and fine adjustment of the composition will be done based on the dissolution test results.

7. **In-vitro dissolution studies**

Developed formulations will be screened in Biorelevant multimedia dissolution condition and final formulation will be tested in QC dissolution condition initially and during complete stability analysis.

8. **Optimization trials (Lab-scale development)**

Based on the initial formulation development trials and their evaluation, qualitative formulation composition will be selected. Final qualitative and quantitative formula composition and manufacturing process will be decided based on the optimization trial results.

9. **Reproducibility trials**

Reproducible batch will be taken with final qualitative and quantitative composition and will evaluate them to check the consistency of the result with previous batches having same qualitative and quantitative composition.

10. **Stability studies & Packaging evaluation**

Initially bench scale development batches with two different packaging systems will be kept in accelerated stability condition (40°C/75%RH) for 3 months to find out stable composition and suitable packaging systems.

11. **Scale up & Process evaluation**

Best stable composition will be scale-up to 10 times than the lab-scale batches with an intention to set-up the tentative process parameter at bigger scale to get the product of desired quality. Process evaluation batches will be taken to check the effect of various process parameters at each stage of product development. So, that the operating range of the process will be finalize to get final product with desired quality.
12. In-vivo Pharmacokinetic studies

Finally, after getting satisfactory in-vitro analytical results of final scale-up batch with 1 month accelerated stability data, an in-vivo bioavailability study of single unit modified release drug delivery system of topiramate with two immediate release dosage form of topiramate (Topamax capsule) will be planned with an intention to check the therapeutic benefit of the modified release dosage form of the topiramate.

Proposed Technologies for formulation development:

1. Modified Release Pellets by extended release coated bead:

*NPS: Non pareil seeds*
2. Modified Release Pellets by Immediate release and Extended release coated bead:

MCC/Sugar pellets → Drug layering → ER Coating → Drug Layering

pellets in Capsule Coating

MCC pellets
Drug layering
ER Coating
Drug layering
Moisture Barrier coating