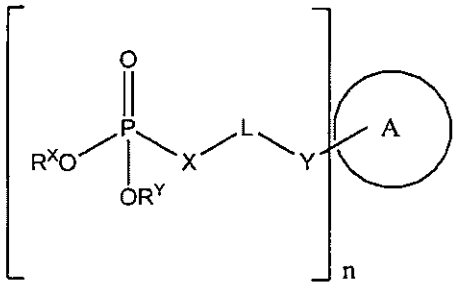
CLAIMS

1. A composition comprising a TLR agonist adsorbed to an insoluble metal salt, provided that the TLR agonist: (a) is not a TLR4 agonist; and (b) is not a TLR9 agonist.

2. The composition of claim 1, wherein the TLR agonist has the formula (A1):



(A1)

wherein:

R^X and R^Y are independently selected from H and C_1-C_6 alkyl;

X is selected from a covalent bond, O and NH;

Y is selected from a covalent bond, O, C(O), S and NH;

L is a linker *e.g.* selected from, C_1-C_6alkylene, C_1-C_6alkenylene, arylene, heteroarylene, C_1-C_6alkyleneoxy and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, $-OP(O)(OH)_2$ and $-P(O)(OH)_2$;

each p is independently selected from 1, 2, 3, 4, 5 and 6;

q is selected from 1, 2, 3 and 4;

n is selected from 1, 2 and 3; and

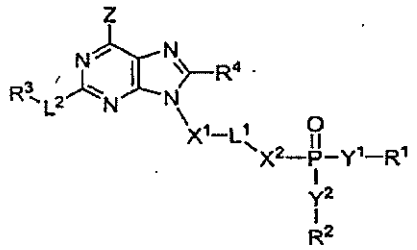
A is a TLR agonist moiety.

3. A TLR agonist comprising at least one adsorptive moiety, with the proviso that the TLR agonist:

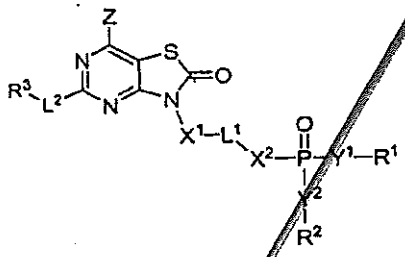
(a) is not a TLR4 agonist;

(b) is not a TLR9 agonist;

(c) is not a compound according to formula (I) or (II):



I



II

wherein:

Z is $-NH_2$ or -OH;

X^1 is alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, carbocyclylene, substituted carbocyclylene, heterocyclylene, or substituted heterocyclylene;

L^1 is a covalent bond, arylene, substituted arylene, heterocyclylene, substituted heterocyclylene, carbocyclylene, substituted carbocyclylene, -S-, -S(O)-, $S(O)_2$, $-NR^5-$, or -O-

X^2 is a covalent bond, alkylene, or substituted alkylene;

L^2 is $-NR^5-$, $-N(R^5)C(O)-$, -O-, -S-, -S(O)-, $S(O)_2$, or a covalent bond;

R^3 is H, alkyl, substituted alkyl, heteroalkyl, substituted heteroalkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

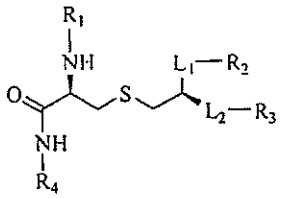
Y^1 and Y^2 are each independently a covalent bond, -O- or $-NR^5-$; or $-Y^1-R^1$ and $-Y^2-R^2$ are each independently $-O-N=C(R^6R^7)$;

R^1 and R^2 are each independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, substituted heterocyclylalkyl, -alkylene-C(O)-O-R^5, -(substituted alkylene)-C(O)-O-R^5, -alkylene-O-C(O)-R^5, -(substituted alkylene)-O-C(O)-R^5, -alkylene-O-C(O)-O-R^5, or -(substituted alkylene)-O-C(O)-O-R^5

R^4 is H, halogen, -OH, -O-alkyl, -O-alkylene-O-C(O)-O-R^5, -O-C(O)-O-R^5, -SH, or $-NH(R^5)$;

each R^5, R^6, and R^7 are independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

(d) is not a compound according to formula (III)



(III)

wherein:

R^1 is H, -C(O)-C_{10}-C_{18}alkyl; R^2 is C_{10}-C_{18}alkyl ; R^3 is C_{10}-C_{18}alkyl;

L_1 is -CH_2O-, -$CH_2OC(O)$-, -$CH_2NR^7C(O)$- or –$C(O)NR^7$-;

L_2 is -O-, -OC(O)- or -$NR^7C(O)$-;

R^4 is -L_3R^5 or -L_4R^5;

R^5 is –$N(R^7)_2$, -OR^7, -$P(O)(OR^7)_2$, -$C(O)OR^7$, -$NR^7C(O)L_3R^8$, -OL_3R^6, -$C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from -OR^9, -OL_3R^6, -OL_4R^6, -OR^7, and -$C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is -$((CR^7R^7)_pO)_q(CR^{10}R^{10})_p$- or -$(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p$-, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, -OR^7, -$N(R^7)_2$, -$C(O)N(R^7)_2$, -$P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from –SR^7, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

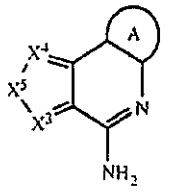
R^9 is phenyl;

each R^{10} is independently selected from H and halo;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4.

(e) is not a compound according to Formula (I-A)



Formula (I-A)

wherein:

X^3 is N;

X^4 is N or CR^3

X^5 is $-CR^4=CR^5-$;

R^1 and R^2 are H;

R^3 is H;

R^4 and R^5 are each independently selected from H, halogen, $-C(O)OR^7$, $-C(O)R^7$, $-C(O)N(R^{11}R^{12})$, $-N(R^{11}R^{12})$, $-N(R^9)_2$, $-NHN(R^9)_2$, $-SR^7$, $-(CH_2)_nOR^7$, $-(CH_2)_nR^7$, $-LR^8$, $-LR^{10}$, $-OLR^8$, $-OLR^{10}$, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^4 and R^5 are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, $-NO_2$, $-R^7$, $-OR^8$, $-C(O)R^8$, $-OC(O)R^8$, $-C(O)OR^8$, $-N(R^9)_2$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$, $-OP(O)(OR^{10})_2$, $-C(O)N(R^9)_2$, $-S(O)_2R^8$, $-S(O)R^8$, $-S(O)_2N(R^9)_2$, and $-NR^9S(O)_2R^8$;

or, R^3 and R^4, or R^4 and R^5, or R^5 and R^6, when present on adjacent ring atoms, can optionally be linked together to form a 5-6 membered ring, wherein the 5-6 membered ring is optionally substituted with R^7;

each L is independently selected from a bond, $-(O(CH_2)_m)_t-$, C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene, wherein the C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene of L are each optionally substituted with 1 to 4 substituents independently selected from halogen, $-R^8$, $-OR^8$, $-N(R^9)_2$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$, and $-OP(O)(OR^{10})_2$;

R^7 is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl groups of R^7 are each optionally substituted with 1 to 3 R^{13} groups, and each R^{13} is independently selected from halogen, -CN, -LR^9, -LOR^9, -OLR^9, -LR^{10}, -LOR^{10}, -OLR^{10}, -LR^8, -LOR^8, -OLR^8, -LSR^8, -LSR^{10}, -$LC(O)R^8$, -$OLC(O)R^8$, -$LC(O)OR^8$, -$LC(O)R^{10}$, -$LOC(O)OR^8$, -$LC(O)NR^9R^{11}$, -$LC(O)NR^9R^8$, -$LN(R^9)_2$, -LNR^9R^8, -LNR^9R^{10}, -$LC(O)N(R^9)_2$, -$LS(O)_2R^8$, -$LS(O)R^8$, -$LC(O)NR^8OH$, -$LNR^9C(O)R^8$, -$LNR^9C(O)OR^8$, -$LS(O)_2N(R^9)_2$, -$OLS(O)_2N(R^9)_2$, -$LNR^9S(O)_2R^8$, -$LC(O)NR^9LN(R^9)_2$, -$LP(O)(OR^8)_2$, -$LOP(O)(OR^8)_2$, -$LP(O)(OR^{10})_2$ and -$OLP(O)(OR^{10})_2$;

each R^8 is independently selected from H, -$CH(R^{10})_2$, C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6heteroalkyl, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy, wherein the C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy groups of R^8 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -$C(O)R^{11}$, -$OC(O)R^{11}$, -$C(O)N(R^9)_2$, -$C(O)OR^{11}$, -$NR^9C(O)R^{11}$, -NR^9R^{10}, -$NR^{11}R^{12}$, -$N(R^9)_2$, -OR^9, -OR^{10}, -$C(O)NR^{11}R^{12}$, -$C(O)NR^{11}OH$, -$S(O)_2R^{11}$, -$S(O)R^{11}$, -$S(O)_2NR^{11}R^{12}$, -$NR^{11}S(O)_2R^{11}$, -$P(O)(OR^{11})_2$, and -$OP(O)(OR^{11})_2$;

each R^9 is independently selected from H, -$C(O)R^8$, -$C(O)OR^8$, -$C(O)R^{10}$, -$C(O)OR^{10}$, -$S(O)_2R^{10}$, -C_1-C_6 alkyl, C_1-C_6 heteroalkyl and C_3-C_6 cycloalkyl, or each R^9 is independently a C_1-C_6alkyl that together with N they are attached to form a C_3-C_8heterocycloalkyl, wherein the C_3-C_8heterocycloalkyl ring optionally contains an additional heteroatom selected from N, O and S, and wherein the C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, or C_3-C_8heterocycloalkyl groups of R^9 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -$C(O)R^{11}$, $OC(O)R^{11}$, -$C(O)0R^{11}$, -$NR^{11}R^{12}$, -$C(O)NR^{11}R^{12}$, -$C(O)NR^{11}OH$, -$S(O)_2R^{11}$, -$S(O)R^{11}$, -$S(O)_2NR^{11}R^{12}$, -$NR^{11}S(O)_2R^{11}$, -$P(O)(OR^{11})_2$ and -$OP(O)(OR^{11})_2$;

each R^{10} is independently selected from aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl, wherein the aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl groups are optionally substituted with 1 to 3 substituents selected from halogen, -R^8, -OR^8, -LR^9, -LOR^9, -$N(R^9)_2$, -$NR^9C(O)R^8$, -$NR^9CO_2R^8$. -CO_2R^8, -$C(O)R^8$ and -$C(O)N(R^9)_2$;

R^{11} and R^{12} are independently selected from H, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^{11} and R^{12} are each optionally substituted with 1 to 3

substituents independently selected from halogen, -CN, R^x, -OR^x, C(O)R^x, OC(O)R^x, -C(O)OR^8, -$N(R^9)_2$, -$NR^8C(O)R^8$, -$NR^8C(O)OR^8$, -$C(O)N(R^9)_2$, C_3-C_8heterocycloalkyl, -$S(O)_2R^8$, -$S(O)_2N(R^9)_2$, -$NR^9S(O)_2R^8$, C_1 -C_6haloalkyl and C_1 -C_6haloalkoxy;

or R^{11} and R^{12} are each independently C_1-C_6alkyl and taken together with the N atom to which they are attached form an optionally substituted C_3-C_8heterocycloalkyl ring optionally containing an additional heteroatom selected from N, O and S;

ring A is an aryl or a heteroaryl, wherein the aryl and heteroaryl groups of Ring A are optionally substituted with 1 to 3 R^A groups, wherein each R^A is independently selected from -R^8, -R^7, -OR^7, -OR^8, -R^{10}, -OR^{10}, -SR^8, -NO_2, -CN, -$N(R^9)_2$, -$NR^9C(O)R^8$, -$NR^9C(S)R^8$, -$NR^9C(O)N(R^9)_2$, - $NR^9C(S)N(R^9)_2$, -$NR^9CO_2R^8$, -$NR^9NR^9C(O)R^8$, -$NR^9NR^9C(O)N(R^9)_2$, -$NR^9NR^9CO_2R^8$, -$C(O)C(O)R^8$, -$C(O)CH_2C(O)R^8$, -CO_2R^8, -$(CH_2)_nCO_2R^8$, -$C(O)R^8$, -$C(S)R^8$, -$C(O)N(R^9)_2$, -$C(S)N(R^9)_2$, -$OC(O)N(R^9)_2$, -$OC(O)R^8$, -$C(O)N(OR^8)R^8$, -$C(NOR^8)R^8$, -$S(O)_2R^8$, -$S(O)_3R^8$, -$SO_2N(R^9)_2$, -$S(O)R^8$, -$NR^9SO_2N(R^9)_2$, -$NR^9SO_2R^8$, -$P(O)(OR^8)_2$, -$OP(O)(OR^8)_2$, -$P(O)(OR^{10})_2$, -$OP(O)(OR^{10})_2$, -$N(0R^8)R^8$, -$CH{=}CHCO_2R^8$, -$C(=NH)$-$N(R^9)_2$, and -$(CH_2)_nNHC(O)R^8$ or two adjacent R^A substituents on Ring A form a 5-6 membered ring that contains up to two heteroatoms as ring members;

n is, independently at each occurrence, 0, 1, 2, 3, 4, 5, 6, 7 or 8;

each m is independently selected from 1, 2, 3, 4, 5 and 6, and

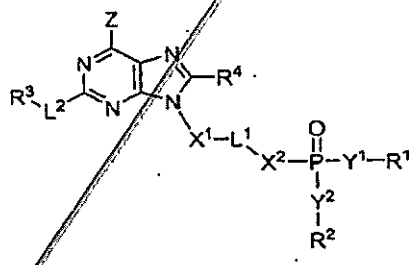
t is 1,2,3,4,5,6,7 or 8.

4. A water-soluble TLR agonist comprising at least one adsorptive moiety, with the proviso that the water-soluble TLR agonist:

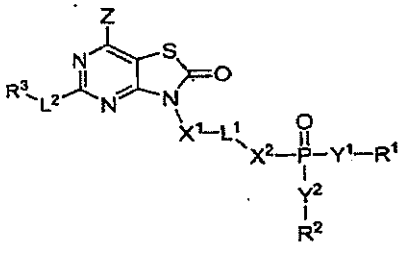
(a) is not a TLR4 agonist;

(b) is not a TLR9 agonist;

(c) is not a compound according to formula (I) or (II)



I



II

wherein:

Z is -NH_2 or -OH;

X^1 is alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, carbocyclylene, substituted carbocyclylene, heterocyclylene, or substituted heterocyclylene;

L^1 is a covalent bond, arylene, substituted arylene, heterocyclylene, substituted heterocyclylene, carbocyclylene, substituted carbocyclylene, -S-, -S(O)-, $S(O)_2$, $-NR^5-$, or -O-

X^2 is a covalent bond, alkylene, or substituted alkylene;

L^2 is $-NR^5-$, $-N(R^5)C(O)-$, -O-, -S-, -S(O)-, $S(O)_2$, or a covalent bond;

R^3 is H, alkyl, substituted alkyl, heteroalkyl, substituted heteroalkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

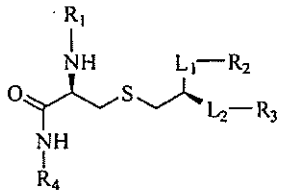
Y^1 and Y^2 are each independently a covalent bond, -O- or $-NR^5-$; or $-Y^1-R^1$ and $-Y^2-R^2$ are each independently $-O-N=C(R^6R^7)$;

R^1 and R^2 are each independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, substituted heterocyclylalkyl, -alkylene-C(O)-O-R^5, —(substituted alkylene)-C(O)-O-R^5, -alkylene-O-C(O)-R^5, -(substituted alkylene)-O-C(O)-R^5, -alkylene-O-C(O)-O-R^5, or -(substituted alkylene)-O-C(O)-O-R^5

R^4 is H, halogen, -OH, -O-alkyl, -O-alkylene-O-C(O)-O-R^5, -O-C(O)-O-R^5, -SH, or $-NH(R^5)$;

each R^5, R^6, and R^7 are independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, or substituted heterocyclylalkyl; and

(d) is not a compound according to formula (III)



(III)

wherein:

R^1 is H, -C(O)-C_{10}-C_{18}alkyl; R^2 is C_{10}-C_{18}alkyl ; R^3 is C_{10}-C_{18}alkyl;

L_1 is $-CH_2O-$, $-CH_2OC(O)-$, $-CH_2NR^7C(O)-$ or $-C(O)NR^7-$;

L_2 is -O-, -OC(O)- or $-NR^7C(O)-$;

R^4 is $-L_3R^5$ or $-L_4R^5$;

R^5 is $-N(R^7)_2$, $-OR^7$, $-P(O)(OR^7)_2$, $-C(O)OR^7$, $-NR^7C(O)L_3R^8$, $-OL_3R^5$, $-C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from $-OR^9$, $-OL_3R^6$, $-OL_4R^6$, $-OR^7$, and $-C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is $-((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$ or $-(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, $-OR^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from $-SR^7$, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

R^9 is phenyl;

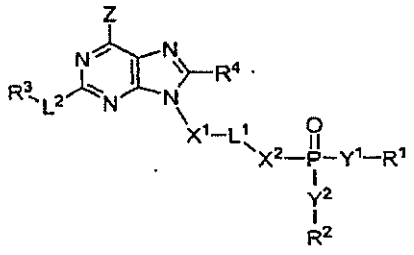
each R^{10} is independently selected from H and halo;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

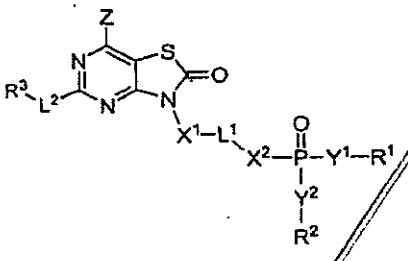
q is 1, 2, 3 or 4.

5. A TLR agonist comprising at least one phosphonate group, with the proviso that the TLR agonist:

(a) is not a phosphonate-containing compound according to formula (I) or (II)



I



II

wherein:

Z is $-NH_2$ or -OH;

X^1 is alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, carbocyclylene, substituted carbocyclylene, heterocyclylene, or substituted heterocyclylene;

L^1 is a covalent bond, arylene, substituted arylene, heterocyclylene, substituted heterocyclylene, carbocyclylene, substituted carbocyclylene, -S-, -S(O)-, $S(O)_2$, $-NR^5-$, or -O-

X^2 is a covalent bond, alkylene, or substituted alkylene;

L^2 is $-NR^5-$, $-N(R^5)C(O)$ -, -O-, -S-, -S(O)-, $S(O)_2$, or a covalent bond;

R^3 is H, alkyl, substituted alkyl, heteroalkyl, substituted heteroalkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

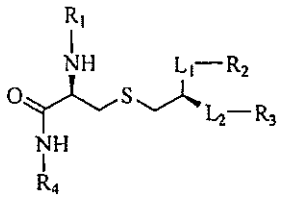
Y^1 and Y^2 are each independently a covalent bond, -O- or $-NR^5-$; or $-Y^1-R^1$ and $-Y^2-R^2$ are each independently $-O-N=C(R^6R^7)$;

R^1 and R^2 are each independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, substituted heterocyclylalkyl, -alkylene-C(O)-O-R^5, —(substituted alkylene)-C(O)-O-R^5, -alkylene-O-C(O)-R^5, -(substituted alkylene)-O-C(O)-R^5, -alkylene-O-C(O)-O-R^5, or -(substituted alkylene)-O-C(O)-O-R^5

R^4 is H, halogen, -OH, -O-alkyl, -O-alkylene-O-C(O)-O-R^5, -O-C(O)-O-R^5, -SH, or $-NH(R^5)$;

each R^5, R^6, and R^7 are independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

(b) is not a phosphonate-containing compound according to formula (III)



(III)

wherein:

R^1 is H, -C(O)-C_{10}-C_{18}alkyl; R^2 is C_{10}-C_{18}alkyl ; R^3 is C_{10}-C_{18}alkyl;

L_1 is -CH_2O-, -$CH_2OC(O)$-, -$CH_2NR^7C(O)$- or –$C(O)NR^7$-;

L_2 is -O-, -OC(O)- or -$NR^7C(O)$-;

R^4 is -L_3R^5 or -L_4R^5;

R^5 is –$N(R^7)_2$, -OR^7, -$P(O)(OR^7)_2$, -$C(O)OR^7$, -$NR^7C(O)L_3R^8$, -OL_3R^6, -$C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from -OR^9, -OL_3R^6, -OL_4R^6, -OR^7, and -$C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is -$((CR^7R^7)_pO)_q(CR^{10}R^{10})_p$- or -$(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p$-, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, -OR^7, -$N(R^7)_2$, -$C(O)N(R^7)_2$, -$P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from –SR^7, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

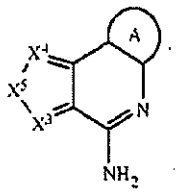
R^9 is phenyl;

each R^{10} is independently selected from H and halo;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4; and

(c) is not a phosphonate-containing compound according to formula (I-A)



Formula (I-A)

wherein:

X^3 is N;

X^4 is N or CR^3

X^5 is $-CR^4=CR^5-$;

R^1 and R^2 are H;

R^3 is H;

R^4 and R^5 are each independently selected from H, halogen, $-C(O)OR^7$, $-C(O)R^7$, $-C(O)N(R^{11}R^{12})$, $-N(R^{11}R^{12})$, $-N(R^9)_2$, $-NHN(R^9)_2$, $-SR^7$, $-(CH_2)_nOR^7$, $-(CH_2)_nR^7$, $-LR^8$, $-LR^{10}$, $-OLR^8$, $-OLR^{10}$, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^4 and R^5 are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, $-NO_2$, $-R^7$, $-OR^8$, $-C(O)R^8$, $-OC(O)R^8$, $-C(O)OR^8$, $-N(R^9)_2$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$. $-OP(O)(OR^{10})_2$, $-C(O)N(R^9)_2$, $-S(O)_2R^8$, $-S(O)R^8$, $-S(O)_2N(R^9)_2$, and $-NR^9S(O)_2R^8$;

or, R^3 and R^4, or R^4 and R^5, or R^5 and R^6, when present on adjacent ring atoms, can optionally be linked together to form a 5-6 membered ring, wherein the 5-6 membered ring is optionally substituted with R^7;

each L is independently selected from a bond, $-(O(CH_2)_m)_t-$, C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene, wherein the C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene of L are each optionally substituted with 1 to 4 substituents independently selected from halogen, $-R^8$, $-OR^8$, $-N(R^9)_2$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$, and $-OP(O)(OR^{10})_2$;

R^7 is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl groups of R^7 are each optionally substituted with 1 to 3 R^{13} groups, and each R^{13} is independently selected from halogen, -CN, -LR^9, -LOR^9, -OLR^9, -LR^{10}, -LOR^{10}, -OLR^{10}, -LR^8, -LOR^8, -OLR^8, -LSR^8, -LSR^{10}, -$LC(O)R^8$, -$OLC(O)R^8$, -$LC(O)OR^8$, -$LC(O)R^{10}$, -$LOC(O)OR^8$, -$LC(O)NR^9R^{11}$, -$LC(O)NR^9R^8$, -$LN(R^9)_2$, -LNR^9R^8, -LNR^9R^{10}, -$LC(O)N(R^9)_2$, -$LS(O)_2R^8$, -$LS(O)R^8$, -$LC(O)NR^8OH$, -$LNR^9C(O)R^8$, -$LNR^9C(O)OR^8$, -$LS(O)_2N(R^9)_2$, -$OLS(O)_2N(R^9)_2$, -$LNR^9S(O)_2R^8$, -$LC(O)NR^9LN(R^9)_2$, -$LP(O)(OR^8)_2$, -$LOP(O)(OR^8)_2$, -$LP(O)(OR^{10})_2$ and -$OLP(O)(OR^{10})_2$;

each R^8 is independently selected from H, -$CH(R^{10})_2$, C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6heteroalkyl, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy, wherein the C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy groups of R^8 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -$C(O)R^{11}$, -$OC(O)R^{11}$, -$C(O)N(R^9)_2$, -$C(O)OR^{11}$, -$NR^9C(O)R^{11}$, -NR^9R^{10}, -$NR^{11}R^{12}$, -$N(R^9)_2$, -OR^9, -OR^{10}, -$C(O)NR^{11}R^{12}$, -$C(O)NR^{11}OH$, -$S(O)_2R^{11}$, -$S(O)R^{11}$, -$S(O)_2NR^{11}R^{12}$, -$NR^{11}S(O)_2R^{11}$, -$P(O)(OR^{11})_2$, and -$OP(O)(OR^{11})_2$;

each R^9 is independently selected from H, -$C(O)R^8$, -$C(O)OR^8$, -$C(O)R^{10}$, -$C(O)OR^{10}$, -$S(O)_2R^{10}$, -C_1-C_6 alkyl, C_1-C_6 heteroalkyl and C_3-C_6 cycloalkyl, or each R^9 is independently a C_1-C_6alkyl that together with N they are attached to form a C_3-C_8heterocycloalkyl, wherein the C_3-C_8heterocycloalkyl ring optionally contains an additional heteroatom selected from N, O and S, and wherein the C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, or C_3-C_8heterocycloalkyl groups of R^9 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -$C(O)R^{11}$, $OC(O)R^{11}$, -$C(O)0R^{11}$, -$NR^{11}R^{12}$, -$C(O)NR^{11}R^{12}$, -$C(O)NR^{11}OH$, -$S(O)_2R^{11}$, -$S(O)R^{11}$, -$S(O)_2NR^{11}R^{12}$, -$NR^{11}S(O)_2R^{11}$, -$P(O)(OR^{11})_2$ and -$OP(O)(OR^{11})_2$;

each R^{10} is independently selected from aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl, wherein the aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl groups are optionally substituted with 1 to 3 substituents selected from halogen, -R^8, -OR^8, -LR^9, -LOR^9, -$N(R^9)_2$, -$NR^9C(O)R^8$, -$NR^9CO_2R^8$. -CO_2R^8, -$C(O)R^8$ and -$C(O)N(R^9)_2$;

R^{11} and R^{12} are independently selected from H, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^{11} and R^{12} are each optionally substituted with 1 to 3

substituents independently selected from halogen, -CN, R^8, -OR^8, $C(O)R^8$, $OC(O)R^8$, -$C(O)OR^8$, -$N(R^9)_2$, -$NR^8C(O)R^8$, -$NR^8C(O)OR^8$, -$C(O)N(R^9)_2$, C_3-C_8heterocycloalkyl, -$S(O)_2R^8$, -$S(O)_2N(R^9)_2$, -$NR^9S(O)_2R^8$, C_1 -C_6haloalkyl and C_1 -C_6haloalkoxy;

or R^{11} and R^{12} are each independently C_1-C_6alkyl and taken together with the N atom to which they are attached form an optionally substituted C_3-C_8heterocycloalkyl ring optionally containing an additional heteroatom selected from N, O and S;

ring A is an aryl or a heteroaryl, wherein the aryl and heteroaryl groups of Ring A are optionally substituted with 1 to 3 R^A groups, wherein each R^A is independently selected from -R^8, -R^7, -OR^7, -OR^8, -R^{10}, -OR^{10}, -SR^8, -NO_2, -CN, -$N(R^9)_2$, -$NR^9C(O)R^8$, -$NR^9C(S)R^8$, -$NR^9C(O)N(R^9)_2$, -$NR^9C(S)N(R^9)_2$, -$NR^9CO_2R^8$, -$NR^9NR^9C(O)R^8$, -$NR^9NR^9C(O)N(R^9)_2$, -$NR^9NR^9CO_2R^8$, -$C(O)C(O)R^8$, -$C(O)CH_2C(O)R^8$, -CO_2R^8, -$(CH_2)_nCO_2R^8$, -$C(O)R^8$, -$C(S)R^8$, -$C(O)N(R^9)_2$, -$C(S)N(R^9)_2$, -$OC(O)N(R^9)_2$, -$OC(O)R^8$, -$C(O)N(OR^8)R^8$, -$C(NOR^8)R^8$, -$S(O)_2R^8$, -$S(O)_3R^8$, -$SO_2N(R^9)_2$, -$S(O)R^8$, -$NR^9SO_2N(R^9)_2$, -$NR^9SO_2R^8$, -$P(O)(OR^8)_2$, -$OP(O)(OR^8)_2$, -$P(O)(OR^{10})_2$, -$OP(O)(OR^{10})_2$, -$N(OR^8)R^8$, -$CH{=}CHCO_2R^8$, -$C(=NH)$-$N(R^9)_2$, and -$(CH_2)_nNHC(O)R^8$ or two adjacent R^A substituents on Ring A form a 5-6 membered ring that contains up to two heteroatoms as ring members;

n is, independently at each occurrence, 0, 1, 2, 3, 4, 5, 6, 7 or 8;

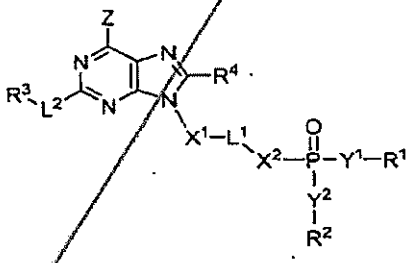
each m is independently selected from 1, 2, 3, 4, 5 and 6, and

t is 1,2,3,4,5, 6,7 or 8.

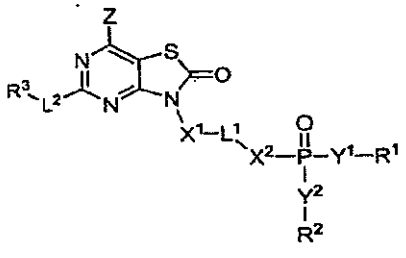
6. A TLR agonist compound comprising at least one adsorptive moiety, wherein the compound is an agonist of TLR1, TLR3, TLR5, TLR6, TLR8 or TLR11.

7. A TLR agonist compound comprising at least one adsorptive moiety, wherein the compound is an agonist of TLR1, TLR2, TLR3, TLR5, TLR6, TLR7, TLR8, or TLR11, with the proviso that the compound:

(a) is not a compound according to formula (I) or (II)



I



II

wherein:

Z is $-NH_2$ or -OH;

X^1 is alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, carbocyclylene, substituted carbocyclylene, heterocyclylene, or substituted heterocyclylene;

L^1 is a covalent bond, arylene, substituted arylene, heterocyclylene, substituted heterocyclylene, carbocyclylene, substituted carbocyclylene, -S-, -S(O)-, $S(O)_2$, $-NR^5-$, or -O-

X^2 is a covalent bond, alkylene, or substituted alkylene;

L^2 is $-NR^5-$, $-N(R^5)C(O)-$, -O-, -S-, -S(O)-, $S(O)_2$, or a covalent bond;

R^3 is H, alkyl, substituted alkyl, heteroalkyl, substituted heteroalkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

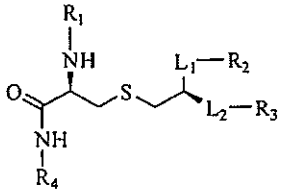
Y^1 and Y^2 are each independently a covalent bond, -O- or $-NR^5-$; or $-Y^1-R^1$ and $-Y^2-R^2$ are each independently $-O-N=C(R^6R^7)$;

R^1 and R^2 are each independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, substituted heterocyclylalkyl, -alkylene-C(O)-O-R^5, —(substituted alkylene)-C(O)-O-R^5, -alkylene-O-C(O)-R^5, -(substituted alkylene)-O-C(O)-R^5, -alkylene-O-C(O)-O-R^5, or -(substituted alkylene)-O-C(O)-O-R^5

R^4 is H, halogen, -OH, -O-alkyl, -O-alkylene-O-C(O)-O-R^5, -O-C(O)-O-R^5, -SH, or $-NH(R^5)$;

each R^5, R^6, and R^7 are independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

(b) is not a compound according to formula (III),



(III)

wherein:

R^1 is H, $-C(O)-C_{10}-C_{18}$alkyl; R^2 is $C_{10}-C_{18}$alkyl ; R^3 is $C_{10}-C_{18}$alkyl;

L_1 is $-CH_2O-$, $-CH_2OC(O)-$, $-CH_2NR^7C(O)-$ or $-C(O)NR^7-$;

L_2 is -O-, -OC(O)- or $-NR^7C(O)-$;

R^4 is $-L_3R^5$ or $-L_4R^5$;

R^5 is $-N(R^7)_2$, $-OR^7$, $-P(O)(OR^7)_2$, $-C(O)OR^7$, $-NR^7C(O)L_3R^8$, $-OL_3R^6$, $-C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from $-OR^9$, $-OL_3R^6$, $-OL_4R^6$, $-OR^7$, and $-C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is $-((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$ or $-(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, $-OR^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from $-SR^7$, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

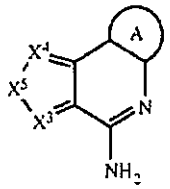
R^9 is phenyl;

each R^{10} is independently selected from H and halo;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4; and

(c) is not a compound according to formula (I-A),



Formula (I-A)

wherein:

X^3 is N;

X^4 is N or CR^3

X^5 is $-CR^4=CR^5-$;

R^1 and R^2 are H;

R^3 is H;

R^4 and R^5 are each independently selected from H, halogen, $-C(O)OR^7$, $-C(O)R^7$, $-C(O)N(R^{11}R^{12})$, $-N(R^{11}R^{12})$, $-N(R^9)_2$, $-NHN(R^9)_2$, $-SR^7$, $-(CH_2)_nOR^7$, $-(CH_2)_nR^7$, $-LR^8$, $-LR^{10}$, $-OLR^8$, $-OLR^{10}$, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^4 and R^5 are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, $-NO_2$, $-R^7$, $-OR^8$, $-C(O)R^8$, $-OC(O)R^8$, $-C(O)OR^8$, $-N(R^9)_2$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$. $-OP(O)(OR^{10})_2$, $-C(O)N(R^9)_2$, $-S(O)_2R^8$, $-S(O)R^8$, $-S(O)_2N(R^9)_2$, and $-NR^9S(O)_2R^8$;

or, R^3 and R^4, or R^4 and R^5, or R^5 and R^6, when present on adjacent ring atoms, can optionally be linked together to form a 5-6 membered ring, wherein the 5-6 membered ring is optionally substituted with R^7;

each L is independently selected from a bond, $-(O(CH_2)_m)_t-$, C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene, wherein the C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene of L are each optionally substituted with 1 to 4 substituents independently selected from halogen, $-R^8$, $-OR^8$, $-N(R^9)_2$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$, and $-OP(O)(OR^{10})_2$;

R^7 is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl groups of R^7 are each optionally substituted with 1 to 3 R^{13} groups, and each R^{13} is independently selected from halogen, -CN, $-LR^9$, $-LOR^9$, $-OLR^9$, $-LR^{10}$, $-LOR^{10}$, $-OLR^{10}$, $-LR^8$, $-LOR^8$, $-OLR^8$, $-LSR^8$, $-LSR^{10}$, $-LC(O)R^8$, $-OLC(O)R^8$, $-LC(O)OR^8$, $-LC(O)R^{10}$, $-LOC(O)OR^8$, $-LC(O)NR^9R^{11}$, $-LC(O)NR^9R^8$, $-LN(R^9)_2$, $-LNR^9R^8$, $-LNR^9R^{10}$, $-LC(O)N(R^9)_2$, $-LS(O)_2R^8$, $-LS(O)R^8$, $-LC(O)NR^8OH$, $-LNR^9C(O)R^8$, $-LNR^9C(O)OR^8$, $-LS(O)_2N(R^9)_2$, $-OLS(O)_2N(R^9)_2$, $-LNR^9S(O)_2R^8$, $-LC(O)NR^9LN(R^9)_2$, $-LP(O)(OR^8)_2$, $-LOP(O)(OR^8)_2$, $-LP(O)(OR^{10})_2$ and $-OLP(O)(OR^{10})_2$;

each R^8 is independently selected from H, $-CH(R^{10})_2$, C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6heteroalkyl, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy, wherein the C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy groups of R^8 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, $-OR^{11}$, $-SR^{11}$, $-C(O)R^{11}$, $-OC(O)R^{11}$, $-C(O)N(R^9)_2$, $-C(O)OR^{11}$, $-NR^9C(O)R^{11}$, $-NR^9R^{10}$, $-NR^{11}R^{12}$, $-N(R^9)_2$, $-OR^9$, $-OR^{10}$, $-C(O)NR^{11}R^{12}$, $-C(O)NR^{11}OH$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-S(O)_2NR^{11}R^{12}$, $-NR^{11}S(O)_2R^{11}$, $-P(O)(OR^{11})_2$, and $-OP(O)(OR^{11})_2$;

each R^9 is independently selected from H, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)R^{10}$, $-C(O)OR^{10}$, $-S(O)_2R^{10}$, $-C_1$-C_6 alkyl, C_1-C_6 heteroalkyl and C_3-C_6 cycloalkyl, or each R^9 is independently a C_1-C_6alkyl that together with N they are attached to form a C_3-C_8heterocycloalkyl, wherein the C_3-C_8heterocycloalkyl ring optionally contains an additional heteroatom selected from N, O and S, and wherein the C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, or C_3-C_8heterocycloalkyl groups of R^9 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, $-OR^{11}$, $-SR^{11}$, $-C(O)R^{11}$, $OC(O)R^{11}$, $-C(O)0R^{11}$, $-NR^{11}R^{12}$, $-C(O)NR^{11}R^{12}$, $-C(O)NR^{11}OH$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-S(O)_2NR^{11}R^{12}$, $-NR^{11}S(O)_2R^{11}$, $-P(O)(OR^{11})_2$ and $-OP(O)(OR^{11})_2$;

each R^{10} is independently selected from aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl, wherein the aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl groups are optionally substituted with 1 to 3 substituents selected from halogen, $-R^8$, $-OR^8$, $-LR^9$, $-LOR^9$, $-N(R^9)_2$, $-NR^9C(O)R^8$, $-NR^9CO_2R^8$, $-CO_2R^8$, $-C(O)R^8$ and $-C(O)N(R^9)_2$;

R^{11} and R^{12} are independently selected from H, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^{11} and R^{12} are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, R^8, $-OR^8$, $C(O)R^8$, $OC(O)R^8$, $-C(O)OR^8$, $-N(R^9)_2$, $-NR^8C(O)R^8$, $-NR^8C(O)OR^8$, $-C(O)N(R^9)_2$, C_3-C_8heterocycloalkyl, $-S(O)_2R^8$, $-S(O)_2N(R^9)_2$, $-NR^9S(O)_2R^8$, C_1-C_6haloalkyl and C_1-C_6haloalkoxy;

or R^{11} and R^{12} are each independently C_1-C_6alkyl and taken together with the N atom to which they are attached form an optionally substituted C_3-C_8heterocycloalkyl ring optionally containing an additional heteroatom selected from N, O and S;

ring A is an aryl or a heteroaryl, wherein the aryl and heteroaryl groups of Ring A are optionally substituted with 1 to 3 R^A groups, wherein each R^A is independently selected from $-R^8$, $-R^7$, $-OR^7$, $-OR^8$, $-R^{10}$, $-OR^{10}$, $-SR^8$, $-NO_2$, -CN, $-N(R^9)_2$, $-NR^9C(O)R^8$, $-NR^9C(S)R^8$, $-NR^9C(O)N(R^9)_2$, $-NR^9C(S)N(R^9)_2$, $-NR^9CO_2R^8$, $-NR^9NR^9C(O)R^8$, $-NR^9NR^9C(O)N(R^9)_2$, $-NR^9NR^9CO_2R^8$, $-C(O)C(O)R^8$, $-C(O)CH_2C(O)R^8$, $-CO_2R^8$, $-(CH_2)_nCO_2R^8$, $-C(O)R^8$, $-C(S)R^8$,

$-C(O)N(R^9)_2$, $-C(S)N(R^9)_2$, $-OC(O)N(R^9)_2$, $-OC(O)R^8$, $-C(O)N(OR^8)R^8$, $-C(NOR^8)R^8$, $-S(O)_2R^8$, $-S(O)_3R^8$, $-SO_2N(R^9)_2$, $-S(O)R^8$, $-NR^9SO_2N(R^9)_2$, $-NR^9SO_2R^8$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$, $-OP(O)(OR^{10})_2$, $-N(OR^8)R^8$, $-CH=CHCO_2R^8$, $-C(=NH)-N(R^9)_2$, and $-(CH_2)_nNHC(O)R^8$ or two adjacent $R^\wedge$ substituents on Ring A form a 5-6 membered ring that contains up to two heteroatoms as ring members;

n is, independently at each occurrence, 0, 1, 2, 3, 4, 5, 6, 7 or 8;

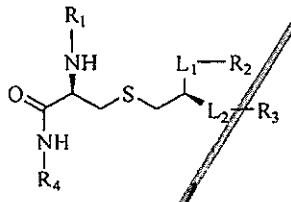
each m is independently selected from 1, 2, 3, 4, 5 and 6, and

t is 1,2,3,4,5, 6,7 or 8.

8. A TLR4 agonist comprising at least one adsorptive moiety, provided that the TLR4 agonist does not include an acyl chain.

9. A TLR9 agonist comprising at least one adsorptive moiety, provided that the TLR9 agonist does not include a cytidine nucleoside.

10. A TLR2 agonist comprising at least one adsorptive moiety, provided that the TLR2 agonist is not a compound according to formula (III)



(III)

wherein:

R^1 is H, $-C(O)-C_{10}-C_{18}$alkyl; R^2 is $C_{10}-C_{18}$alkyl ; R^3 is $C_{10}-C_{18}$alkyl;

L_1 is $-CH_2O-$, $-CH_2OC(O)-$, $-CH_2NR^7C(O)-$ or $-C(O)NR^7-$;

L_2 is -O-, -OC(O)- or $-NR^7C(O)-$;

R^4 is $-L_3R^5$ or $-L_4R^5$;

R^5 is $-N(R^7)_2$, $-OR^7$, $-P(O)(OR^7)_2$, $-C(O)OR^7$, $-NR^7C(O)L_3R^8$, $-OL_3R^6$, $-C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from $-OR^9$, $-OL_3R^6$, $-OL_4R^6$, $-OR^7$, and $-C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is $-((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$ or $-(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, $-OR^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from $-SR^7$, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

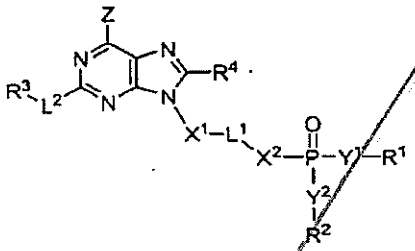
R^9 is phenyl;

each R^{10} is independently selected from H and halo;

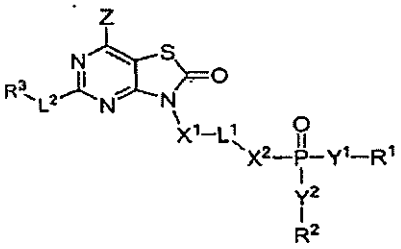
each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4.

11. A TLR7 agonist comprising at least one adsorptive moiety, provided that the TLR7 agonist is not: (a) a compound according to formula (I) or (II)



I



II

wherein:

Z is $-NH_2$ or -OH;

X^1 is alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, carbocyclylene, substituted carbocyclylene, heterocyclylene, or substituted heterocyclylene;

L^1 is a covalent bond, arylene, substituted arylene, heterocyclylene, substituted heterocyclylene, carbocyclylene, substituted carbocyclylene, -S-, -S(O)-, $S(O)_2$, $-NR^5$-, or -O-

X^2 is a covalent bond, alkylene, or substituted alkylene;

L^2 is $-NR^5-$, $-N(R^5)C(O)-$, -O-, -S-, -S(O)-, $S(O)_2$, or a covalent bond;

R^3 is H, alkyl, substituted alkyl, heteroalkyl, substituted heteroalkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

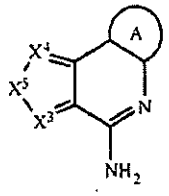
Y^1 and Y^2 are each independently a covalent bond, -O- or $-NR^5-$; or $-Y^1-R^1$ and $-Y^2-R^2$ are each independently $-O-N=C(R^6R^7)$;

R^1 and R^2 are each independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, substituted heterocyclylalkyl, -alkylene-C(O)-O-R^5, —(substituted alkylene)-C(O)-O-R^5, -alkylene-O-C(O)-R^5, -(substituted alkylene)-O-C(O)-R^5, -alkylene-O-C(O)-O-R^5, or -(substituted alkylene)-O-C(O)-O-R^5

R^4 is H, halogen, -OH, -O-alkyl, -O-alkylene-O-C(O)-O-R^5, -O-C(O)-O-R^5, -SH, or $-NH(R^5)$;

each R^5, R^6, and R^7 are independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, or substituted heterocyclylalkyl; or

(b) a compound according to formula (I-A)



Formula (I-A)

wherein:

X^3 is N;

X^4 is N or CR^3

X^5 is $-CR^4=CR^5-$;

R^1 and R^2 are H;

R^3 is H;

R^4 and R^5 are each independently selected from H, halogen, -C(O)OR′, -C(O)R′, -C(O)N($R^{11}R^{12}$), -N($R^{11}R^{12}$), -N(R^9)$_2$, -NHN(R^9)$_2$, -SR^7, -$(CH_2)_n$OR^7, -$(CH_2)_n R^7$, -LR^8, -LR^{10}, -OLR^8, -OLR^{10}, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^4 and R^5 are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, -NO_2, -R^7, -OR^8, -C(O)R^8, -OC(O)R^8, -C(O)OR^8, -N(R^9)$_2$, -P(O)(OR^8)$_2$, -OP(O)(OR^8)$_2$, -P(O)(OR^{10})$_2$. -OP(O)(OR^{10})$_2$, -C(O)N(R^9)$_2$, -S(O)$_2R^8$, -S(O)R^8, -S(O)$_2$N(R^9)$_2$, and -NR^9S(O)$_2R^8$;

or, R^3 and R^4, or R^4 and R^5, or R^5 and R^6, when present on adjacent ring atoms, can optionally be linked together to form a 5-6 membered ring, wherein the 5-6 membered ring is optionally substituted with R^7;

each L is independently selected from a bond, -$(O(CH_2)_m)_t$-, C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene, wherein the C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene of L are each optionally substituted with 1 to 4 substituents independently selected from halogen, -R^8, -OR^8, -N(R^9)$_2$, -P(O)(OR^8)$_2$, -OP(O)(OR^8)$_2$, -P(O)(OR^{10})$_2$, and -OP(O)(OR^{10})$_2$;

R^7 is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl groups of R^7 are each optionally substituted with 1 to 3 R^{13} groups, and each R^{13} is independently selected from halogen, -CN, -LR^9, -LOR^9, -OLR^9, -LR^{10}, -LOR^{10}, -OLR^{10}, -LR^8, -LOR^8, -OLR^8, -LSR^8, -LSR^{10}, -LC(O)R^8, -OLC(O)R^8, -LC(O)OR^8, -LC(O)R^{10}, -LOC(O)OR^8, -LC(O)NR^9R^{11}, -LC(O)NR^9R^8, -LN(R^9)$_2$, -LNR^9R^8, -LNR^9R^{10}, -LC(O)N(R^9)$_2$, -LS(O)$_2R^8$, -LS(O)R^8, -LC(O)NR^8OH, -LNR^9C(O)R^8, -LNR^9C(O)OR^8, -LS(O)$_2$N(R^9)$_2$, -OLS(O)$_2$N(R^9)$_2$, -LNR^9S(O)$_2R^8$, -LC(O)NR^9LN(R^9)$_2$, -LP(O)(OR^8)$_2$, -LOP(O)(OR^8)$_2$, -LP(O)(OR^{10})$_2$ and -OLP(O)(OR^{10})$_2$;

each R^8 is independently selected from H, -CH(R^{10})$_2$, C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6heteroalkyl, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy, wherein the C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy groups of R^8 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -C(O)R^{11}, -OC(O)R^{11}, -C(O)N(R^9)$_2$, -C(O)OR^{11}, -NR^9C(O)R^{11}, -NR^9R^{10}, -N$R^{11}R^{12}$, -

$N(R^9)_2$, $-OR^9$, $-OR^{10}$, $-C(O)NR^{11}R^{12}$, $-C(O)NR^{11}OH$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-S(O)_2NR^{11}R^{12}$, $-NR^{11}S(O)_2R^{11}$, $-P(O)(OR^{11})_2$, and $-OP(O)(OR^{11})_2$;

each R^9 is independently selected from H, $-C(O)R^8$, $-C(O)OR^8$, $-C(O)R^{10}$, $-C(O)OR^{10}$, $-S(O)_2R^{10}$, $-C_1$-C_6 alkyl, C_1-C_6 heteroalkyl and C_3-C_6 cycloalkyl, or each R^9 is independently a C_1-C_6alkyl that together with N they are attached to form a C_3-C_8heterocycloalkyl, wherein the C_3-C_8heterocycloalkyl ring optionally contains an additional heteroatom selected from N, O and S, and wherein the C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, or C_3-C_8heterocycloalkyl groups of R^9 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, $-OR^{11}$, $-SR^{11}$, $-C(O)R^{11}$, $OC(O)R^{11}$, $-C(O)0R^{11}$, $-NR^{11}R^{12}$, $-C(O)NR^{11}R^{12}$, $-C(O)NR^{11}OH$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-S(O)_2NR^{11}R^{12}$, $-NR^{11}S(O)_2R^{11}$, $-P(O)(OR^{11})_2$ and $-OP(O)(OR^{11})_2$;

each R^{10} is independently selected from aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl, wherein the aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl groups are optionally substituted with 1 to 3 substituents selected from halogen, $-R^8$, $-OR^8$, $-LR^9$, $-LOR^9$, $-N(R^9)_2$, $-NR^9C(O)R^8$, $-NR^9CO_2R^8$. $-CO_2R^8$, $-C(O)R^8$ and $-C(O)N(R^9)_2$;

R^{11} and R^{12} are independently selected from H, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^{11} and R^{12} are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, R^8, $-OR^8$, $C(O)R^8$, $OC(O)R^8$, $-C(O)OR^8$, $-N(R^9)_2$, $-NR^8C(O)R^8$, $-NR^8C(O)OR^8$, $-C(O)N(R^9)_2$, C_3-C_8heterocycloalkyl, $-S(O)_2R^8$, $-S(O)_2N(R^9)_2$, $-NR^9S(O)_2R^8$, C_1 -C_6haloalkyl and C_1 -C_6haloalkoxy;

or R^{11} and R^{12} are each independently C_1-C_6alkyl and taken together with the N atom to which they are attached form an optionally substituted C_3-C_8heterocycloalkyl ring optionally containing an additional heteroatom selected from N, O and S;

ring A is an aryl or a heteroaryl, wherein the aryl and heteroaryl groups of Ring A are optionally substituted with 1 to 3 R^A groups, wherein each R^A is independently selected from $-R^8$, $-R^7$, $-OR^7$, $-OR^8$, $-R^{10}$, $-OR^{10}$, $-SR^8$, $-NO_2$, -CN, $-N(R^9)_2$, $-NR^9C(O)R^8$, $-NR^9C(S)R^8$, $-NR^9C(O)N(R^9)_2$, $-NR^9C(S)N(R^9)_2$, $-NR^9CO_2R^8$, $-NR^9NR^9C(O)R^8$, $-NR^9NR^9C(O)N(R^9)_2$, $-NR^9NR^9CO_2R^8$, $-C(O)C(O)R^8$, $-C(O)CH_2C(O)R^8$, $-CO_2R^8$, $-(CH_2)_nCO_2R^8$, $-C(O)R^8$, $-C(S)R^8$, $-C(O)N(R^9)_2$, $-C(S)N(R^9)_2$, $-OC(O)N(R^9)_2$, $-OC(O)R^8$, $-C(O)N(OR^8)R^8$, $-C(NOR^8)R^8$, $-S(O)_2R^8$, $-S(O)_3R^8$, $-SO_2N(R^9)_2$, $-S(O)R^8$, $-NR^9SO_2N(R^9)_2$, $-NR^9SO_2R^8$, $-P(O)(OR^8)_2$, $-OP(O)(OR^8)_2$, $-P(O)(OR^{10})_2$, $-OP(O)(OR^{10})_2$, $-N(0R^8)R^8$, $-CH=CHCO_2R^8$, $-C(=NH)-N(R^9)_2$, and $-(CH_2)_nNHC(O)R^8$ or two adjacent R^A substituents on Ring A form a 5-6 membered ring that contains up to two heteroatoms as ring members;

n is, independently at each occurrence, 0, 1, 2, 3, 4, 5, 6, 7 or 8;

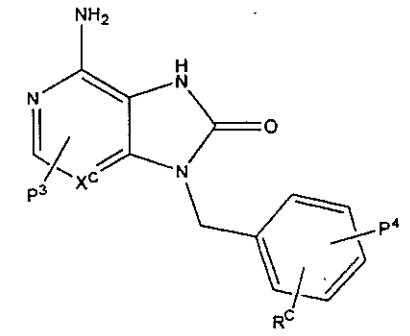
each m is independently selected from 1, 2, 3, 4, 5 and 6, and

t is 1,2,3,4,5, 6,7 or 8.

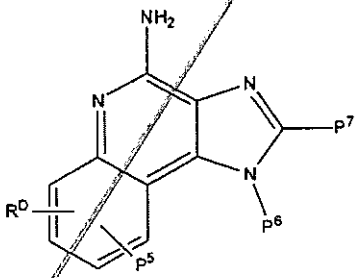
12. A TLR4 agonist comprising at least one adsorptive moiety, wherein the TLR agonist has a molecular weight of less than 1000 Da.

13. A TLR9 agonist comprising at least one adsorptive moiety, wherein the TLR agonist has a molecular weight of less than 1000 Da.

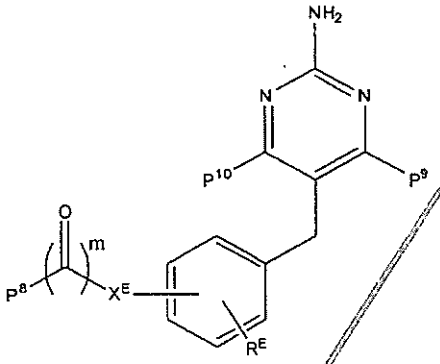
14. A TLR7 agonist selected from compounds according to any of formulae (C), (D), (E) or (H):



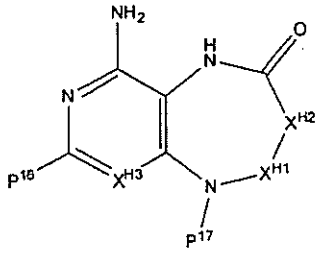
(C)



(D)



(E)



(H)

wherein:

(a) P^3 is selected from H, C_1-C_6alkyl, CF_3, and -$((CH_2)_pO)_q(CH_2)_pO_s$- and -Y-L-X-$P(O)(OR^X)(OR^Y)$; and P^4 is selected from H, C_1-C_6alkyl, -C_1-C_6alkylaryl and -Y-L-X-$P(O)(OR^X)(OR^Y)$; with the proviso that at least one of P^3 and P^4 is -Y-L-X-$P(O)(OR^X)(OR^Y)$,

(b) P^5 is selected from H, C_1-C_6alkyl, and -Y-L-X-$P(O)(OR^X)(OR^Y)$; P^6 is selected from H, C_1-C_6alkyl each optionally substituted with 1 to 3 substituents selected from C_1-C_4alkyl and OH, and -Y-L-X-$P(O)(OR^X)(OR^Y)$; and P^7 is selected from H, C_1-C_6alkyl, -$((CH_2)_pO)_q(CH_2)_pO_s$-, -NHC_1-C_6alkyl and -Y-L-X-$P(O)(OR^X)(OR^Y)$; with the proviso that at least one of P^5, P^6 and P^7 is -Y-L-X-$P(O)(OR^X)(OR^Y)$;

(c) P^8 is selected from H, C_1-C_6alkyl, C_1-C_6alkoxy, -NHC_1-C_6alkyl each optionally substituted with OH, and -Y-L-X-P(O)(OR^X)(OR^Y); and P^9 and P^{10} are each independently selected from H, C_1-C_6alkyl, C_1-C_6alkoxy, -NHC_1-C_6alkyl each optionally substituted with OH and C_1-C_6alkyl, and -Y-L-X-P(O)(OR^X)(OR^Y); with the proviso that at least one of P^8, P^9 or P^{10} is -Y-L-X-P(O)(OR^X)(OR^Y);

(d) P^{16} and each P^{18} are each independently selected from H, C_1-C_6alkyl, and -Y-L-X-P(O)(OR^X)(OR^Y); P^{17} is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_1-C_6alkylaryl, C_1-C_6alkyl heteroaryl, C_1-C_6alkylaryl-Y-L-X-P(O)(OR^X)(OR^Y) and -Y-L-X-P(O)(OR^X)(OR^Y), each optionally substituted with 1 to 2 substituents selected from C_1-C_6alkyl or heterocyclyl with the proviso that at least one of P^{16}, P^{17} or a P^{18} contains a -Y-L-X-P(O)(OR^X)(OR^Y) moiety;

R^X and R^Y are independently selected from H and C_1-C_6alkyl;

R^C, R^D and R^H are each independently selected from H and C_1-C_6alkyl;

X^C is selected from CH and N;

R^E is selected from H, C_1-C_6alkyl, C_1-C_6alkoxy, C(O)C_1-C_6alkyl, halogen and -$((CH_2)_pO)_q(CH_2)_p$-;

X^E is selected from a covalent bond, $CR^{E2}R^{E3}$ and NR^{E4};

R^{E2}, R^{E3} and R^{E4} are independently selected from H and C_1-C_6alkyl;

X^{H1}-X^{H2} is selected from -$CR^{H2}R^{H3}$-, -$CR^{H2}R^{H3}$-$CR^{H2}R^{H3}$-, -C(O)$CR^{H2}R^{H3}$-, -C(O)$CR^{H2}R^{H3}$-, -$CR^{H2}R^{H3}$C(O)-, -NR^{H4}C(O)-, C(O)NR^{H4}-, $CR^{H2}R^{H3}S(O)_2$ and –CR^{H2}=CR^{H2}-;

R^{H2}, R^{H3} and R^{H4} are each independently selected from H, C_1-C_6alkyl and P^{18};

X^{H3} is selected from N and CN;

X is selected from a covalent bond, O and NH;

Y is selected from a covalent bond, O, C(O), S and NH;

L is selected from, a covalent bond C_1-C_6alkylene, C_1-C_6alkenylene, arylene, heteroarylene, C_1-C_6alkyleneoxy and -$((CH_2)_pO)_q(CH_2)_p$- each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, -OP(O)$(OH)_2$ and –P(O)$(OH)_2$;

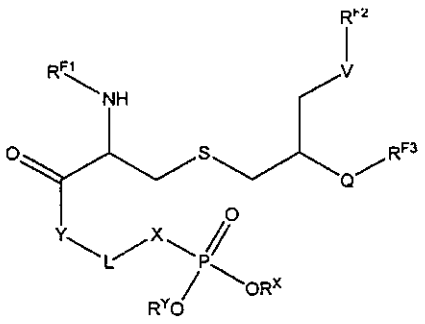
m is selected from 0 or 1;

each p is independently selected from 1, 2, 3, 4, 5 and 6;

q is selected from 1, 2, 3 and 4; and

s is selected from 0 and 1.

15. A compound of formula (F):



wherein:

R^X and R^Y are independently selected from H and C_1-C_6alkyl;

Q and V are independently selected from a covalent bond, NH, S, C(O) and O;

X is selected from a covalent bond, O and NH;

Y is selected from a covalent bond, O, C(O), S and NH;

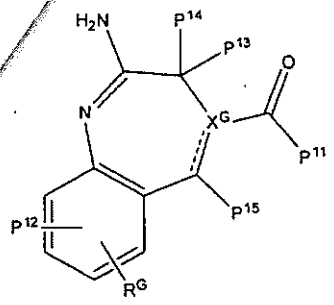
L is selected from, a covalent bond C_1-C_6alkylene, C_1-C_6alkenylene, arylene, heteroarylene, C_1-C_6alkyleneoxy and $-((CH_2)_pO)_q(CH_2)_p-$, each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, $-OP(O)(OH)_2$ and $-P(O)(OH)_2$; and

R^{F1}, R^{F2} and R^{F3} are independently selected from H, C_1-C_{18} alkyl, C_1-C_{18}alkenyl, $C(O)C_1$-C_{18}alkyl and $C(O)C_1$-C_{18}alkenyl;

each p is independently selected from 1, 2, 3, 4, 5 and 6; and

q is selected from 1, 2, 3 and 4.

16. A compound of formula (G)



(G)

wherein:

P^{11} is selected from H, C_1-C_6alkyl, C_1-C_6 alkoxy, NR^VR^W and $-Y-L-X-P(O)(OR^X)(OR^Y)$;

P^{12} is selected from H, C_1-C_6alkyl, aryl optionally substituted by $-C(O)NR^VR^W$, and -Y-L-X-$P(O)(OR^X)(OR^Y)$;

P^{13}, P^{14} and P^{15} are independently selected from H, C_1-C_6alkyl, C_1-C_6 alkoxy and -Y-L-X-$P(O)(OR^X)(OR^Y)$;

with the proviso that at least one of P^{11}, P^{12}, P^{13}, P^{14} or P^{15} is -Y-L-X-$P(O)(OR^X)(OR^Y)$;

R^V and R^W are independently selected from H, C_1-C_6alkyl or together with the nitrogen atom to which they are attached form a 4 to 7 remembered heterocyclic ring;

X^G is selected from C, CH and N;

----- represents an optional double bond, wherein X^G is C if ----- is a double bond; and

R^G is selected from H and C_1-C_6alkyl;

X is selected from a covalent bond, O and NH;

Y is selected from a covalent bond, O, C(O), S and NH;

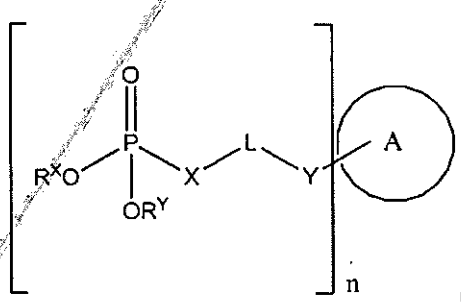
L is selected from, a covalent bond C_1-C_6alkylene, C_1-C_6alkenylene, arylene, heteroarylene, C_1-C_6alkyleneoxy and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, $-OP(O)(OH)_2$ and $-P(O)(OH)_2$;

each p is independently selected from 1, 2, 3, 4, 5 and 6 and

q is selected from 1, 2, 3 and 4.

17. A TLR agonist including between two and fifteen adsorptive moieties.

18. A TLR agonist according to any preceding claim, having the formula (A1):



(A1)

wherein:

R^X and R^Y are independently selected from H and C_1-C_6 alkyl;

X is selected from a covalent bond, O and NH;

Y is selected from a covalent bond, O, C(O), S and NH;

L is a linker *e.g.* selected from, C_1-C_6alkylene, C_1-C_6alkenylene, arylene, heteroarylene, C_1-C_6alkyleneoxy and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, $-OP(O)(OH)_2$ and $-P(O)(OH)_2$;

each p is independently selected from 1, 2, 3, 4, 5 and 6;

q is selected from 1, 2, 3 and 4;

n is selected from 1, 2 and 3; and

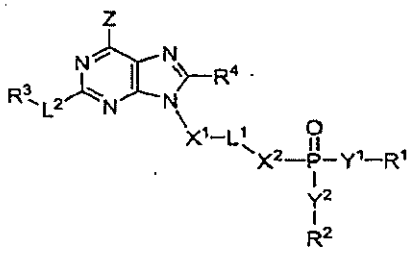
A is a TLR agonist moiety;

with the proviso that the TLR agonist:

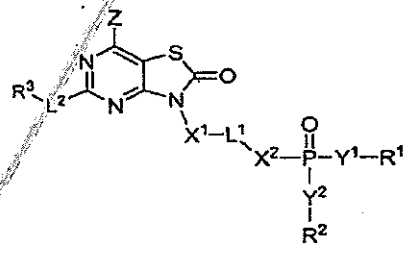
a. is not a TLR4 agonist;

b. is not a TLR9 agonist;

c. is not a compound according to formula (I) or (II)



I



II

wherein:

Z is $-NH_2$ or -OH;

X^1 is alkylene, substituted alkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, carbocyclylene, substituted carbocyclylene, heterocyclylene, or substituted heterocyclylene;

L^1 is a covalent bond, arylene, substituted arylene, heterocyclylene, substituted heterocyclylene, carbocyclylene, substituted carbocyclylene, -S-, -S(O)-, $S(O)_2$, $-NR^5-$, or -O-

X^2 is a covalent bond, alkylene, or substituted alkylene;

L^2 is $-NR^5-$, $-N(R^5)C(O)-$, -O-, -S-, -S(O)-, $S(O)_2$, or a covalent bond;

R^3 is H, alkyl, substituted alkyl, heteroalkyl, substituted heteroalkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

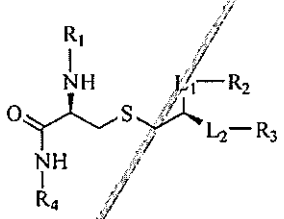
Y^1 and Y^2 are each independently a covalent bond, -O- or $-NR^3-$; or $-Y^1-R^1$ and $-Y^2-R^2$ are each independently $-O-N=C(R^6R^7)$;

R^1 and R^2 are each independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, substituted heterocyclylalkyl, -alkylene-C(O)-O-R^5, —(substituted alkylene)-C(O)-O-R^5, -alkylene-O-C(O)-R^5, -(substituted alkylene)-O-C(O)-R^5, -alkylene-O-C(O)-O-R^5, or -(substituted alkylene)-O-C(O)-O-R^5

R^4 is H, halogen, -OH, -O-alkyl, -O-alkylene-O-C(O)-O-R^5, -O-C(O)-O-R^5, -SH, or $-NH(R^5)$;

each R^5, R^6, and R^7 are independently H, alkyl, substituted alkyl, carbocyclyl, substituted carbocyclyl, heterocyclyl, substituted heterocyclyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, arylalkyl, substituted arylalkyl, heterocyclylalkyl, or substituted heterocyclylalkyl;

d. is not a compound according to formula (III)



(III)

wherein:

R^1 is H, $-C(O)-C_{10}-C_{18}$alkyl; R^2 is $C_{10}-C_{18}$alkyl ; R^3 is $C_{10}-C_{18}$alkyl;

L_1 is $-CH_2O-$, $-CH_2OC(O)-$, $-CH_2NR^7C(O)-$ or $-C(O)NR^7-$;

L_2 is -O-, -OC(O)- or $-NR^7C(O)-$;

R^4 is $-L_3R^5$ or $-L_4R^5$;

R^5 is $-N(R^7)_2$, $-OR^7$, $-P(O)(OR^7)_2$, $-C(O)OR^7$, $-NR^7C(O)L_3R^8$, $-OL_3R^6$, $-C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from $-OR^9$, $-OL_3R^6$, $-OL_4R^6$, $-OR^7$, and $-C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is $-((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$ or $-(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, $-OR^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from $-SR^7$, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

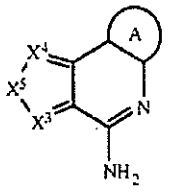
R^9 is phenyl;

each R^{10} is independently selected from H and halo;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4;

e. is not a compounds according to formula (I-A)



Formula (I-A)

wherein:

X^3 is N;

X^4 is N or CR^3

X^5 is $-CR^4=CR^5-$;

R^1 and R^2 are H;

R^3 is H;

R^4 and R^5 are each independently selected from H, halogen, $-C(O)OR^7$, $-C(O)R^7$, $-C(O)N(R^{11}R^{12})$, $-N(R^{11}R^{12})$, $-N(R^9)_2$, $-NHN(R^9)_2$, $-SR^7$, $-(CH_2)_nOR^7$, $-(CH_2)_nR^7$, $-LR^8$, $-LR^{10}$, $-OLR^8$, $-OLR^{10}$, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-

C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^4 and R^5 are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, -NO_2, -R^7, -OR^8, -$C(O)R^8$, -$OC(O)R^8$, -$C(O)OR^8$, -$N(R^9)_2$, -$P(O)(OR^8)_2$, -$OP(O)(OR^8)_2$, -$P(O)(OR^{10})_2$. -$OP(O)(OR^{10})_2$, -$C(O)N(R^9)_2$, -$S(O)_2R^8$, -$S(O)R^8$, -$S(O)_2N(R^9)_2$, and -$NR^9S(O)_2R^8$;

or, R^3 and R^4, or R^4 and R^5, or R^5 and R^6, when present on adjacent ring atoms, can optionally be linked together to form a 5-6 membered ring, wherein the 5-6 membered ring is optionally substituted with R^7;

each L is independently selected from a bond, -$(O(CH_2)_m)_t$-, C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene, wherein the C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene of L are each optionally substituted with 1 to 4 substituents independently selected from halogen, -R^8, -OR^8, -$N(R^9)_2$, -$P(O)(OR^8)_2$, -$OP(O)(OR^8)_2$, -$P(O)(OR^{10})_2$, and -$OP(O)(OR^{10})_2$;

R^7 is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl groups of R^7 are each optionally substituted with 1 to 3 R^{13} groups, and each R^{13} is independently selected from halogen, -CN, -LR^9, -LOR^9, -OLR^9, -LR^{10}, -LOR^{10}, -OLR^{10}, -LR^8, -LOR^8, -OLR^8, -LSR^8, -LSR^{10}, -$LC(O)R^8$, -$OLC(O)R^8$, -$LC(O)OR^8$, -$LC(O)R^{10}$, -$LOC(O)OR^8$, -$LC(O)NR^9R^{11}$, -$LC(O)NR^9R^8$, -$LN(R^9)_2$, -LNR^9R^8, -LNR^9R^{10}, -$LC(O)N(R^9)_2$, -$LS(O)_2R^8$, -$LS(O)R^8$, -$LC(O)NR^8OH$, -$LNR^9C(O)R^8$, -$LNR^9C(O)OR^8$, -$LS(O)_2N(R^9)_2$, -$OLS(O)_2N(R^9)_2$, -$LNR^9S(O)_2R^8$, -$LC(O)NR^9LN(R^9)_2$, -$LP(O)(OR^8)_2$, -$LOP(O)(OR^8)_2$, -$LP(O)(OR^{10})_2$ and -$OLP(O)(OR^{10})_2$;

each R^8 is independently selected from H, -$CH(R^{10})_2$, C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6heteroalkyl, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy, wherein the C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy groups of R^8 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -$C(O)R^{11}$, -$OC(O)R^{11}$, -$C(O)N(R^9)_2$, -$C(O)OR^{11}$, -$NR^9C(O)R^{11}$, -NR^9R^{10}, -$NR^{11}R^{12}$, -$N(R^9)_2$, -OR^9, -OR^{10}, -$C(O)NR^{11}R^{12}$, -$C(O)NR^{11}OH$, -$S(O)_2R^{11}$, -$S(O)R^{11}$, -$S(O)_2NR^{11}R^{12}$, -$NR^{11}S(O)_2R^{11}$, -$P(O)(OR^{11})_2$, and -$OP(O)(OR^{11})_2$;

each R^9 is independently selected from H, -C(O)R^8, -C(O)OR^8, -C(O)R^{10}, -C(O)OR^{10}, -S(O)$_2$$R^{10}$, -$C_1$-$C_6$ alkyl, C_1-C_6 heteroalkyl and C_3-C_6 cycloalkyl, or each R^9 is independently a C_1-C_6alkyl that together with N they are attached to form a C_3-C_8heterocycloalkyl, wherein the C_3-C_8heterocycloalkyl ring optionally contains an additional heteroatom selected from N, O and S, and wherein the C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, or C_3-C_8heterocycloalkyl groups of R^9 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -C(O)R^{11}, OC(O)R^{11}, -C(O)0R^{11}, -N$R^{11}$$R^{12}$, -C(O)N$R^{11}$$R^{12}$, -C(O)N$R^{11}$OH, -S(O)$_2$$R^{11}$, -S(O)$R^{11}$, -S(O)$_2NR^{11}$$R^{12}$, -N$R^{11}$S(O)$_2$$R^{11}$, -P(O)(O$R^{11}$)$_2$ and -OP(O)(OR^{11})$_2$;

each R^{10} is independently selected from aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl, wherein the aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl groups are optionally substituted with 1 to 3 substituents selected from halogen, -R^8, -OR^8, -LR^9, -LOR^9, -N(R^9)$_2$, -NR^9C(O)R^8, -NR^9C$O_2$$R^8$. –C$O_2$$R^8$, -C(O)$R^8$ and -C(O)N(R^9)$_2$;

R^{11} and R^{12} are independently selected from H, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^{11} and R^{12} are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, R^8, -OR^8, C(O)R^8, OC(O)R^8, -C(O)OR^8, -N(R^9)$_2$, -NR^8C(O)R^8, -NR^8C(O)OR^8, -C(O)N(R^9)$_2$, C_3-C_8heterocycloalkyl, -S(O)$_2$$R^8$, -S(O)$_2$N($R^9$)$_2$, -N$R^9$S(O)$_2$$R^8$, C_1 -C_6haloalkyl and C_1 -C_6haloalkoxy;

or R^{11} and R^{12} are each independently C_1-C_6alkyl and taken together with the N atom to which they are attached form an optionally substituted C_3-C_8heterocycloalkyl ring optionally containing an additional heteroatom selected from N, O and S;

ring A is an aryl or a heteroaryl, wherein the aryl and heteroaryl groups of Ring A are optionally substituted with 1 to 3 R^A groups, wherein each R^A is independently selected from -R^8, -R^7, -OR^7, -OR^8, -R^{10}, -OR^{10}, -SR^8, -NO_2, -CN, -N(R^9)$_2$, -NR^9C(O)R^8, -NR^9C(S)R^8, -NR^9C(O)N(R^9)$_2$, - NR^9C(S)N(R^9)$_2$, -NR^9C$O_2$$R^8$, -N$R^9NR^9$C(O)$R^8$, -N$R^9NR^9$C(O)N($R^9$)$_2$, -N$R^9NR^9CO_2$$R^8$, -C(O)C(O)$R^8$, -C(O)C$H_2$C(O)$R^8$, -C$O_2$$R^8$, -(C$H_2$)$_nCO_2$$R^8$, -C(O)$R^8$, -C(S)$R^8$, -C(O)N($R^9$)$_2$, -C(S)N($R^9$)$_2$, -OC(O)N($R^9$)$_2$, -OC(O)$R^8$, -C(O)N(O$R^8$)$R^8$, -C(NO$R^8$)$R^8$, -S(O)$_2$$R^8$, -S(O)$_3$$R^8$, -S$O_2$N($R^9$)$_2$, -S(O)$R^8$, -N$R^9SO_2$N($R^9$)$_2$, -N$R^9SO_2$$R^8$, -P(O)(O$R^8$)$_2$, -OP(O)(O$R^8$)$_2$, -P(O)(O$R^{10}$)$_2$, -OP(O)(O$R^{10}$)$_2$, -N(0$R^8$)$R^8$, -CH=CHC$O_2$$R^8$, -C(=NH)-N($R^9$)$_2$, and -(C$H_2$)$_n$NHC(O)$R^8$ or two adjacent R^A substituents on Ring A form a 5-6 membered ring that contains up to two heteroatoms as ring members;

n is, independently at each occurrence, 0, 1, 2, 3, 4, 5, 6, 7 or 8;

each m is independently selected from 1, 2, 3, 4, 5 and 6, and

t is 1,2,3,4,5, 6,7 or 8.

19. A TLR agonist according to claim 18, wherein R^X and R^Y are H; X is O; L is selected from C_1-C_6 alkylene and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 2 halogen atoms; p is selected from 1, 2 and 3; q is selected from 1 and 2; and n is 1.

20. A TLR agonist according to claim 18, wherein R^X and R^Y are H; X is a covalent bond; L is selected from C_1-C_6 alkylene and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 2 halogen atoms; p is selected from 1, 2 or 3; q is selected from 1 or 2; and n is 1.

21. A composition comprising a TLR agonist of any preceding claim and an insoluble metal salt.

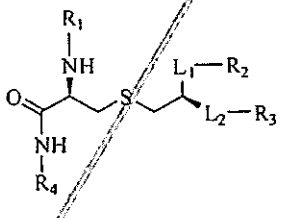
22. The composition of claim 21, wherein the TLR agonist is adsorbed onto the insoluble metal salt.

23. A composition comprising a TLR agonist and an insoluble metal salt, with the proviso that the TLR agonist:

(a) is not a TLR4 agonist;

(b) is not a TLR9 agonist;

(c) is not a compound according to formula (III)



(III)

wherein:

R^1 is H, $-C(O)-C_{10}$-C_{18}alkyl; R^2 is C_{10}-C_{18}alkyl ; R^3 is C_{10}-C_{18}alkyl;

L_1 is $-CH_2O-$, $-CH_2OC(O)-$, $-CH_2NR^7C(O)-$ or $-C(O)NR^7-$;

L_2 is -O-, -OC(O)- or $-NR^7C(O)-$;

R^4 is $-L_3R^5$ or $-L_4R^5$;

R^5 is $-N(R^7)_2$, $-OR^7$, $-P(O)(OR^7)_2$, $-C(O)OR^7$, $-NR^7C(O)L_3R^8$, $-OL_3R^6$, $-C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from $-OR^9$, $-OL_3R^6$, $-OL_4R^6$, $-OR^7$, and $-C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the

same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is $-((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$ or $-(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p-$, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, $-OR^7$, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from $-SR^7$, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

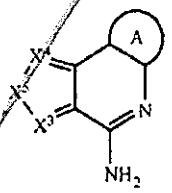
R^9 is phenyl;

each R^{10} is independently selected from H and halo;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4; and

(d) is not a compound according to Formula (I-A)



Formula (I-A)

wherein:

X^3 is N;

X^4 is N or CR^3;

X^5 is $-CR^4=CR^5-$;

R^1 and R^2 are H;

R^3 is H;

R^4 and R^5 are each independently selected from H, halogen, $-C(O)OR^7$, $-C(O)R^7$, $-C(O)N(R^{11}R^{12})$, $-N(R^{11}R^{12})$, $-N(R^9)_2$, $-NHN(R^9)_2$, $-SR^7$, $-(CH_2)_nOR^7$, $-(CH_2)_nR^7$, $-LR^8$, $-LR^{10}$, $-OLR^8$, $-OLR^{10}$, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-

C_6haloalkoxy, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^4 and R^5 are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, -NO_2, -R^7, -OR^8, -$C(O)R^8$, -$OC(O)R^8$, -$C(O)OR^8$, -$N(R^9)_2$, -$P(O)(OR^8)_2$, -$OP(O)(OR^8)_2$, -$P(O)(0R^{10})_2$. -$OP(O)(OR^{10})_2$, -$C(O)N(R^9)_2$, -$S(O)_2R^8$, -$S(O)R^8$, -$S(O)_2N(R^9)_2$, and -$NR^9S(O)_2R^8$;

or, R^3 and R^4, or R^4 and R^5, or R^5 and R^6, when present on adjacent ring atoms, can optionally be linked together to form a 5-6 membered ring, wherein the 5-6 membered ring is optionally substituted with R^7;

each L is independently selected from a bond, -$(O(CH_2)_m)_t$-, C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene, wherein the C_1-C_6alkyl, C_2-C_6alkenylene and C_2-C_6alkynylene of L are each optionally substituted with 1 to 4 substituents independently selected from halogen, -R^8, -OR^8, -$N(R^9)_2$, -$P(O)(OR^8)_2$, -$OP(O)(OR^8)_2$, -$P(O)(OR^{10})_2$, and -$OP(O)(OR^{10})_2$;

R^7 is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6alkoxy, C_1-C_6haloalkoxy, and C_3-C_8heterocycloalkyl groups of R^7 are each optionally substituted with 1 to 3 R^{13} groups, and each R^{13} is independently selected from halogen, -CN, -LR^9, -LOR^9, -OLR^9, -LR^{10}, -LOR^{10}, -OLR^{10}, -LR^8, -LOR^8, -OLR^8, -LSR^8, -LSR^{10}, -$LC(O)R^8$, -$OLC(O)R^8$, -$LC(O)OR^8$, -$LC(O)R^{10}$, -$LOC(O)OR^8$, -$LC(O)NR^9R^{11}$, -$LC(O)NR^9R^8$, -$LN(R^9)_2$, -LNR^9R^8, -LNR^9R^{10}, -$LC(O)N(R^9)_2$, -$LS(O)_2R^8$, -$LS(O)R^8$, -$LC(O)NR^8OH$, -$LNR^9C(O)R^8$, -$LNR^9C(O)OR^8$, -$LS(O)_2N(R^9)_2$, -$OLS(O)_2N(R^9)_2$, -$LNR^9S(O)_2R^8$, -$LC(O)NR^9LN(R^9)_2$, -$LP(O)(OR^8)_2$, -$LOP(O)(OR^8)_2$, -$LP(O)(OR^{10})_2$ and -$OLP(O)(OR^{10})_2$;

each R^8 is independently selected from H, -$CH(R^{10})_2$, C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_1-C_6heteroalkyl, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy, wherein the C_1-C_8alkyl, C_2-C_8alkene, C_2-C_8alkyne, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, C_1-C_6alkoxy, C_3-C_8cycloalkyl, C_2-C_8heterocycloalkyl, C_1-C_6hydroxyalkyl and C_1-C_6haloalkoxy groups of R^8 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -$C(O)R^{11}$, -$OC(O)R^{11}$, -$C(O)N(R^9)_2$, -$C(O)OR^{11}$, -$NR^9C(O)R^{11}$, -NR^9R^{10}, -$NR^{11}R^{12}$, -$N(R^9)_2$, -OR^9, -OR^{10}, -$C(O)NR^{11}R^{12}$, -$C(O)NR^{11}OH$, -$S(O)_2R^{11}$, -$S(O)R^{11}$, -$S(O)_2NR^{11}R^{12}$, -$NR^{11}S(O)_2R^{11}$, -$P(O)(OR^{11})_2$, and -$OP(O)(OR^{11})_2$;

each R^9 is independently selected from H, -$C(O)R^8$, -$C(O)OR^8$, -$C(O)R^{10}$, -$C(O)OR^{10}$, -$S(O)_2R^{10}$, -C_1-C_6 alkyl, C_1-C_6 heteroalkyl and C_3-C_6 cycloalkyl, or each R^9 is independently a C_1-C_6alkyl that together with N they are attached to form a C_3-C_8heterocycloalkyl, wherein the C_3-C_8heterocycloalkyl ring optionally contains an additional

heteroatom selected from N, O and S, and wherein the C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_3-C_6 cycloalkyl, or C_3-C_8heterocycloalkyl groups of R^9 are each optionally substituted with 1 to 3 substituents independently selected from -CN, R^{11}, -OR^{11}, -SR^{11}, -C(O)R^{11}, OC(O)R^{11}, -C(O)0R^{11}, -$NR^{11}R^{12}$, -C(O)$NR^{11}R^{12}$, -C(O)NR^{11}OH, -$S(O)_2R^{11}$, -S(O)R^{11}, -$S(O)_2NR^{11}R^{12}$, -$NR^{11}S(O)_2R^{11}$, -P(O)$(OR^{11})_2$ and -OP(O)$(OR^{11})_2$;

each R^{10} is independently selected from aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl, wherein the aryl, C_3-C_8cycloalkyl, C_3-C_8heterocycloalkyl and heteroaryl groups are optionally substituted with 1 to 3 substituents selected from halogen, -R^8, -OR^8, -LR^9, -LOR^9, -$N(R^9)_2$, -$NR^9C(O)R^8$, -$NR^9CO_2R^8$. –CO_2R^8, -C(O)R^8 and -C(O)$N(R^9)_2$;

R^{11} and R^{12} are independently selected from H, C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl, wherein the C_1-C_6alkyl, C_1-C_6heteroalkyl, C_1-C_6haloalkyl, aryl, heteroaryl, C_3-C_8cycloalkyl, and C_3-C_8heterocycloalkyl groups of R^{11} and R^{12} are each optionally substituted with 1 to 3 substituents independently selected from halogen, -CN, -R^8, -OR^8, C(O)R^8, OC(O)R^8, -C(O)OR^8, -$N(R^9)_2$, -$NR^8C(O)R^8$, -$NR^8C(O)OR^8$, -C(O)$N(R^9)_2$, C_3-C_8heterocycloalkyl, -$S(O)_2R^8$, -$S(O)_2N(R^9)_2$, -$NR^9S(O)_2R^8$, C_1-C_6haloalkyl and C_1-C_6haloalkoxy;

or R^{11} and R^{12} are each independently C_1-C_6alkyl and taken together with the N atom to which they are attached form an optionally substituted C_3-C_8heterocycloalkyl ring optionally containing an additional heteroatom selected from N, O and S;

ring A is an aryl or a heteroaryl, wherein the aryl and heteroaryl groups of Ring A are optionally substituted with 1 to 3 R^A groups, wherein each R^A is independently selected from -R^8, -R^7, -OR^7, -OR^8, -R^{10}, -OR^{10}, -SR^8, -NO_2, -CN, -$N(R^9)_2$, -$NR^9C(O)R^8$, -$NR^9C(S)R^8$, -$NR^9C(O)N(R^9)_2$, -$NR^9C(S)N(R^9)_2$, -$NR^9CO_2R^8$, -$NR^9NR^9C(O)R^8$, -$NR^9NR^9C(O)N(R^9)_2$, -$NR^9NR^9CO_2R^8$, -C(O)C(O)R^8, -C(O)$CH_2C(O)R^8$, -CO_2R^8, -$(CH_2)_nCO_2R^8$, -C(O)R^8, -C(S)R^8, -C(O)$N(R^9)_2$, -C(S)$N(R^9)_2$, -OC(O)$N(R^9)_2$, -OC(O)R^8, -C(O)$N(OR^8)R^8$, -C(NOR^8)R^8, -$S(O)_2R^8$, -$S(O)_3R^8$, -$SO_2N(R^9)_2$, -S(O)R^8, -$NR^9SO_2N(R^9)_2$, -$NR^9SO_2R^8$, -P(O)$(OR^8)_2$, -OP(O)$(OR^8)_2$, -P(O)$(OR^{10})_2$, -OP(O)$(OR^{10})_2$, -$N(0R^8)R^8$, -CH=$CHCO_2R^8$, -C(=NH)-$N(R^9)_2$, and -$(CH_2)_nNHC(O)R^8$ or two adjacent R^A substituents on Ring A form a 5-6 membered ring that contains up to two heteroatoms as ring members;

n is, independently at each occurrence, 0, 1, 2, 3, 4, 5, 6, 7 or 8;

each m is independently selected from 1, 2, 3, 4, 5 and 6, and

t is 1,2,3,4,5, 6,7 or 8.

24. A composition comprising a TLR agonist, an insoluble metal salt, and a buffer, with the proviso that:

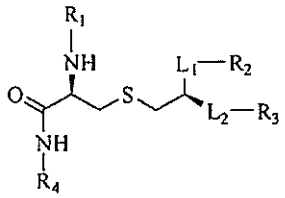
(a) the buffer is not a phosphate buffer;

(b) the TLR agonist is:

(i) not a TLR4 agonist;

(ii) not a TLR9 agonist;

(iii) not a compound of formula (III)



(III)

wherein:

R^1 is H, -C(O)-C_{10}-C_{18}alkyl; R^2 is C_{10}-C_{18}alkyl ; R^3 is C_{10}-C_{18}alkyl;

L_1 is -CH_2O-, -$CH_2OC(O)$-, -$CH_2NR^7C(O)$- or -$C(O)NR^7$-;

L_2 is -O-, -OC(O)- or -$NR^7C(O)$-;

R^4 is -L_3R^5 or -L_4R^5;

R^5 is $-N(R^7)_2$, -OR^7, -$P(O)(OR^7)_2$, -$C(O)OR^7$, -$NR^7C(O)L_3R^8$, -OL_3R^6, -$C(O)NR^7L_3R^8$, C_1-C_6alkyl, a C_6 aryl, a C_{10} aryl, a C_{14} aryl, 5 to 14 membered heteroaryl containing 1 to 3 heteroatoms selected from O, S and N, C_3-C_8cycloalkyl or a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O, S and N, wherein the aryl, heteroaryl, cycloalkyl and heterocycloalkyl of R^5 are each optionally substituted with 1 to 3 substituents independently selected from -OR^9, -OL_3R^6, -OL_4R^6, -OR^7, and -$C(O)OR^7$;

L_3 is a C_1-C_{10}alkylene, wherein the C_1-C_6alkylene of L_3 is optionally substituted with 1 to 4 R^6 groups, or the C_1-C_6alkylene of L_3 is substituted with 2 C_1-C_6alkyl groups on the same carbon atom which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

L_4 is -$((CR^7R^7)_pO)_q(CR^{10}R^{10})_p$- or -$(CR^{11}R^{11})((CR^7R^7)_pO)_q(CR^{10}R^{10})_p$-, wherein each R^{11} is a C_1-C_6alkyl groups which together, along with the carbon atom they are attached to, form a C_3-C_8cycloakyl;

each R^6 is independently selected from halo, C_1-C_6alkyl, -OR^7, $-N(R^7)_2$, $-C(O)N(R^7)_2$, $-P(O)(OR^7)_2$, a C_6 aryl, a C_{10} aryl and a C_{14} aryl;

each R^7 is independently selected from H and C_1-C_6alkyl;

R^8 is selected from $-SR^7$, -C(O)OH and a 5 to 6 membered heterocycloalkyl containing 1 to 3 heteroatoms selected from O and N;

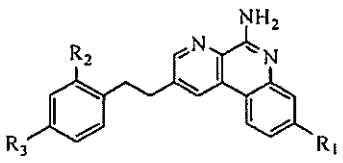
R^9 is phenyl;

each R^{10} is independently selected from H and halo;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4; and/or

(iv) not a compound of formula (IV)



(IV)

wherein:

R^1 is H, C_1-C_6alkyl, -$C(R^5)_2OH$, -L^1R^5, -L^1R^6, -L^2R^5, -L^2R^6, -OL^2R^5, or -OL^2R^6;

L^1 is –C(O)- or –O-;

L^2 is C_1-C_6alkylene, C_2-C_6alkenylene, arylene, heteroarylene or -$((CR^4R^4)_pO)_q(CH_2)_p$-, wherein the C_1-C_6alkylene and C_2-C_6alkenylene of L^2 are optionally substituted with 1 to 4 fluoro groups;

each L^3 is independently selected from C_1-C_6alkylene and -$((CR^4R^4)_pO)_q(CH_2)_p$-, wherein the C_1-C_6alkylene of L^3 is optionally substituted with 1 to 4 fluoro groups;

L^4 is arylene or heteroarylene;

R^2 is H or C_1-C_6alkyl;

R^3 is selected from C_1-C_4alkyl, -L^3R^5, -L^1R^5, -L^3R^7, -$L^3L^4L^3R^7$, -$L^3L^4R^5$, -$L^3L^4L^3R^5$, -OL^3R^5, -OL^3R^7, -$OL^3L^4R^7$, -$OL^3L^4L^3R^7$, -OR^8, -$OL^3L^4R^5$, -$OL^3L^4L^3R^5$ and -$C(R^5)_2OH$;

each R^4 is independently selected from H and fluoro;

R^5 is -$P(O)(OR^9)_2$,

R^6 is –$CF_2P(O)(OR^9)_2$ or -$C(O)OR^{10}$;

R^7 is –$CF_2P(O)(OR^9)_2$ or -$C(O)OR^{10}$;

R^8 is H or C_1-C_4alkyl;

each R^9 is independently selected from H and C_1-C_6alkyl;

R^{10} is H or C_1-C_4alkyl;

each p is independently selected from 1, 2, 3, 4, 5 and 6, and

q is 1, 2, 3 or 4.

25. The composition of claim 23 or claim 24, wherein the TLR agonist is adsorbed onto the insoluble metal salt.

26. The composition of claim 22 or claim 25, wherein at least 80% of the total TLR agonist in the composition is adsorbed onto insoluble metal salt.

27. The composition of any of claims 22, 25 or 26, wherein the adsorbed TLR agonist is, when injected intramuscularly, still present in the injected muscle at least 12 hours later.

28. The composition of any of claims 22, 25 or 26, wherein the adsorbed TLR agonist, when injected intramuscularly, has a lower peak serum concentration (Cmax) than the same TLR agonist when injected intramuscularly in non-adsorbed form.

29. A process for preparing an adjuvant complex, comprising a step of mixing a TLR agonist with an insoluble metal salt such that the TLR agonist interact to form the complex *e.g.* wherein the TLR agonist adsorbs to the insoluble metal salt.

30. A process for preparing a sterile adjuvant complex, comprising steps of: (i) mixing a TLR agonist with an insoluble metal salt such that the TLR agonist and the insoluble metal salt form the complex *e.g.* by adsorption of the TLR agonist to the salt; and (ii) sterilising the complex.

31. A process for preparing an immunogenic composition, wherein the process comprises mixing a TLR agonist, an insoluble metal salt, and an immunogen, thereby providing the immunogenic composition.

32. A method for modifying the pharmacokinetic profile and/or intramuscular retention time of an immunopotentiator, the method comprising: chemically modifying the immunopotentiator to form a modified immunopotentiator by the introduction of an adsorptive group.

33. A composition comprising: (a) an adjuvant complex comprising a TLR agonist and an insoluble metal salt; and (b) at least two different immunogens.

34. The composition of claim 33, wherein the adjuvant complex comprises the TLR agonist adsorbed to the insoluble metal salt.

35. The composition of claim 33 or claim 34, wherein the TLR agonist is not a TLR4 agonist and is not a TLR9 agonist.

36. The composition of claim 33 or claim 34 or claim 35, wherein the composition includes (i) a diphtheria toxoid, a tetanus toxoid, and an acellular pertussis antigen; (ii) a diphtheria toxoid, a tetanus toxoid, a pertussis antigen, and a *H.influenzae* type B capsular saccharide conjugate; (iii) a diphtheria toxoid, a tetanus toxoid, a pertussis antigen, and a hepatitis B virus surface antigen; (iv) a diphtheria toxoid, a tetanus toxoid, a pertussis antigen, a hepatitis B virus surface antigen and a *H.influenzae* type B capsular saccharide conjugate; (v) a diphtheria toxoid, a tetanus toxoid, a pertussis antigen, and an inactivated poliovirus antigen; or (vi) a diphtheria toxoid, a

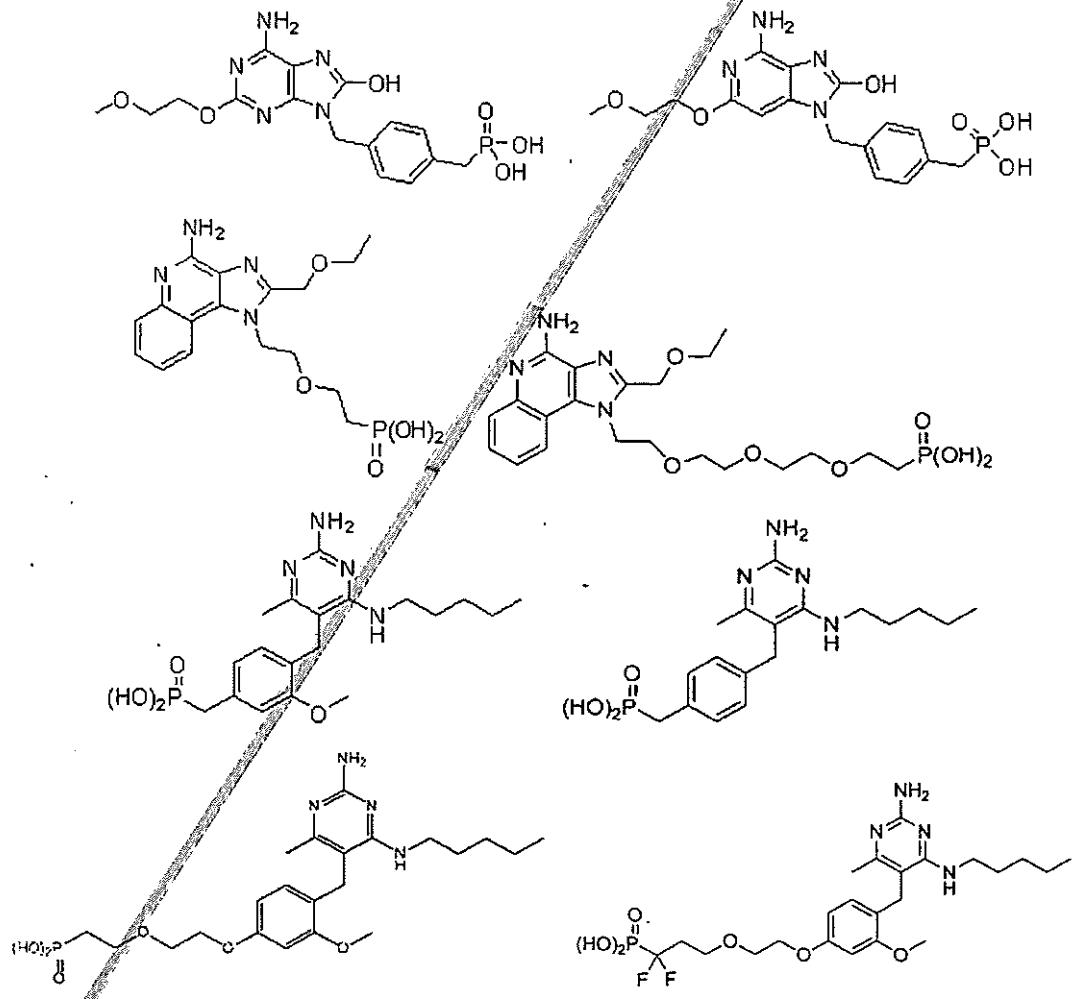
tetanus toxoid, a pertussis antigen, a *H.influenzae* type B capsular saccharide conjugate, a hepatitis B virus surface antigen, and an inactivated poliovirus antigen.

37. The composition of claim 36, wherein the composition also includes further antigens, such as from *N.meningitidis* or *S.pneumoniae*.

38. The composition of any one of claims 33 to 37, wherein the composition includes at least one bacterial antigen and at least one viral antigen.

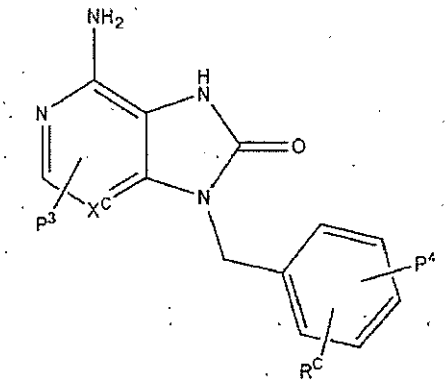
39. A process for preparing the immunogenic composition of claims 33 to 38, comprising one of: (i) combining at least two different immunogens with a mixture comprising a TLR agonist and an insoluble metal salt; (ii) combining an insoluble metal salt with a mixture comprising a TLR agonist and at least two different immunogens; (iii) combining a TLR agonist with a mixture comprising an insoluble metal salt and at least two different immunogens; or (iv) combining in any order a TLR agonist, an insoluble metal salt, a first immunogen and a second immunogen.

40. One of the following compounds:

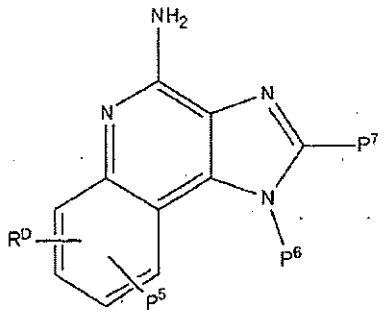


Claims

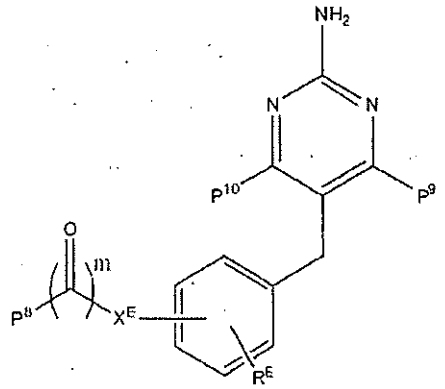
1. A TLR7 agonist selected from compounds according to any of formulae (C), (D), (E) or (H):



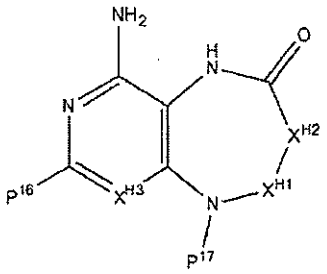
(C)



(D)



(E)



(H)

wherein:

(a) P^3 is selected from H, C_1-C_6alkyl, CF_3, and -$(((CH_2)_pO)_q(CH_2)_pO_s$- and -Y-L-X-P(O)($OR^X$)($OR^Y$); and P^4 is selected from H, C_1-C_6alkyl, -C_1-C_6alkylaryl and -Y-L-X-P(O)(OR^X)(OR^Y); with the proviso that at least one of P^3 and P^4 is -Y-L-X-P(O)(OR^X)(OR^Y),

(b) P^5 is selected from H, C_1-C_6alkyl, and -Y-L-X-P(O)(OR^X)(OR^Y); P^6 is selected from H, C_1-C_6alkyl each optionally substituted with 1 to 3 substituents selected from C_1-C_4alkyl and OH, and -Y-L-X-P(O)(OR^X)(OR^Y); and P^7 is selected from H, C_1-C_6alkyl, -$(((CH_2)_pO)_q(CH_2)_pO_s$-, -NH$C_1$-$C_6$alkyl and -Y-L-X-P(O)($OR^X$)($OR^Y$); with the proviso that at least one of P^5, P^6 and P^7 is -Y-L-X-P(O)(OR^X)(OR^Y);

(c) P^8 is selected from H, C_1-C_6alkyl, C_1-C_6alkoxy, -NHC_1-C_6alkyl each optionally substituted with OH, and -Y-L-X-P(O)(OR^X)(OR^Y); and P^9 and P^{10} are each independently selected from H, C_1-C_6alkyl, C_1-C_6alkoxy, -NHC_1-C_6alkyl each optionally substituted with OH and C_1-C_6alkyl, and -Y-L-X-P(O)(OR^X)(OR^Y); with the proviso that at least one of P^8, P^9 or P^{10} is -Y-L-X-P(O)(OR^X)(OR^Y);

(d) P^{16} and each P^{18} are each independently selected from H, C_1-C_6alkyl, and -Y-L-X-P(O)(OR^X)(OR^Y); P^{17} is selected from H, C_1-C_6alkyl, aryl, heteroaryl, C_1-C_6alkylaryl, C_1-C_6alkyl heteroaryl, C_1-C_6alkylaryl-Y-L-X-P(O)(OR^X)(OR^Y) and -Y-L-X-P(O)(OR^X)(OR^Y), each optionally substituted with 1 to 2 substituents selected from C_1-C_6alkyl or heterocyclyl with the proviso that at least one of P^{16}, P^{17} or a P^{18} contains a -Y-L-X-P(O)(OR^X)(OR^Y) moiety;

R^X and R^Y are independently selected from H and C_1-C_6alkyl;

R^C, R^D and R^H are each independently selected from H and C_1-C_6alkyl;

X^C is selected from CH and N;

R^E is selected from H, C_1-C_6alkyl, C_1-C_6alkoxy, C(O)C_1-C_6alkyl, halogen and -$(((CH_2)_pO)_q(CH_2)_p$-;

X^E is selected from a covalent bond, $CR^{E2}R^{E3}$ and NR^{E4};

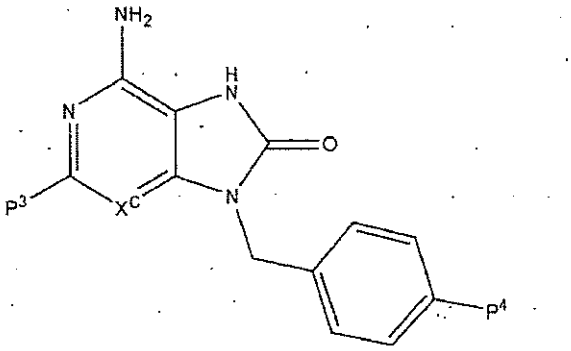
R^{E2}, R^{E3} and R^{E4} are independently selected from H and C_1-C_6alkyl;

X^{H1}-X^{H2} is selected from -$CR^{H2}R^{H3}$-, -$CR^{H2}R^{H3}$-$CR^{H2}R^{H3}$-, -C(O)$CR^{H2}R^{H3}$-, -C(O)$CR^{H2}R^{H3}$-, -$CR^{H2}R^{H3}$C(O)-, -NR^{H4}C(O)-, C(O)NR^{H4}-, $CR^{H2}R^{H3}S(O)_2$ and -CR^{H2}=CR^{H2}-;

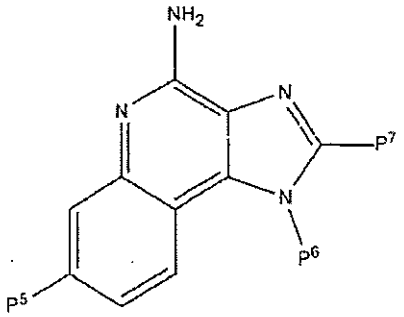
R^{H2}, R^{H3} and R^{H4} are each independently selected from H, C_1-C_6alkyl and P^{18};

X^{H3} is selected from N and CN;
X is selected from a covalent bond, O and NH;
Y is selected from a covalent bond, O, C(O), S and NH;
L is selected from, a covalent bond C_1-C_6alkylene, C_1-C_6alkenylene, arylene, heteroarylene, C_1-C_6alkyleneoxy and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, $-OP(O)(OH)_2$ and $-P(O)(OH)_2$;
m is selected from 0 or 1;
each p is independently selected from 1, 2, 3, 4, 5 and 6;
q is selected from 1, 2, 3 and 4; and
s is selected from 0 and 1.

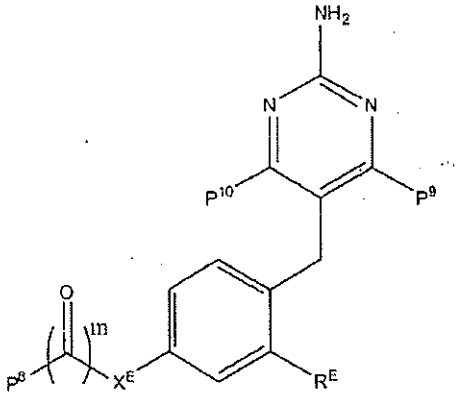
2. The TLR7 agonist as claimed in claim 1, selected from compounds of formulae (C), (D) and (E), wherein the compounds have structures according to formulae (C'), (D') and (E'), shown below:



(C')



(D')



(E')

wherein the substituents P^3, P^4, x^c, P^5, P^6, P^7, P^8, P^9, P^{10}, X^E and R^E are as defined in claim 1.

3. The TLR7 agonist as claimed in claims 1 or 2, selected from formulae (C) or (C'), wherein P^3 is selected from C_1-C_6alkyl, CF_3, and $-((CH_2)_pO)_q(CH_2)_pO_s-$ and -Y-L-X-P(O)(OR^X)(OR^Y); P^4 is selected from $-C_1$-C_6alkylaryl and -Y-L-X-P(O)(OR^X)(OR^Y); X^C is CH; X is a covalent bond; L is selected from C_1-C_6alkylene and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, $-OP(O)(OH)_2$ and $-P(O)(OB)_2$; each p is independently selected from 1, 2 and 3; q is 1 or 2.

4. The TLR7 agonist as claimed in claims 1 or 2, selected from formulae (C) or (C'), wherein P^3 is selected from C_1-C_6alkyl, CF_3, and $-((CH_2)_pO)_q(CH_2)_pO_s-$ and -Y-L-X-P(O)(OR^X)(OR^Y); P^4 is selected from $-C_1$-C_6alkylaryl and -Y-L-X-P(O)(OR^X)(OR^Y); X^C is N; X is a covalent bond; L is selected from C_1-C_6alkylene and $-((CH_2)_pO)_q(CH_2)_p-$ each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, $-OP(O)(OH)_2$ and $-P(O)(OH)_2$; each p is independently selected from 1, 2 and 3; q is selected from 1 and 2.

5. The TLR7 agonist as claimed in claims 1 or 2, selected from formulae (D) or (D'), wherein P^5 is selected from C_1-C_6alkyl, and -Y-L-X-P(O)(OR^X)(OR^Y).

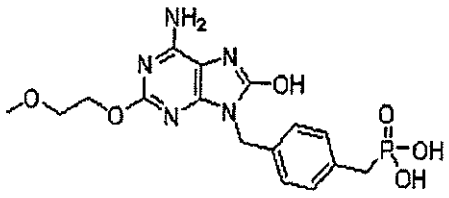
6. The TLR7 agonist as claimed in claims I or 2, selected from formulae (E) or (E'), wherein X^E is CH_2, P^8 is C_1-C_6alkoxy optionally substituted with -Y-L-X-P(O)(OR^X)(OR^Y).

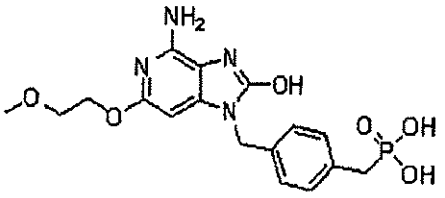
7. The TLR7 agonist as claimed in claims 1 or 2, selected from formula (E) or (E'), wherein P^9 is - NHC_1-C_6alkyl optionally substituted with OH and C_1-C_6alkyl, and -Y-L-X-P(O)(OR^X)(OR^Y).

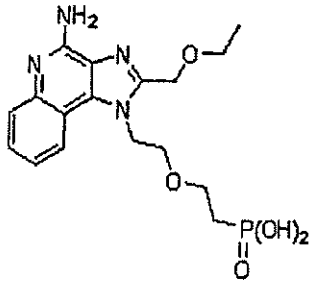
8. The TLR7 agonist as claimed in claims I or 2, selected from formulae (C) or (C'), which is not a compound in which P^4 is -Y-L-X-P(O)(OR^X)(OR^Y).

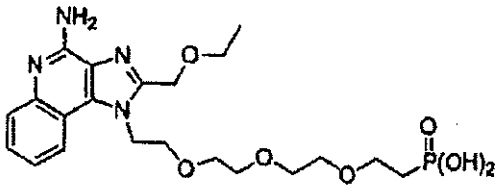
9. The TLR7 agonist as claimed in claims 1 or 2, selected from formulae (C) or (C'), wherein P^4 is selected from H, C_1-C_6alkyl, -C_1-C_6alkylaryl.

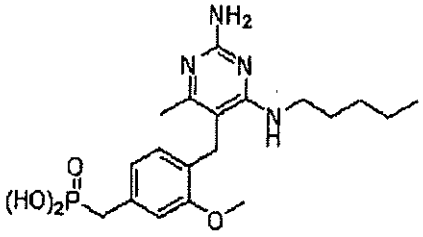
10. One of the following compounds:

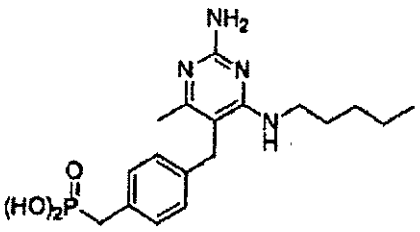


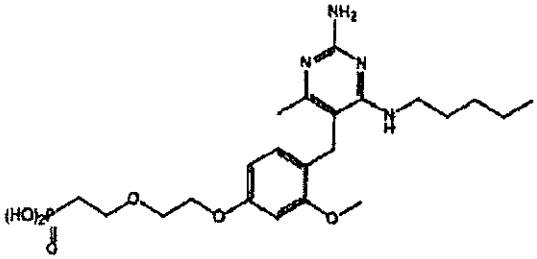


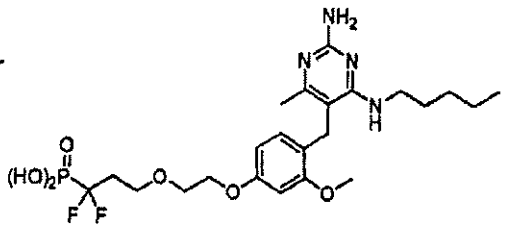




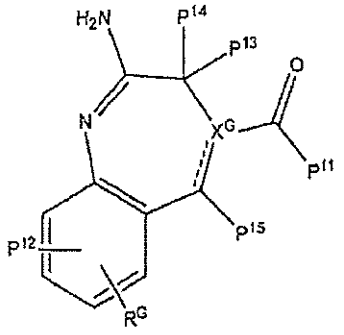








11. A compound of formula (G)

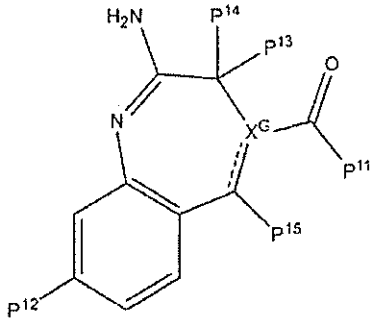


(G)

wherein:

P^{11} is selected from H, C_1-C_6alkyl, C_1-C_6 alkoxy, NR^VR^W and -Y-L-X-P(O)(OR^X)(OR^Y);
P^{12} is selected from H, C_1-C_6alkyl, aryl optionally substituted by -C(O)NR^VR^W, and -Y-L-X-P(O)(OR^X)(OR^Y);
P^{13}, P^{14} and P^{15} are independently selected from H, C_1-C_6alkyl, C_1-C_6 alkoxy and -Y-L-X-P(O)(OR^X)(OR^Y);
with the proviso that at least one of P^{11}, P^{12}, P^{13}, P^{14} or P^{15} is -Y-L-X-P(O)(OR^X)(OR^Y);
R^V and R^W are independently selected from H, C_1-C_6alkyl or together with the nitrogen atom to which they are attached form a 4 to 7 remembered heterocyclic ring;
X^G is selected from C, CH and N;
---- represents an optional double bond, wherein X^G is C if ---- is a double bond; and
R^G is selected from H and C_1-C_6alkyl;
X is selected from a covalent bond, O and NH;
Y is selected from a covalent bond, O, C(O), S and NH;
L is selected from, a covalent bond C_1-C_6alkylene, C_1-C_6alkenylene, arylene, heteroarylene, C_1-C_6alkyleneoxy and -$(CH_2)_pO)_q(CH_2)_p$- each optionally substituted with I to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, -OP(O)$(OH)_2$ and-P(O)$(OH)_2$;
each p is independently selected from 1, 2, 3, 4, 5 and 6 and
q is selected from 1, 2, 3 and 4.

12. The compound as claimed in claim 11, wherein the compound of formula (G) has a structure according to formula (G') shown below:



(G')

wherein the substituents P^{11}, P^{12}, P^{13}, P^{14}, P^{15} and X^G are as defined in claim 11.

13. The TLR7 agonist as claimed in claims 1 or 2, or the compound as claimed in claims 11 or 12, wherein X is O; L is selected from C_1-C_6alkylene and -$(CH_2)_pO)_q(CH_2)_p$- each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl,-OP(O)$(OH)_2$ and -P(O)$(OH)_2$; each p is independently selected from 1, 2 and 3; and q is selected from 1 and 2.

14. The TLR7 agonist as claimed in claims 1 or 2, or the compound as claimed in claims 11 or 12, wherein X is a covalent bond; L is selected from C_1-C_6alkylene and -$((CH_2)_pO)_q(CH_2)_p$- each optionally substituted with 1 to 4 substituents independently selected from halo, OH, C_1-C_4alkyl, -$OP(O)(OH)_2$ and -$P(O)(OH)_2$; each p is independently selected from 1, 2 and 3; and q is selected from 1 and 2.

15. A composition comprising a TLR agonist or a compound of any preceding claim and an insoluble metal salt.