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Nanotechnologies — Vocabulary — Liposomes

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Foreword

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This document was prepared by Technical Committee TC 229, *Nanotechnologies*.

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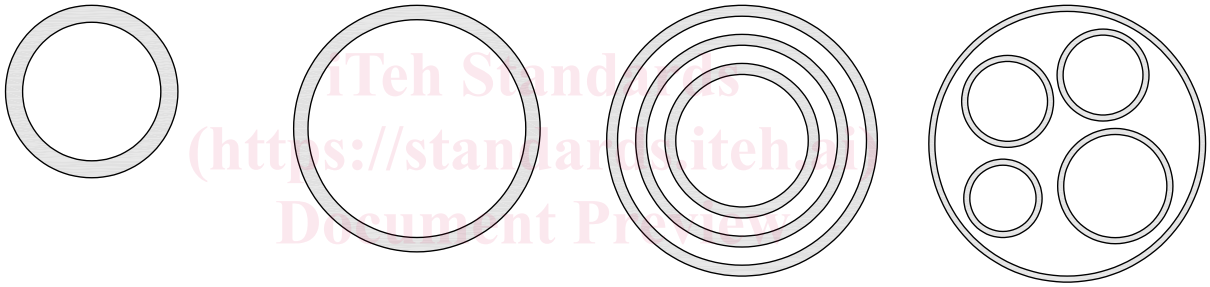
Introduction

Lipid-based nanomaterials represent an important class of carriers for the in vivo transport and delivery of active pharmaceutical ingredients (APIs). By encapsulating the API inside a lipid-based structure, payloads can be protected from degradation while potent APIs can be delivered with reduced adverse physiological effects. These lipid-based carriers are carefully formulated to achieve specific properties and are generally well tolerated and biocompatible.

Lipid particles include different structural forms or subclasses that can be differentiated by structure, composition and chemistry (e.g. liposomes, solid lipid nanoparticles). The first lipid-based nanomaterial product to obtain regulatory approval in the US and EU was liposomal doxorubicin, approved in 1995 in the US for the treatment of ovarian cancer and AIDS-related Kaposi sarcoma. More recently, cationic lipid-containing nanoparticles complexed with mRNA were formulated as highly effective vaccines against the coronavirus SARS-CoV-2. This document aims to standardize the terminology associated with the most studied and mature form of lipid-based carriers, namely liposomes.

Liposomes are synthetic vesicles composed of a single bilayer (most common form for drug delivery) or of multiple concentric or non-concentric bilayers separated by aqueous compartments. Figure 1 schematically illustrates these basic structural forms of liposome as used within a biomedical context. An example of pharmaceutical relevance (e.g. a drug product) is provided for each vesicle form defined in 3.2.



a) Small unilamellar vesicle ≤100 nm | **b) Large unilamellar vesicle >100 nm** | **c) Multilamellar vesicle ≥500 nm** | **d) Multivesicular liposome >1 000 nm**

NOTE Images are not drawn to scale.

SOURCE Scientific Publications, Graphics and Media, Frederick National Laboratory for Cancer Research.

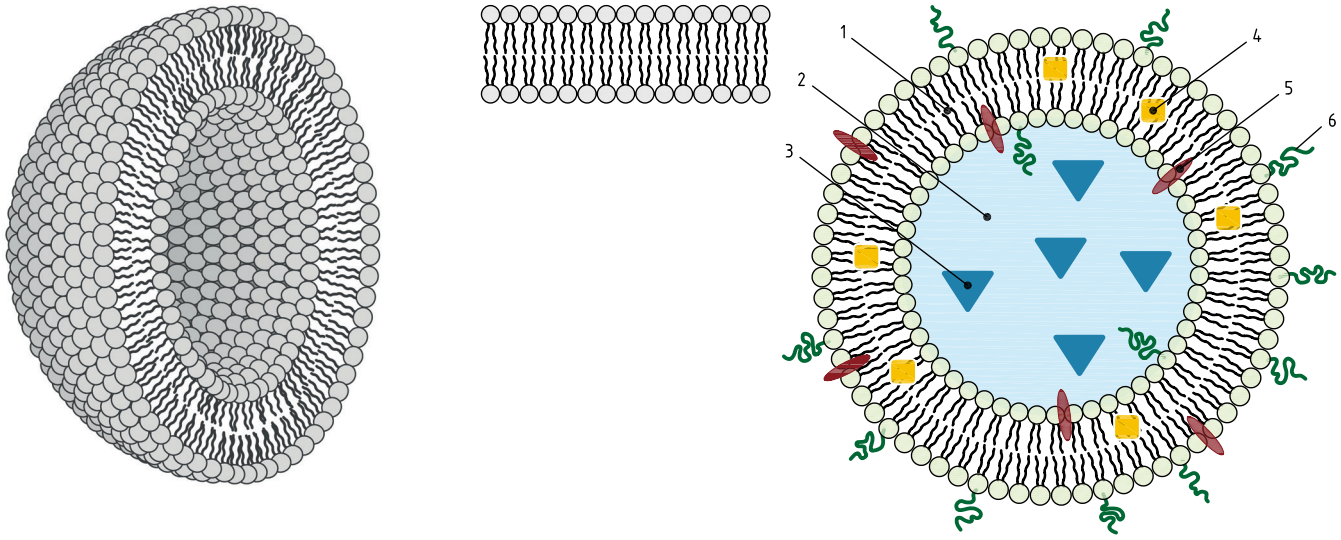
Figure 1 — Schematic illustration showing lamellar structure of different vesicle types

The bilayers are formed by amphipathic molecules, primarily phospholipids, but can include other molecular components necessary for membrane integrity (e.g. cholesterol) or avoidance of opsonization and reticuloendothelial clearance [e.g. polyethylene glycol (PEG)].

The size of liposomes can range from approximately 20 nm to over 1 000 nm, though therapeutic delivery most commonly involves particles in the 50 nm to 200 nm diameter range. Therefore, while not all liposomes are nano-objects as defined in this document, all liposomes consist of bilayers of nanoscale thickness and are therefore generally considered both nanomaterials and nanostructured materials.

Figure 2 depict a 3D cross-sectional perspective of an idealized unilamellar liposome, a lipid bilayer and a liposomal drug formulation showing the location of compartments and APIs.

Figure 3 illustrates the three principal structural phases associated with lipid bilayers. These phases are principally dependent on composition and temperature, but other factors such as pH can also play a role.



a) 3D hemispherical view **b) Cross-section of bilayer segment** **c) Liposome cross-section showing bilayer with details**

Key

1 hydrophobic compartment (lipid bilayer)
2 hydrophilic compartment (aqueous phase core)
3 hydrophilic active pharmaceutical ingredient (API)
4 hydrophobic API
5 amphiphilic API
6 polyethylene glycol (PEG)

NOTE 1 Images are not drawn to scale.

NOTE 2 In Figure 2 b), polar headgroups are shown in green and hydrophobic tails are shown in black.

SOURCE Scientific Publications, Graphics and Media, Frederick National Laboratory for Cancer Research.

Figure 2 — Idealized unilamellar liposome showing phospholipid bilayer structure, internal compartments and representative details