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(54) Title **IMPROVED LIPID NANOPARTICLES FOR DELIVERY OF NUCLEIC ACIDS**

(56) References Cited:
WO-A1-2018/081480
US-A1- 2015 203 446
WO-A1-2019/089828
WO-A1-2018/107026

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (http://worldwide.espacenet.com) or via the search engine on our website here: https://search.patentstyret.no/

Patentkrav

1. Lipidnanopartikler (LNP'er) for bruk i en fremgangsmåte ved behandling eller forebygging av sykdom hos en primat med behov for dette, hvor fremgangsmåten omfatter å administrere LNP'ene til primaten, hvor hver av LNP'ene omfatter:

i) en nukleinsyre, eller et farmasøytisk akseptabelt salt derav, innkapslet inne i LNP'en;

ii) et kationisk lipid;

iii) et nøytralt lipid;

iv) et steroid; og

v) et polymer-konjugert lipid,

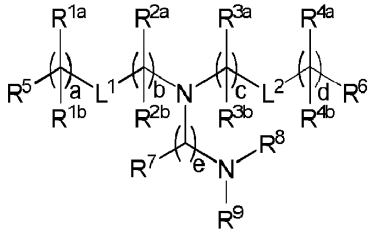
hvor en midlere partikkeldiameter til LNP'ene er i området fra 40 nm til 68 nm, bestemt gjennom kvasielastisk lysspredning.

2. LNP'er for bruk ifølge krav 1, hvor den midlere partikkeldiameteren er i området fra 50 nm til 68 nm, fra 55 nm til 65 nm, fra 50 nm til 60 nm eller fra 60 nm til 68 nm.

3. LNP'er for bruk ifølge krav 1, hvor den midlere partikkeldiameteren er omtrent 47 nm, omtrent 48 nm, omtrent 49 nm, omtrent 50 nm, omtrent 51 nm, omtrent 52 nm, omtrent 53 nm, omtrent 54 nm, omtrent 55 nm, omtrent 56 nm, omtrent 57 nm, omtrent 58 nm, omtrent 59 nm, omtrent 60 nm, omtrent 61 nm, omtrent 62 nm, omtrent 63 nm, omtrent 64 nm eller omtrent 65 nm.

4. LNP'er for bruk ifølge et hvilket som helst av kravene 1-3, hvor:

i) det kationiske lipidet har en struktur med formel (I):



(I)

eller et farmasøytisk akseptabelt salt, tautomer eller stereoisomer derav, hvor:

én av L^1 eller L^2 er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -$S(O)_x$-, -S-S-, -C(=O)S-, SC(=O)-, -$NR^aC(=O)$-, -$C(=O)NR^a$-, $NR^aC(=O)NR^a$-, -$OC(=O)NR^a$- eller

-$NR^aC(=O)O$-, og den andre av L^1 eller L^2 er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -$S(O)_x$-, -S-S-, -C(=O)S-, SC(=O)-, -$NR^aC(=O)$-, -$C(=O)NR^a$-, ,$NR^aC(=O)NR^a$-, -$OC(=O)NR^a$- eller-$NR^aC(=O)O$- eller en direkte binding;

R^a er H eller C_1-C_{12}-alkyl;

R^{1a} og R^{1b}, i hver forekomst, uavhengig er enten (a) H eller C_1-C_{12}-alkyl, eller (b) R^{1a} er H eller C_1-C_{12}-alkyl, og R^{1b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{1b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{2a} og R^{2b}, i hver forekomst, uavhengig er enten (a) H eller C_1-C_{12}-alkyl, eller (b) R^{2a} er H eller C_1-C_{12}-alkyl, og R^{2b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{2b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{3a} og R^{3b}, i hver forekomst, uavhengig er enten (a) H eller C_1-C_{12}-alkyl, eller (b) R^{3a} er H eller C_1-C_{12}-alkyl, og R^{3b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{3b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{4a} og R^{4b}, i hver forekomst, uavhengig er enten (a) H eller C_1-C_{12}-alkyl, eller (b) R^{4a} er H eller C_1-C_{12}-alkyl, og R^{4b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{4b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

hver av R^5 og R^6 uavhengig er metyl eller sykloalkyl;

R^7, i hver forekomst, uavhengig er H eller C_1-C_{12}-alkyl;

hver av R^8 og R^9 uavhengig er usubstituert C_1-C_{12}-alkyl; eller R^8 og R^9, sammen med det nitrogenatomet som de er tilknyttet, danner en 5-, 6- eller 7-leddet heterosyklisk ring omfattende ett nitrogenatom;

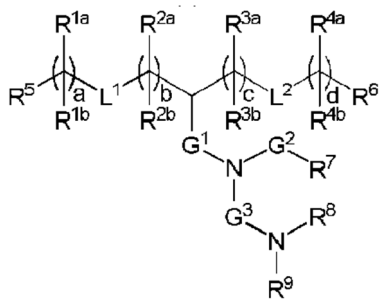
hver av a og d uavhengig er et heltall fra 0 til 24;

hver av b og c uavhengig er et heltall fra 1 til 24;

e er 1 eller 2; og

x er 0, 1 eller 2; eller

ii) det kationiske lipidet har en struktur med formel (II):



(II)

eller et farmasøytisk akseptabelt salt, tautomer eller stereoisomer derav, hvor:

én av L^1 eller L^2 er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -$S(O)_x$-, -S-S-, -C(=O)S-, SC(=O)-, -$NR^aC(=O)$-, -C(=O)NR^a-, $NR^aC(=O)NR^a$-, -OC(=O)NR^a- eller -$NR^aC(=O)O$-, og den andre av L^1 eller L^2 er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -$S(O)_x$-, -S-S-, -C(=O)S-, SC(=O)-, -$NR^aC(=O)$-, -C(=O)NR^a-, $NR^aC(=O)NR^a$-, -OC(=O)NR^a- eller-$NR^aC(=O)O$- eller en direkte binding;

G^1 er C_1-C_2-alkylen, -(C=O)-, -O(C=O)-, -SC(=O)-, -$NR^aC(=O)$- eller en direkte binding;

G^2 er -C(=O)-, -(C=O)O-, -C(=O)S-, -C(=O)NR^a- eller en direkte binding;

G^3 er C_1-C_6-alkylen;

R^a er H eller C_1-C_{12}-alkyl;

R^{1a} og R^{1b}, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R^{1a} er H eller C_1-C_{12}-alkyl, og R^{1b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{1b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{2a} og R^{2b}, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R^{2a} er H eller C_1-C_{12}-alkyl, og R^{2b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{2b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{3a} og R^{3b}, i hver forekomst, uavhengig er enten (a): H eller C_1-C_{12}-alkyl; eller (b) R^{3a} er H eller C_1-C_{12}-alkyl, og R^{3b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{3b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{4a} og R^{4b}, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R^{4a} er H eller C_1-C_{12}-alkyl, og R^{4b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{4b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

hver av R^5 og R^6 uavhengig er H eller metyl;

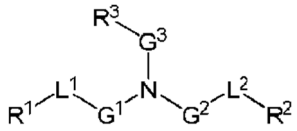
R^7 er C_4-C_{20}-alkyl;

hver av R^8 og R^9 uavhengig er C_1-C_{12}-alkyl; eller R^8 og R^9, sammen med det nitrogenatomet som de er tilknyttet, danner en 5-, 6- eller 7-leddet heterosyklisk ring;

hver av a, b, c og d uavhengig er et heltall fra 1 til 24; og

x er 0, 1 eller 2; eller

iii) det kationiske lipidet har en struktur med formel III:



III

eller et farmasøytisk akseptabelt salt eller stereoisomer derav, hvor:

én av L^1 eller L^2 er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -S(O)$_x$-, -S-S-, -C(=O)S-, SC(=O)-, -NR^aC(=O)-, -C(=O)NR^a-, NR^aC(=O)NR^a-, -OC(=O)NR^a- eller -NR^aC(=O)O-, og den andre av L^1 eller L^2 er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -S(O)$_x$-, -S-S-, -C(=O)S-, SC(=O)-, -NR^aC(=O)-, -C(=O)NR^a-, NR^aC(=O)NR^a-, -OC(=O)NR^a- eller-NR^aC(=O)O- eller en direkte binding;

hver av G^1 og G^2 uavhengig er usubstituert C_1-C_{12}-alkylen eller C_1-C_{12}-alkenylen;

G^3 er C_1-C_{24}-alkylen, C_1-C_{24}-alkenylen, C_3-C_8-sykloalkylen, C_3-C_8-sykloalkenylen;

R^a er H eller C_1-C_{12}-alkyl;

hver av R^1 og R^2 uavhengig er C_6-C_{24}-alkyl eller C_6-C_{24}-alkenyl;

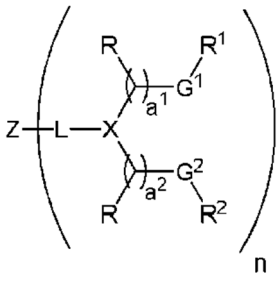
R^3 er H, OR^5, CN, -C(=O)OR^4, -OC(=O)R^4 eller -NR^5C(=O)R^4;

R^4 er C_1-C_{12}-alkyl;

R^5 er H eller C_1-C_6-alkyl; og

x er 0, 1 eller 2; eller

iv) det kationiske lipidet har følgende formel (IV):



(IV)

eller et farmasøytisk akseptabelt salt eller stereoisomer derav, hvor:

én av G^1 eller G^2, i hver forekomst, er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -S(O)$_y$-, -S-S-, -C(=O)S-, SC(=O)-, -N(R^a)C(=O)-, -C(=O)N(R^a)-, -N(R^a)C(=O)N(R^a)-, -OC(=O)N(R^a)- eller -N(R^a)C(=O)O-, og den andre av G^1 eller G^2, i hver forekomst, er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -S(O)$_y$-, -S-S-, -

C(=O)S-, -SC(=O)-, -N(R^a)C(=O)-, -C(=O)N(R^a)-, -N(R^a)C(=O)N(R^a)-, -OC(=O)N(R^a)- eller -N(R^a)C(=O)O- eller en direkte binding;

L, i hver forekomst, er ~O(C=O)-, hvor ~ representerer en kovalent binding til X;

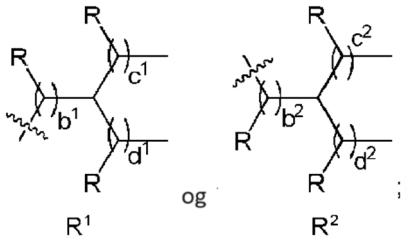
X er CR^a;

Z er alkyl, sykloalkyl eller en monovalent enhet omfattende minst én polar funksjonell gruppe når n er 1; eller Z er alkylen, sykloalkylen eller en polyvalent enhet omfattende minst én polar funksjonell gruppe når n er større enn 1;

R^a, i hver forekomst, uavhengig er H, C_1-C_{12}-alkyl, C_1-C_{12}-hydroksylalkyl, C_1-C_{12}-aminoalkyl, C_1-C_{12}-alkylaminylalkyl, C_1-C_{12}-alkoksyalkyl, C_1-C_{12}-alkoksykarbonyl, C_1-C_{12}-alkylkarbonyloksy, C_1-C_{12}-alkylkarbonyloksyalkyl eller C_1-C_{12}-alkylkarbonyl;

R, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^1 og R^2, i hver forekomst, henholdsvis har følgende struktur:



a^1 og a^2, i hver forekomst, uavhengig er et heltall fra 3 til 12;

b^1 og b^2, i hver forekomst, uavhengig er 0 eller 1;

c^1 og c^2, i hver forekomst, uavhengig er et heltall fra 5 til 10;

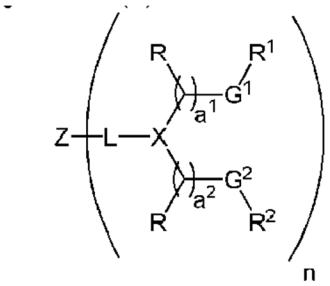
d^1 og d^2, i hver forekomst, uavhengig er et heltall fra 5 til 10;

y, i hver forekomst, uavhengig er et heltall fra 0 til 2; og

n er et heltall fra 1 til 6,

hvor hvert alkyl, alkylen, hydroksylalkyl, aminoalkyl, alkylaminylalkyl, alkoksyalkyl, alkoksykarbonyl, alkylkarbonyloksy, alkylkarbonyloksyalkyl og alkylkarbonyl eventuelt er substituert med én eller flere substituenter; eller

v) det kationiske lipidet har følgende formel (V):



(V)

eller et farmasøytisk akseptabelt salt eller stereoisomer derav, hvor:

én av G^1 eller G^2, i hver forekomst, er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -$S(O)_y$-, -S-S-, -C(=O)S-, SC(=O)-, -N(R^a)C(=O)-, -C(=O)N(R^a)-, -N(R^a)C(=O)N(R^a)-, -OC(=O)N(R^a)- eller -N(R^a)C(=O)O-, og den andre av G^1 eller G^2, i hver forekomst, er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -$S(O)_y$-, -S-S-, -C(=O)S-, -SC(=O)-, -N(R^a)C(=O)-, -C(=O)N(R^a)-, -N(R^a)C(=O)N(R^a)-, -OC(=O)N(R^a)- eller -N(R^a)C(=O)O- eller en direkte binding;

L, i hver forekomst, er ~O(C=O)-, hvor ~ representerer en kovalent binding til X;

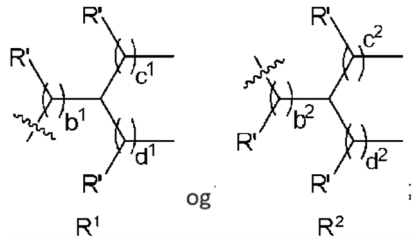
X er CR^a;

Z er alkyl, sykloalkyl eller en monovalent enhet omfattende minst én polar funksjonell gruppe når n er 1; eller Z er alkylen, sykloalkylen eller en polyvalent enhet omfattende minst én polar funksjonell gruppe når n er større enn 1;

R^a, i hver forekomst, uavhengig er H, C_1-C_{12}-alkyl, C_1-C_{12}-hydroksylalkyl, C_1-C_{12}-aminoalkyl, C_1-C_{12}-alkylaminylalkyl, C_1-C_{12}-alkoksyalkyl, C_1-C_{12}-alkoksykarbonyl, C_1-C_{12}-alkylkarbonyloksy, C_1-C_{12}-alkylkarbonyloksyalkyl eller C_1-C_{12}-alkylkarbonyl;

R, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^1 og R^2, i hver forekomst, henholdsvis har følgende struktur:



R', i hver forekomst, uavhengig er H eller C_1-C_{12}-alkyl;

a^1 og a^2, i hver forekomst, uavhengig er et heltall fra 3 til 12;

b^1 og b^2, i hver forekomst, uavhengig er 0 eller 1;

c^1 og c^2, i hver forekomst, uavhengig er et heltall fra 2 til 12;

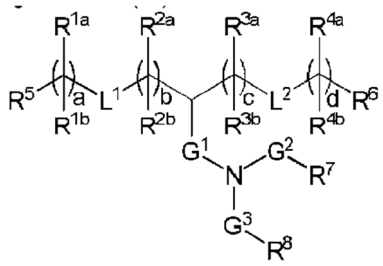
d^1 og d^2, i hver forekomst, uavhengig er et heltall fra 2 til 12;

y, i hver forekomst, uavhengig er et heltall fra 0 til 2; og

n er et heltall fra 1 til 6,

hvor a^1, a^2, c^1, c^2, d^1 og d^2 er valgt slik at summen av $a^1+c^1+d^1$ er et heltall fra 18 til 30, og summen av $a^2+c^2+d^2$ er et heltall fra 18 til 30, og hvor hvert alkyl, alkylen, hydroksylalkyl, aminoalkyl, alkylaminylalkyl, alkoksyalkyl, alkoksykarbonyl, alkylkarbonyloksy, alkylkarbonyloksyalkyl og alkylkarbonyl eventuelt er substituert med én eller flere substituenter; eller

vi) det kationiske lipidet har følgende formel (VI):



(VI)

eller et farmasøytisk akseptabelt salt, tautomer eller stereoisomer derav, hvor:

hver av L^1 og L^2 uavhengig er -O(C=O)-, -(C=O)O-, -C(=O)-, -O-, -$S(O)_x$-, -S-S-, -C(=O)S-, -SC(=O)-, -$NR^aC(=O)$-, -C(=O)NR^a-, -$NR^aC(=O)NR^a$-, -OC(=O)NR^a-, -$NR^aC(=O)O$- eller en direkte binding;

G^1 er C_1-C_2-alkylen, -(C=O)-, -O(C=O)-, -SC(=O)-, -$NR^aC(=O)$- eller en direkte binding;

G^2 er -C(=O)-, -(C=O)O-, -C(=O)S-, -C(=O)NR^a- eller en direkte binding;

G^3 er C_1-C_6-alkylen;

R^a er H eller C_1-C_{12}-alkyl;

R^{1a} og R^{1b}, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R^{1a} er H eller C_1-C_{12}-alkyl, og R^{1b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{1b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{2a} og R^{2b}, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R^{2a} er H eller C_1-C_{12}-alkyl, og R^{2b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{2b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{3a} og R^{3b}, i hver forekomst, uavhengig er enten (a): H eller C_1-C_{12}-alkyl; eller (b) R^{3a} er H eller C_1-C_{12}-alkyl, og R^{3b}, sammen med det karbonatomet som den er bundet til, er tatt sammen

med en tilstøtende R^{3b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

R^{4a} og R^{4b}, i hver forekomst, uavhengig er enten: (a) H eller C_1-C_{12}-alkyl; eller (b) R^{4a} er H eller C_1-C_{12}-alkyl, og R^{4b}, sammen med det karbonatomet som den er bundet til, er tatt sammen med en tilstøtende R^{4b} og det karbonatomet som den er bundet til for å danne en karbon-karbon-dobbeltbinding;

hver av R^5 og R^6 uavhengig er H eller metyl;

R^7 er H eller C_1-C_{20}-alkyl;

R^8 er OH, -N(R^9)(C=O)R^{10}, -(C=O)NR^{9R10}, -NR^{9R10}, -(C=O)OR^{11} eller -O(C=O)R^{11}, forutsatt at G^3 er C_4-C_6-alkylen når R^8 er -NR^{9R10},

hver av R^9 og R^{10} uavhengig er H eller C_1-C_{12}-alkyl;

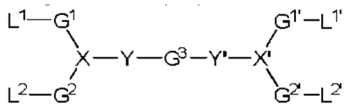
R^{11} er aralkyl;

hver av a, b, c og d uavhengig er et heltall fra 1 til 24; og

x er 0, 1 eller 2,

hvor hvert alkyl, alkylen og aralkyl eventuelt er substituert; eller

vii) det kationiske lipidet har følgende formel (VII):



(VII)

eller et farmasøytisk akseptabelt salt eller stereoisomer derav, hvor:

hver av X og X' uavhengig er N eller CR;

hver av Y og Y' uavhengig er fraværende, -O(C=O)-, -(C=O)O- eller NR, forutsatt at:

a) Y er fraværende når X er N;

b) Y' er fraværende når X' er N;

c) Y er -O(C=O)-, -(C=O)O- eller NR når X er CR; og

d) Y' er -O(C=O)-, -(C=O)O- eller NR når X' er CR,

hver av L^1 og $L^{1'}$ uavhengig er -O(C=O)R^1, -(C=O)OR^1, -C(=O)R^1, -OR^1, - S(O)$_z$$R^1$, -S-S$R^1$, -C(=O)S$R^1$, -SC(=O)$R^1$, -N$R^a$C(=O)$R^1$, -C(=O)N$R^b$$R^c$, -N$R^a$C(=O)N$R^b$$R^c$, - OC(=O)N$R^b$$R^c$ eller -NR^aC(=O)OR^1;

hver av L^2 og $L^{2'}$ uavhengig er -O(C=O)R^2, -(C=O)OR^2, -C(=O)R^2, -OR^2, - S(O)$_z$$R^2$, -S-S$R^2$, -C(=O)S$R^2$, -SC(=O)$R^2$, -N$R^d$C(=O)$R^2$, -C(=O)N$R^e$$R^f$, -N$R^d$C(=O)N$R^e$$R^f$, - OC(=O)N$R^e$$R^f$;- N$R^d$C(=O)O$R^2$ eller en direkte binding til R^2;

hver av G^1, $G^{1'}$, G^2 og G^2 uavhengig er C_2-C_{12}-alkylen eller C_2-C_{12}-alkenylen;

G^3 er C_2-C_{24}-heteroalkylen eller C_2-C_{24}-heteroalkenylen;

R^a, R^b, R^d og R^e, i hver forekomst, uavhengig er H, C_1-C_{12}-alkyl eller C_2-C_{12}-alkenyl;

R^c og R^f, i hver forekomst, uavhengig er C_1-C_{12}-alkyl eller C_2-C_{12}-alkenyl;

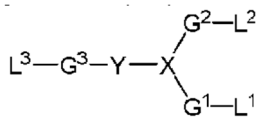
R, i hver forekomst, uavhengig er H eller C_1-C_{12}-alkyl;

R^1 og R^2, i hver forekomst, uavhengig er forgrenet C_6-C_{24}-alkyl eller forgrenet C_6-C_{24}-alkenyl;

z er 0, 1 eller 2, og

hvor hvert alkyl, alkenyl, alkylen, alkenylen, heteroalkylen og heteroalkenylen uavhengig er substituert eller usubstituert dersom ikke annet er angitt; eller

viii) det kationiske lipidet har følgende formel (VIII):



(VIII)

eller et farmasøytisk akseptabelt salt eller stereoisomer derav, hvor:

X er N og Y er fraværende; eller X er CR og Y er NR;

L^1 er-O(C=O)R^1, -(C=O)OR^1, -C(=O)R^1, -OR^1, -S(O)$_x$$R^1$, -S-S$R^1$, -C(=O)S$R^1$, -SC(=O)$R^1$, -N$R^a$C(=O)$R^1$, -C(=O)N$R^b$$R^c$, -N$R^a$C(=O)N$R^b$$R^c$, -OC(=O)N$R^b$$R^c$ eller -NR^aC(=O)OR^1;

L^2 er -O(C=O)R^2, -(C=O)OR^2, -C(=O)R^2, -OR^2, -S(O)$_x$$R^2$, -S-S$R^2$, -C(=O)S$R^2$, -SC(=O)$R^2$, -N$R^d$C(=O)$R^2$, -C(=O)N$R^e$$R^f$, -N$R^d$C(=O)N$R^e$$R^f$, -OC(=O)N$R^e$$R^f$; -N$R^d$C(=O)O$R^2$ eller en direkte binding til R^2;

L^3 er -O(C=O)R^3 eller -(C=O)OR^3;

hver av G^1 og G^2 uavhengig er C_2-C_{12}-alkylen eller C_2-C_{12}-alkenylen;

G^3 er C_1-C_{24}-alkylen, C_2-C_{24}-alkenylen, C_1-C_{24}-heteroalkylen eller C_2-C_{24}-heteroalkenylen når X er CR og Y er NR; og G^3 er C_1-C_{24}-heteroalkylen eller C_2-C_{24}-heteroalkenylen når X er N og Y er fraværende;

hver av R^a, R^b, R^d og R^e uavhengig er H eller C_1-C_{12}-alkyl eller C_1-C_{12}-alkenyl;

hver av R^c og R^f uavhengig er C_1-C_{12}-alkyl eller C_2-C_{12}-alkenyl;

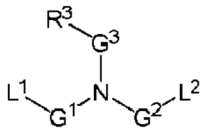
hver R uavhengig er H eller C_1-C_{12}-alkyl;

hver av R^1, R^2 og R^3 uavhengig er C_1-C_{24}-alkyl eller C_2-C_{24}-alkenyl; og

x er 0, 1 eller 2, og

hvor hvert alkyl, alkenyl, alkylen, alkenylen, heteroalkylen og heteroalkenylen uavhengig er substituert eller usubstituert dersom ikke annet er angitt; eller

ix) det kationiske lipidet har følgende formel (IX):



(IX)

eller et farmasøytisk akseptabelt salt eller stereoisomer derav, hvor:

L^1 er -O(C=O)R^1, -(C=O)OR^1, -C(=O)R^1, -OR^1, -S(O)$_x$$R^1$, -S-S$R^1$, -C(=O)S$R^1$, - SC(=O)$R^1$, -$NR^aC(=O)R^1$, -C(=O)$NR^bR^c$, -$NR^aC(=O)NR^bR^c$, -OC(=O)$NR^bR^c$ eller -$NR^aC(=O)OR^1$;

L^2 er -O(C=O)R^2, -(C=O)OR^2, -C(=O)R^2, -OR^2, -S(O)$_x$$R^2$, -S-S$R^2$, -C(=O)S$R^2$, - SC(=O)$R^2$, -$NR^dC(=O)R^2$, -C(=O)$NR^eR^f$, -$NR^dC(=O)NR^eR^f$, -OC(=O)$NR^eR^f$; -$NR^dC(=O)OR^2$ eller en direkte binding til R^2;

hver av G^1 og G^2 uavhengig er C_2-C_{12}-alkylen eller C_2-C_{12}-alkenylen;

G^3 er C_1-C_{24}-alkylen, C_2-C_{24}-alkenylen, C_3-C_8-sykloalkylen eller C_3-C_8-sykloalkenylen;

hver av R^a, R^b, R^d og R^e uavhengig er H eller C_1-C_{12}-alkyl eller C_1-C_{12}-alkenyl;

hver av R^c og R^f uavhengig er C_1-C_{12}-alkyl eller C_2-C_{12}-alkenyl;

hver av R^1 og R^2 uavhengig er forgrenet C_6-C_{24}-alkyl eller forgrenet C_6-C_{24}-alkenyl;

R^3 er -N(R^4)R^5;

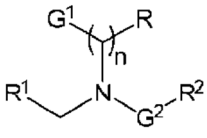
R^4 er C_1-C_{12}-alkyl;

R^5 er substituert C_1-C_{12}-alkyl; og

x er 0, 1 eller 2, og

hvor hvert alkyl, alkenyl, alkylen, alkenylen, sykloalkylen, sykloalkenylen, aryl og aralkyl uavhengig er substituert eller usubstituert dersom ikke annet er angitt; eller

x) det kationiske lipidet har følgende formel (X):



(X)

eller et farmasøytisk akseptabelt salt eller stereoisomer derav, hvor:

G^1 er -OH, -NR^3R^4, -(C=O)NR^5 eller -NR^3(C=O)R^5;

G^2 er -CH_2- eller -(C=O)-;

R, i hver forekomst, uavhengig er H eller OH;

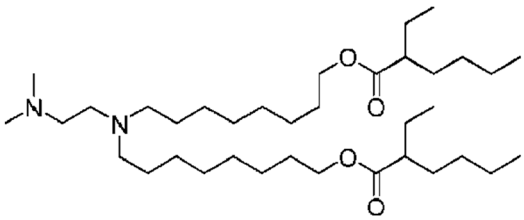
hver av R^1 og R^2 uavhengig eventuelt er substituert forgrenet, mettet eller umettet C_{12}-C_{36}-alkyl;

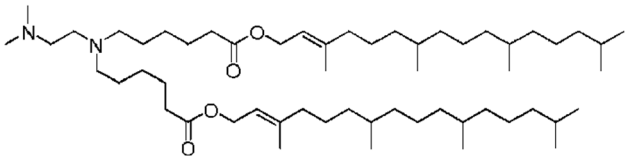
hver av R^3 og R^4 uavhengig er H eller eventuelt substituert rett eller forgrenet, mettet eller umettet C_1-C_6-alkyl;

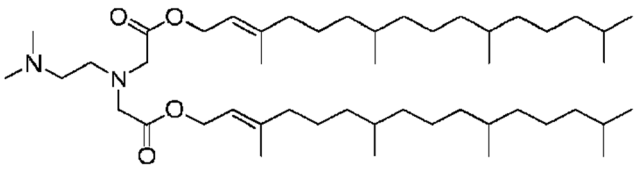
R^5 eventuelt er substituert rett eller forgrenet, mettet eller umettet C_1-C_6-alkyl; og

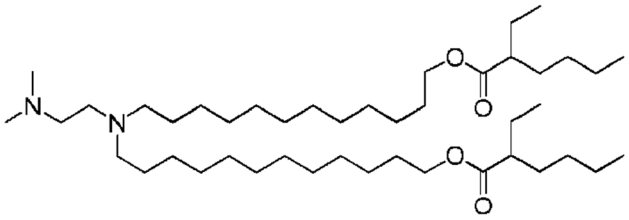
n er et heltall fra 2 til 6.

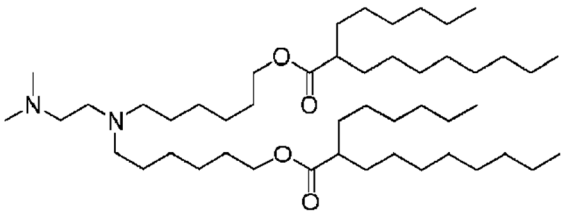
5. LNP'er for bruk ifølge et hvilket som helst av kravene 1-4, hvor det kationiske lipidet er dannet fra en lipidstruktur valgt fra:

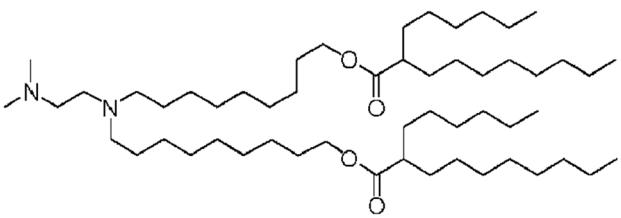


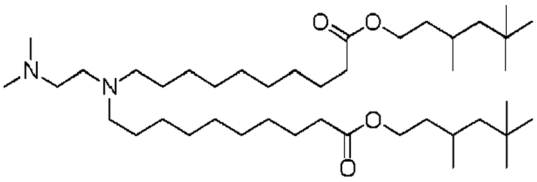


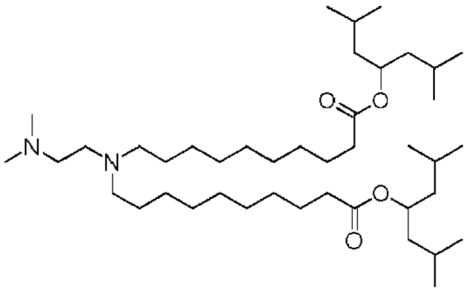


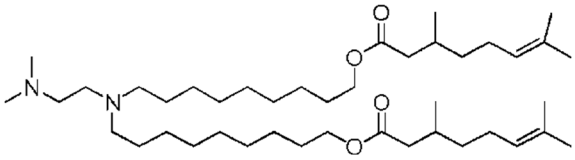


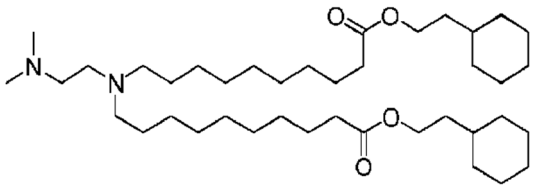


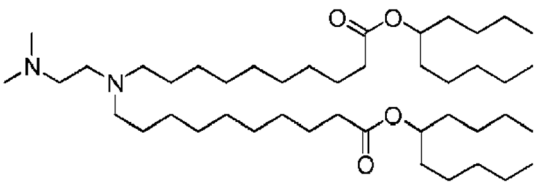


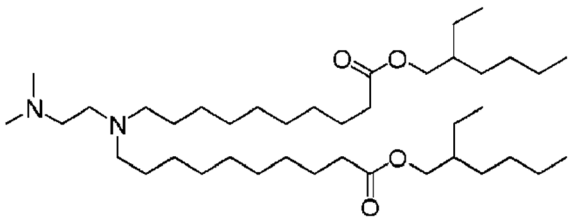


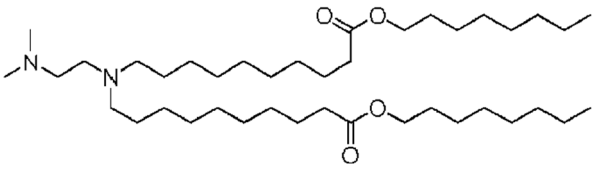


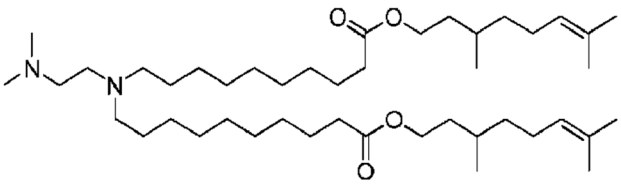


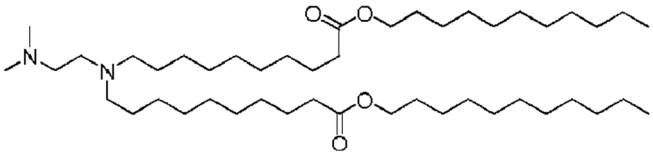


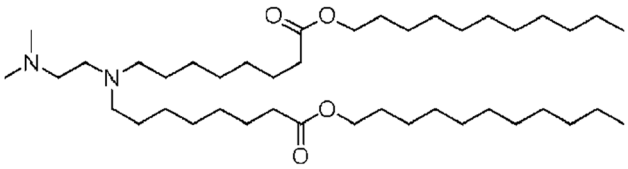


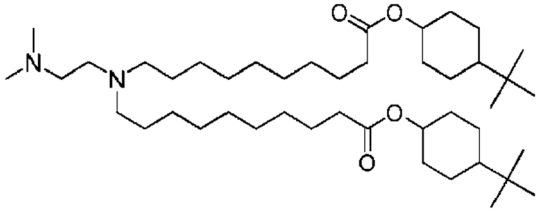


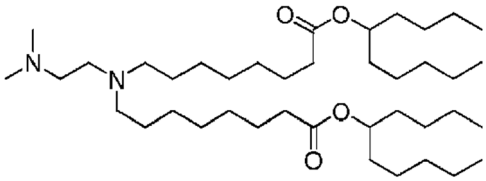


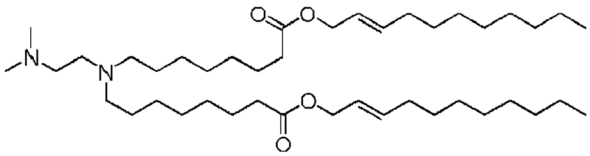


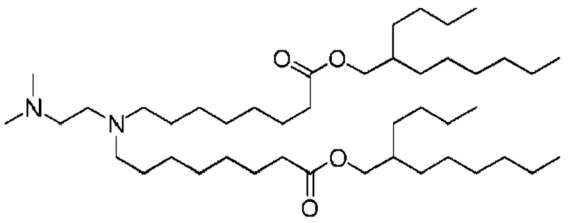


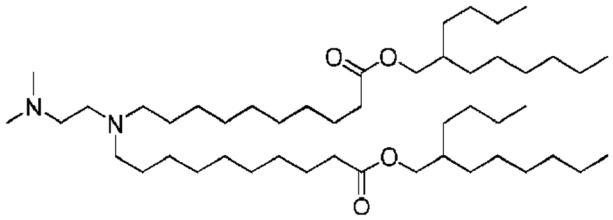


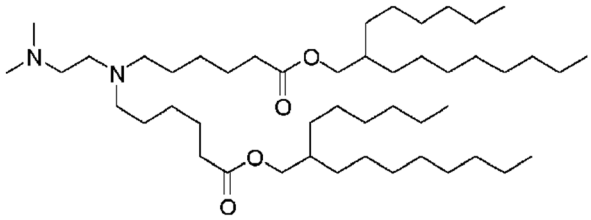


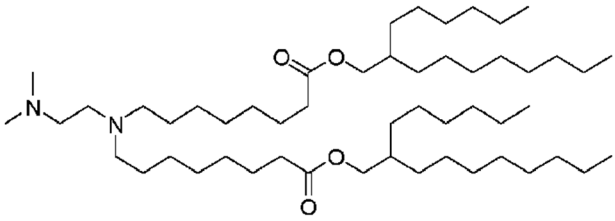


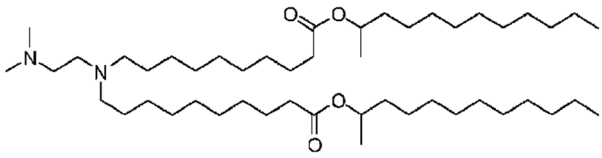


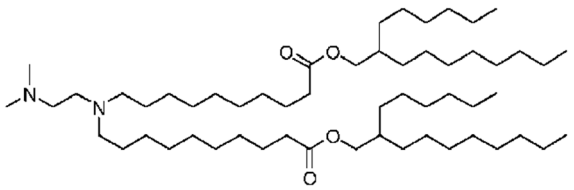


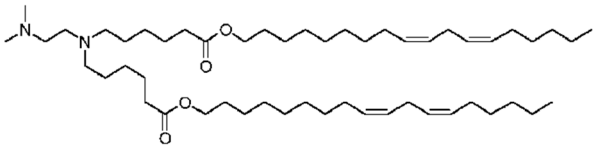


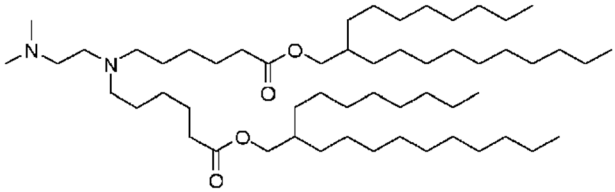


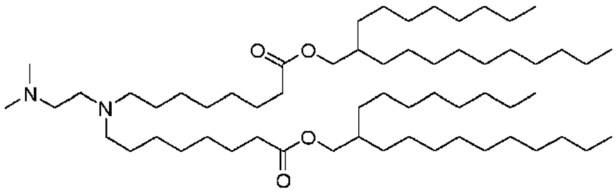


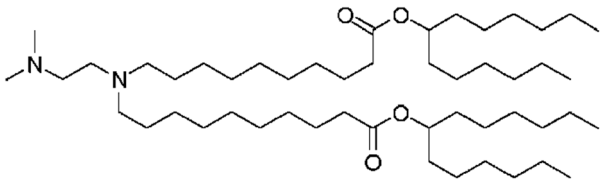


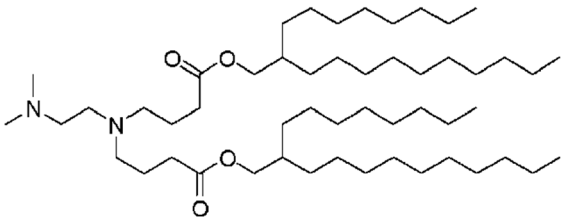


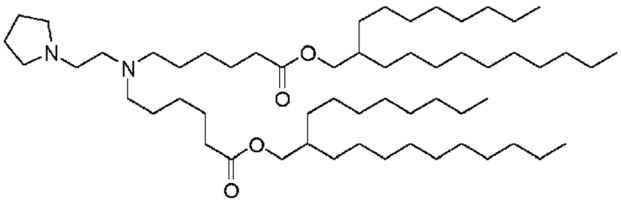


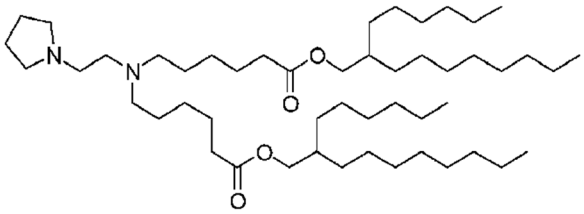


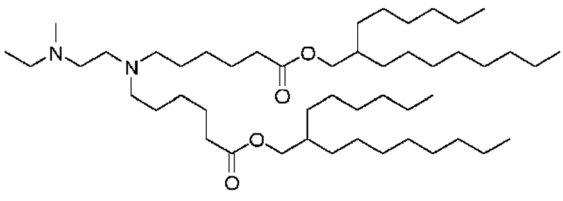


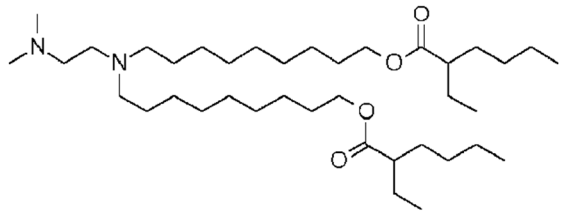


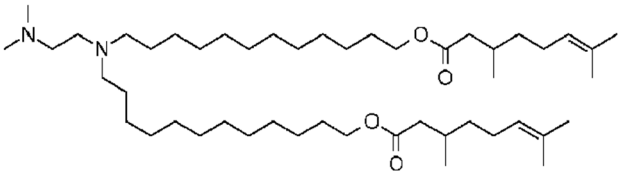


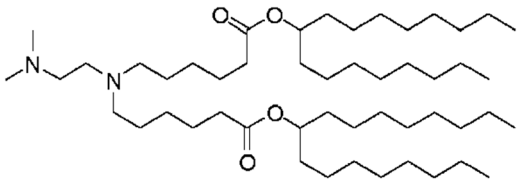


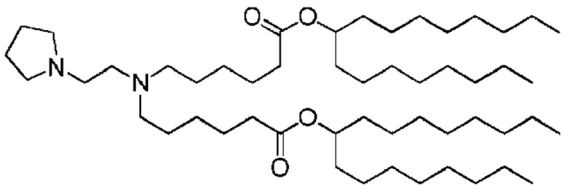


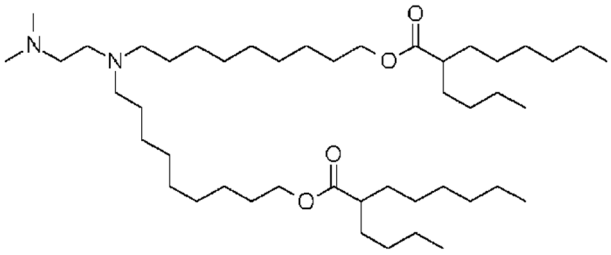


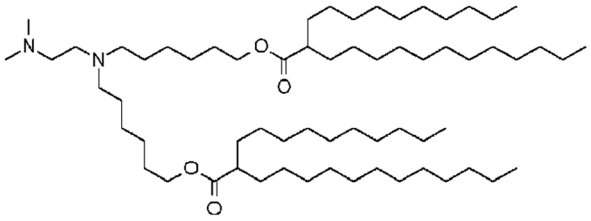


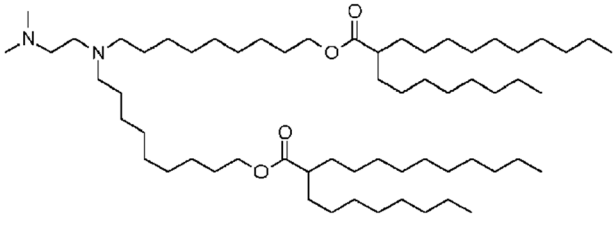


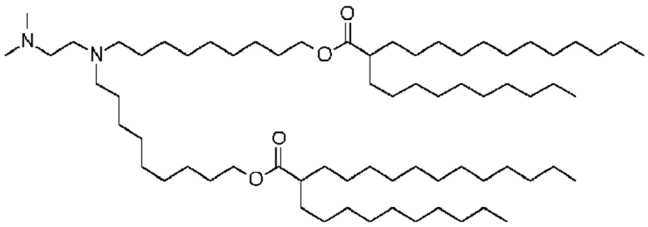


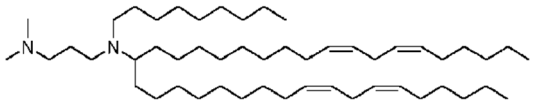


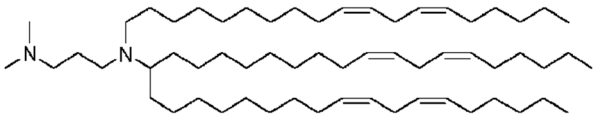


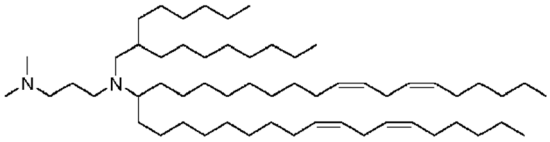


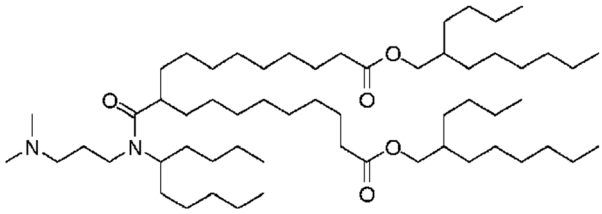


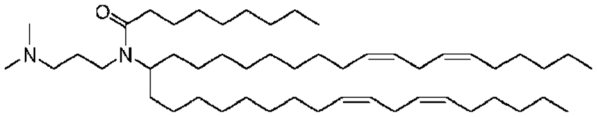


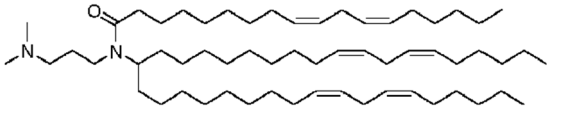


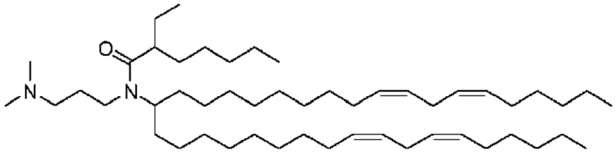


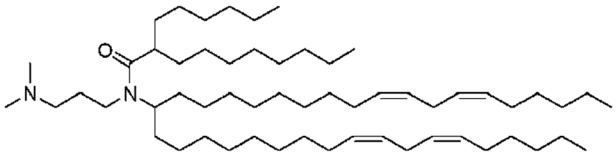


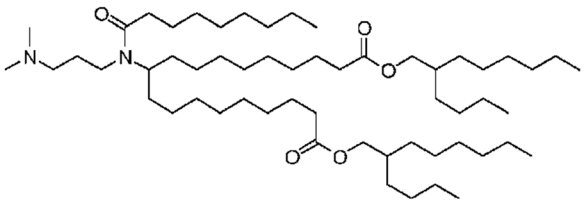


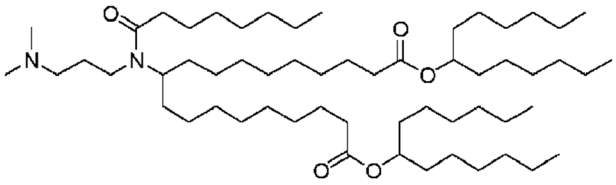


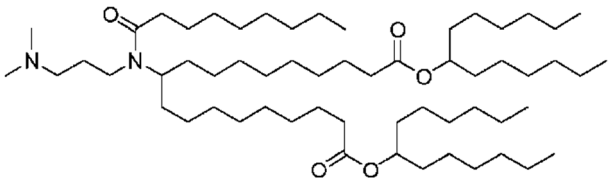


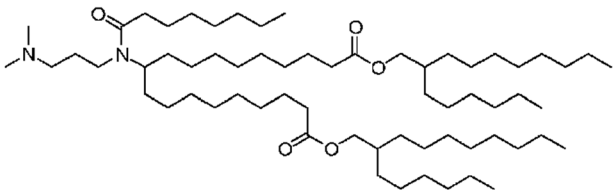


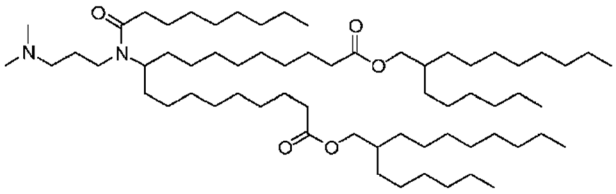


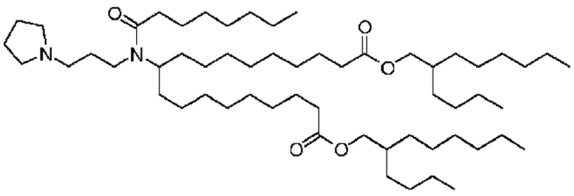


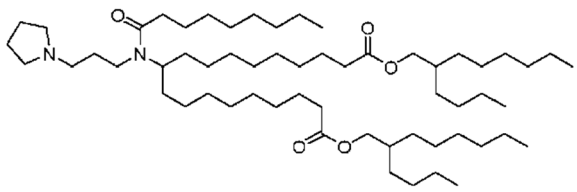


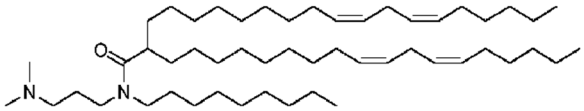


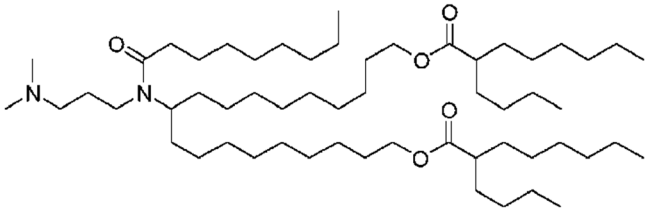


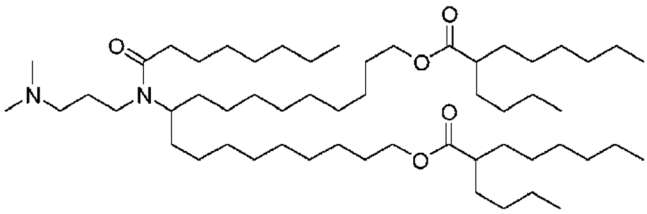


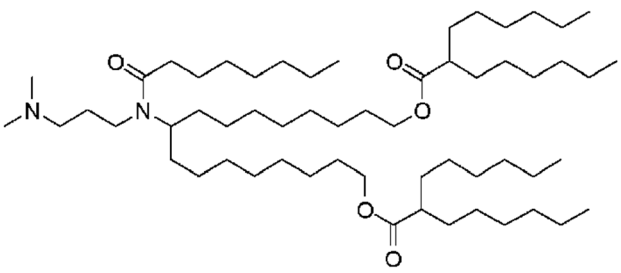


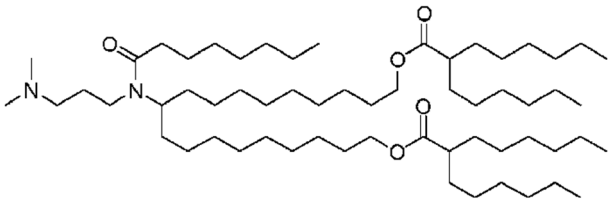


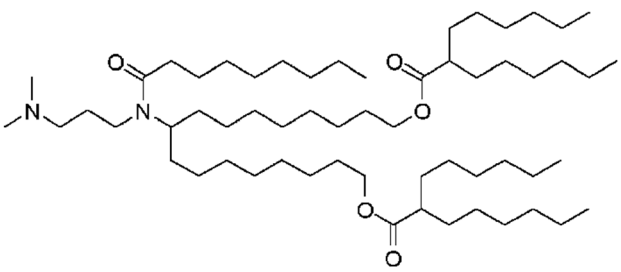


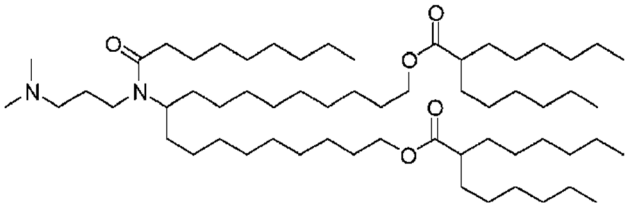


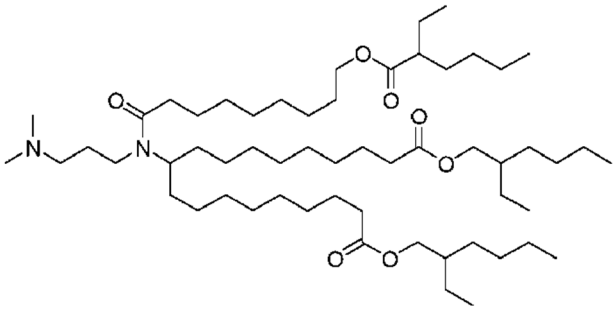


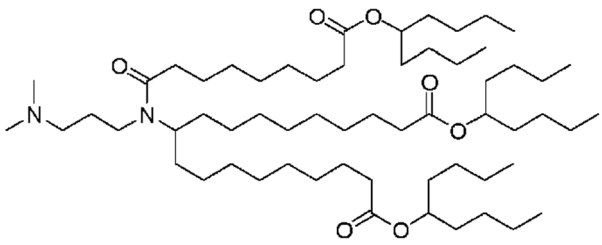


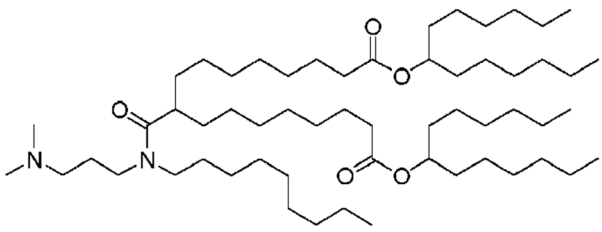


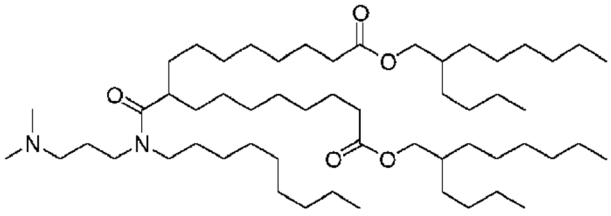


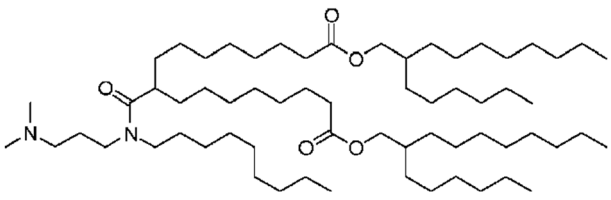


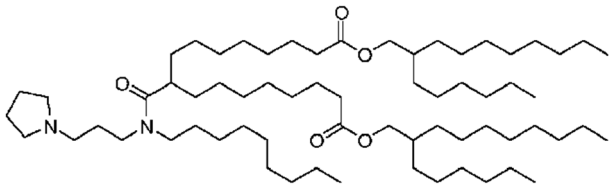


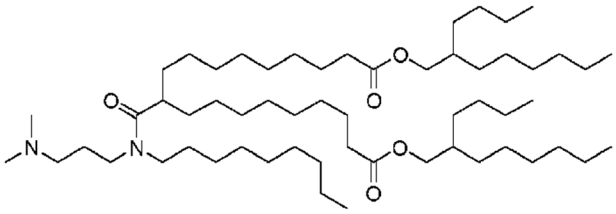


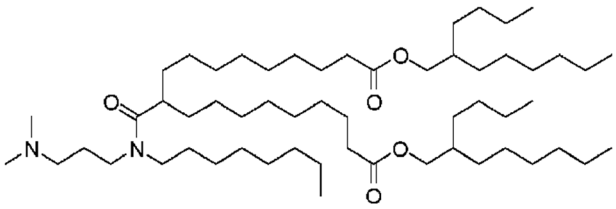


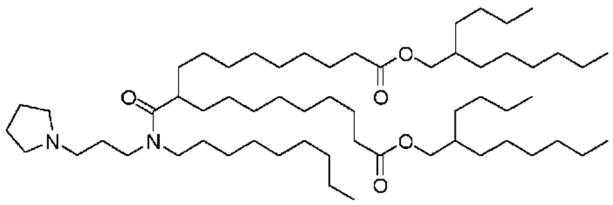


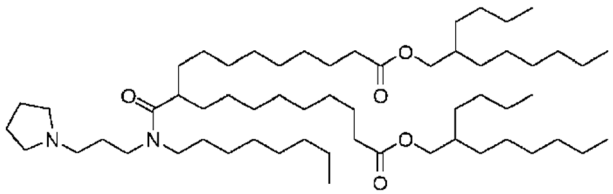


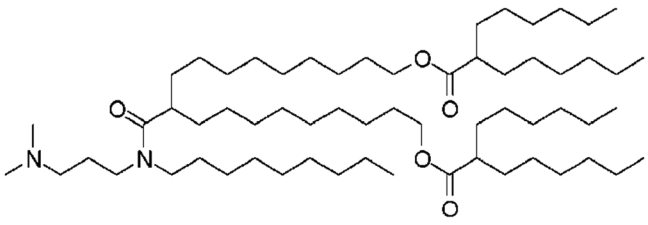


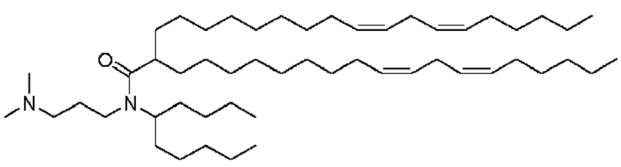


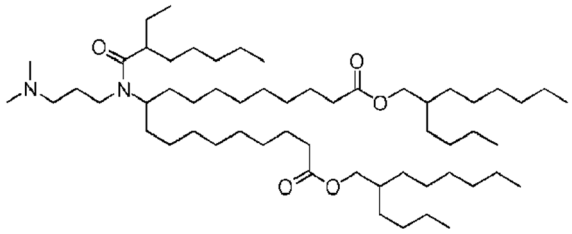


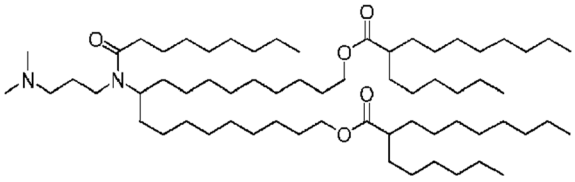


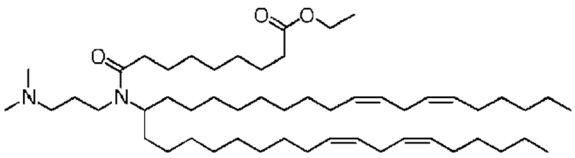


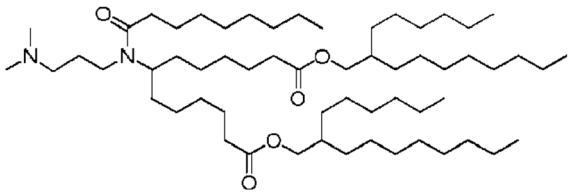


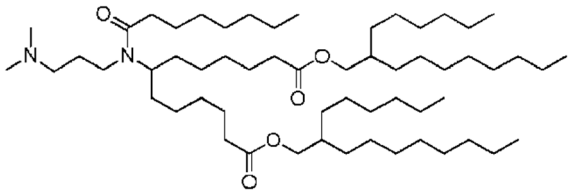


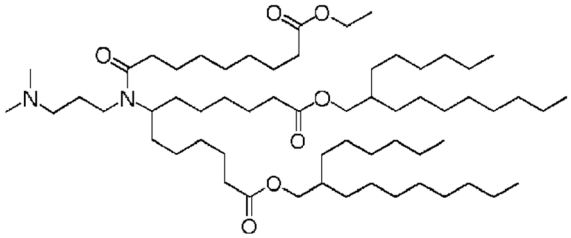


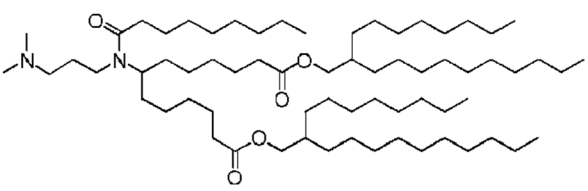


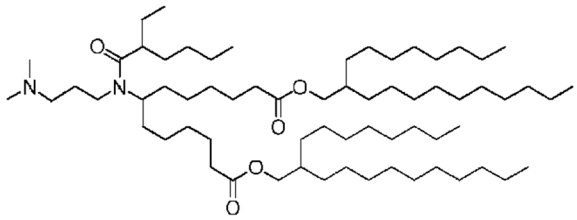


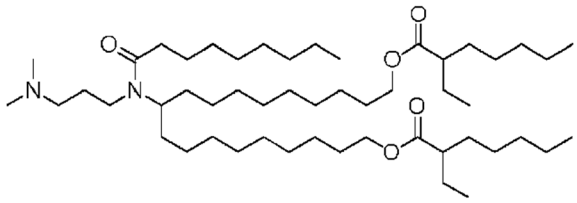


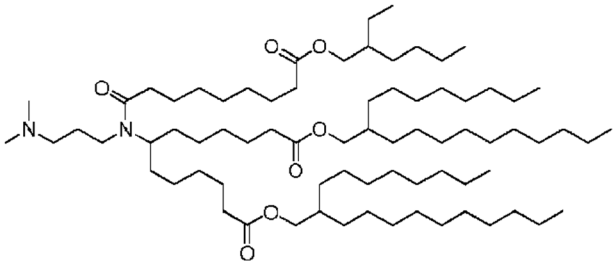


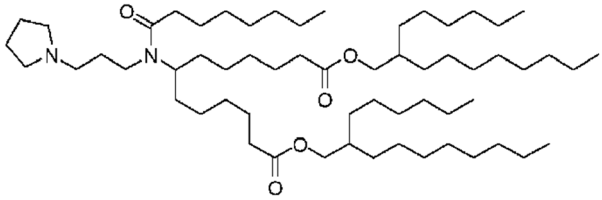


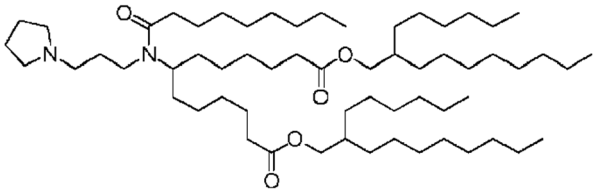


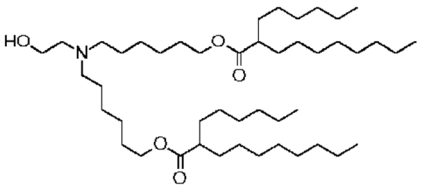


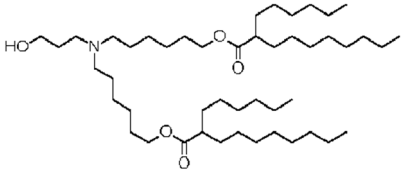


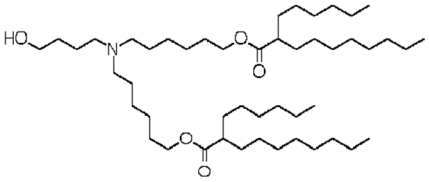


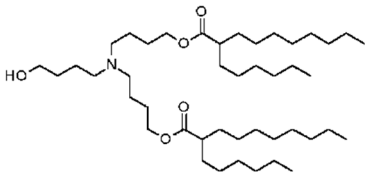


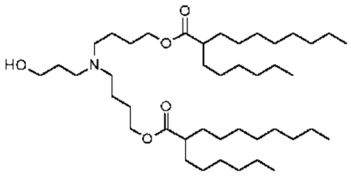


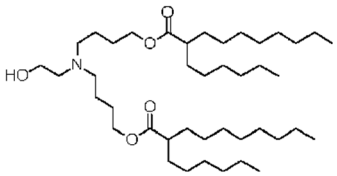


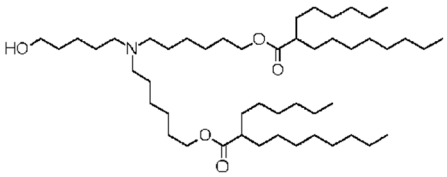


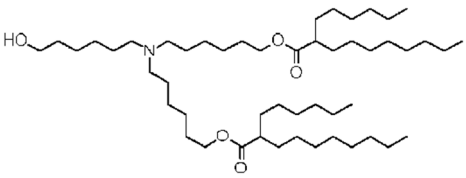


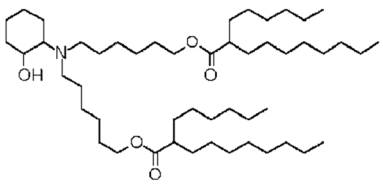


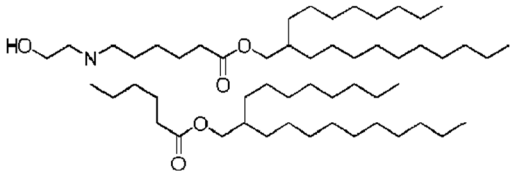


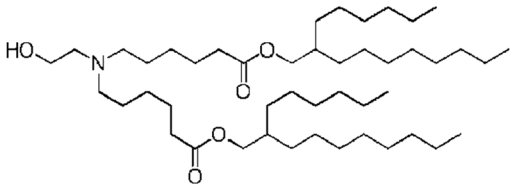


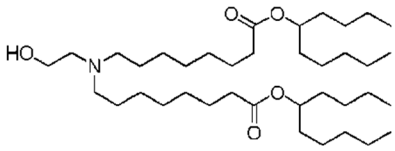


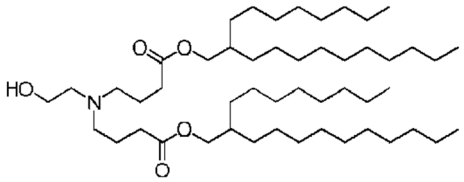


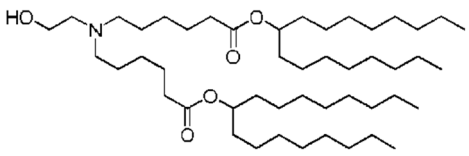


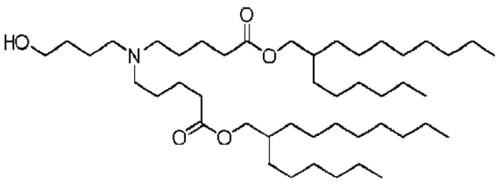


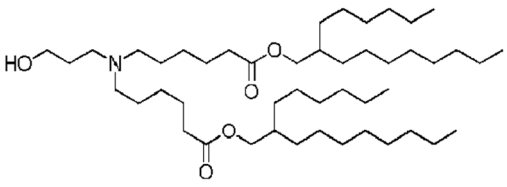


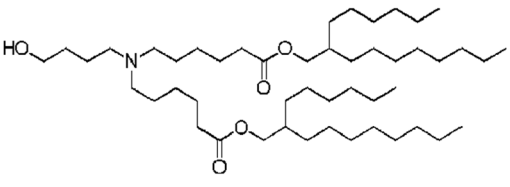


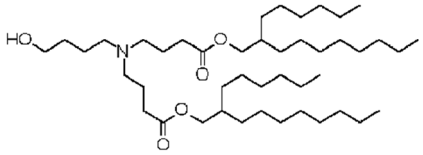


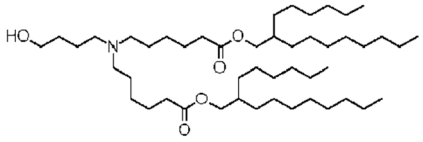


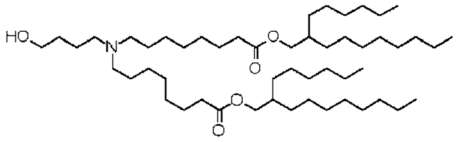


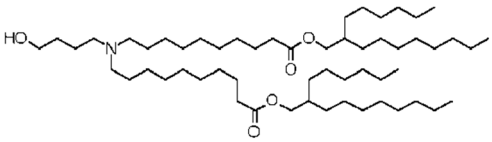


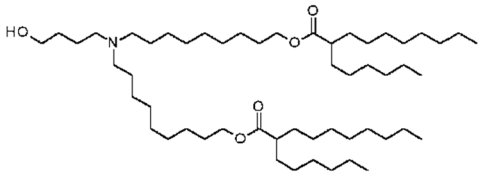


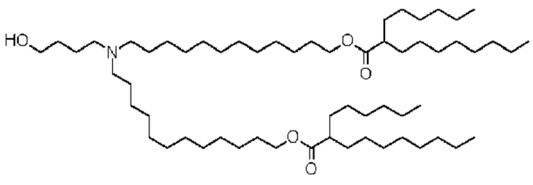


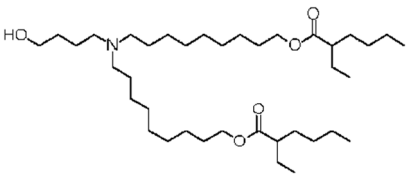


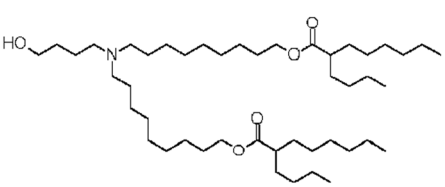


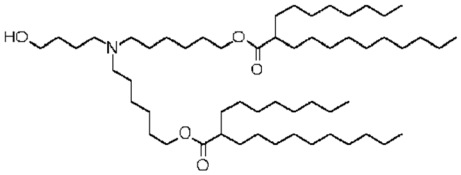


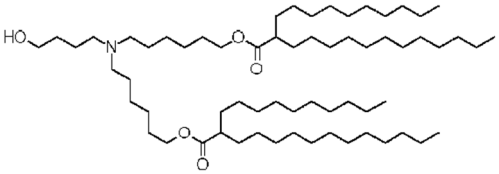


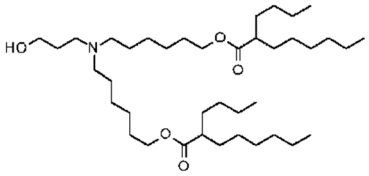


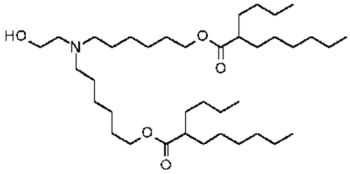


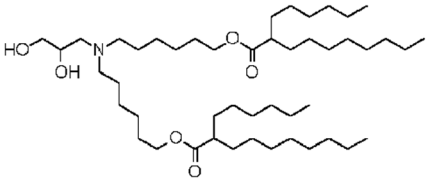


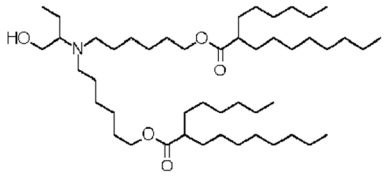


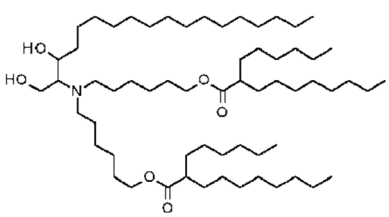


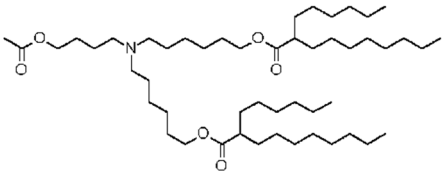


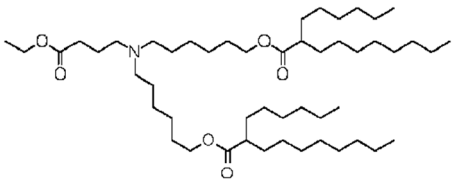


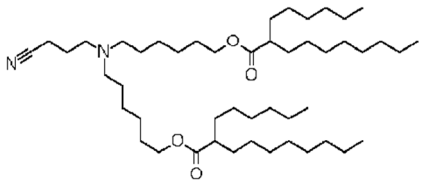


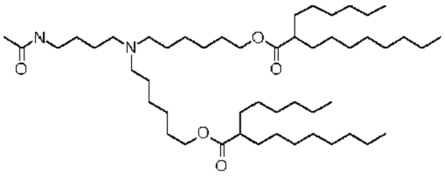


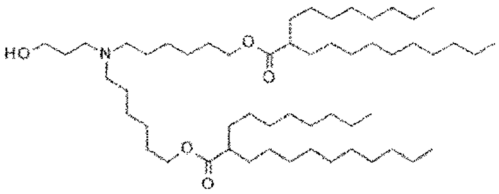


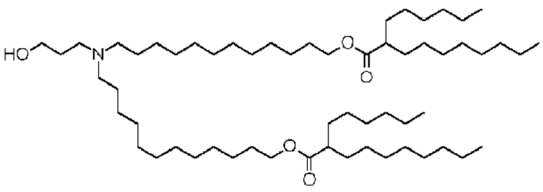


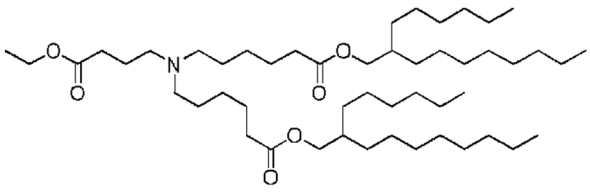


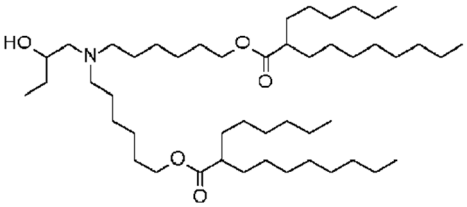


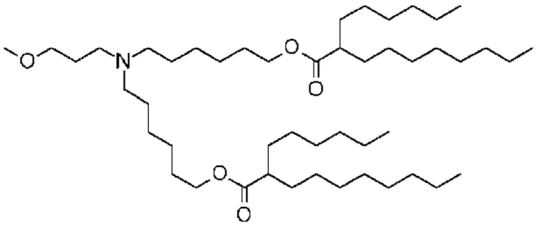


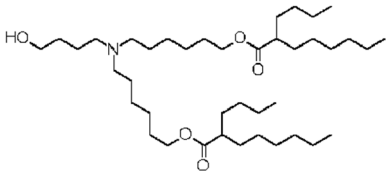


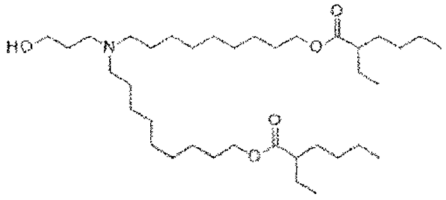


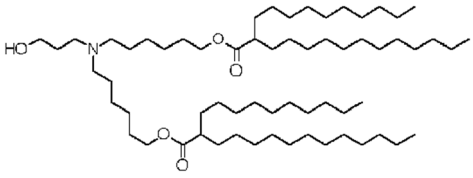


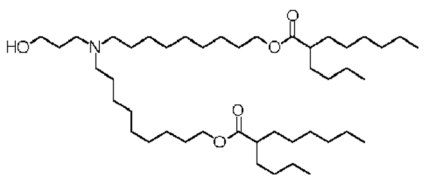


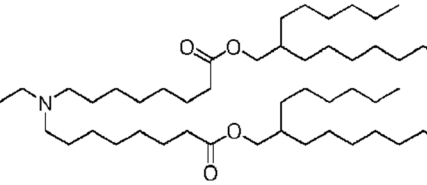


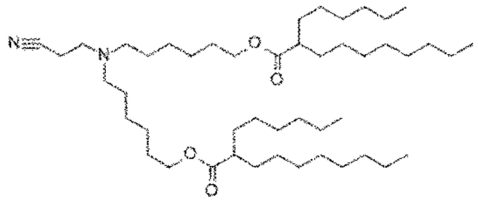


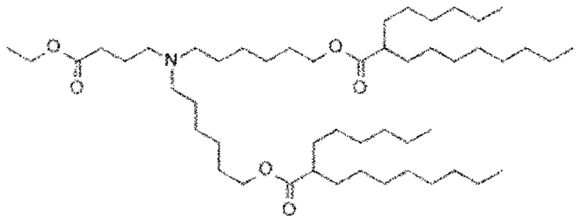


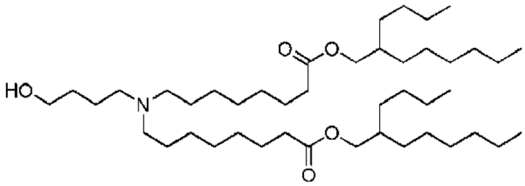


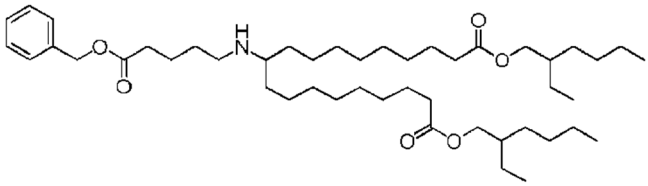


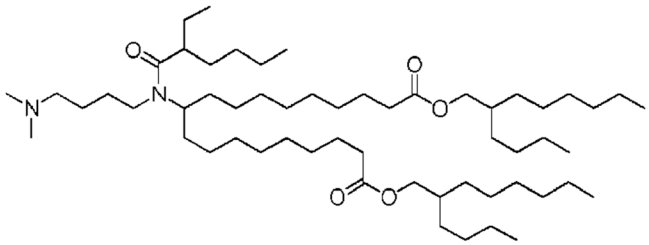


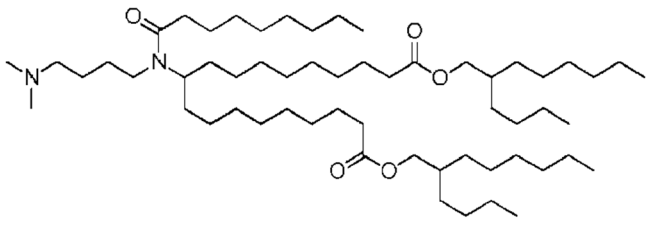


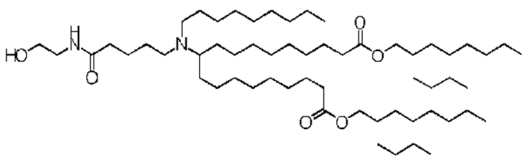


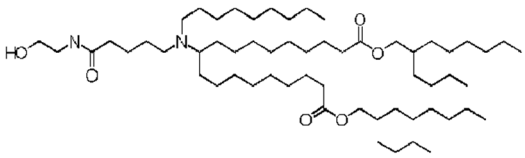


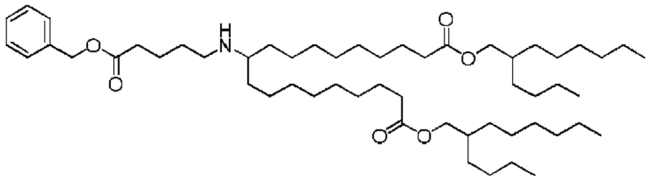


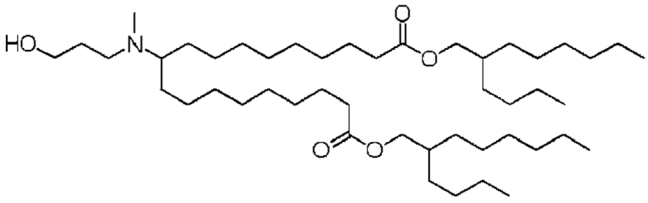


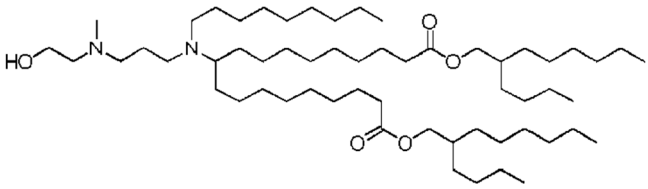


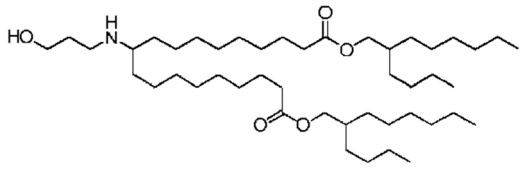


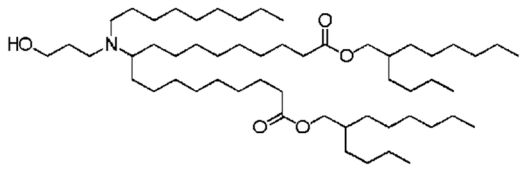


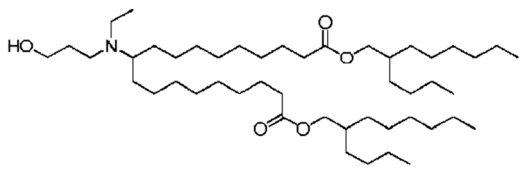


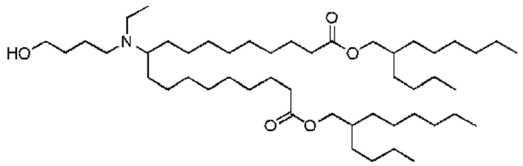


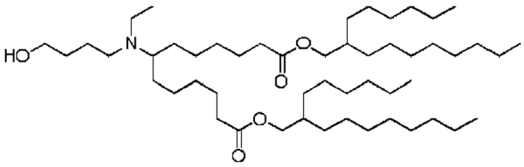


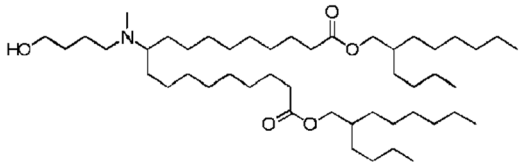


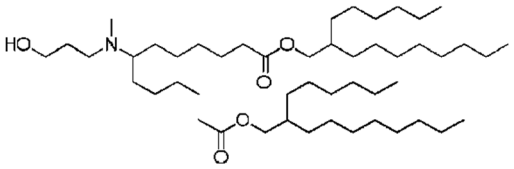


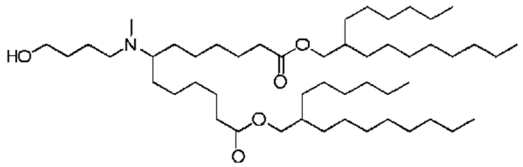


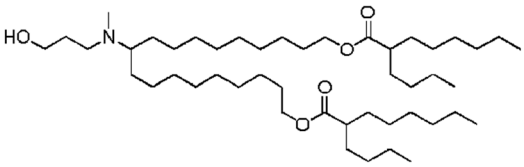


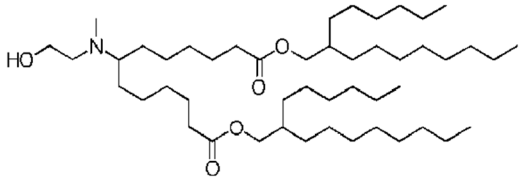


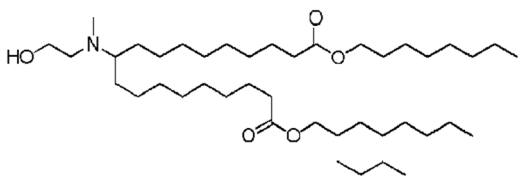


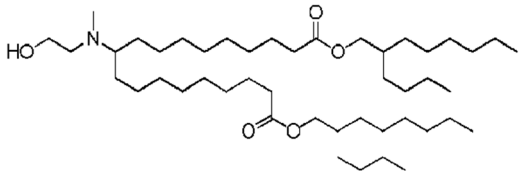


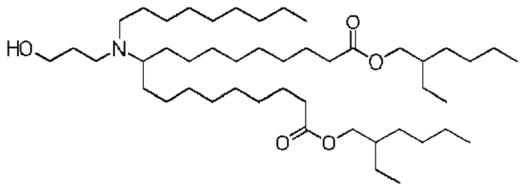


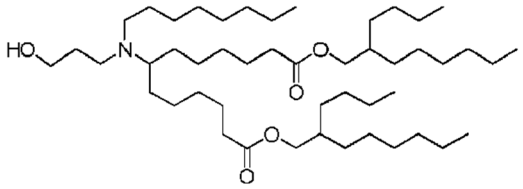


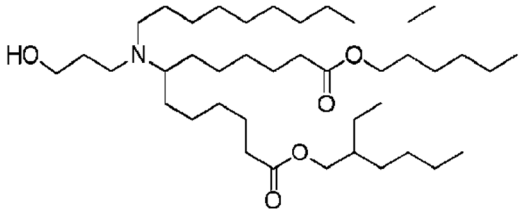


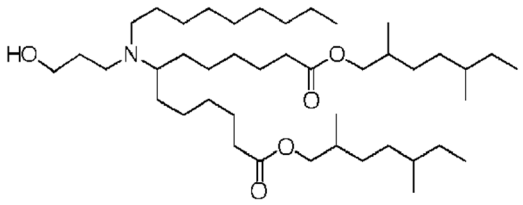


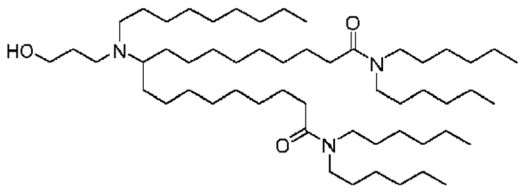


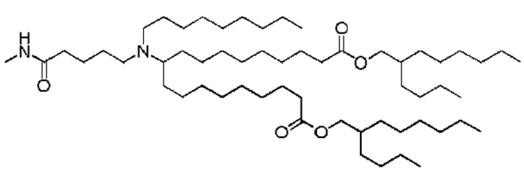


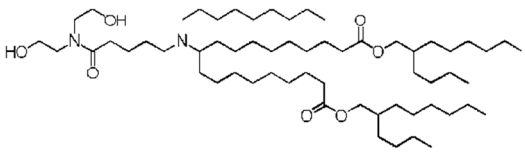


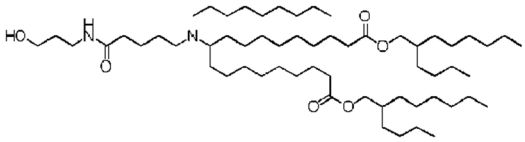


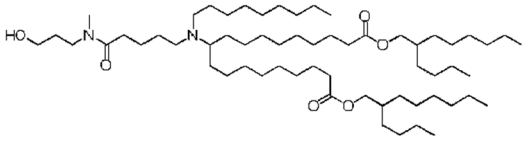


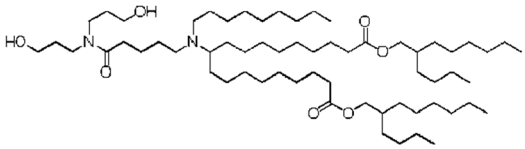


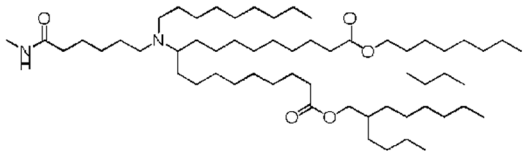


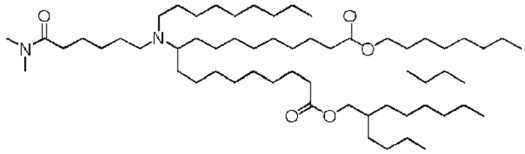


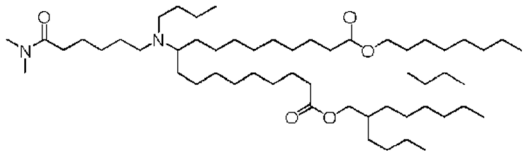


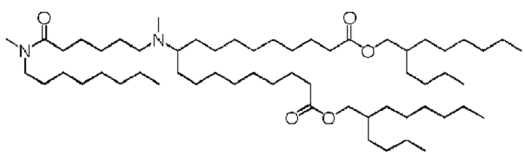


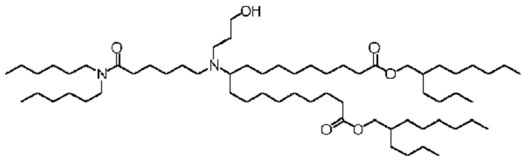


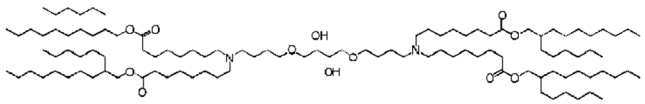


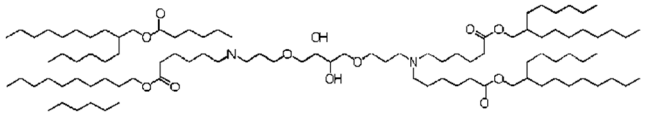


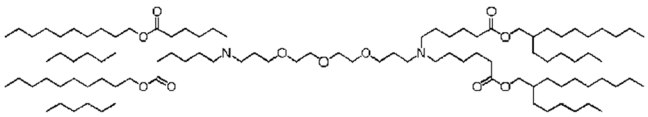


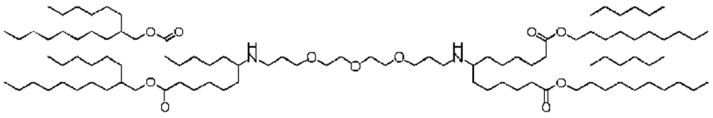


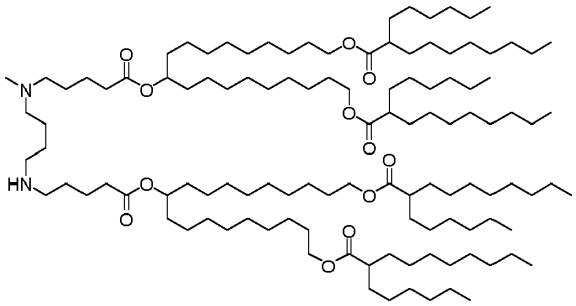


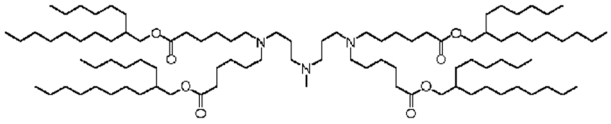


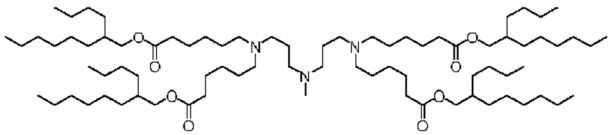


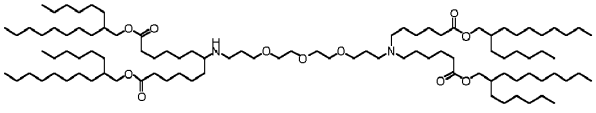


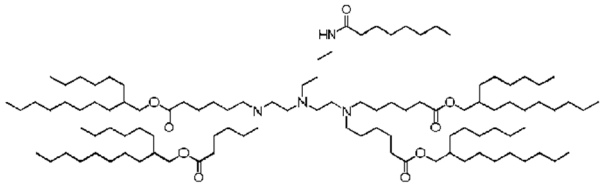


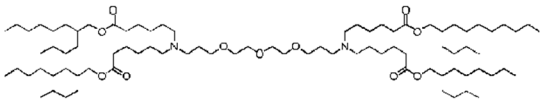


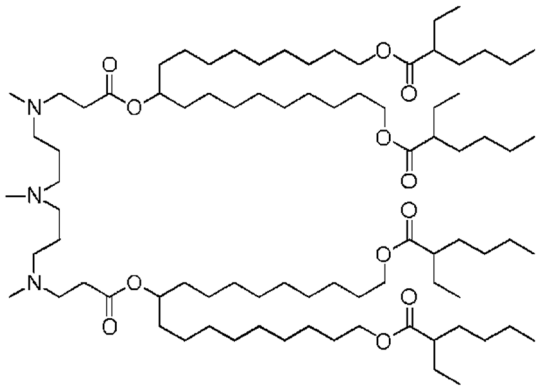


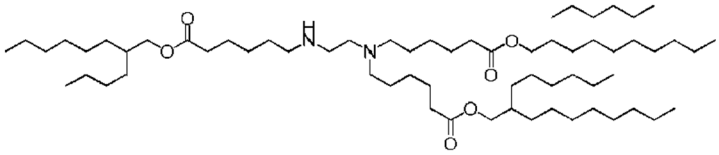


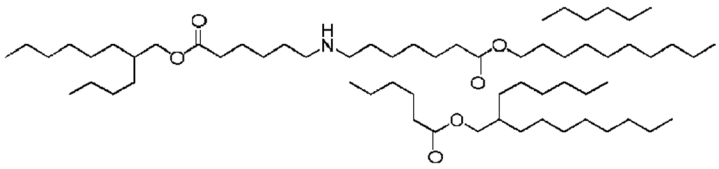


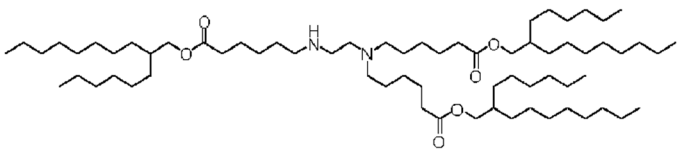


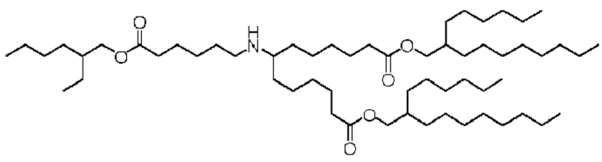


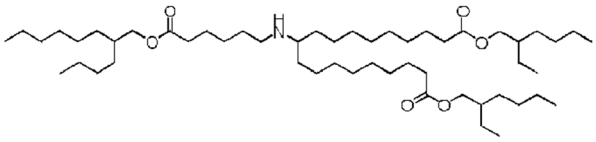


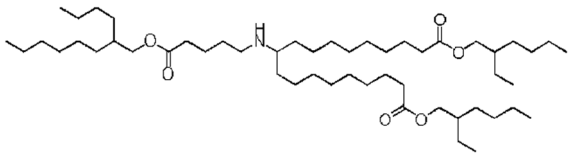


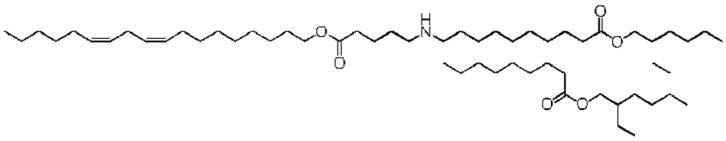


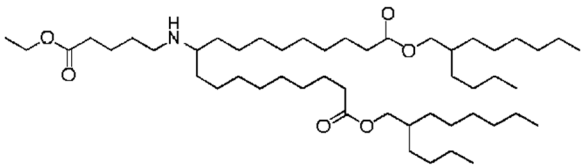


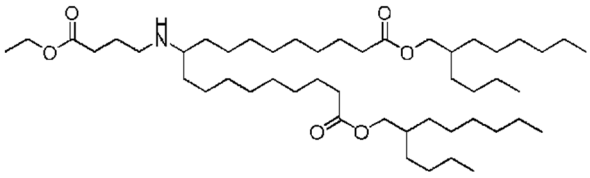


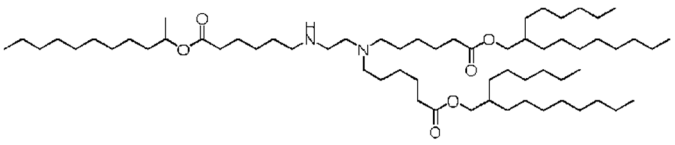


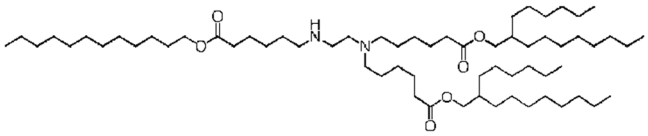


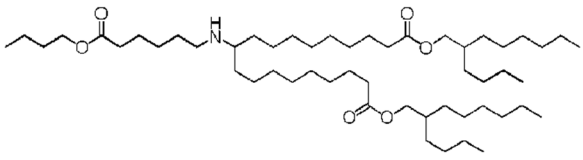


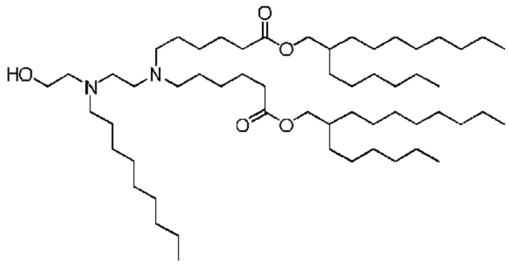


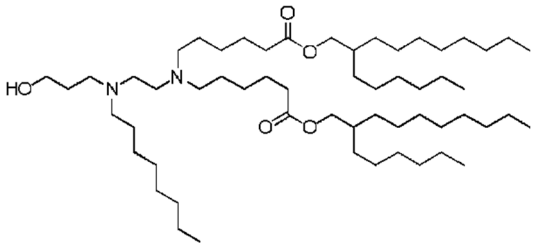


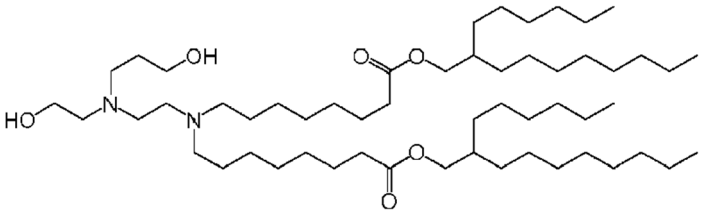


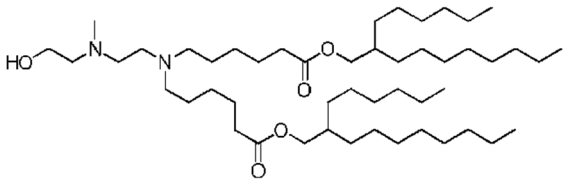


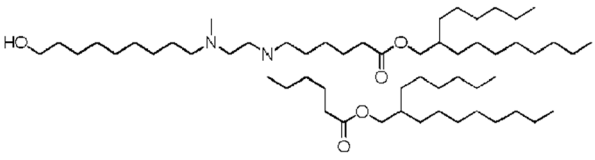


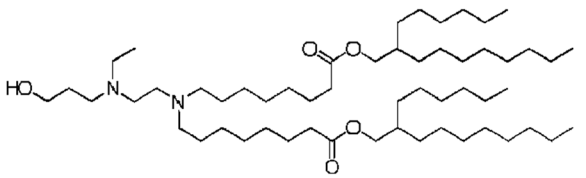


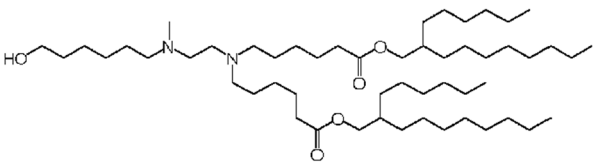


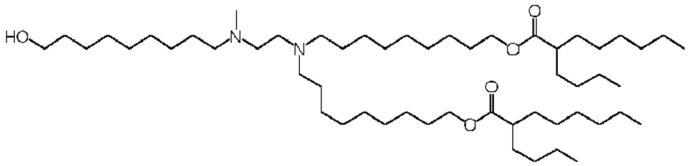


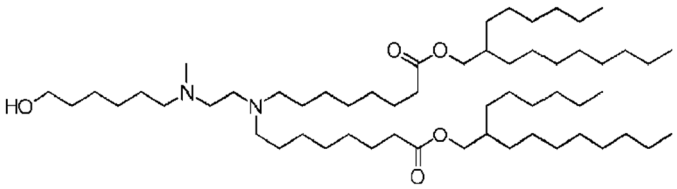


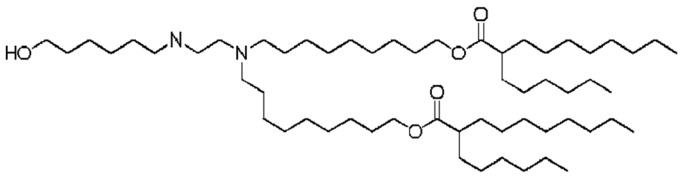


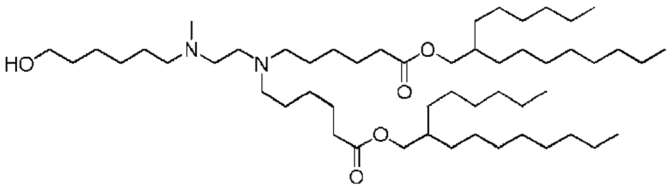


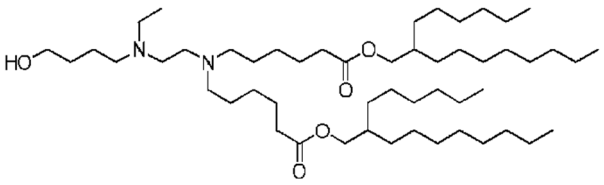


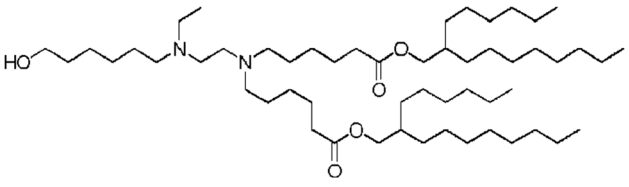


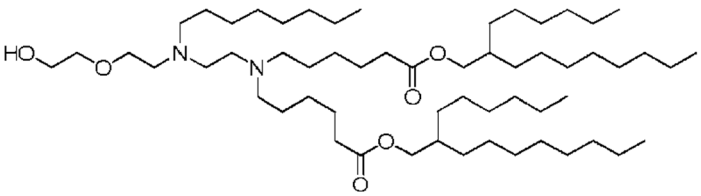


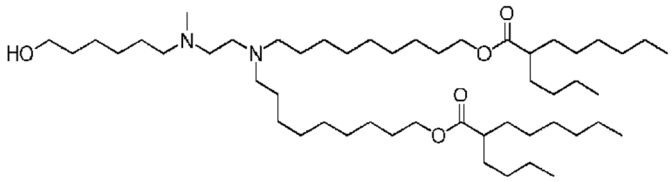


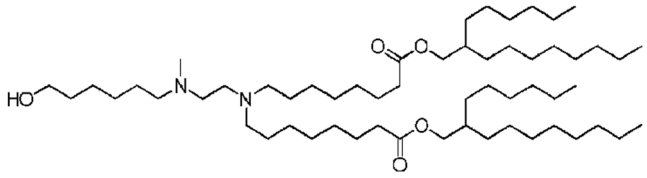


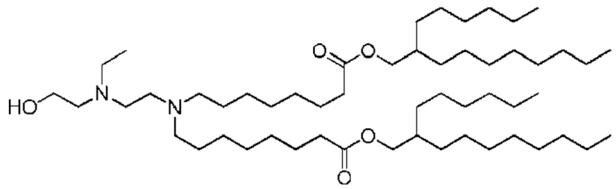


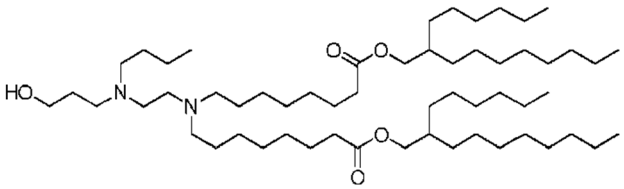


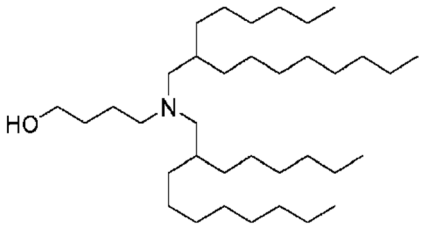


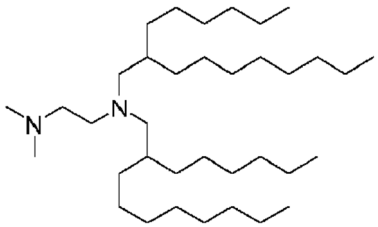


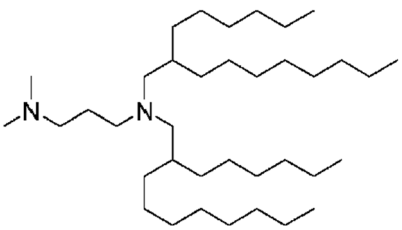


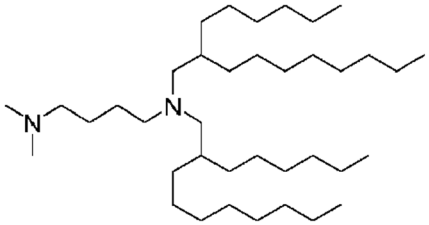


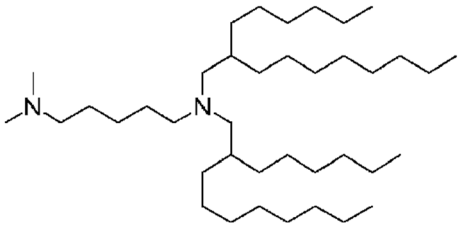


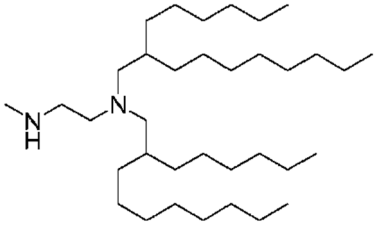


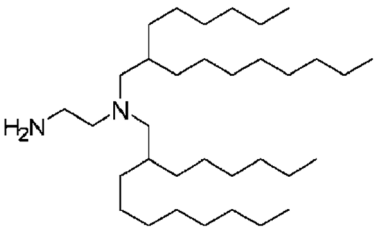


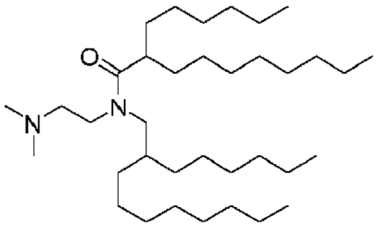


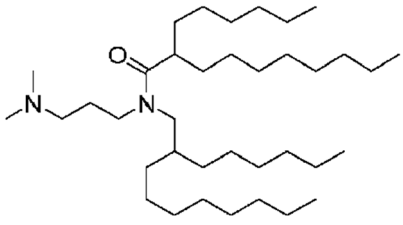


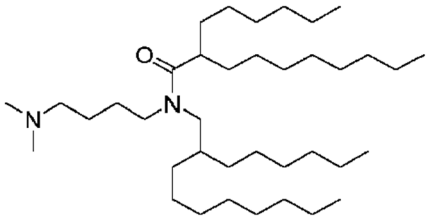


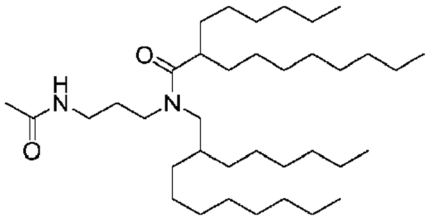


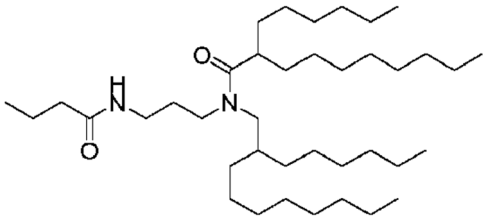


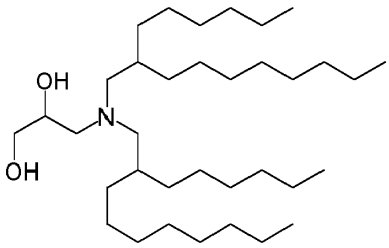


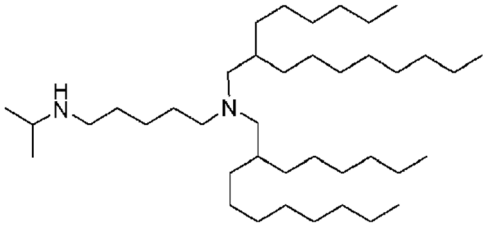


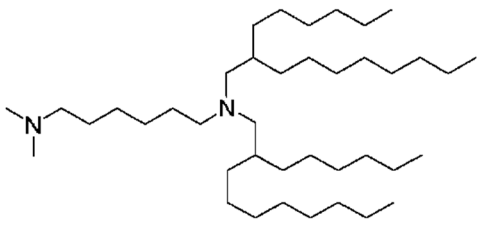


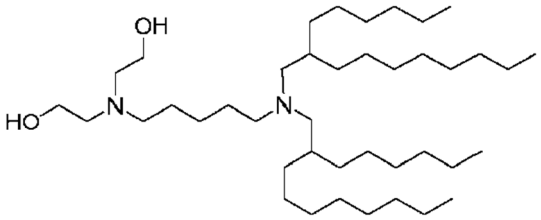


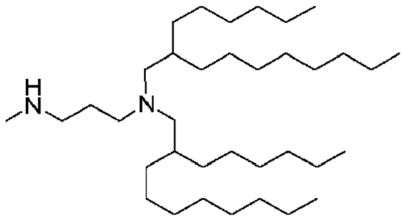


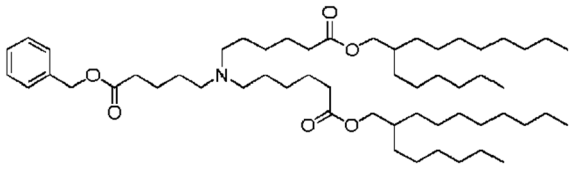


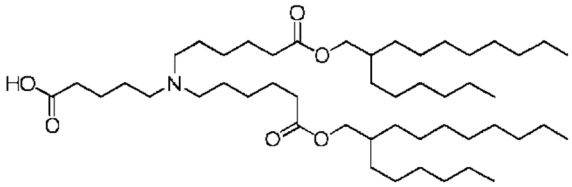


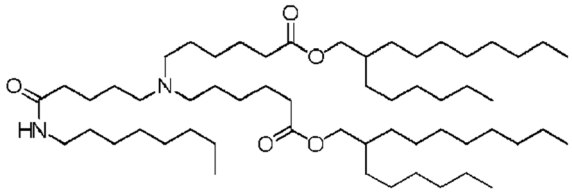


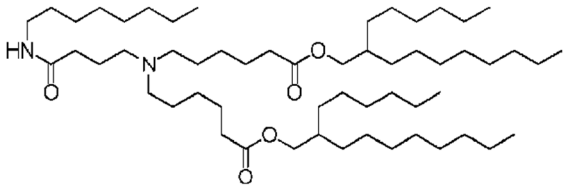


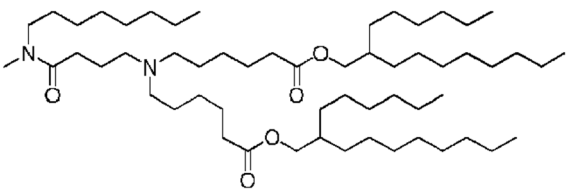


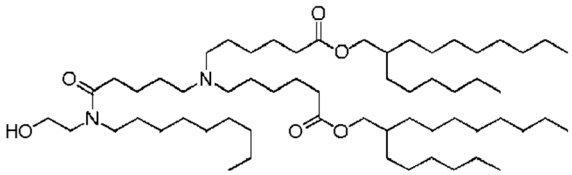


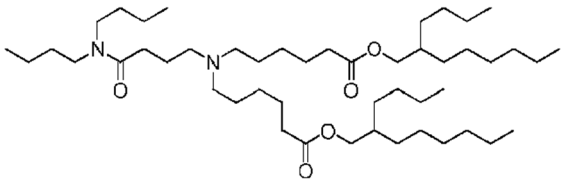


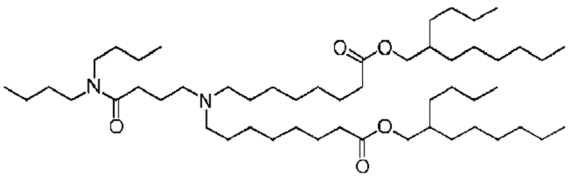


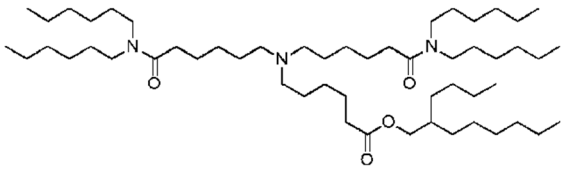


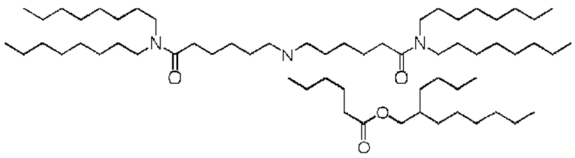


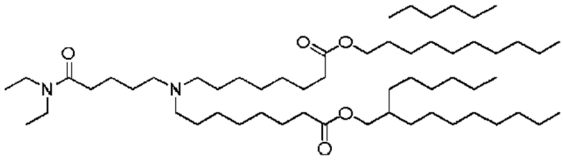


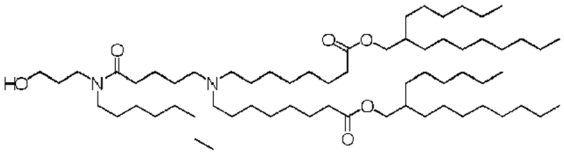


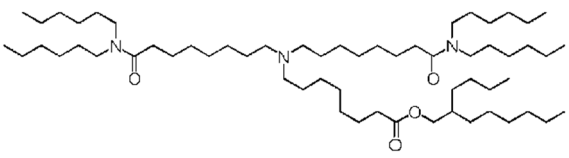


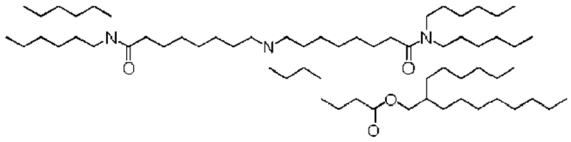


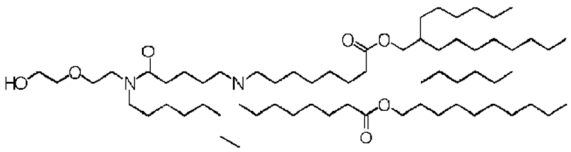


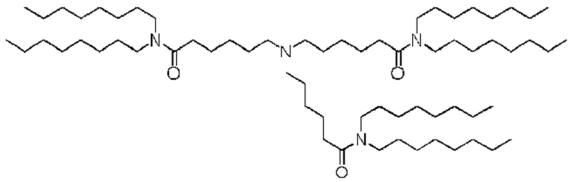


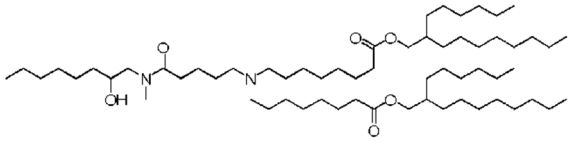


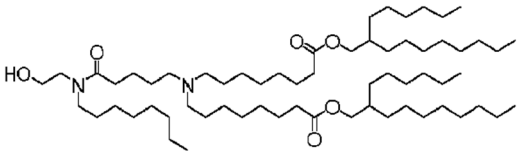


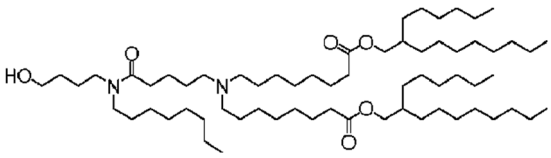


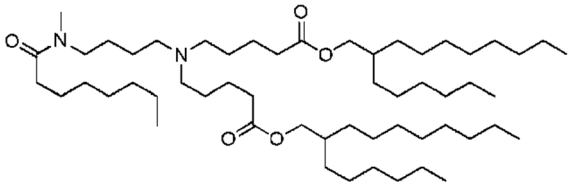


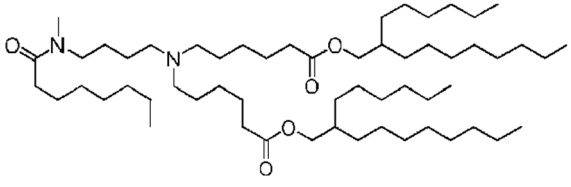


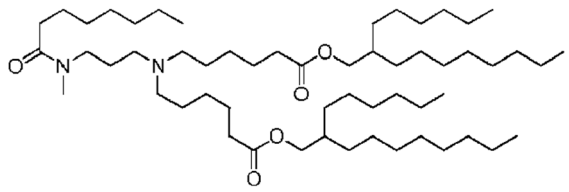


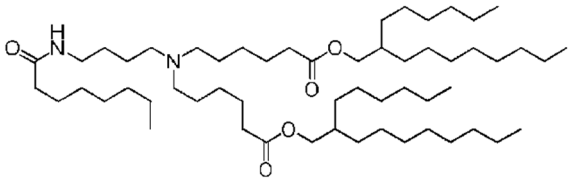


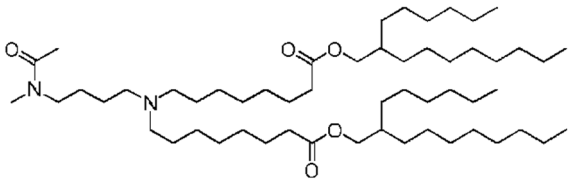


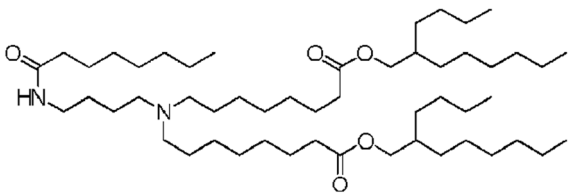


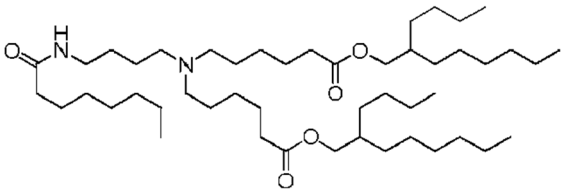


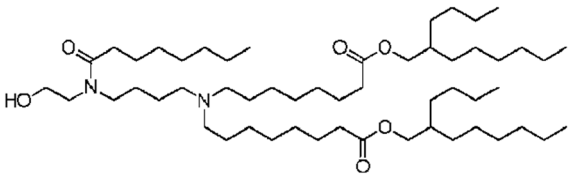


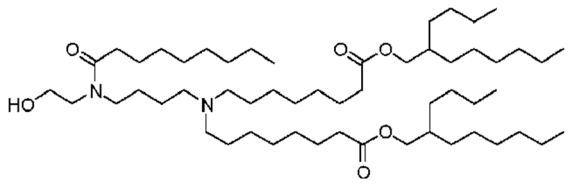


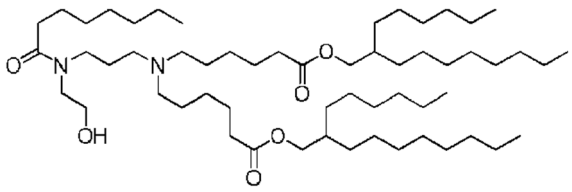


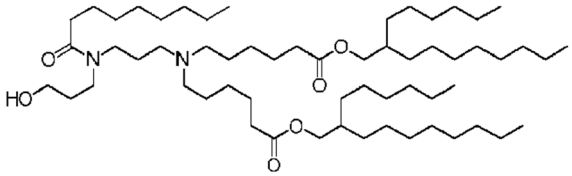


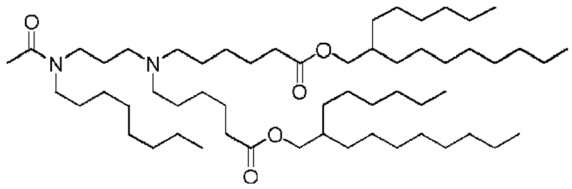


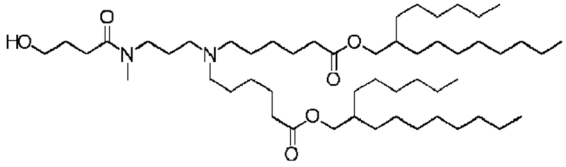


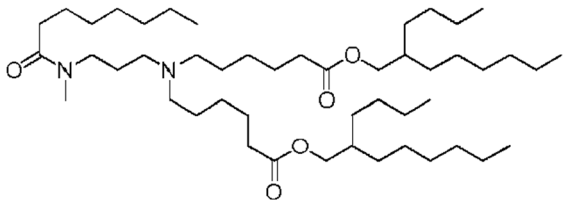


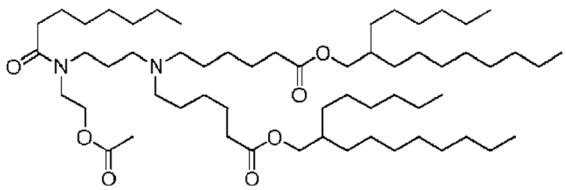


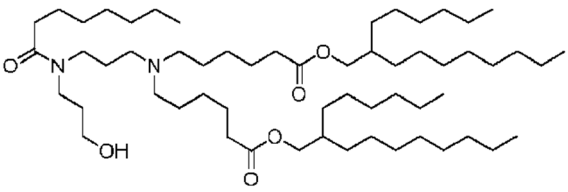


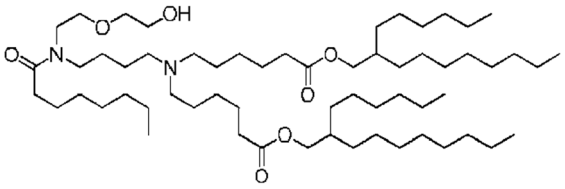


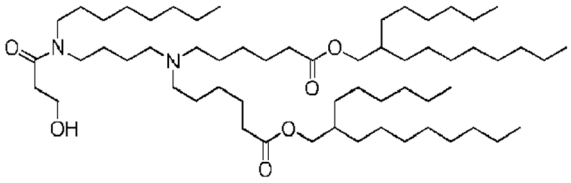


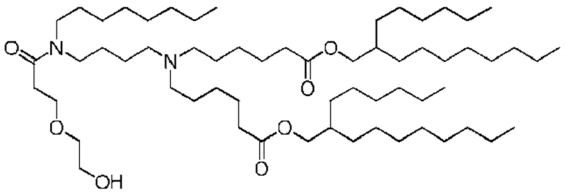


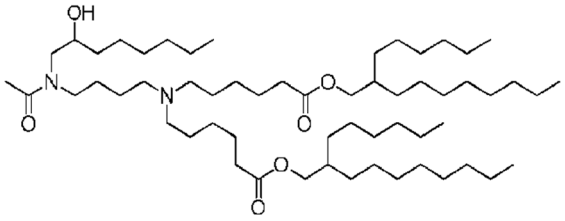


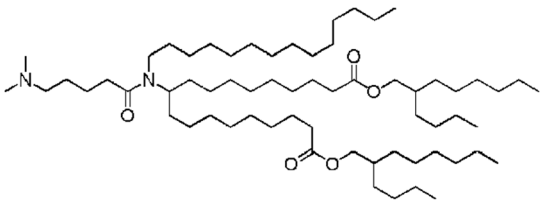


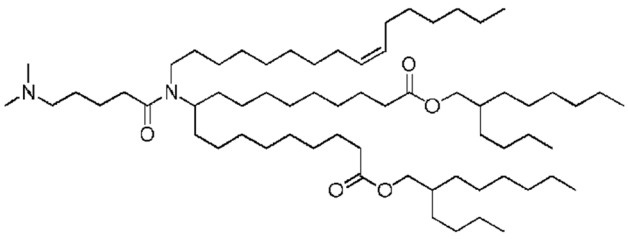


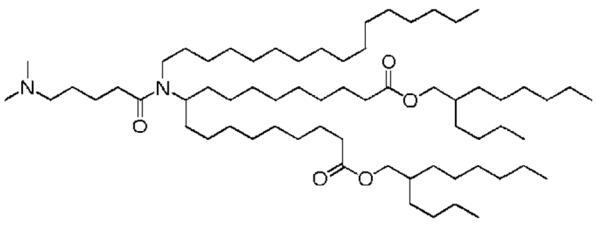


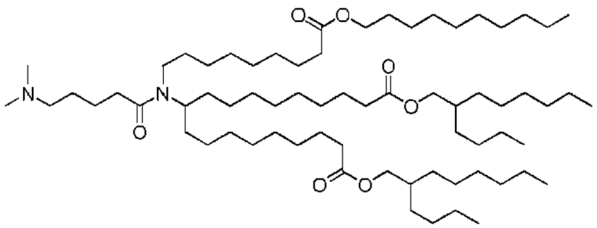


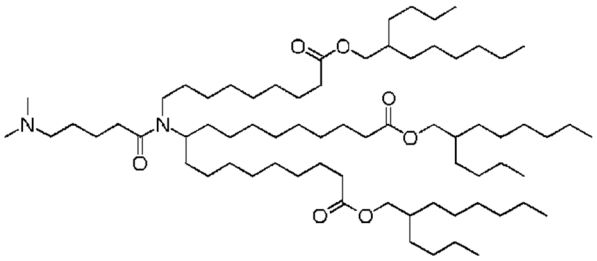


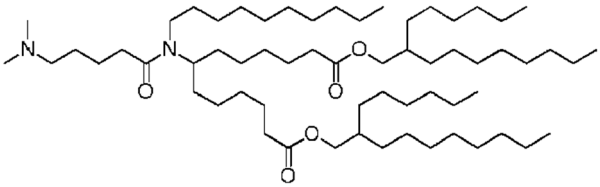


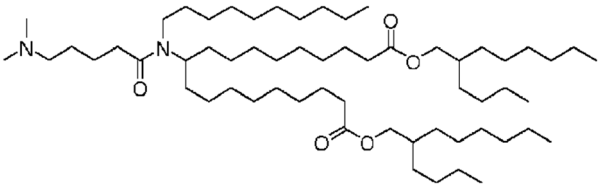


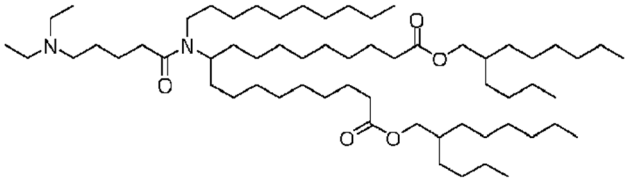


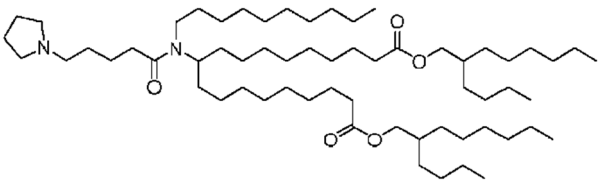


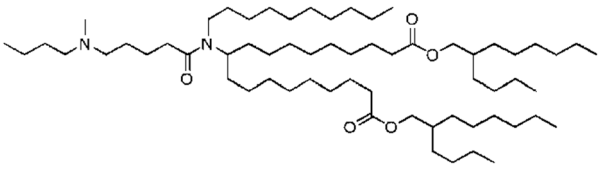


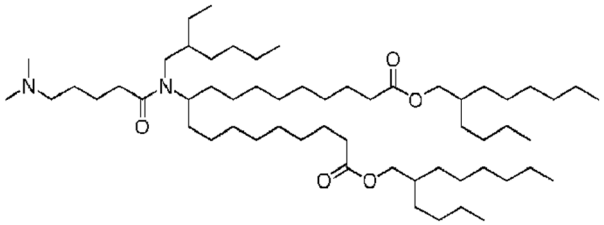


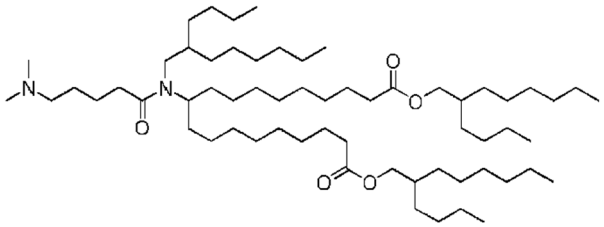


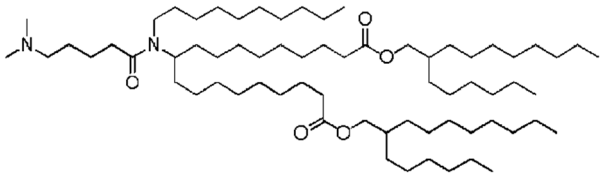


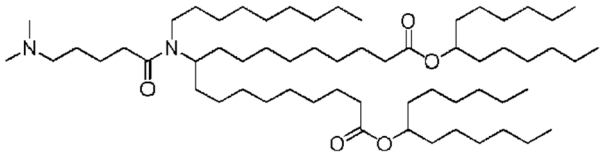


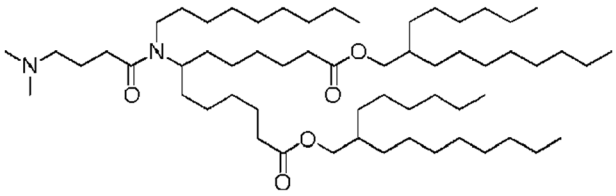


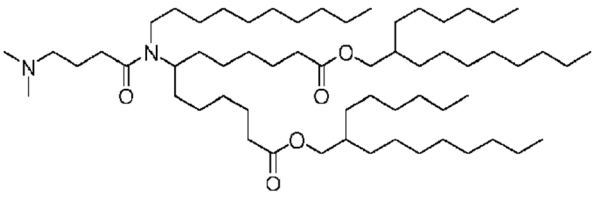


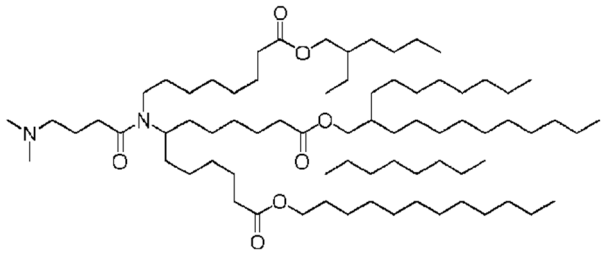


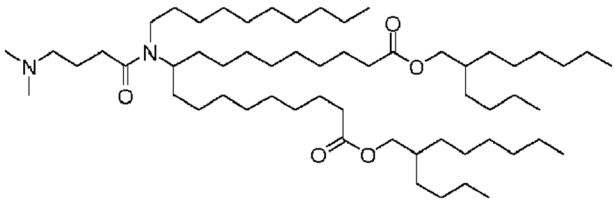


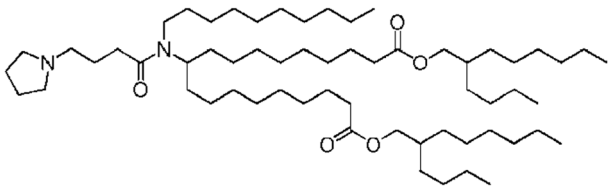


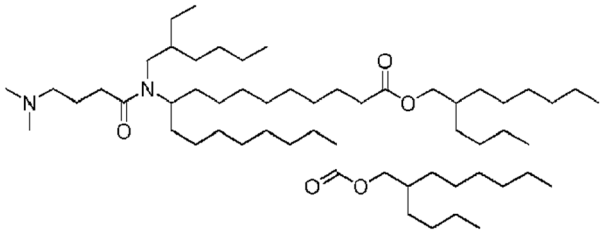


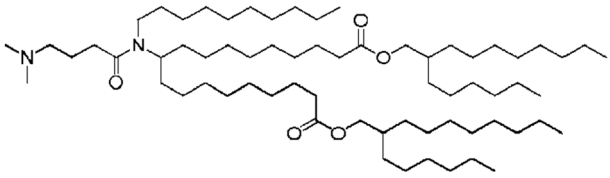


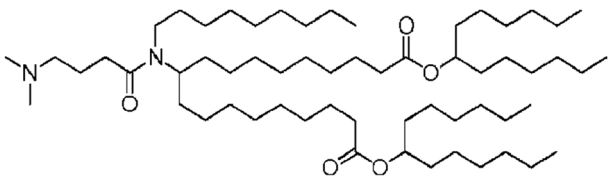


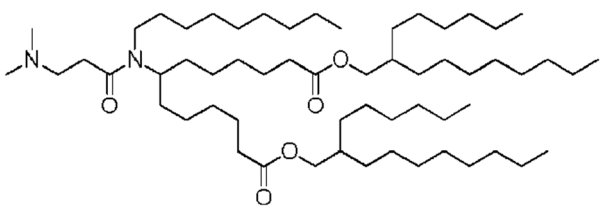


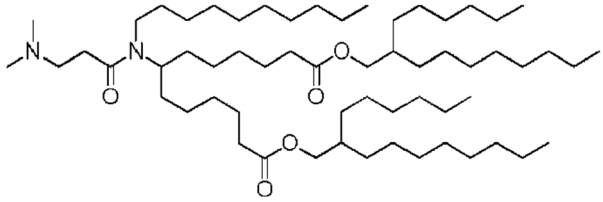


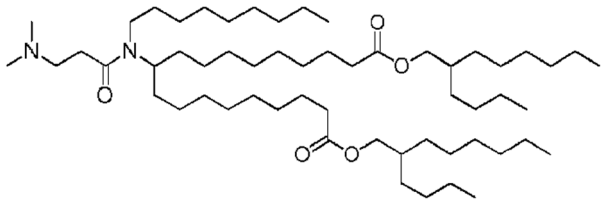


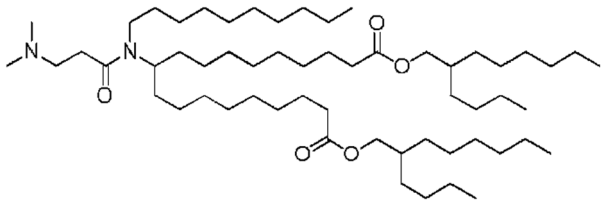


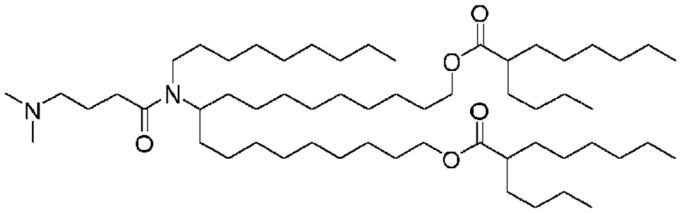


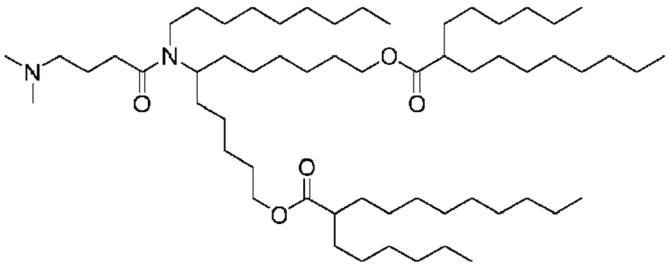


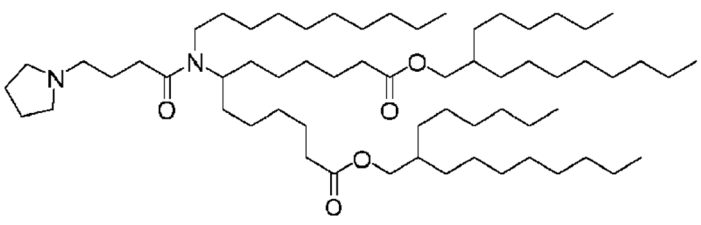


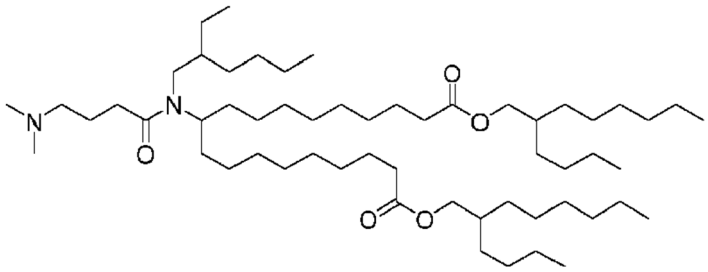


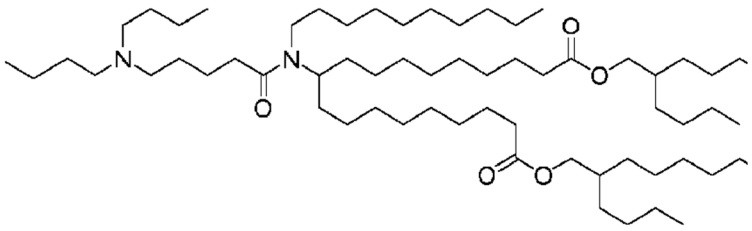


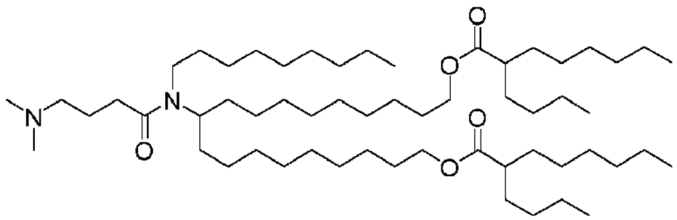


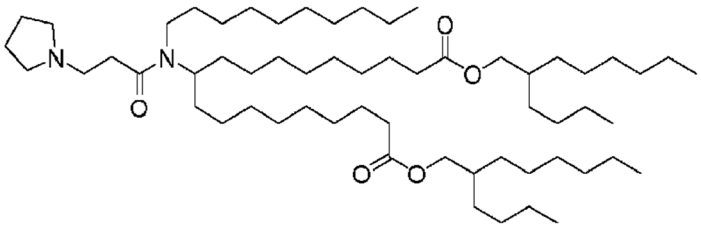


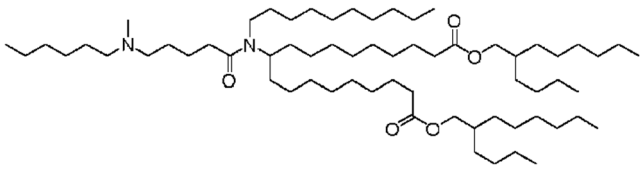


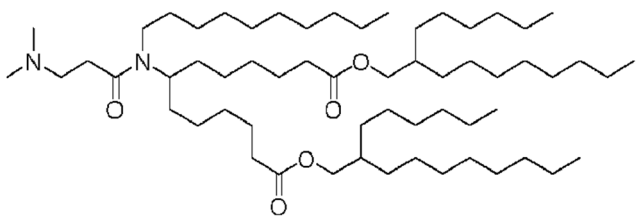


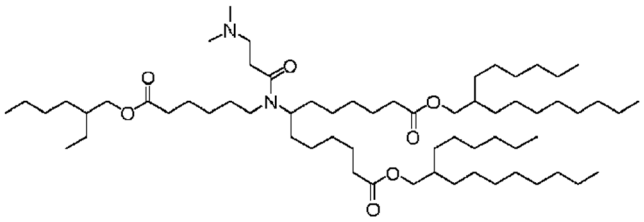


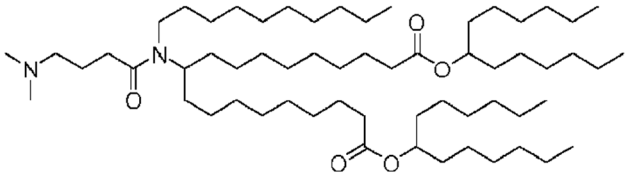


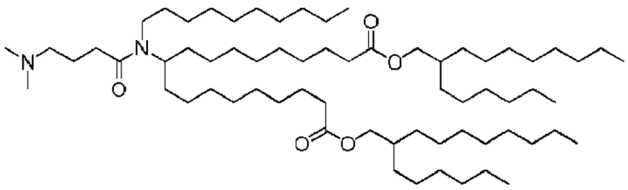


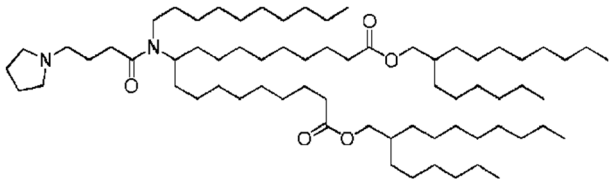


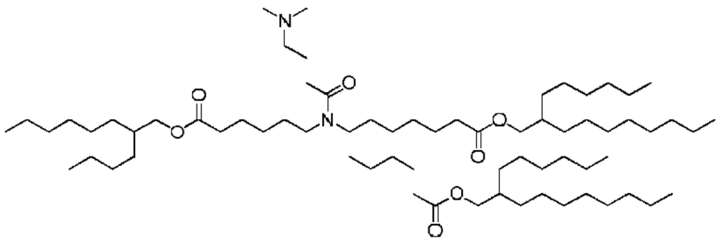












6. LNP'er for bruk ifølge et hvilket som helst av kravene 1-5, hvor molforholdet av kationisk lipid til nøytralt lipid er i området fra omtrent 2:1 til omtrent 8:1.

7. LNP'er for bruk ifølge et hvilket som helst av kravene 1-6, hvor det nøytrale lipidet er distearoylfosfatidylkolin (DSPC), dioleoylfosfatidylkolin (DOPC), dipalmitoylfosfatidylkolin (DPPC), dioleoylfosfatidylglyserol (DOPG), dipalmitoylfosfatidylglyserol (DPPG), dioleoyl-fosfatidyletanolamin (DOPE), palmitoyloleoylfosfatidylkolin (POPC), palmitoyloleoyl-fosfatidyletanolamin (POPE) og dioleoyl-fosfatidyletanolamin 4-(N-maleimidometyl)-sykloheksan-1-karboksylat (DOPE-mal),

dipalmitoyl-fosfatidyl-etanolamin (DPPE), dimyristoylfosfoetanolamin (DMPE), distearoyl-fosfatidyletanolamin (DSPE), 16-O-monometyl PE, 16-O-dimetyl PE, 18-1-trans PE, 1-stearioyl-2-oleoylfosfatidyetanol-amin (SOPE) eller 1,2-dielaidoyl-sn-glysero-3-fofoetanolamin (transDOPE).

8. LNP'er for bruk ifølge et hvilket som helst av kravene 1-6, hvor det nøytrale lipidet er DSPC, DPPC, DMPC, DOPC, POPC, DOPE eller SM.

9. LNP'er for bruk ifølge et hvilket som helst av kravene 1-6, hvor det nøytrale lipidet er DSPC.

10. LNP'er for bruk ifølge et hvilket som helst av kravene 1-9, hvor steroidet er kolesterol.

11. LNP'er for bruk ifølge et hvilket som helst av kravene 1-10, hvor molforholdet av kationisk lipid til steroid er i området fra 5:1 til 1:1.

12. LNP'er for bruk ifølge et hvilket som helst av kravene 1-11, hvor molforholdet av kationisk lipid til polymer-konjugert lipid er i området fra omtrent 100:1 til omtrent 20:1.

13. LNP'er for bruk ifølge et hvilket som helst av kravene 1-12, hvor nukleinsyren er valgt fra antisense- og messenger-RNA.

14. LNP'er for bruk ifølge et hvilket som helst av kravene 1-13, hvor nukleinsyren omfatter et mRNA i stand til å translatere et immunogent protein.

15. LNP'er for bruk ifølge et hvilket som helst av kravene 1-14, hvor administreringen omfatter intravenøs administrering.