

Annex A

EP 626 – Amendment A

1. A liposome for *in vivo* delivery of RNA to a vertebrate cell, the liposome having a lipid bilayer encapsulating an aqueous core, wherein: (i) the lipid bilayer comprises a lipid having a pKa in the range of 5.0 to 6.8 when measured as described in the section "pKa measurement" of the description; and (ii) the aqueous core includes a RNA which encodes an immunogen, and wherein the liposome includes an amphiphilic lipid whose hydrophilic portion is PEGylated.

The remaining claims are as granted.

Annex B

EP 626 – Amendment B1

1. A liposome for *in vivo* delivery of RNA to a vertebrate cell, the liposome having a lipid bilayer encapsulating an aqueous core, wherein: (i) the lipid bilayer comprises a lipid having a pKa in the range of 5.0 to 6.8 when measured as described in the section "pKa measurement" of the description; and (ii) the aqueous core includes a RNA which encodes an immunogen, wherein the liposome is formed from a mixture of lipids, wherein the proportion of those lipids which have a pKa within the range of 5.0 to 6.8 is between 20-80 mol% of the total amount of lipids.

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1. A liposome for *in vivo* delivery of RNA to a vertebrate cell, the liposome having a lipid bilayer encapsulating an aqueous core, wherein: (i) the lipid bilayer comprises a lipid having a pKa in the range of 5.0 to 6.8 when measured as described in the section "pKa measurement" of the description; and (ii) the aqueous core includes a RNA which encodes an immunogen, wherein the liposome is formed from a mixture of lipids, wherein the proportion of those lipids which have a pKa within the range of 5.0 to 6.8 is between 40-60 mol% of the total amount of lipids.

In each case, the remaining claims are as granted.

Annex C

EP 626 – Amendment C

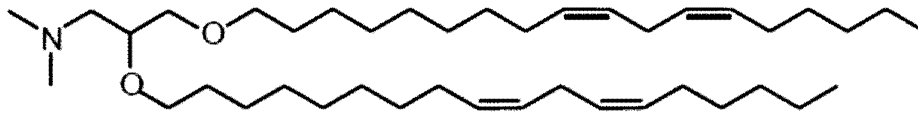
1. A liposome for *in vivo* delivery of RNA to a vertebrate cell, the liposome having a lipid bilayer encapsulating an aqueous core, wherein: (i) the lipid bilayer comprises a lipid having a pKa in the range of 5.0 to 6.8 when measured as described in the section "pKa measurement" of the description; and (ii) the aqueous core includes a RNA which encodes an immunogen, wherein the liposome is formed from a mixture of lipids, wherein the proportion of those lipids which have a pKa within the range of 5.0 to 6.8 is between 40-60 mol% of the total amount of lipids, wherein the remainder is made of 35-50 mol% cholesterol, PEGylated DMG and DSPC.

The remaining claims are as granted.

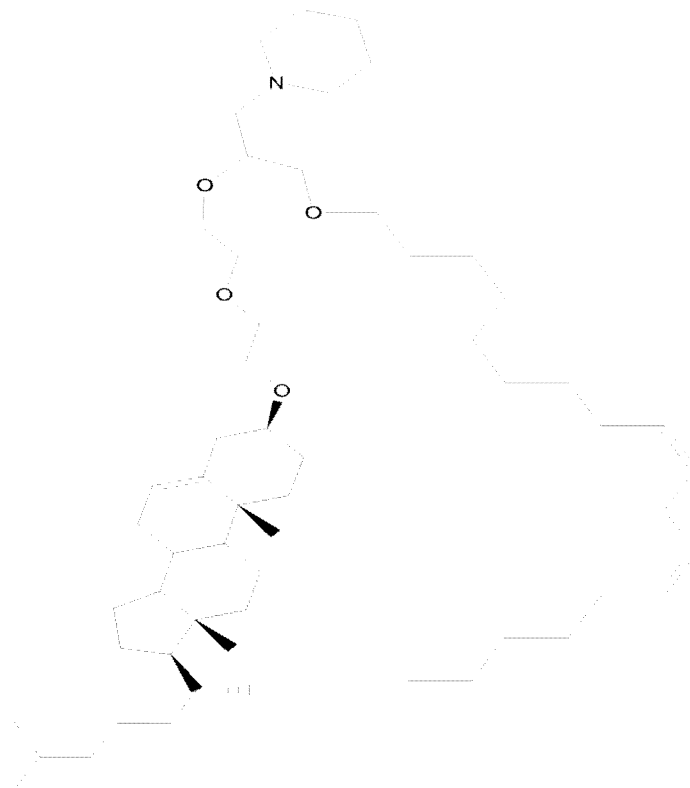
Annex D

EP 626 – Amendment D

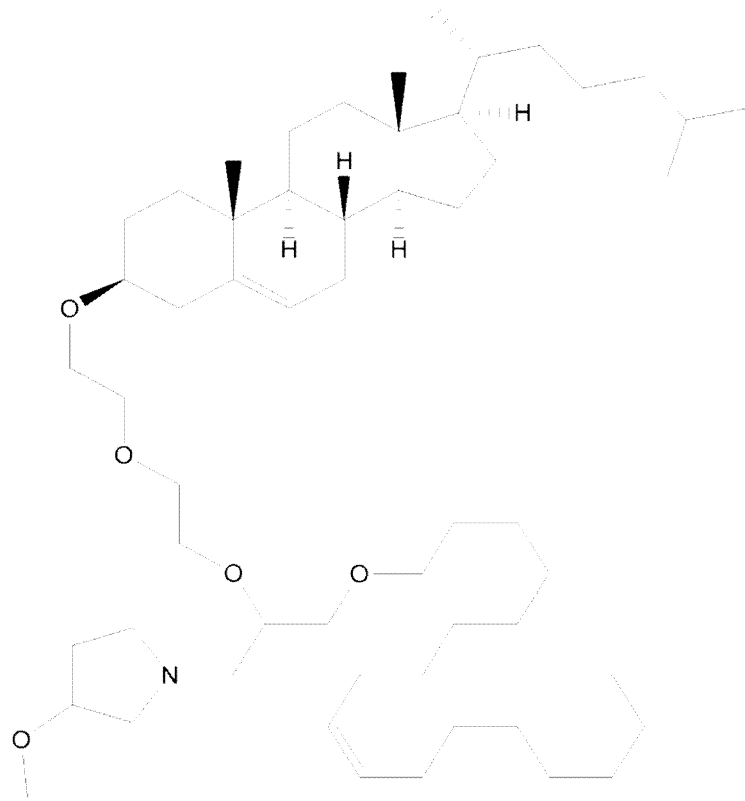
1. A liposome for *in vivo* delivery of RNA to a vertebrate cell, the liposome having a lipid bilayer encapsulating an aqueous core, wherein: (i) the lipid bilayer comprises a lipid having a pKa in the range of 5.6 to 6.8 when measured as described in the section "pKa measurement" of the description; and (ii) the aqueous core includes a RNA which encodes an immunogen.
2. The liposome of claim 0, wherein the lipid having a pKa in the range of 5.6 to 6.8 has a tertiary amine.
3. The liposome of any preceding claim, wherein pKa in the range of 5.0 to 6.8 is between 5.6 and 6.8.
4. The liposome of any preceding claim, wherein pKa in the range of 5.6 to 6.8 is between 5.7 and 5.9.
5. The liposome of claim 0, wherein the lipid having a pKa in the range of 5.6 to 6.8 has the formula shown herein for RV01:



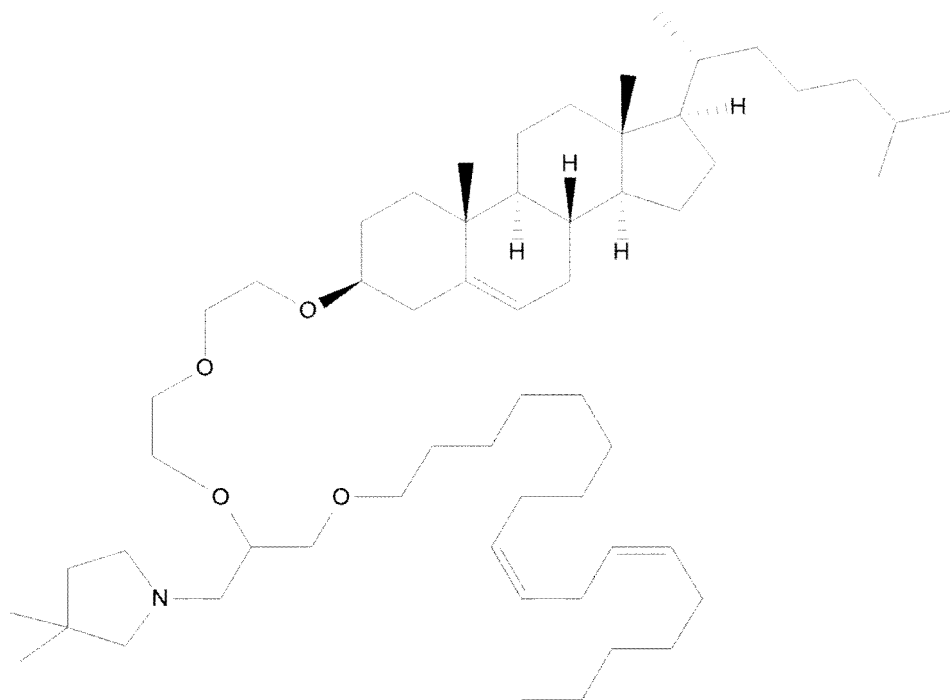
RV03:



RV04:



RV05:



RV07: