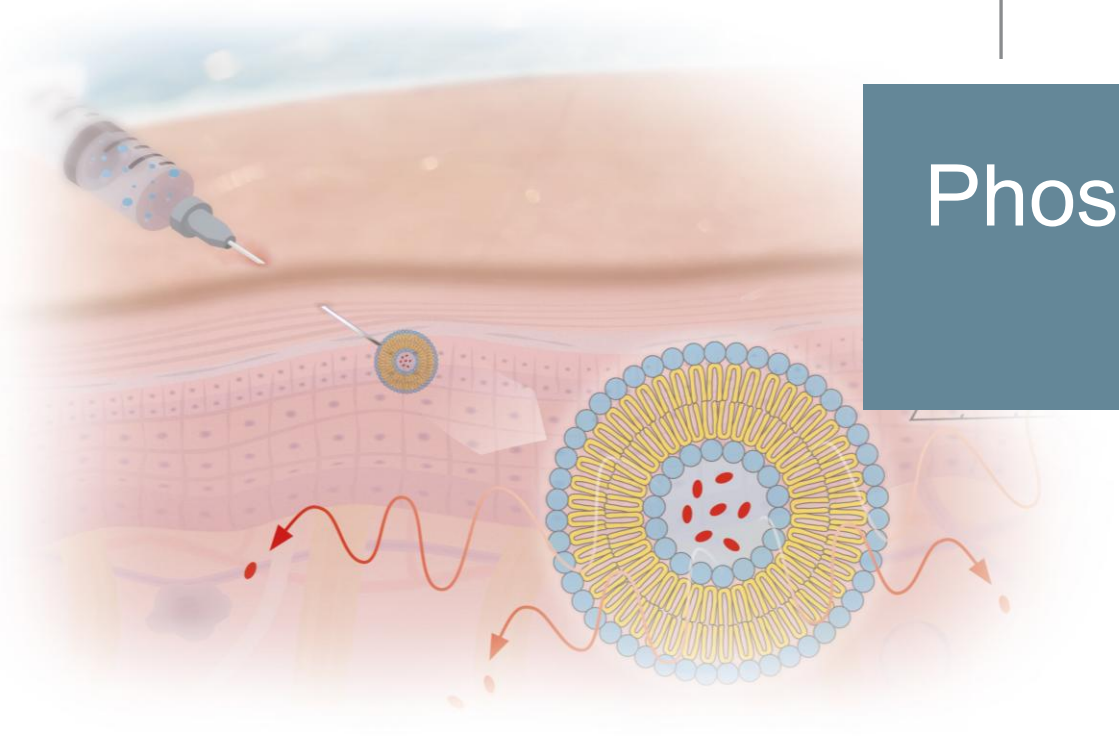
Lipoid

CRS Annual Meeting
PRC Workshop
Philadelphia, 10 August 2026

Dr. Michael Kahn
Lipoid, Inc.



Phospholipids in Parenteral Applications

We Invest in Quality.

LIPOID AT A GLANCE

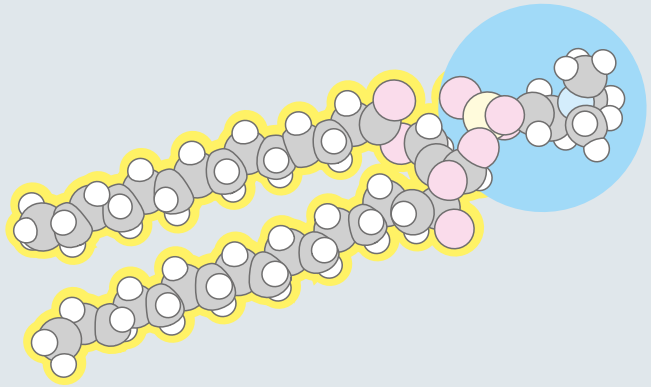
Lipoid

- World market leader in the field of phospholipids for pharmaceutical applications
- Expertise in phospholipids in the industrial benchmark since 1977
- Comprehensive portfolio
- 4 independent production sites
- Global presence and distribution network
- About 500 employees
- GMP & ISO certified
- US FDA audited (“no findings”)
- DMFs for many products
- Reference standards

PHOSPHOLIPID FUNDAMENTALS

Characteristics and Appearance

- Amphiphilic molecules
- Surface-active compounds with characteristic self-assemblies
- Available from natural and synthetic sources



Phospholipids fulfill essential physiological functions:

- Building block of cell membranes and organelles
- Building block of lipoproteins
- Part of the digestion process
- Mucosal lining
- Source of choline and fatty acids

PHOSPHOLIPID FUNDAMENTALS

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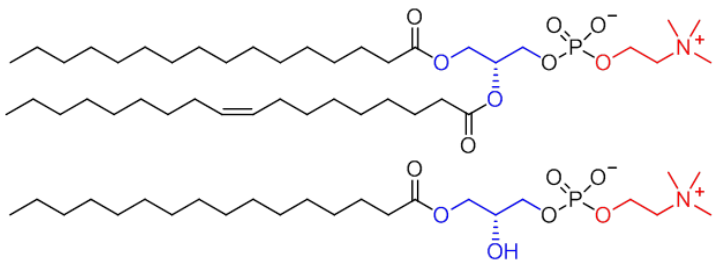
Structures:

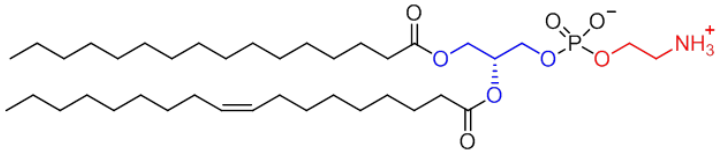
Phosphatidylcholine (PC)

Monoacyl PC (LPC)



Zwitterionic
at physiological pH

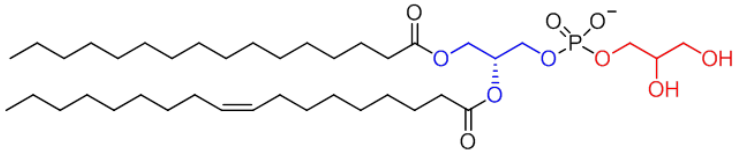
Phosphatidylethanolamine (PE)



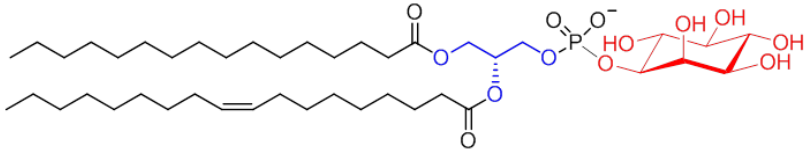
Zwitterionic
at physiological pH

Negatively charged
at basic pH

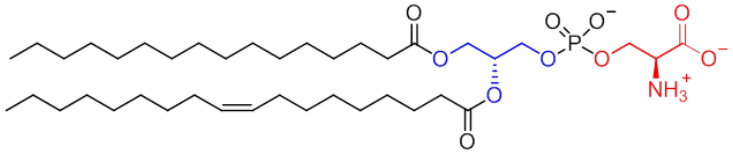
Phosphatidylglycerol (PG)



Phosphatidylinositol (PI)



Phosphatidylserine (PS)



Negatively charged
at physiological pH

INJECTABLE DEPOTS

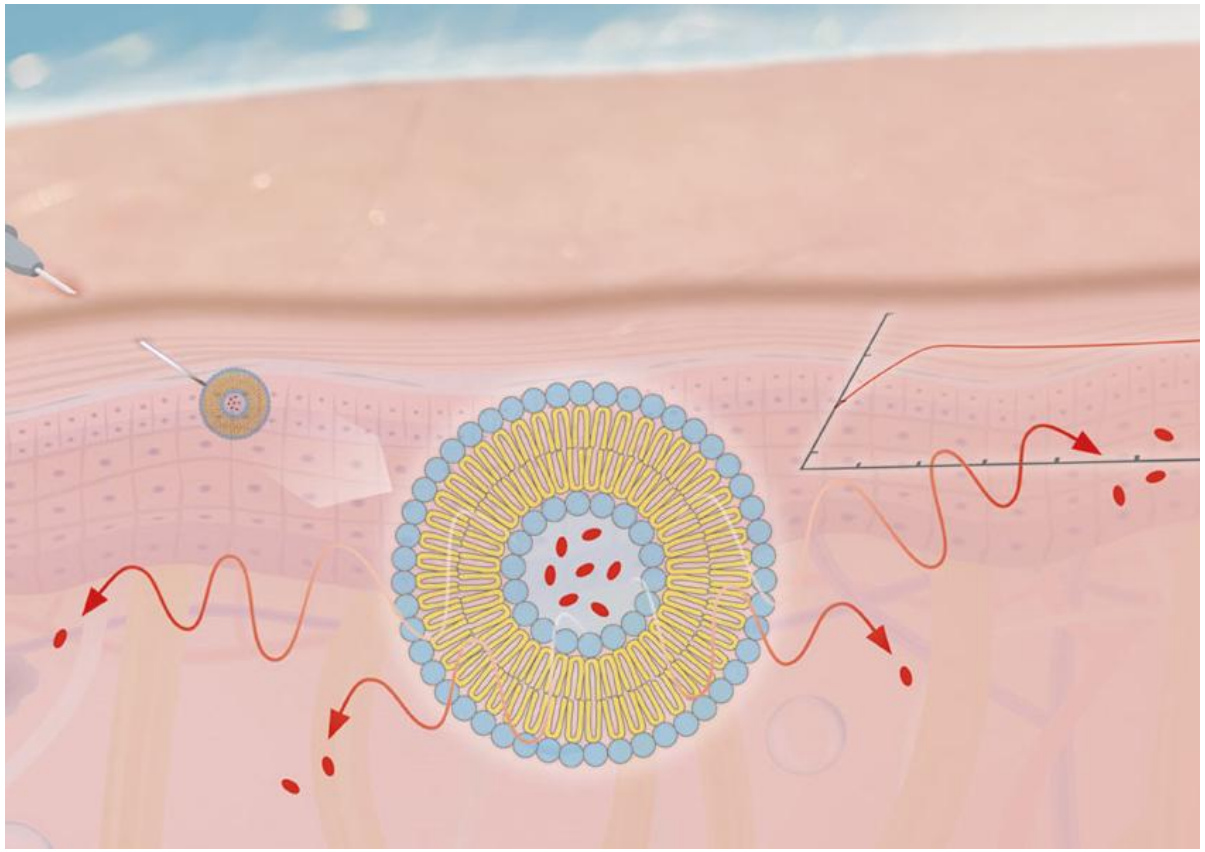
Benefits and Applications

Benefits

- Reduced administration frequency
- Stable plasma levels
- Improved patient compliance

Applications

- Psychological disorders
- Hormonal contraceptives
- Diabetes management
- Chronic pain management
- Oncology
- Pediatric growth disorders



PHOSPHOLIPID-BASED DEPOTS

Lipoid

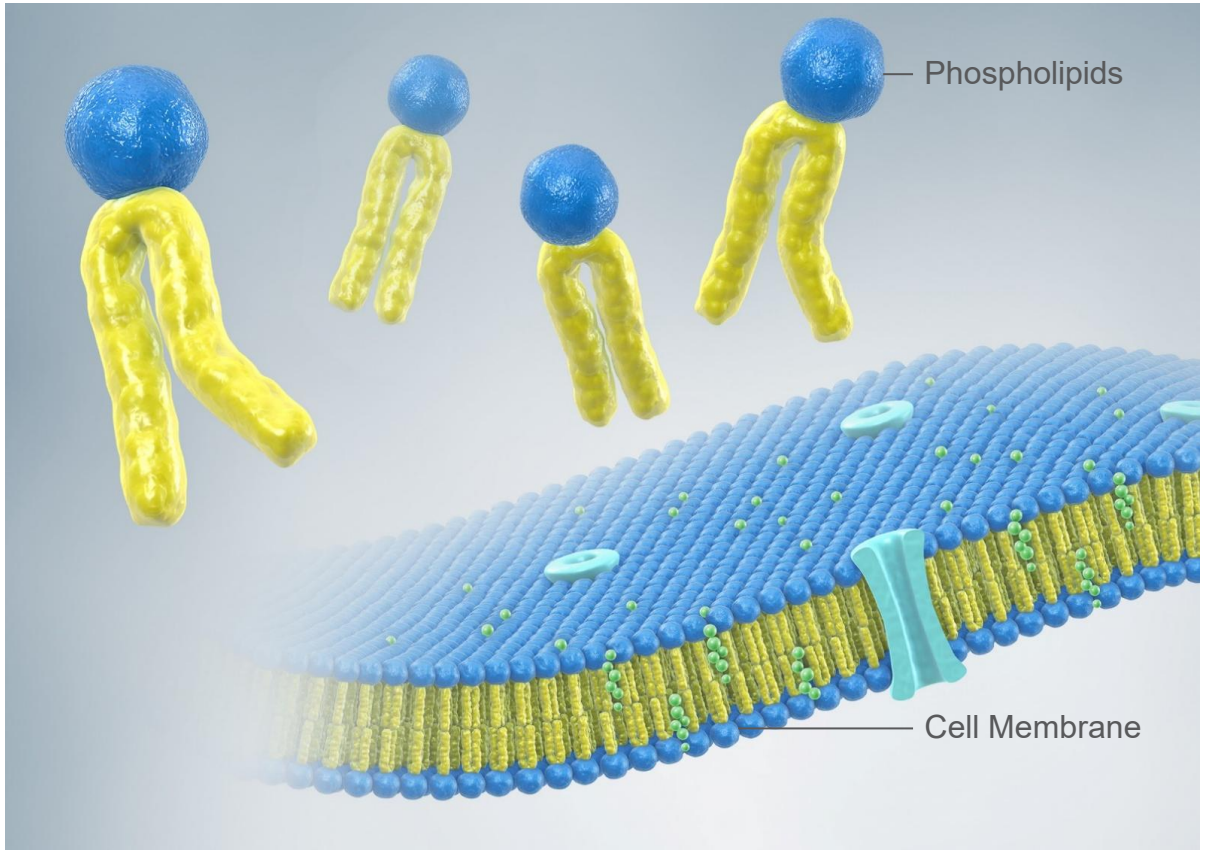
Challenges and Solutions

Challenges

- Compatibility and degradability of depot matrix and its degradation products
- Realization of appropriate release periods for drug and indication

Key advantages of phospholipids

- Tissue-friendly and no harmful degradation products
- Suitable for any administration route
- Compatible with hydrophilic and lipophilic drugs
- Diverse formulation options (in situ, preformed solid, preformed semisolid)
- Extended drug release from hours up to several weeks



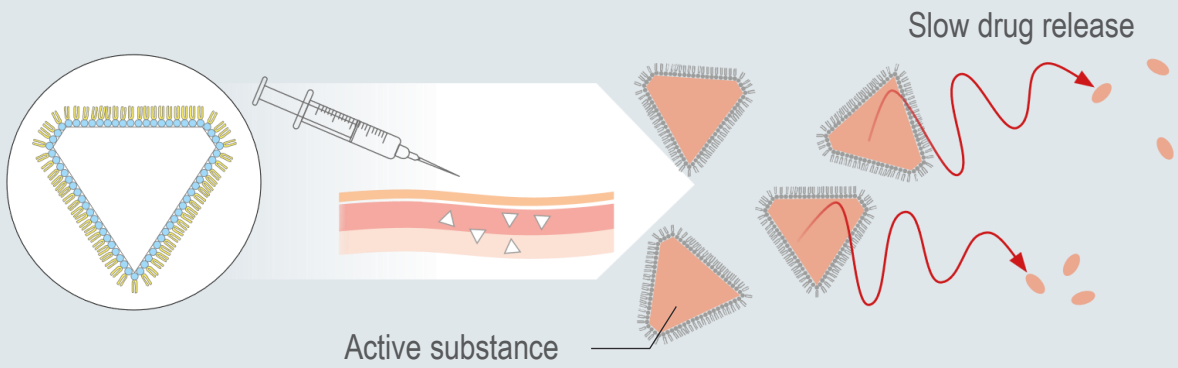
PHOSPHOLIPID-BASED DEPOTS

Lipoid

Technologies – Suspension

Project/Product	Drug Substance	(Phospho-)Lipid	Administration Route	Indication	Company
Pendysin®, Tardocillin®	Benzylpenicillin benzathine	**Soybean phospholipids**	Intramuscular	Bacterial infections	InfectoPharm

Drug Suspension



Duration of action › Days to weeks

Applied APIs › Benzylpenicillin benzathine

PHOSPHOLIPID-BASED DEPOTS

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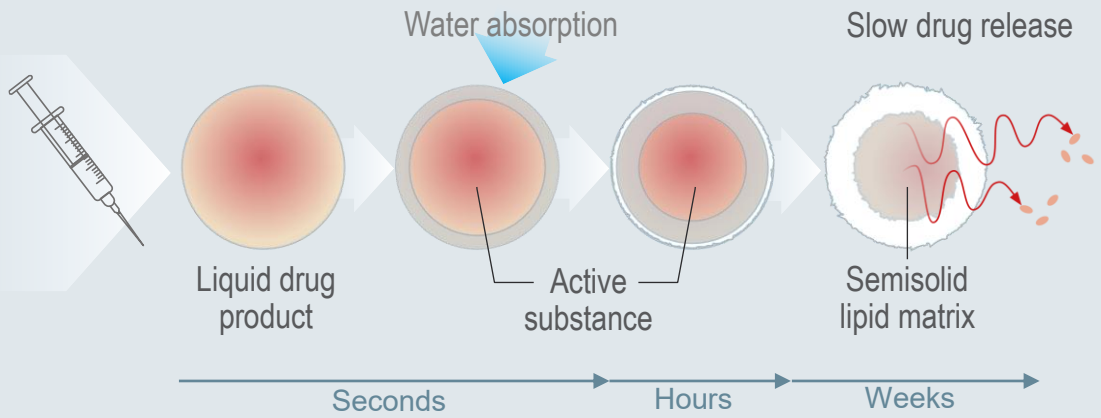
Technologies – *In situ* Formed Depot

Project/Product	Drug Substance	(Phospho-)Lipid	Administration Route	Indication	Company
Buvidal® Brixadi™	Buprenorphine	**Soybean PC**, glycerol dioleate	Subcutaneous	Opioid addiction	Camurus Braeburn

In situ Formed Depot



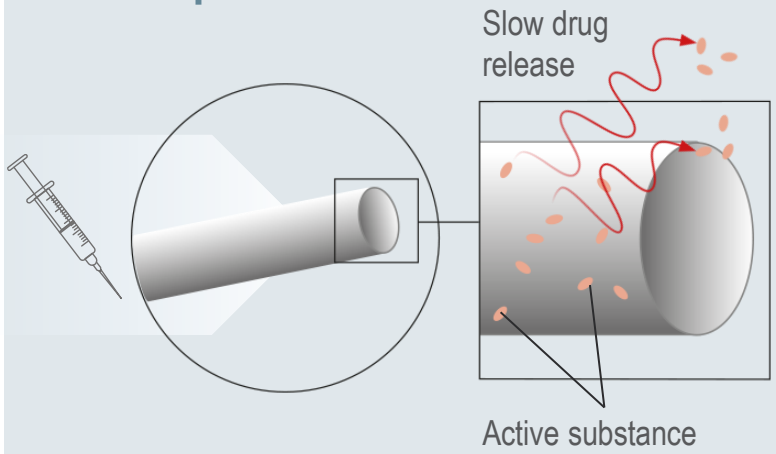
Duration of action
- Weeks to months

Applied APIs
- Buprenorphine
- Minocycline
- Doxorubicin, docetaxel
- Octreotide, setmelanotide
- siRNA

PHOSPHOLIPID-BASED DEPOTS

Explorative Formulations

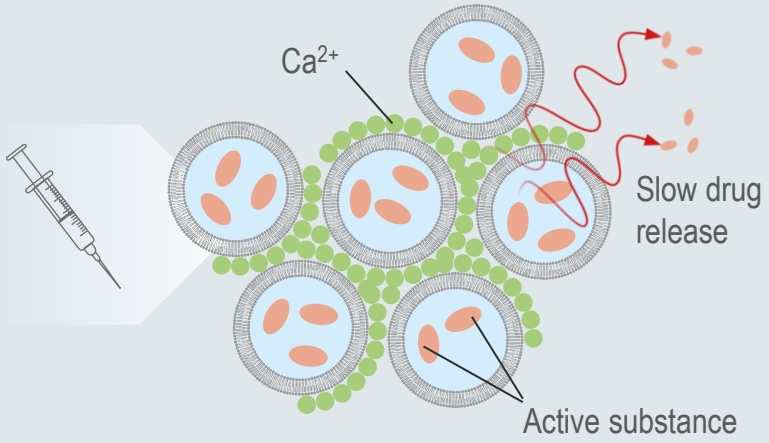
Solid Implant



Duration of action
› Days to weeks

Applied APIs
› Nicardipine

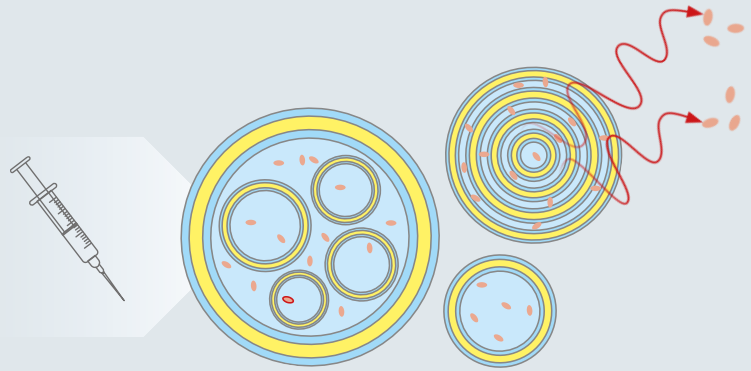
In situ Aggregating Liposomes



Duration of action
› Days

Applied APIs
› Flurbiprofen

Vesicular Phospholipid Gels



Duration of action
› Days to weeks

Applied APIs
› Interferon-beta-1b, exenatide, G-CSF

PHOSPHOLIPID-BASED DEPOTS

Lipoid

Approved Products

Project/Product	Drug Substance	(Phospho-)Lipid	Administration Route	Indication	Company
Pendysin®, Tardocillin®	Benzylpenicillin benzathine	**Soybean phospholipids**	Intramuscular	Bacterial infections	InfectoPharm
Buvidal® Brixadi™	Buprenorphine	**Soybean PC**, glyceroldioleate	Subcutaneous	Opioid addiction	Camurus Braeburn
Exparel®	Bupivacaine	**DEPC, DPPG**, tricaprylin	At surgical site	Postsurgical analgesia	Pacira Pharmaceuticals
MagicTouch	Sirolimus	**Egg phospholipids**	Stent inserted along with balloon catheter	In-stent restenosis, small vessels, bifurcation lesions and *de-novo* lesions	Concept Medical

PHOSPHOLIPIDS FOR INJECTABLE DEPOTS

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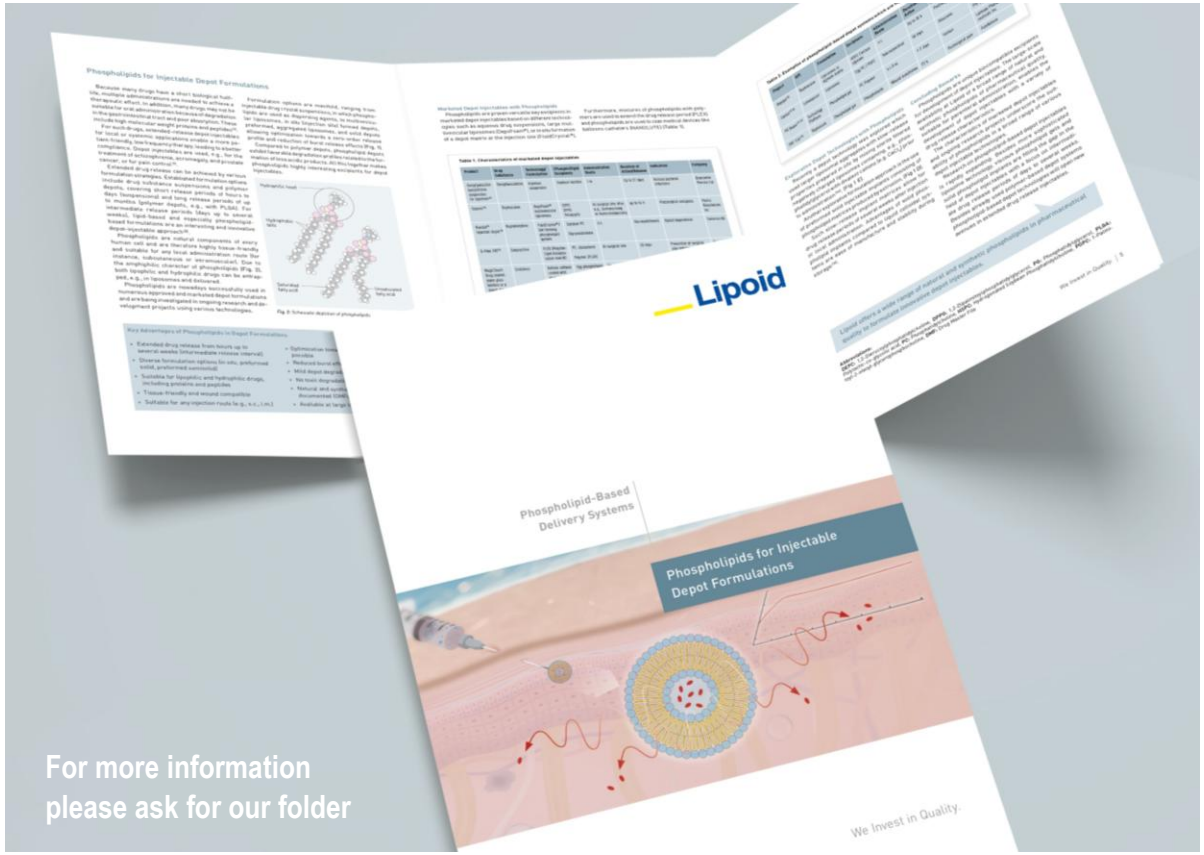
Summary and Conclusion

- Phospholipids are **natural, well-tolerated materials** with **physiological degradation** pathways
- Phospholipids offer **versatile formulation options** covering release periods from hours up to several weeks
- Phospholipids are key ingredients of marketed and R&D depot systems
- Phospholipids are **fully documented** and provide **compendial compliance**

Phospholipids are ideal excipients to formulate innovative depot injectables.



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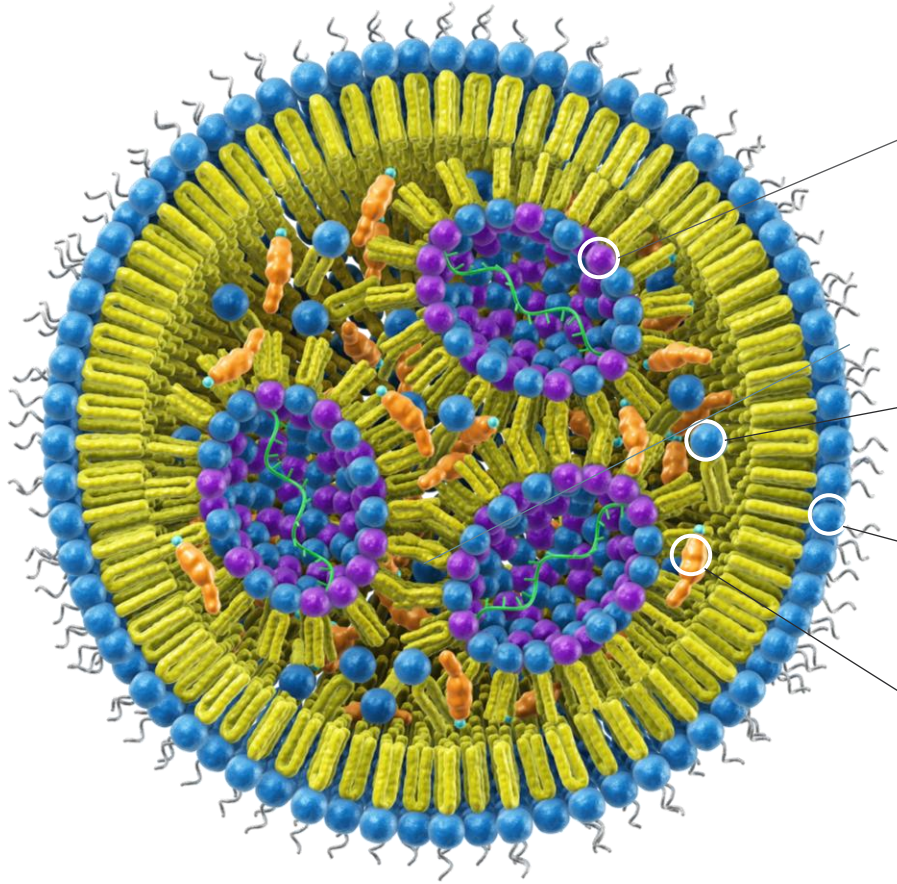
Role of Excipients



Ionizable Cationic Lipid

- Complexes & protects RNA
- Facilitates endosomal escape
- Neutral charge at pH 7.4
- Positive charge at pH 4

Phospholipid

- Essential structural component
- Stabilization

PEG-ylated lipids

- Stabilization
- Protection from opsonization

Cholesterol

- Stabilization

Voight, E. *et al.* A self-amplifying RNA vaccine against COVID-19 with long-term room-temperature stability, npj Vaccines (2022)

mRNA-LNP COVID-19 VACCINES

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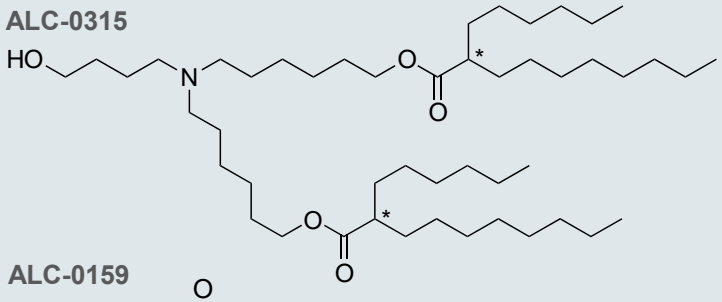
Excipients and Composition

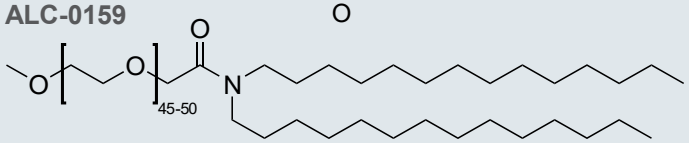
Comirnaty® of Biontech/Pfizer

ALC-0315



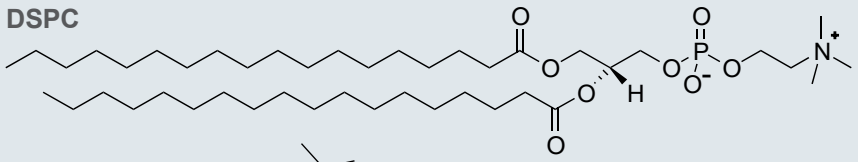
0.43 mg / dose

ALC-0159



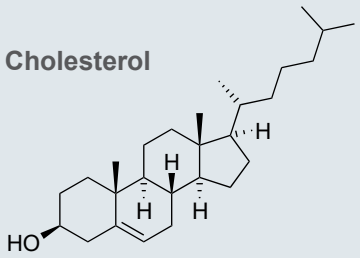
0.05 mg / dose

DSPC



0.09 mg / dose

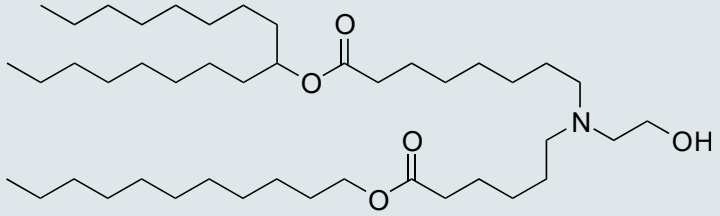
Cholesterol



0.2 mg / dose

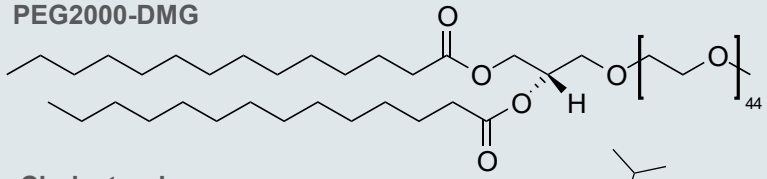
Spikevax® of Moderna

SM-102



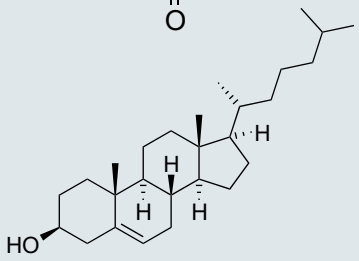
1.09 mg / dose

PEG2000-DMG



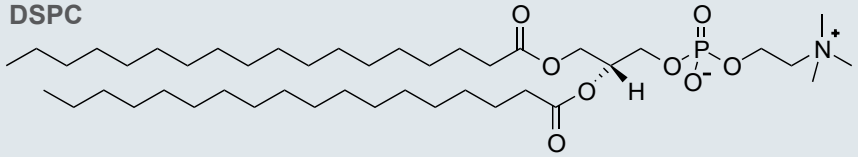
0.13 mg / dose

Cholesterol



0.47 mg / dose

DSPC



0.24 mg / dose

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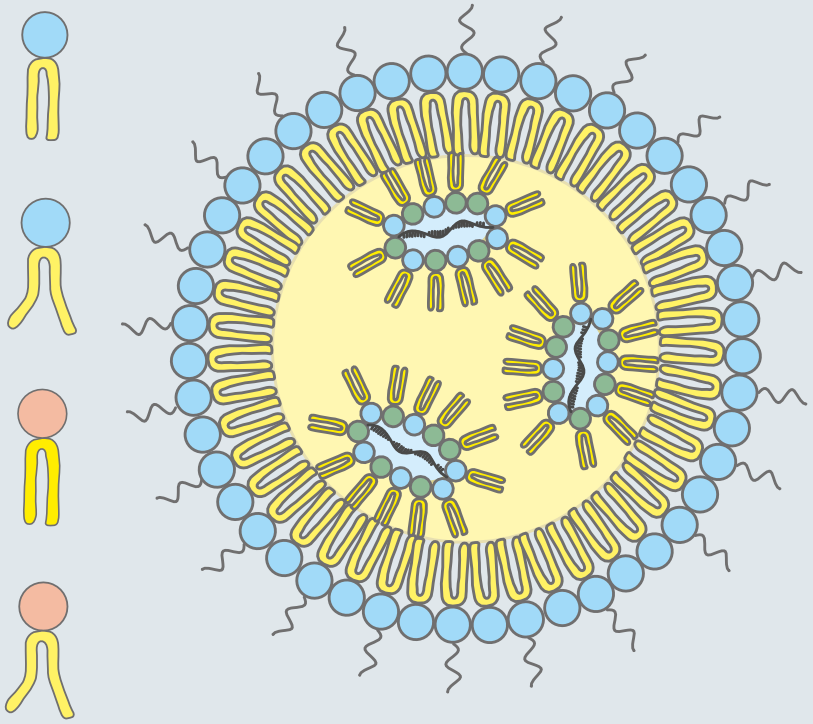
Function of Phospholipids

- Defined as **“helper lipids”** which are a range of lipids such as sterols, phospholipids, and glycerolipids that are *typically* non-cationic
- The prevailing hypothesis regarding the role of helper lipids in LNP is that they **support stability during storage and circulation** as with liposomes.
- Ongoing research efforts in academia and industry investigate **amount and type of phospholipids to modulate functionalities of LNPs**

Design space for helper lipids



ENDOSOMAL ESCAPE OF LIPID NANOPARTICLES

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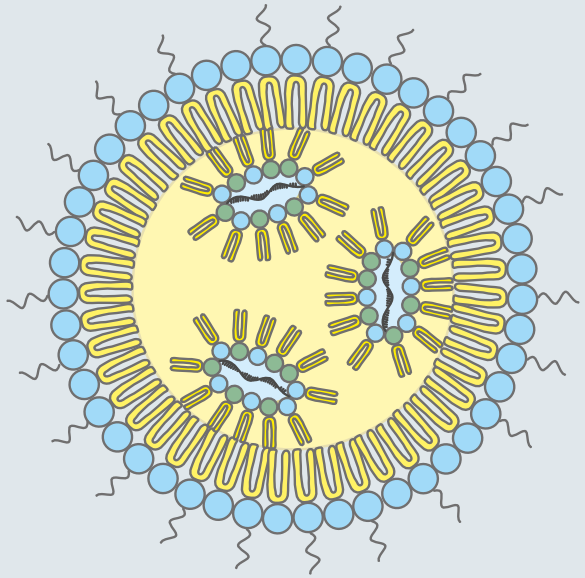
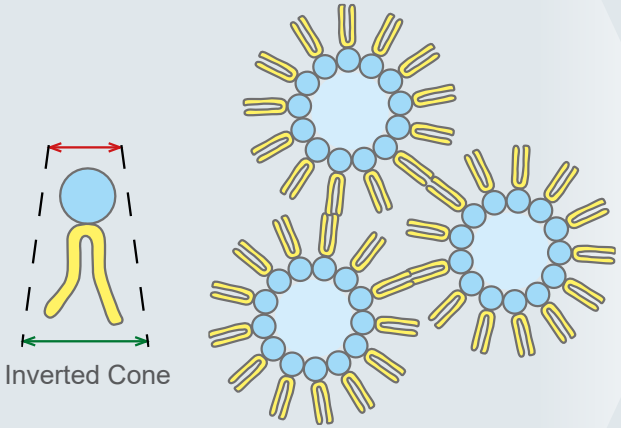
Phospholipids Offer a Versatile Toolbox to Modulate Functional Properties of LNPs.

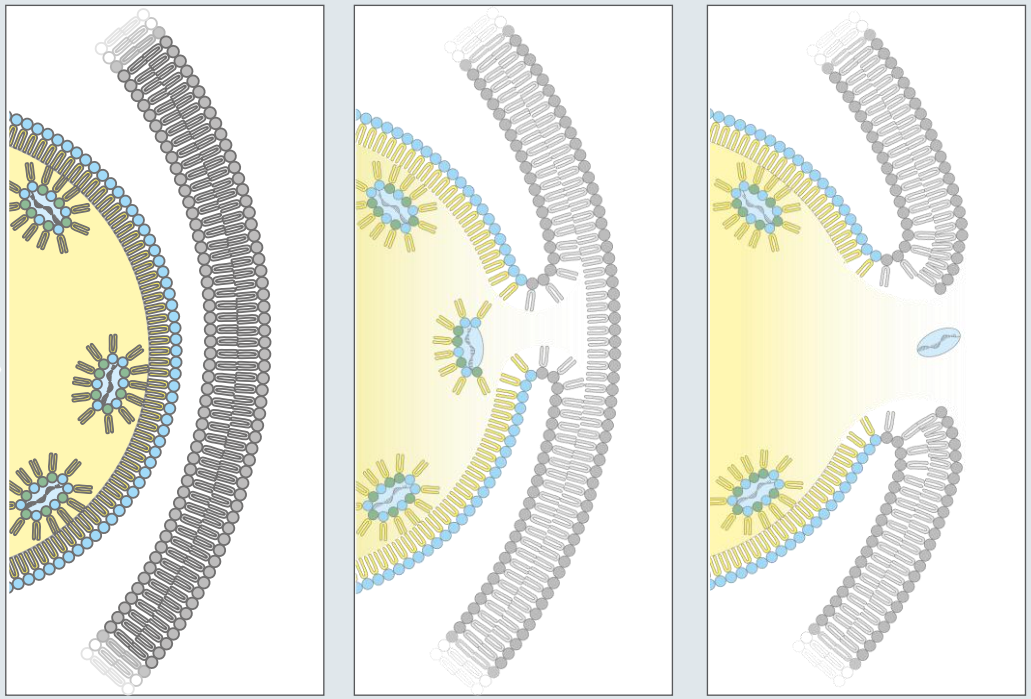
Lipid Nanoparticle (LNP)



Enhancing Endosomal Escape with Fusogenic Phospholipids
e.g., DOPE



Unsaturated phosphatidylethanolamines adopt hexagonal (H_{II}) phases



H_{II} phase-adopting phospholipids stimulate membrane fusion events and thereby promote endosomal escape of nucleic acids.

MODULATION OF LNP CHARACTERISTICS

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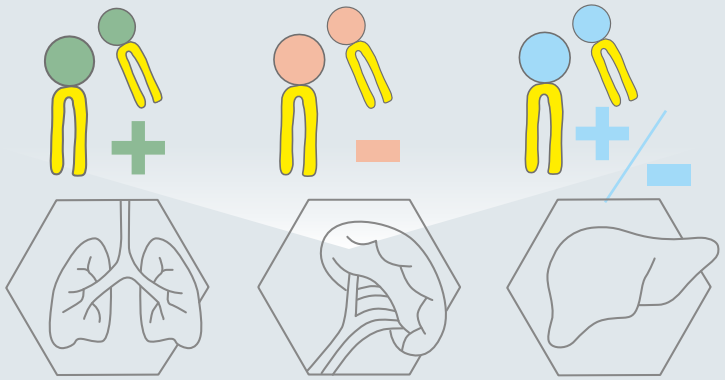
Phospholipids Can Improve Circulation Time, Tissue Tropism, and Efficacy

SORT lipids

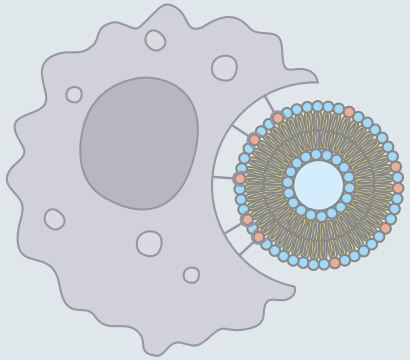
Tissue-specific delivery to lung, spleen and liver



- Extrahepatic targeting of LNPs by addition of SORT lipids
- Zwitterionic (phospho-)lipids → liver
- Anionic (phospho-)lipids → spleen
- Cationic (phospho-)lipids → lung

Phosphatidylserine (PS)

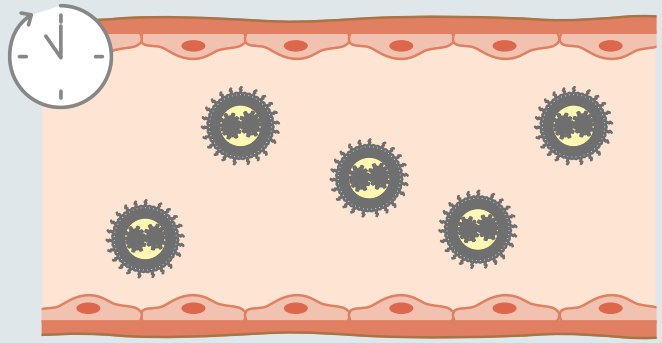
Improved gene delivery and targeting of immune cells



- Mimicry of apoptotic cells and viruses that display externalized PS
- Improved transfection efficacy and potency with pDNA and mRNA
- Preferential uptake by immune cells

Egg sphingomyelin (ESM)

Increased circulation time and extra-hepatic accumulation



- Unique morphology of ESM-supplemented LNPs
- Increased stability in presence of plasma
- Accumulation and improved gene expression in spleen and bone marrow

LIPID NANOPARTICLES

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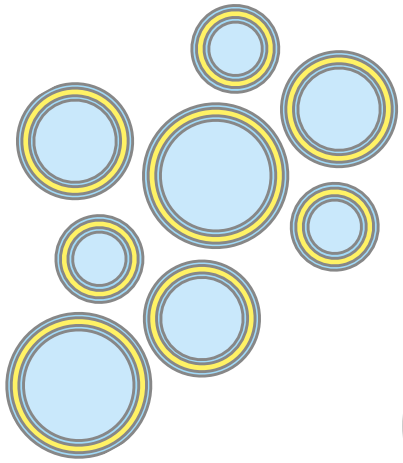
Market products

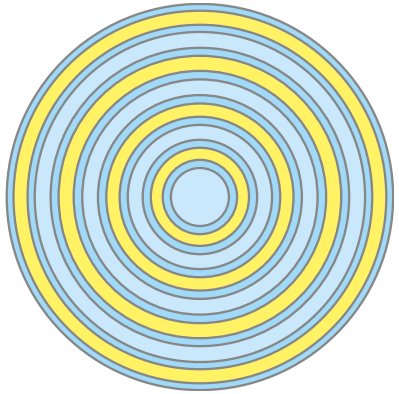
Trade product	Indication	Nucleic acid cargo	(Lipid) Composition	Company
Comirnaty®	COVID-19	mRNA	DSPC, Cholesterol, ALC-0315, ALC-0159	BioNTech / Pfizer
Spikevax®	COVID-19	mRNA	DSPC, Cholesterol, SM-102, PEG2000-DMG	Moderna
mRESVIA™	Respiratory syncytial virus (RSV)	mRNA	DSPC, Cholesterol, SM-102, PEG2000-DMG	Moderna
Onpattro®	Polyneuropathy of hereditary transthyretin-mediated amyloidosis	siRNA	DSPC, Cholesterol, DLin-MC3-DMA, PEG2000-DMG	Alnylam

LIPOSOMES – CLASSIFICATION / TYPES

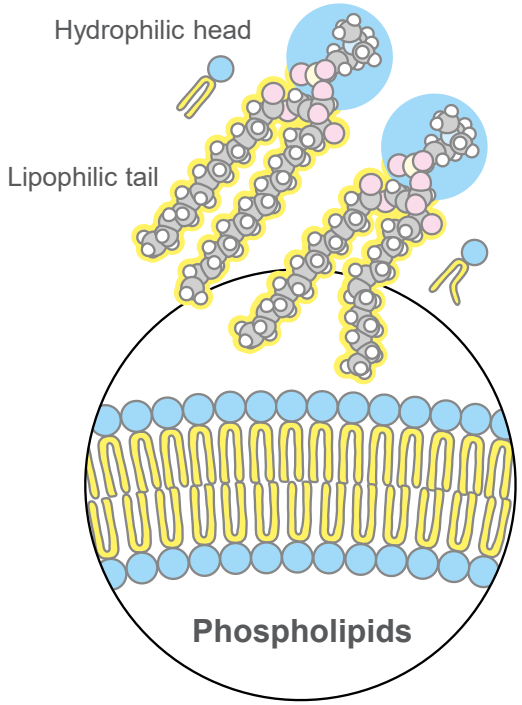
Lipoid

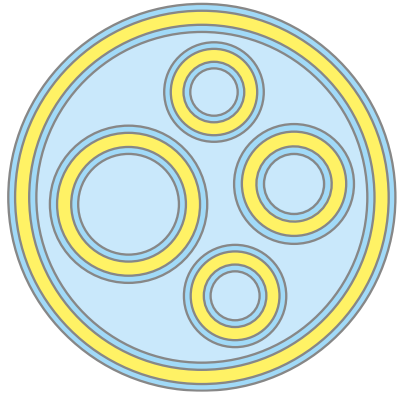


SUV
Small Unilamellar
Vesicles

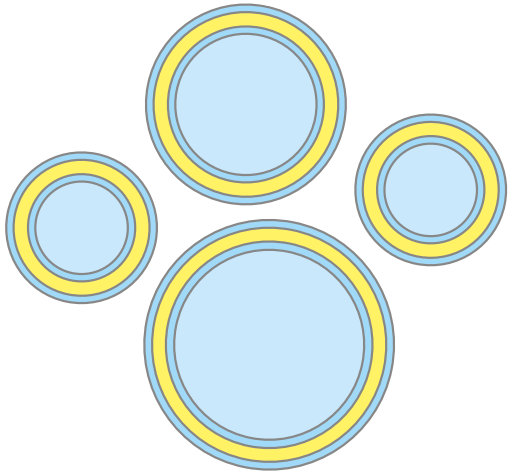


MLV
Multilamellar
Vesicles





MVV
Multivesicular
Vesicles



LUV
Large Unilamellar
Vesicles

BENEFITS OF LIPOSOMES

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General Advantages

- Delivery system for hydrophilic, lipophilic, and amphiphilic APIs
- Solubilization of lipophilic and amphiphilic APIs
- Protection of the API
- Reduction of side effects - toxicity of the API
- Sustained release
- Drug targeting
- Increased therapeutic index

Advantages Compared to Other Solubilizers

- Biocompatible carrier with low toxicity
- No drug precipitation at injection site and after dilution
- Transfer of drug from liposomal membrane to lipoproteins
- Disintegrating liposomes
- Mostly no change of body distribution and PK of drug

STABILIZATION OF LIPOSOMES

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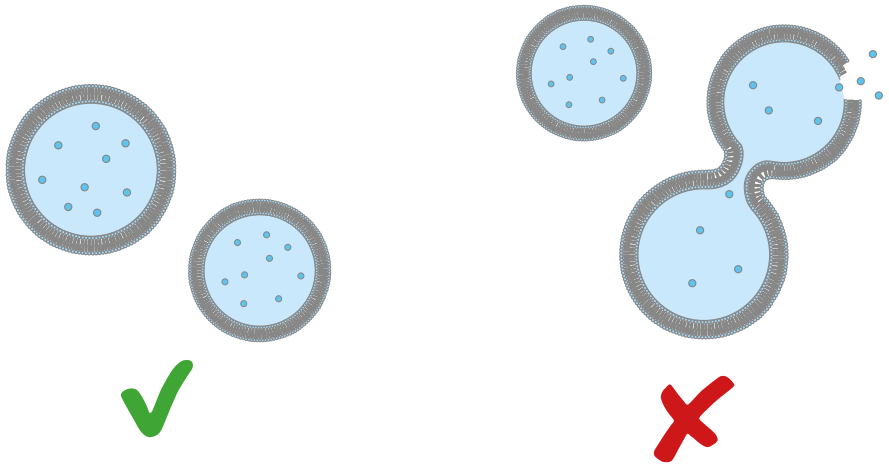
Prevention from chemical degradation

- Suitable storage temperature
- Optimal pH (ca. pH 6.8 for phospholipids)
- Protective gas: nitrogen or argon
- Freeze drying (cryoprotectants: lactose or sucrose)



Improvement of physical stability

- Prevention from drug leakage:
- pH or ammonium gradient
- Insoluble salt
- Addition of negatively charged PL (e.g. PG)

Note: Drug might be the stability limiting factor!

MAIN PREPARATION METHODS OF LIPOSOMES

Methods based on solutions of lipids in organic solvents

- Thin Film Hydration Method
- Injection Method

Mainly lab and pilot scale

Methods with impact of mechanical energy

- High Pressure Homogenization
- Membrane Extrusion

Also applied on plant scale

PHOSPHOLIPIDS IN LIPOSOMAL VACCINES

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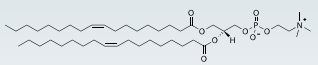
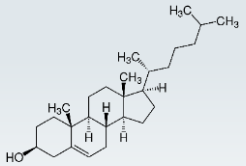
SHINGRIX, AREXVY, and MOSQUIRIX Adjuvant System

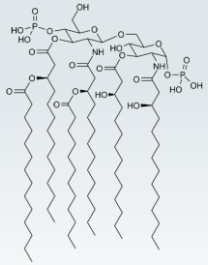
DOPC



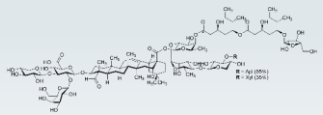
Cholesterol

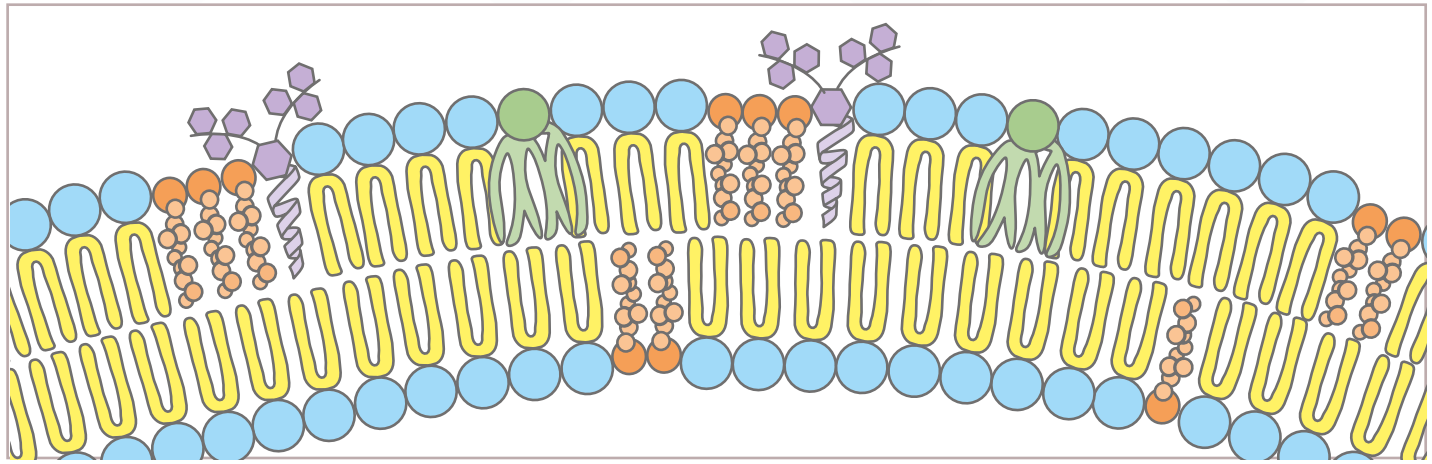


Monophosphoryl Lipid A

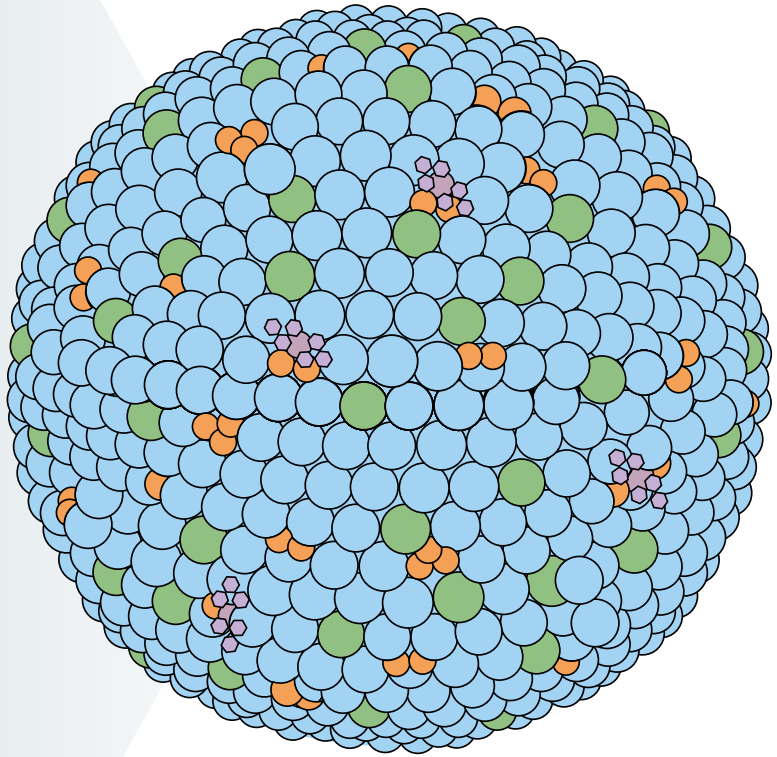


QS-21 Saponin





Sectional view



COMMERCIALIZED DRUG - AMBISOME

Lipoid

AmBisome®

Company:	Gilead
Active:	Amphotericin B
Composition:	50 mg Amphotericin B 213 mg **Hydrogenated Soybean Phosphatidylcholine** 84 mg **DSPG** 84 mg Cholesterol 0.64 mg a-Tocopherol 900 mg Sucrose 27 mg Disodium Succinate Hexahydrate, pH 5-6 following reconstitution
How supplied:	50 mg as lyophilisate
Administration:	Reconstruction with 12 ml water for injection, 5 µm-filtration into 5% dextrose injection
Indication:	Fungal infections

EXAMPLES OF COMMERCIAL DRUGS WITH LIPOSOMES I

Lipoid

Brand Name	API	Type of PL	Role of Lipid System	Indication	Year*	Company
Abelcet®	Amphothericin B	DMPC, DMPG	Increase therap. index, solubilizer	Fungal infection	1995	Leadiant (USA, Canada) Teva
Doxil®/ Caelyx®	Doxorubicin-HCL	HSPC, MPEG-2000-DSPE	Increase therap. Index, passive targeting/EPR	Metastatic cancer	1995	Baxter
AmBisome®	Amphotericin B	HSPC, DSPG	Increase therap. index, solubilizer	Systemic mycosis	1997	Gilead
Myocet®	Doxorubicin-HCl	E PC	Increase therap. index	Cancer	2000	Sopherion Teva
Visudyne®	Verteporfin	DMPC, E PG	Solubilizer	Photodyn. therapy	2000	Bausch + Lomb
DEFINITY®	**Perflutren**	**DPPA, DPPC, MPEG-5000-DPPE**	**Ultrasound contrast agent**	**Echocardiography**	**2001**	**Lantheus**
Lipusu®	Paclitaxel	Egg Phospholipids	Increase therap. index, solubilizer	non-small cell lung cancer, breast cancer, ovarian cancer	2005**	Luye Pharma China
Mepact®	Mifamurtide (MTP-PE)	POPC, DOPS	Increase therap. Index, passive targeting/MPS	Osteosarcoma	2009 (EU)	Takeda
EXPAREL®	Bupivacaine	DEPC, DPPG	Slow release (it)	Pain control	2011	Pacira

* Year of FDA approval ** Year of NMPA approval

EXAMPLES OF COMMERCIAL DRUGS WITH LIPOSOMES II

Lipoid

Brand Name	API	Type of PL	Role of Lipid System	Indication	Year*	Company
Lipodox®	Doxorubicin	DSPC, MPEG-2000-DSPE	Generic of DOXIL®	Metastatic Cancer	2012	Sun Pharma
Onivyde®	Irinotecan	DSPC, MPEG-2000-DSPE	Increase therap. index	Pancreatic cancer	2015	Ipsen
Nocita®	Bupivacaine	DEPC:DPPG	Slow release	Pain control (Dogs)	2017	Aratana/Elanco
Vyxeos™	Cytarabine / Daunorubicin	DSPC, DSPG	Increase therap. index	Acute myeloid leukemia	2017	Jazz Pharmaceuticals
Shingrix	Antigenes	DOPC	Adjuvant	Herpes zoster vaccine	2017	GSK

* Year of FDA approval

PHOSPHOLIPID-BASED VACCINES

Summary and Conclusion

- Certain phospholipids may direct extrahepatic targeting
- Phospholipids are **essential parts of lipid nanoparticles** that are applied for nucleic acid vaccines
- Lipoid offers a comprehensive range of **natural and synthetic phospholipids in cGMP quality**

Phospholipids are key ingredients for innovative vaccines.

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FURTHER INFORMATION

Lipoid

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or consult our webpage: https://lipoid.com/en/