Artificial lipidic membranes are considered as the part of liposomes that influence their behavior, their biophysical and thermodynamic properties and consequently the therapeutic outcome of the encapsulated drug. It is of interest to shed special attention in the metastable phases of artificial lipidic based nanomedicines such as liposomal membranes as well to their physicochemical changes. The quantitative measurements of these changes need a more reliable and realistic strategic research. This could be an emerged approach for disclosing the smartness of the artificial liposomal membrane behavior. Taking into account the importance of the state of matter (i.e. liquid crystalline state) of the liposomal membrane and the sub transitions over the main transition from the gel to crystalline phase, it is obvious that the changes from one phase to another could be adapted to its masked biophysical and thermodynamic behavior. Thermal and biophysical analysis are promising tools that can identify their thermotropic and biophysical behavior. By using the recently emerged thermodynamic theories, such as Hill's theory on *thermodynamics of small systems* and by re-defining the limits of the so called 'size' of a liposomal membrane, we are obliged to use nanothermodynamics for better approaching strange phenomena that are occurred in the interfacial area between liposomal membranes with their surroundings. Studies that determine the interactions between liposomal membrane surfaces as well as their interactions with the biological elements (proteins, metals etc) can be conducted by using thermal analysis techniques. The grade of curvature and the hydration forces that are taken place on the liposomal membrane surface are major partners that affect the properties of membrane and produce difficulties for creating similar to prototype liposomal membranes. The regulatory issues concerning the design and the development of liposomal nanomedicines involve a combination of valuable techniques and the complexity of liposomal membranes, need more and precise studies by using nanothermodynamics and stimulation as Monte Carlo and quantum mechanisms, in order to overcome the classical thermodynamics limitations, and to rational design nanosimilars.